

Prevalence of Double Diabetes in Benha City, Egypt

Hospital Based Cross Sectional Study

Amina M. Ahmed, Mohamed S. Saleh, Ayman M. El Badawy, Amira M. Elsayed, Walaa M. Ibrahim

Internal Medicine Department,
Faculty of Medicine, Benha
University, Egypt.

Corresponding to: Amina M.
Ahmed, Internal Medicine
Department, Faculty of Medicine
Benha University, Egypt.

Email:
mgnagy44@gmail.com

Received: 9 December 2024

Accepted: 22 December 2024

Abstract

Objective: This study aimed to assess the prevalence of double diabetes (DD) among type 1 and type 2 diabetes mellitus (DM) patients in Benha city, Egypt, and to evaluate the clinical and metabolic differences between DD and typical DM. **Methods:** This cross-sectional study included 528 patients who attended Benha University Hospital between July 2023 and January 2024. Group I consisted of 435 type 2 DM patients aged >40 years, while Group II included 93 type 1 DM patients aged <18 years. Diagnosis of DD was established by positive anti-GAD65 antibodies in type 2 DM patients and elevated HOMA-IR (>2.5) in type 1 DM patients. **Results:** The prevalence of DD was 13.6% (59/435) in type 2 DM patients and 25.8% (24/93) in type 1 DM patients. In Group I, DD patients were younger (59.5 vs. 60.1 years, $p=0.569$), had lower BMI (24.9 vs. 28.9 kg/m², $p<0.001$), and higher prevalence of autoimmune disease family history (40.7% vs. 9%, $p<0.001$) compared to typical type 2 DM patients. In Group II, DD patients were older (14.3 vs. 12.9 years, $p=0.005$), with higher BMI (23.8 vs. 16.3 kg/m², $p<0.001$) and waist circumference (73.6 vs. 62.5 cm, $p<0.001$) compared to typical type 1 DM patients. DD patients in both groups exhibited higher HbA1c levels (Group I: 9.05% vs. 8.09%, $p<0.001$; Group II: 10.7% vs. 8.04%, $p<0.001$). **Conclusion:** Double diabetes is prevalent among both type 1 and type 2 DM patients, with distinct clinical and metabolic profiles.

Keywords: Double diabetes, Type 1 diabetes, Type 2 diabetes, Insulin resistance, Anti-GAD65.

Introduction

Since 1991, evidence has emerged supporting the existence of a distinct form of diabetes, termed 'double diabetes' (DD). This condition was initially recognized through the concurrent presence of insulin deficiency and insulin resistance. However, the precise classification of DD was

complicated by the lack of reliable methods to quantify insulin resistance. The term 'double diabetes' refers to a clinical scenario where features of both T1D and T2D coexist in a patient. Early epidemiological studies, coupled with hereditary patterns, suggested that approximately 4% of individuals with

T1D are predisposed to developing features characteristic of T2D (1).

Over the past two decades, the worldwide obesity epidemic has contributed to approximately 25% of adolescents with T1D presenting with excess body weight. This phenomenon is often linked to suboptimal diabetes management, increased insulin requirements, and fluctuating blood glucose levels. Addressing the diagnosis and treatment of the DD phenotype is particularly crucial, as managing this condition poses significant challenges for affected individuals, who are frequently diagnosed during childhood (2).

Recent studies have reaffirmed that approximately 25.5% of individuals with T1D are affected by similar comorbidities, including a heightened prevalence of macrovascular complications such as coronary artery disease and stroke, as well as an increased incidence of microvascular conditions. These associations are observed independently of glycemic control (3).

Another study, which included 200 patients with youth-onset diabetes, identified 7% as having DD, with a mean BMI of 29.8 and mean age of 22.2 years. Additionally, 29% of the participants were classified as having an indeterminate form of the condition (4).

A large-scale epidemiological study also revealed that 25.5% of patients with T1D exhibited characteristics of metabolic syndrome (3). In a study conducted among individuals with juvenile-onset diabetes from East Delhi and surrounding areas of India, investigators determined that 7% of the subjects presented with DD (4). Recent estimates from the KSA suggest that approximately one-third of young diabetic

patients are affected by atypical forms of diabetes (5).

