AL-KUFA JOURNAL FOR BIOLOGY
ISSN (Print): 2073-8854 **ISSN (online):** 2311-6544

Original Research Paper

Clinical Stratification and Demographic Profiling of Patients with Insulin Resistance and Type 2 Diabetes Mellitus: A Cross-Sectional Study

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Article history
Received: 12/4/2025
Revised: 23/4/2025
Accepted: 12/5/2025

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Abstract: The increasing global health concern of insulin resistance (IR) and type 2 diabetes mellitus (T2DM) highlights the need for improved patient categorization to better understand the various forms of these conditions and inform individualized treatment plans. This research sought to systematically group 100 participants based on the presence or absence of IR and T2DM, subsequently examining demographic and clinical characteristics such as age, gender, the occurrence of autoimmune diseases, and hypertension rates within these defined groups. The study's findings revealed significant differences in the distribution of these factors across the cohorts. Specifically, older age and co-existing hypertension were more common in individuals with both T2DM and IR, while autoimmune diseases were more frequently seen in those with T2DM, irrespective of whether they also had IR. In conclusion, classifying patients using clinical and demographic features offers important understanding into the diverse nature of metabolic disorders, a stratification that is crucial for refining diagnostic and treatment approaches tailored to specific patient subgroups.

Keywords: Insulin resistance, Type 2 diabetes mellitus, Clinical stratification, Hypertension, Autoimmune diseases.

1.Introduction

The prevalence of type 2 diabetes mellitus (T2DM) and insulin resistance (IR) continues to escalate globally, posing substantial public health challenges and economic burdens [1] . T2DM, accounting for the vast majority of diabetes cases worldwide, is characterized by chronic hyperglycemia resulting from a combination of insulin secretory defects and insulin resistance [2] . Insulin resistance, a key feature in the pathogenesis of T2DM, represents a pathological state in which target tissues, including the liver, skeletal muscle, and adipose tissue, exhibit impaired biological responses to insulin [3] . This impairment disrupts glucose homeostasis, leading to elevated blood glucose levels and ultimately contributing to the development of T2DM.[4] Both conditions are frequently accompanied by a cluster of metabolic and inflammatory abnormalities, including dyslipidemia, hypertension, and increased oxidative stress, further complicating their clinical presentation and management [5, 6]. The interplay between metabolic dysfunction and inflammation, often referred to as "metabolic inflammation" or "metaflammation," plays a critical role in the development and progression of both T2DM and IR, necessitating a deeper understanding of their clinical heterogeneity to enhance patient management and outcomes.Recent studies have highlighted the role of pro-inflammatory cytokines, such as interleukin-15 (IL-15), in autoimmune pathologies, including hematological

DOI: 10.36320/ajb/v17.i2.19549

complications like hemolytic anemia in systemic lupus erythematosus (SLE) [7]. This underscores the broader relevance of immune dysregulation in metabolic and autoimmune disorders . Additionally, evidence suggests that weight gain, irrespective of T2DM status, can affect the central nervous system by altering levels of noradrenaline (NA), brain-derived neurotrophic factor (BDNF), and nerve growth factor (NGF) [8] . In patients with T2DM, studies have shown reduced expression of dopamine receptor 2 (D2R), elevated insulin levels, and increased hepatic enzyme activity (AST and ALT), all of which reflect systemic metabolic stress. [9] A regional study conducted in Basrah, Iraq, further demonstrated significant differences in insulin, C-peptide, lipid profiles, and other biochemical markers between T2DM patients and healthy individuals, underscoring the multifaceted nature of disease manifestation. [10] Clinical stratification of patients with T2DM and IR is critical for identifying distinct phenotypes that may respond differently to therapeutic interventions. The traditional view of T2DM as a homogenous disease has been challenged by evidence suggesting significant heterogeneity in its etiology, progression, and response to treatment [11, 12]. Factors such as age, gender, ethnicity, genetic predisposition, comorbid autoimmune diseases, and hypertension have been implicated in modifying disease progression and severity [13, 14]. For instance, the presence of comorbid autoimmune conditions may influence the course of T2DM and the choice of treatment strategies. Furthermore, elucidating demographic and clinical variations among patients provides insight into the complex pathophysiology of these conditions and facilitates the refinement of individualized treatment approaches, moving towards a more personalized medicine paradigm.

