

## BRIEF REPORT

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

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### 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”

[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-

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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.

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### 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.

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