The presence of GAD antibodies may contribute to the onset of type 2 diabetes, a condition that is characteristic of DD. In individuals with T1D, common manifestations of DD include insulin resistance, obesity, and a variant known as LADA. Furthermore, autoantibodies such as insulin antibodies, GAD65, and IA2 are typically detected. DD represents a significant clinical event in patients with juvenile-onset diabetes (ages 11–19), as it often results from weight gain and insulin resistance, which are side effects of insulin therapy. Clinical indicators that may help distinguish DD from classic T1D include a positive family history and an elevated BMI, particularly when it exceeds the 85th percentile (4).

DD is emerging as an independent and prospective risk factor for the development of both macrovascular and microvascular complications in patients with T1D. In DD, microvascular complications are linked to an elevated risk of nephropathy and retinopathy, while macrovascular comorbidities, such as metabolic syndrome, are prevalent. However, there remains a significant gap in awareness regarding these metabolic comorbidities. It is crucial to intensify efforts aimed at identifying affected individuals and implementing strategies to mitigate the incidence of metabolic syndrome in T1D (3).

To prevent complications and improve glycemic control associated with diabetes, these patients require a comprehensive treatment approach that integrates lifestyle modifications with an appropriate insulin regimen (4). Behavioural lifestyle

modifications, including tailored dietary and physical activity plans, may play a crucial role in the prevention and management of both T1D and T2D (6).

This study aimed to assess the prevalence of DD among type 1 and type 2 DM patients in Benha city, Egypt, and to evaluate the clinical and metabolic differences between DD and typical DM.

Patients and Methods

Study design:

This is cross-sectional observational study was conducted on 528 patients divided into two groups: Group I included 435 cases of type 2 DM over 40 years old, and Group II included 93 cases of type 1 DM below 18 years old., who attend to Benha university hospital in the period from July 2023 to January 2024(Code Number: Ms21-8-2023), The aim of this study is to assess prevalence of double diabetes in both types through asses' insulin resistance in type 1 through HOMA IR (homeostasis model assessment estimated IR), in type 2 check for positive anti GAD antibodies (glutamic acid decarboxylase antibodies)

Sample size:

The calculated sample size of the study were; group I: 435 cases of DM over 40 years, and group II: 93 cases of DM below 18 years participants at 5% level of significance and 80% power of the study, using the following formula (7).

$$n = \frac{Z^2 * P * (1 - P)}{d^2}$$

Where:

Z = 1.96 for 95% confidence level.

p = Expected proportion of children and adolescents who have metabolic syndrome (21%).

d = precision (Margin of error) = 0.05

Inclusion criteria:

Patients eligible for the study included those diagnosed with type 1 or type 2 diabetes mellitus (DM), with an age criterion of below 18 years for type 1 DM and above 40 years for type 2 DM. Both male and female patients were included in the study.

Exclusion criteria:

Patients were excluded if they were pregnant, had impaired renal or liver function, were undergoing cancer treatment, had secondary types of diabetes (such as pancreatic, drug-induced, or endocrinopathy-related diabetes), or were diagnosed with monogenic diabetes.

Methods

A thorough history was taken from each patient, focusing on sociodemographic characteristics such as age, gender, nationality, marital status, education, and work status. Particular attention was given to a positive family history of diabetes or autoimmune diseases, duration of diabetes, treatment modalities, medication adherence, and any diabetes-related comorbidities or complications.

Full clinical examination:

The clinical examination emphasized vital parameters, including pulse and blood pressure.

Anthropometric measurements:

Body height was measured using a stadiometer with participants standing barefoot, recorded to the nearest 0.1 cm. Body weight was assessed using digital scales with participants in minimal clothing, measured to the nearest 0.01 kg. Waist circumference (WC) was measured at the level of the umbilicus while participants

stood upright and breathed naturally. A non-elastic plastic tape was used for precise measurements, recorded to the nearest 0.1 cm. Pediatric and adolescent measurements were adjusted for age and sex according to the Egyptian growth charts (8). Truncal obesity was classified as a waist circumference of ≥ 80 cm in females and ≥ 94 cm in males (9). Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). For pediatric and adolescent populations, BMI was evaluated using the Egyptian growth charts with appropriate age- and gender-specific adjustments (10).

Manifestations of IR e.g. Acanthosis nigricans.

Complication of DM.

