

## BRIEF REPORT

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

Fatih Oner Kaya<sup>1\*</sup>, Muhammet Emir Kaya<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, Maltepe University Faculty of Medicine, Istanbul, Turkiye

<sup>2</sup>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  $\beta$ -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- $\alpha$ , 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"

**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: 10.35841/1590-8577-26.6.943

**Correspondence:** Fatih Oner Kaya

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

**E-mail:** fatihonerkaya1@gmail.com

[2,9]. Leptin promotes Th1 polarization and inhibits T-regulatory function, thus bridging obesity and autoimmunity [10]. Cytokines such as IL-1 $\beta$  and TNF- $\alpha$  activate the NF- $\kappa$ B and JNK pathways, impairing insulin signaling and  $\beta$ -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  $\beta$ -cells, triggering MHC expression and presentation of self-antigens [14]. These events make  $\beta$ -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-

**Citation:** Kaya FO (2025) Pancreatic Involvement in Metabolic-Autoimmune Cross-Talk: Emerging Evidence from Turkiye. J Pancreas. 26:943.

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  $\beta$ -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  $\beta$ -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. Charoennangam 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.