This study aims to stratify patients into distinct clinical groups based on the presence or absence of IR and T2DM and to assess the distribution of demographic and clinical variables across these groups. Through this analysis, we seek to highlight the diversity of clinical presentations in these metabolic disorders and underscore the value of tailored diagnostic and therapeutic strategies. A better understanding of the distinct clinical phenotypes within T2DM and IR populations will not only improve patient care but also contribute to the development of more targeted and effective interventions.

2.Methodology

Study Design and Population

This cross-sectional study was conducted at the Diabetes Center in Najaf, Iraq, between October 1, 2024, and January 22, 2025. The study aimed to investigate the clinical profiles of patients with type 2 diabetes mellitus (T2DM) and insulin resistance (IR), with a focus on detailed clinical stratification. A total of 100 participants were recruited consecutively following the provision of informed consent. The study protocol was approved by the Iraqi Ministry of Health Ethics Committee (Approval No. 1036, dated May 24, 2024), and all procedures adhered to the ethical principles outlined in the Declaration of Helsinki.

Participant Classification

Participants were categorized into four groups based on clinical and laboratory assessments, according to the diagnostic criteria of the American Diabetes Association (ADA) and the World Health Organization (WHO):

Group 1 (IR): Individuals diagnosed with insulin resistance without diabetes mellitus (n = 30). The specific criteria used for the diagnosis of insulin resistance should be explicitly stated here (e.g., HOMA-IR threshold).

Group 2 (DM + IR): Individuals diagnosed with both type 2 diabetes mellitus and insulin resistance (n = 20).

Group 3 (DM - IR): Individuals diagnosed with type 2 diabetes mellitus without evidence of insulin resistance (n = 20). The criteria for excluding insulin resistance in these patients should be clearly defined.

Group 4 (Healthy Controls, HC): Age- and gender-matched healthy individuals without diabetes or insulin resistance (n = 30). The criteria for "healthy" should be defined (e.g., normal fasting glucose, HbA1c, absence of metabolic disorders).

Data Collection

DOI: 10.36320/ajb/v17.i2.19549

For each participant, comprehensive clinical and demographic data were collected using standardized protocols and validated data collection forms. The following data were included: Age: Recorded in years and categorized for analysis as ≤40 years or >40 years.

Gender: Male or Female.

Autoimmune Disease Status: Presence or absence of a documented clinical diagnosis of any autoimmune disorder. The specific autoimmune diseases considered in the study should be listed (e.g., rheumatoid arthritis, Hashimoto's thyroiditis).

Hypertension Status: Presence or absence of a clinical diagnosis of hypertension, defined according to established criteria (e.g., systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg, or use of antihypertensive medication) [15]. The method of blood pressure measurement should be specified.

Clinical diagnoses were established through standard laboratory assessments, physical examination, and a thorough review of patient medical history by qualified endocrinologists. Details of the laboratory assays used (e.g., specific assays for glucose, insulin) should be provided, including information on the assay manufacturer and precision. The physical examination should be briefly described, including any relevant components.

3.Results and discussion

Age and Disease Progression

Age distribution differed significantly among the groups ($p < 0.01$). Participants with DM + IR were more likely to be older than 40 years compared to other groups. Table 1 summarizes the age distribution across the study cohorts. Age distribution differed significantly among the groups ($p < 0.01$). Participants with T2DM (DM + IR and DM - IR) were more likely to be older than 40 years compared to those with isolated IR or healthy controls. Specifically, 60% of the DM + IR group and 80% of the DM - IR group were older than 40 years, compared to 27% in the IR group and 20% in the healthy control group. This observation aligns with established evidence indicating that aging is a major risk factor for the development of T2DM due to progressive declines in insulin sensitivity and pancreatic β-cell function [16, 17]. The current study's findings support the notion that the accumulation of age-related metabolic changes contributes to the increased prevalence of T2DM in older individuals.Aging is also associated with an increased inflammatory burden, termed "inflammaging," which may contribute to the pathogenesis of both IR and diabetes [18, 19]. Chronic low-grade inflammation, a hallmark of aging, can impair insulin signaling and promote pancreatic beta-cell dysfunction, thereby exacerbating the development of T2DM.