Investigations

The following investigations were performed for every patient:

- ❖ **Fasting insulin** was estimated by chemiluminescent microparticle immunoassay (CMIA) method on Abbott Architect i2000 (Abbott Diagnostic, USA) analyser (11).
- ❖ **HbA1c** analysis was performed in our laboratory employing a standardized method accredited by the National Glycohemoglobin Standardization Program and calibrated to align with the assay utilized in the Diabetes Control and Complications Trial (12).
- ❖ **Anti-GAD** antibodies were measured using the GAD Autoantibody ELISA assay (RSR Limited), with the assay's lower detection threshold set at 0.57 units/mL. For antibody concentrations ranging from 5.7 to 97 units/mL, the intra-assay and interassay coefficients of variation were found to be between

3.5% and 7.3%, and 5.2% and 6.4%, respectively (13).

- ❖ **Insulin resistance** was calculated using homeostasis model assessment (HOMA-IR) formula, $HOMA-IR = (Fasting\ glucose\ in\ mg/dL \times Fasting\ insulin\ in\ \mu U/mL) / 405$. (14).
- ❖ Prior to breakfast, venous blood samples were drawn by trained nurses from the antecubital vein and collected into vacuum tubes. The samples were subsequently centrifuged at 3000 rpm, aliquoted, and stored at $-80^\circ C$. All biochemical analyses were performed using the Cobas 6000 biomedical analyzer. The glucose oxidase and enzymatic methods were employed for the quantification of FG, TC, LDL, and TG, respectively, while HDL-C was measured using the clearance method (15).

Definition of the double diabetes

The term 'double diabetes' describes the condition in which individuals with type 1 diabetes develop insulin resistance, as well as those with type 2 diabetes who test positive for anti-GAD antibodies. **Group II:** 93 cases of DM below 18 years who had recruited in the study were initially classified as T1DM on the basis of pre-defined WHO criteria (16) and then were re-categorized as typical type 1 and double diabetes based on their Anti-GAD65-antibody and HOMA-IR- level. Subjects positive for Anti-GAD65 (>1.05 U/ml) and HOMA-IR- levels more than 2.5 were characterized as double diabetes subjects; and subjects with HOMA-IR- levels less than 2.5 and positive Anti-GAD-antibody, were kept under the category of typical type 1 DM category (4).

Group I: 435 cases of DM over 40 years who had recruited in the study were initially classified as T2DM on the basis of pre-defined WHO criteria (16) and then were re-categorized as typical type 2 and double diabetes based on their Anti-GAD 65-antibody, Subjects with positive Anti-GAD65 were characterized as double diabetes subjects; and subjects with negative Anti-GA D65-antibody, were kept under the category of typical type 2 DM category.

Administrative design:

Ethical consideration: A written informed consent has been taken from the parents/guardians of participants and old aged participants with explanation of the study purpose, steps, possible hazards. Approval was attained from IRB (Approval code: 21-8-2023).

Statistical analysis:

The data analysis was performed using IBM SPSS version 23.0 for Windows (SPSS Inc., Chicago, IL, USA) and NCSS version 11 for Windows (NCSS LLC, Kaysville, UT, USA). Qualitative variables were represented as frequencies and percentages, while quantitative variables were expressed as means with standard deviations (SD). The Kolmogorov-Smirnov test was applied to assess the normality of the data distribution.

Various statistical tests were utilized for the analysis. The Chi-square test was employed to compare qualitative data. An independent sample t-test was used to compare the means of normally distributed quantitative data between two groups, while the Mann-Whitney test was used for non-normally distributed quantitative data. For comparisons involving multiple means in normally distributed quantitative data, the analysis of variance (ANOVA, F-test) was

applied. The Kruskal-Wallis test was used for comparisons involving multiple sets of non-normally distributed quantitative data. A p-value of <0.05 was considered statistically significant, <0.001 was considered highly significant, and >0.05 was considered non-significant.

Results

The study participants were divided into two groups: Group I, which included 435 cases of type 2 diabetes mellitus (DM) aged over 40 years, and Group II, which included 93 cases of type 1 DM aged below 18 years.

Table (1) shows basic demographic and anthropometric data of all studied patients. This table summarizes the demographic and anthropometric measures of all studied patients. Fifty-four percent of the patients were male, with a mean age of 51.8 years. Among them, 38.6% had a positive family history of type II DM, and 17.9% had a positive family history of autoimmune disease.

Table (2) shows basic demographic and anthropometric data of the studied groups. This table shows demographic and anthropometric measures among both groups. Fifty-four percent of studied group 1 cases (> 40 years) were males with mean age of 60.1 years, 41.1% of them had positive family history of type II DM and 13.3% had positive family history of Autoimmune disease. 52.7% of group 2 were males with mean age of 13.4 years. While 26.9% and 39.8% of them had positive family history of type 2 DM and autoimmune disease respectively. Except for gender distribution and family history of DM, all other parameters in this table showing highly significant difference between both groups.

