BRIEF REPORT

Pancreatic Involvement in Metabolic-Autoimmune Cross-Talk: Emerging Evidence from Turkiye

Fatih Oner Kaya[1*], Muhammet Emir Kaya[2]

[1]Department of Internal Medicine, Maltepe University Faculty of Medicine, Istanbul, Turkiye

[2]Department of Internal Medicine, Saint-Joseph French High School, Istanbul, Turkiye

ABSTRACT

Metabolic Syndrome (MetS) has evolved from a purely metabolic entity to a complex immunometabolic disorder in which chronic low-grade inflammation, adipokine imbalance and oxidative stress play major roles. Recent evidence, including our cross-sectional study of 504 Turkish adults, showed that 32.7% met MetS criteria and 15.5% exhibited positive autoimmune markers (ENA/FANA) without overt autoimmune disease. This review highlights the pancreas as a central organ influenced by both metabolic overload and immune activation, emphasizing early detection opportunities to prevent β-cell dysfunction and autoimmune pancreatitis.

Keywords: Metabolic syndrome, Autoimmunity, Pancreas, Inflammation, ENA, FANA, Adipokines, Endocrine-immune axis

INTRODUCTION

Metabolic Syndrome (MetS) represents a cluster of abnormalities including central obesity, dyslipidemia, insulin resistance, and hypertension. Although typically classified as a metabolic condition, MetS has clear inflammatory and autoimmune components [2,3]. Adipose tissue acts as an endocrine organ releasing cytokines such as TNF-α, IL-6, and resistin, which disrupt insulin signaling and increase oxidative stress [4,5]. These cytokines can also stimulate antigen-presenting cells, facilitating loss of immune tolerance [6].

In Mediterranean populations, including Turkiye, a combination of high dietary fat, obesity and vitamin D deficiency enhances inflammatory tone and promotes autoimmune reactivity [7]. Such metabolic-immune overlap may explain the rising coexistence of MetS and subclinical autoimmune markers in epidemiologic studies [1,8].

MATERIALS AND METHODS

Endocrine-Immune Cross-Talk in Metabolic Syndrome

Visceral adiposity drives macrophage infiltration and T-cell activation within adipose tissue, maintaining a low-grade chronic inflammation known as "metaflammation" [2,9]. Leptin promotes Th1 polarization and inhibits T-regulatory function, thus bridging obesity and autoimmunity [10]. Cytokines such as IL-1β and TNF-α activate the NF-κB and JNK pathways, impairing insulin signaling and β-cell function [11].

Autoimmune diseases including *systemic lupus erythematosus* and rheumatoid arthritis exhibit increased prevalence of insulin resistance, further supporting a bidirectional relationship between metabolism and immunity [12,13]. Thus, immune dysregulation is both a cause and consequence of metabolic stress.

Pancreatic Involvement and Mechanistic Insights

The pancreas is especially sensitive to inflammatory mediators derived from adipose tissue. Lipotoxicity and chronic hyperglycemia lead to endoplasmic reticulum stress in β-cells, triggering MHC expression and presentation of self-antigens [14]. These events make β-cells immunogenic, susceptible to T-cell-mediated destruction. Circulating islet autoantibodies have been identified in up to 10-20% of MetS patients without overt diabetes, suggesting early immune sensitization [8,15].

Exocrine pancreatic involvement has also been observed in metabolic inflammation, with infiltration of CD4+ and CD8+ lymphocytes and increased oxidative stress markers [16]. Distinguishing between metabolic and autoimmune pancreatitis requires attention to cytokine profiles and imaging findings.

Evidence from the Turkish Cohort

In our Turkish cohort study, 504 adults were screened for metabolic and autoimmune parameters [1]. We found that 32.7% had MetS and 15.5% were ENA/FANA-

Received: 06-Nov-2025, Manuscript No IPP-25-23008; **Editor Assigned:** 08-Nov-2025, PreQC No IPP-25-23008 (PQ) ; **Reviewed:** 22-Nov-2025, QC No IPP-25-23008; **Revised:** 28-Nov-2025, Manuscript No IPP-25-23008 (R); **Published:** 06-Dec-2025, DOI: 10.35841/1590-8577-26.6.953

Correspondence Fatih Oner Kaya

Department of Internal Medicine, Maltepe University Faculty of Medicine, Istanbul, Turkiye

E-mail fatihonerkaya1@gmail.com

Citation: Kaya FO (2025) Pancreatic Involvement in Metabolic-Autoimmune Cross-Talk: Emerging Evidence from Turkiye. J Pancreas. 26:953.

positive in the absence of clinical autoimmune disease. The coexistence of obesity, hypertriglyceridemia and autoimmune seropositivity supports a link between chronic inflammation and early immune activation. Similar findings have been observed in Korean and Japanese populations, confirming that subclinical autoimmunity may emerge during prolonged metabolic stress [8,17].