Table 1: Age Distribution

Age group	IR (n=30)	DM-IR(n=20)	DM+IR(n=20)	HC(n=30)
≤ 40	22(73%)	4(20%)	8(40%)	24(80%)
>40	8(27%)	16(80%)	12(60%)	6(20%)

Gender Disparities

While gender differences were not statistically significant across the groups, the distribution of females varied across the groups. Females constituted 67% of the IR group, 65% of the DM + IR group, 50% of the DM - IR group, and 60% of the healthy control group. Previous epidemiological studies have suggested that hormonal, genetic, and lifestyle factors might modulate susceptibility to metabolic diseases differently between sexes [20]. Specifically, postmenopausal hormonal changes, characterized by estrogen deficiency, have been implicated in increased insulin resistance among women, potentially explaining the observed trend [21].

Table 1: gender Distribution

Gender	IR (n=30)	DM-IR(n=20)	DM+IR(n=20)	HC(n=30)
Female	20(67%)	10(50%)	13(65%)	18(60%)
Male	10(33%)	10(50%)	7(35%)	12(40%)

Autoimmune Disease Associations

DOI: 10.36320/ajb/v17.i2.19549

The prevalence of autoimmune diseases varied significantly between groups. Patients with T2DM (DM + IR: 45% and DM - IR: 40%) exhibited a higher incidence of autoimmune conditions compared to IR (7%) and healthy controls (20%). This finding underscores the complex interplay between metabolic and immune dysfunctions. Several studies have reported an increased incidence of autoimmune phenomena, including thyroid disorders and latent autoimmune diabetes in adults (LADA), among individuals with T2DM [22, 23]. LADA, in particular, shares characteristics of both type 1 and type 2 diabetes, highlighting the heterogeneity within T2DM. Chronic low-grade inflammation and immune dysregulation may serve as common mechanistic links between autoimmunity and impaired glucose metabolism. The higher prevalence of autoimmune diseases in T2DM patients in our study suggests that immune-mediated mechanisms may play a more significant role in the pathogenesis of T2DM than previously recognized, particularly in this population. Notably, the healthy control group also had a non-negligible prevalence of autoimmune diseases (20%), which warrants further investigation

Table 3 :Autoimmune Disease Prevalence

Autoimmune disease status	IR (n=30)	DM-IR(n=20)	DM+IR(n=20)	HC(n=30)
With autoimmune disease	2(7%)	8(40%)	9(45%)	6(20%)
Without autoimmune disease	28(93%)	12(60%)	11(55%)	24(80%)

Hypertension and Metabolic Risk

Hypertension was significantly more prevalent among participants with T2DM (DM + IR: 30% and DM - IR: 40%) compared to the IR (0%) group. Interestingly, the prevalence of hypertension in healthy controls (20%) was similar to that in the T2DM groups. This finding contrasts with the typical understanding of hypertension as a major comorbidity of T2DM [24]. The absence of hypertension in the IR group is also notable. These findings may suggest a complex relationship between insulin resistance, T2DM, and hypertension in this specific study population, potentially influenced by factors such as ethnicity, lifestyle, or other confounding variables.

Table 4 : Hypertension Prevalence

Hypertension status	IR (n=30)	DM-IR(n=20)	DM+IR(n=20)	HC(n=30)
With hypertension	0(0%)	8(40%)	6(30%)	6(20%)
Without hypertension	30(100%)	12(60%)	14(70%)	24(80%)

Conclusion

In conclusion, this study demonstrates that distinct clinical and demographic profiles exist among patients with insulin resistance (IR) and type 2 diabetes mellitus (T2DM). Specifically, T2DM, both with and without IR, is more prevalent in older individuals, highlighting the significant impact of age on the development of this metabolic disorder. While gender distribution was similar across the groups, T2DM patients, regardless of IR status, exhibited a higher prevalence of autoimmune diseases. Interestingly, hypertension, while expected to be associated with T2DM, was observed in both T2DM groups and, to a notable extent, in the healthy control group, suggesting a complex interplay of factors beyond just diabetes and insulin resistance in its etiology within this study population. These findings underscore the importance of stratifying patients with T2DM and IR based on age, autoimmune disease status, and hypertension, which may help in tailoring more effective and individualized treatment strategies and improving patient outcomes.

Acknowledgement

Research facilities provided by various hospitals in Najaf, city recognized

Author's Contributions

Hawraa Fadhel Gaber: Conceptualization, Data curation.Writing – original draft.

Muslim Idan Mohsin: Formal analysis

Ethics

This research was approved to use human samples from patients and approved to contain these samples by MOH committee for ethics in Iraq with legal paper 1036, 24 may of 2024.

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