Table (2) shows Laboratory data among studied groups. This table shows lipid profile among both old and young age group (TG, TC, HDL and LDL), also levels of hemoglobin A1c, fasting insulin, FBG and HOMAIR. 13.6% of group I cases (>40 years old) had positive Anti-GAD versus 100% of group II cases (<18 years old). There were significant differences between both groups regarding all lab parameters except fasting insulin level and HDL level in male cases.

Table (3) shows Comparison between cases of DD and typical type 2 diabetic patients of the studied group I regarding demographic data, duration of DM, blood pressure, family history, and laboratory data. This table shows that there was no significant difference regarding age, gender between cases of DD and typical type 2 diabetic patients of the studied group I.

This table shows that 20.3% of DD subgroup had positive family history of type 2 DM and 40.7% had positive family history of autoimmune disease versus 55.6% and 9% of cases of typical type 2 DM respectively, with statistically significant difference among them. While there was no significant difference regarding duration of

DM, also significant decrease in levels of systolic and diastolic blood pressure than cases with typical type 2 DM.

This table shows a high statistically significant lower levels of lipid profile (TG, TC, LDL) among cases with DD of group I and higher HDL, also there was a significant decrease in levels of fasting insulin and HOMA IR than cases with typical type 2 DM.

Table 4 shows Comparison between cases of DD and typical type 1 diabetic patients of the studied group II regarding demographic data, duration of DM, blood pressure and family history. This table shows a statistically significant difference among cases of DD and cases of typical type 1 DM as regard age while gender showed insignificant difference between both subgroups. This table shows a statistically significant difference among cases of typical type 1 DM as regard family history of type 2 DM. while family history of Autoimmune Disease showed insignificant difference between both subgroups, also significant increase in levels of systolic and diastolic blood pressure than cases with typical type 1 DM.

Table (1): Basic demographic and anthropometric data of all studied patients.

| All patients N=528 | | | |
|--|--------|---------------|----------|
| Mean ± SD | | | |
| Age\ years | | 51.81 ± 18.85 | |
| Duration of DM\ years | | 10.8 ± 5.9 | |
| Weight (kg) | | 75.09 ± 17.68 | |
| Height (m) | | 1.66 ± 0.11 | |
| BMI | | 26.7 ± 5.44 | |
| Waist circumference (cm) | male | 98.25 ± 15.94 | |
| | female | 99.21 ± 16.43 | |
| | | N | % |
| Gender | Male | 284 | 53.8 |
| | Female | 244 | 46.2 |
| Family history of type 2 DM | | 204 | 38.6 |
| Family history of Auto-immune disease | | 95 | 17.9 |

Data are represented as mean ± SD or N (%), N: Number of patients, SD: Standard deviation, DM: Diabetes mellitus, BMI: Body mass index.

Table (2): Demographic, Anthropometric, And Laboratory Data of the studied groups.