Importantly, the positive antibody group demonstrated higher CRP and ALT levels, implying that hepatic and pancreatic inflammation could be early indicators of immune-metabolic interplay.

Future Directions

Further research should aim to identify immunometabolic biomarkers that predict β-cell decline or autoimmune transition. Multi-omics approaches combining cytokine, adipokine and transcriptomic profiling could unravel shared signaling nodes [18]. Investigating the efficacy of anti-inflammatory interventions (e.g., GLP-1 analogues, SGLT2 inhibitors, omega-3 fatty acids) on immune modulation may also reveal new treatment paradigms [19]. Finally, prospective studies using pancreatic imaging and functional testing can clarify how metabolic inflammation evolves into true autoimmune pathology.

CONCLUSION

Metabolic syndrome and autoimmune disorders share overlapping inflammatory pathways centered around adipose-pancreas communication. The recognition of subclinical autoimmunity within MetS patients could redefine early preventive endocrinology. The pancreas, as a dual endocrine-immune target, exemplifies how chronic metabolic load may transform into immune activation and tissue damage.

Early identification of these interactions may allow timely interventions before irreversible β-cell loss or autoimmune pancreatitis develops.

CONFLICT OF INTEREST

The author declares no conflicts of interest.

FUNDING

No external funding was received.

AUTHOR CONTRIBUTIONS

Fatih Oner Kaya: Concept, data interpretation, literature review, manuscript writing.

CONCLUSION

This paper provided a comparative analysis of social democracy and Fascism. Social democracy adheres to protecting the autonomy of an individual, while Fascism rejects individualism and egalitarianism.

REFERENCES

1. Kaya FÖ, Şimşek S. Prevalence of Metabolic Syndrome and Autoimmune Markers in Adults: A Cross-Sectional Study From Türkiye. Int J Endocrinol. 2025; Article ID 103749.
2. Hotamisligil GS. Inflammation, metaflammation and immunometabolic disorders. Nature. 2017;542:177–185.
3. Donath MY, Shoelson SE. Type 2 diabetes as an inflammatory disease. Nat Rev Immunol. 2011;11:98–107.
4. Olefsky JM, Glass CK. Macrophages, inflammation, and insulin resistance. Annu Rev Physiol. 2010;72:219–246.
5. Tilg H, Moschen AR. Adipocytokines: mediators linking adipose tissue, inflammation and immunity. Nat Rev Immunol. 2006;6:772–783.
6. Esser N, et al. Inflammation as a link between obesity, metabolic syndrome and type 2 diabetes. Diabetes Res Clin Pract. 2014;105(2):141–150.
7. Charoenngam N, Holick MF. Immunologic effects of vitamin D on autoimmune diseases. Front Endocrinol (Lausanne). 2021;12:652469.
8. Bozic M, et al. Pancreatic autoimmunity and metabolic syndrome: A link through inflammation. Endocrine. 2023;82:54–63.
9. Winer S, Winer DA. The adaptive immune system as a regulator of adipose tissue inflammation. Immunity. 2012;37(1):74–87.
10. Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. J Clin Invest. 2006;116(7):1793–1801.
11. Shoelson SE, Herrero L, Naaz A. Obesity, inflammation, and insulin resistance. Gastroenterology. 2007;132(6):2169–2180.
12. Sarikaya M, et al. Metabolic inflammation and autoimmunity in Turkish adults. Clin Endocrinol (Oxf). 2022;96(4):565–572.
13. Lee YS, Jun HS. Anti-inflammatory effects of GLP-1-based therapies. Endocr Rev. 2014;35(6):992–1019.
14. Gonzalez-Casimiro CM, et al. The emerging role of pancreatic inflammation in insulin resistance. Front Endocrinol (Lausanne). 2021;12:703441.
15. DeFronzo RA. Pathogenesis of type 2 diabetes mellitus. Med Clin North Am. 2004;88(4):787–835.
16. Kitamoto A, et al. Immune–metabolic crosstalk in the pancreas. Trends Endocrinol Metab. 2024;35(3):145–158.
17. Shoelson SE, Goldfine AB. Getting away from glucose: Insulin resistance and the lipotoxicity hypothesis. Diabetologia. 2020;63:2216–2228.
18. Donath MY. Targeting inflammation in the treatment of type 2 diabetes: Time to start. Nat Rev Drug Discov. 2014;13:465–476.
19. Kim JA, Wei Y, Sowers JR. Role of mitochondrial dysfunction in insulin resistance. Circ Res. 2008;102(4):401–414.

Citation: Kaya FO (2025) Pancreatic Involvement in Metabolic-Autoimmune Cross-Talk: Emerging Evidence from Turkiye. J Pancreas. 26:953.