| | | Group I N=435 | | Group II N=93 | | t | p |
|--|--------|--------------------------------|------|--------------------------------|------|----------------|----------|
| | | | | Mean \pm SD | | | |
| Age\ years | | 60.1 \pm 6.89 | | 13.4 \pm 2.36 | | 64.518 | <0.001HS |
| Duration of DM\ years | | 12.1 \pm 5.58 | | 4.42 \pm 2.11 | | 13.0665 | <0.001HS |
| Weight (kg) | | 81.6 \pm 9.45 | | 44.5 \pm 14.9 | | 29.9886 | <0.001HS |
| Height (m) | | 1.71 \pm 0.08 | | 1.51 \pm 0.12 | | 19.8232 | <0.001HS |
| BMI | | 28.4 \pm 4.17 | | 19.3 \pm 4.35 | | 18.9562 | <0.001HS |
| Waist circumference (cm) | male | 105.82 \pm 5.24 | | 67.34 \pm 8.42 | | 49.3553 | <0.001HS |
| | female | 105.21 \pm 6.43 | | 66.98 \pm 7.11 | | 48.447 | <0.001HS |
| Gender | | N | % | N | % | X ² | p |
| | Male | 235 | 54.0 | 49 | 52.7 | 0.34 | 0.55 NS |
| | Female | 200 | 46.0 | 44 | 47.3 | | |
| Family history of type 2 DM | +ve | 179 | 41.1 | 25 | 26.9 | 2.3 | 0.12 NS |
| | -ve | 256 | 58.9 | 68 | 73.1 | | |
| Family history of Auto-immune disease | +ve | 58 | 13.3 | 37 | 39.8 | 8.4 | 0.004 S |
| | -ve | 377 | 86.7 | 56 | 60.2 | | |
| Triglycerides (mg\dl) | | 161.7 \pm 16.75 | | 121.4 \pm 19.4 | | 20.4485 | <0.001HS |
| Total cholesterol (mg\dl) | | 210 \pm 26.8 | | 164.5 \pm 27.8 | | 14.7631 | <0.001HS |
| HDL (mg\dl) | male | 49.2 \pm 4.34 | | 48.23 \pm 6.76 | | 2.4445 | 0.076 NS |
| | female | 49.4 \pm 5.74 | | 47.98 \pm 8.35 | | 1.9807 | 0.0481 S |
| LDL (mg\dl) | | 111.5 \pm 13.5 | | 88.1 \pm 16.4 | | 14.5779 | <0.001HS |
| HbA1c | | 8.22 \pm 1.11 | | 9.11 \pm 1.94 | | 6.0526 | <0.001HS |
| Fasting insulin (μIU\ml) | | 17.8 \pm 10.72 | | 19.6 \pm 20.2 | | 1.2222 | 0.2222NS |
| FBS (mg\dl) | | 137.8 \pm 19.9 | | 144.4 \pm 31.5 | | 2.5829 | 0.0101 S |
| HOMAIR | | 5.89 \pm 3.38 | | 7.42 \pm 8.18 | | 2.9135 | 0.0037 S |
| Positive Anti-GAD | | N (%) | | N (%) | | X ² | P |
| | | 59 (13.6%) | | 93 (100%) | | 30.7 | <0.001HS |

N: Number of participants, t: t-statistic, p: p-value, SD: Standard deviation, DM: Diabetes mellitus, BMI: Body mass index, cm: Centimeters, X²: Chi-square, NS: Not significant, S: Significant, HS: Highly significant, +ve: Positive, -ve: Negative, mg/dL: Milligrams per deciliter, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, HbA1c: Hemoglobin A1c, μ IU/mL: Micro international units per milliliter, FBS: Fasting blood sugar, HOMA-IR: Homeostasis model assessment of insulin resistance, Anti-GAD: Anti-glutamic acid decarboxylase antibodies.

Table 3: Comparison between cases of DD and typical type 2 diabetic patients of the studied group I regarding demographic data.

| Group I | | DD N=59 | | Typical type 2 DM N=376 | | t-test\ MW [#] | P |
|---|-------------------|--------------------------|------|----------------------------|------|--------------------------------|--------------|
| | | Mean ± SD | | | | | |
| Age\ years | | 59.5 ± 5.07 | | 60.1 ± 7.13 | | 0.571 | 0.569 NS |
| Gender | Male | N | % | N | % | X ² 0.772 | P 0.402 |
| | Female | 35 | 59.3 | 200 | 53.2 | | |
| Group I | DD | 24 | 40.7 | 176 | 46.8 | t-test | NS P |
| | Typical type 2 DM | N=59 | | N=376 | | | |
| Duration of DM\ years | | Mean ± SD 12.9 ± 5.32 | | 11.99 ± 5.61 | | 1.14 [#] | 0.255 NS |
| SBP (mmHg) | | 127.98 ± 16.2 | | 133.4 ± 15.39 | | 2.43 | 0.02 S |
| DBP (mmHg) | | 79.6 ± 11.3 | | 84.4 ± 15.22 | | 2.93 | 0.004 S |
| Family history of type 2 DM | +ve | N | % | N | % | X ² 12.2 | P 0.001 |
| | -ve | 12 | 20.3 | 209 | 55.6 | | |
| Family history of Autoimmune Disease | +ve | 47 | 79.7 | 167 | 44.4 | 44.2 | S <0.001 |
| | -ve | 24 | 40.7 | 34 | 9.0 | | |
| Group I | DD | 35 | 59.3 | 342 | 91.0 | t- test/ MW [#] | HS P |
| | Typical type 2 DM | N=59 | | N=376 | | | |
| | | Mean ± SD | | | | | |
| Triglycerides (mg\dl) | | 145.3 ± 4.52 | | 164.3 ± 16.4 | | 8.79 | <0.001 HS |
| Total cholesterol (mg\dl) | | 183.6 ± 9.02 | | 214.2 ± 26.1 | | 8.93 | <0.001 HS |
| HDL (mg\dl) | | 58.2 ± 3.33 | | 48.1 ± 4.88 | | 15.4 | <0.001 HS |
| LDL (mg\dl) | | 101.5 ± 3.75 | | 113.1 ± 13.8 | | 6.38 | <0.001 HS |
| HbA1c | | 9.05 ± 0.71 | | 8.09 ± 0.99 | | 7.12 | <0.001 HS |
| Fasting insulin (µIU\ml) | | 5.81 ± 1.32 | | 19.6 ± 10.5 | | 12.2 [#] | <0.001 HS |
| FBS (mg\dl) | | 143.8 ± 8.65 | | 136.8 ± 21.1 | | 4.47 | <0.001 HS |
| HOMAIR | | 2.05 ± 0.48 | | 6.49 ± 3.25 | | 12.3 [#] | <0.001 HS |

N: Number of participants, DM: Diabetes mellitus, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, HbA1c: Hemoglobin A1c, FBS: Fasting blood sugar, HOMA-IR: Homeostasis model assessment of insulin resistance, MW#: Mann-Whitney test, NS: Not significant, S: Significant, HS: Highly significant.

Table (4): Comparison between cases of DD and typical type 1 diabetic patients of the studied group II regarding demographic data.

| Group II | | DD N=24 | | Typical type 1 DM N=69 | | t-test\ MW [#] | P |
|---|--------|-------------|-----------|---------------------------------|-----------|----------------------------|-----------------|
| | | Mean ± SD | | | | | |
| Age\ years | | 14.3 ± 2.34 | | 12.9 ± 2.25 | | 2.87 | 0.005 S |
| Gender | Male | N 10 | % 41.7 | N 30 | % 43.5 | X ² 3.55 | P 0.06 NS |
| | Female | 14 | 58.3 | 39 | 56.5 | | |
| Group II | | DD N=24 | | Typical type 1 DM N=69 | | t-test | P |
| | | Mean ± SD | | | | | |
| Duration of DM\ years | | 4.29 ± 1.91 | | 4.51 ± 2.24 | | 0.464# | 0.451 NS |
| SBP (mmHg) | | 114 ± 6.12 | | 100.3 ± 6.09 | | 10.55 | <0.001 HS |
| DBP (mmHg) | | 69.9 ± 5.43 | | 59.9 ± 5.31 | | 8.66 | <0.001 HS |
| Family history of type 2 DM | +ve | N 9 | % 37.5 | N 12 | % 17.4 | X ² 5.86 | P 0.02 S |
| | -ve | 15 | 62.5 | 57 | 82.6 | | |
| Family history of Autoimmune Disease | +ve | 7 | 29.2 | 22 | 31.8 | 2.33 | 0.107 NS |
| | -ve | 17 | 70.8 | 47 | 68.2 | | |

N: Number of participants, DM: Diabetes mellitus, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MW#: Mann-Whitney test, NS: Not significant, S: Significant, HS: Highly significant, +ve: Positive, -ve: Negative, X²: Chi-square.

Discussion

In our study, the prevalence of DD among type 2 DM patients (Group I) was 13.6% (59 out of 435 patients) .

This finding is comparable to a study reported a prevalence of 10-20% of DD among adult-onset diabetes patients (6).

However, our result is lower than that reported by a study found a prevalence of 25% of DD among type 2 DM patients. This difference could be attributed to variations in study populations, diagnostic criteria, and environmental factors. (3)

In our study, prevalence of 25.8 % DD among type 1 DM patients (Group II), (24 out of 93 patients) .

This is consistent with the findings of Pozzilli and Buzzetti, who reported a prevalence of 20-30% among children and adolescents with type 1 DM. (6)

Our result is slightly higher than that reported by Wilkin, who found a prevalence of 15-20% in young type 1 DM patients (17) .

The higher prevalence in our study might be due to increasing rates of obesity and insulin resistance in the Egyptian population.

In our study, in Group I, DD patients were significantly younger than typical type 2 DM patients (59.5 vs 60.1 years, p=0.569) .

This aligns with findings from a study reported that DD patients tend to be diagnosed at a younger age than typical type 2 DM patients (18).

In our study, the DD subgroup also had a higher prevalence of family history of autoimmune diseases (40.7% of DD vs 9% of typical type 2 DM, $p<0.001$). In our study, the DD subgroup also had a higher prevalence of family history of type 2 DM (37.5% vs 17.4%, $p=0.02$), supporting the role of genetic factors in DD development.

A cross-sectional study involving 658 participants from the Pittsburgh Epidemiology of Diabetes Complications (EDC) cohort, which included 112 individuals with a documented family history of type 2 diabetes and 119 who had a history of CHD, found that a positive family history notably heightened the risk of CHD (HR 1.89, 95% CI 1.27, 2.84). A study reported that the risk escalated in proportion to the number of affected family members ($p = 0.001$ for trend). Having one family member with the condition resulted in an OR of 1.62, while the presence of two affected family members elevated the OR to 5.13 (19).

In our study, in Group II, DD patients were significantly older than typical type 1 DM patients (14.3 vs 12.9 years, $p=0.005$).

This is consistent with the findings of some authors noted that DD in type 1 DM patients often develops during puberty or later adolescence. (2)

Our study revealed significant differences in metabolic profiles between DD patients and their typical diabetes counterparts. In our study, in Group I, DD patients had significantly lower BMI (24.9 vs 28.9 kg/m²,

$p<0.001$) and waist circumference (96.8 vs 106.1 cm, $p<0.001$) compared to typical type 2 DM patients.

This is contrary to a study found higher BMI in DD patients (3). Another study found that patients with latent autoimmune diabetes in adults (LADA), a form of DD, had lower BMI and higher HDL cholesterol levels compared to antibody-negative T2DM patients, which aligns with our findings in the T2DM group (20).

In our study, in Group II, DD patients had significantly higher BMI (23.8 vs 16.3 kg/m², $p<0.001$) and waist circumference (73.6 vs 62.5 cm, $p<0.001$) compared to typical type 1 DM patients.

This aligns with the findings of Pozzilli and Buzzetti, who reported that DD in type 1 DM is often associated with increased weight and insulin resistance. (6)

A study documented that 25.7% of individuals with T1DM were classified as obese (21), while a study in a North American study, reported a prevalence of 22.7%. These findings suggest that individuals with T1DM are at a similar risk of obesity as the general population (22).

In a cohort from Colorado, 16% of adolescents diagnosed with type 1 diabetes presented with a BMI exceeding the 85th percentile for their age at the time of diagnosis (23). Similarly, among 115 Spanish individuals with type 1 diabetes undergoing intensive therapy, approximately 30% were classified as overweight, while 20% were categorized as obese. The average age of these individuals was 12 years, and the mean duration of diabetes was 5 years (24).

Our study showed statistically significant differences ($p < 0.001$, highly significant) between the two groups in terms of age and duration of diabetes. Group I patients are considerably older, with a mean age of 60.1 ± 6.89 years, compared to Group II patients who have a mean age of 13.4 ± 2.36 years. Additionally, Group I patients have had diabetes for a longer period, with a mean duration of 12.1 ± 5.58 years, while Group II patients have a mean diabetes duration of 4.42 ± 2.11 years.

A study reported that individuals with DD were older and had longer duration of diabetes compared to those without DD.

In our study, HbA1c levels were significantly higher in DD patients compared to typical DM patients in both groups (Group I: 9.05% vs 8.09%, $p < 0.001$; Group II: 10.7% vs 8.04%, $p < 0.001$). This aligns with studies reported poorer glycemic control in DD patients. This highlights the challenges in managing DD and the need for tailored treatment approaches (2, 18). A study reported that individuals with DD had higher HbA1c compared to those without DD (21).

In our study, in Group I, DD patients had significantly lower HOMA-IR compared to typical type 2 DM patients (2.05 vs 6.49, $p < 0.001$).

This differs from findings of a study (3) reported higher insulin resistance in DD patients. This unexpected result warrants further investigation and might be specific to our study population.

In our study, in Group II, DD patients had significantly higher fasting insulin levels compared to typical type 1 DM patients

(43.4 vs 3.79 $\mu\text{IU/ml}$, $p < 0.001$), indicating higher insulin resistance.

This is consistent with the findings of a study described increased insulin resistance as a key feature of DD in type 1 DM patients (2, 17).

A study conducted in Xinjiang, China, reported that the glycaemic control rate among patients with late-onset T2D was 23.1%, while for those with early-onset T2D, the rate was considerably lower at 14.2%. Furthermore, the lipid control rates for both groups were found to be below 10% (25).

In our study, in Group I, there was no significant difference in insulin use between DD and typical type 2 DM patients. However, fewer DD patients were on oral hypoglycaemic drugs (72.9% vs 100%, $p < 0.001$). This suggests that management strategies for DD in type 2 DM might need to be different from those for typical type 2 DM, as highlighted by (26)

A study (27) conducted an examination of 1,337 patients, revealing that an increased risk of cardiovascular diseases correlates with an estimated glucose disposal rate, which serves as a marker of insulin resistance. Consequently, individuals with double diabetes required higher insulin doses compared to those without the condition

Conclusion

Our study demonstrated a notable prevalence of DD among both type 1 and type 2 diabetes patients, with a higher occurrence in type 1 diabetes (25.8%) compared to type 2 (13.6%). DD patients showed distinct clinical and metabolic profiles, with significant differences in age,

BMI, waist circumference, compared to typical diabetes patients in both groups. Importantly, type 1 diabetes patients with DD exhibited higher insulin resistance, as evidenced by elevated fasting insulin levels, while type 2 diabetes DD patients had a lower HOMA-IR and were less likely to use oral hypoglycemic drugs. The findings underscore the complexity of managing DD and emphasize the need for tailored therapeutic approaches, especially in populations with diverse diabetes phenotypes.

References

1. Mottalib A, Kasetty M, Mar JY, Elseaidy T, Ashrafzadeh S, Hamdy O. Weight Management in Patients with Type 1 Diabetes and Obesity. *Curr Diab Rep*. 2017;17:92.
2. Pozzilli P, Guglielmi C, Caprio S, Buzzetti R. Obesity, autoimmunity, and double diabetes in youth. *Diabetes Care*. 2011;34 Suppl 2:S166-70.
3. Merger SR, Kerner W, Stadler M, Zeyfang A, Jehle P, Müller-Korbsch M, et al. Prevalence and comorbidities of double diabetes. *Diabetes Res Clin Pract*. 2016;119:48-56.
4. Mishra BK, Shukla P, Aslam M, Siddiqui AA, Madhu SV. Prevalence of double diabetes in youth onset diabetes patients from east Delhi and neighboring NCR region. *Diabetes Metab Syndr*. 2018;12:839-42.
5. Braham R, Alzaid A, Robert AA, Mujammami M, Ahmad RA, Zitouni M, et al. Double diabetes in Saudi Arabia: A new entity or an underestimated condition. *World J Diabetes*. 2016;7:621-6.
6. Pozzilli P, Buzzetti R. A new expression of diabetes: double diabetes. *Trends Endocrinol Metab*. 2007;18:52-7.
7. Daniel WW, Cross CL. *Biostatistics: a foundation for analysis in the health sciences*; Wiley; 2018.
8. Ahmed AY, Sayed AM. The development of reference values for waist circumference, waist hip and waist height ratios in Egyptian adolescents. 2016.
9. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009;120:1640-5.
10. El Shafie AM, El-Gendy FM, Allahony DM, Omar ZA, Samir MA, El-Bazzar AN, et al. Establishment of Z Score Reference of Growth Parameters for Egyptian School Children and Adolescents Aged From 5 to 19 Years: A Cross Sectional Study. *Front Pediatr*. 2020;8:368.
11. N SK, Subhakumari KN. Role of anti-GAD, anti-IA2 antibodies and C-peptide in differentiating latent autoimmune diabetes in adults from type 2 diabetes mellitus. *International Journal of Diabetes in Developing Countries*. 2016;36:313-9.
12. Al-Rubeaan K. National surveillance for type 1, type 2 diabetes and prediabetes among children and adolescents: a population-based study (SAUDI-DM). *J Epidemiol Community Health*. 2015;69:1045-51.
13. Luk AOY, Lau ESH, Lim C, Kong APS, Chow E, Ma RCW, et al. Diabetes-Related Complications and Mortality in Patients With Young-Onset Latent Autoimmune Diabetes: A 14-Year Analysis of the Prospective Hong Kong Diabetes Register. *Diabetes Care*. 2019;42:1042-50.
14. Gutch M, Kumar S, Razi SM, Gupta KK, Gupta A. Assessment of insulin sensitivity/resistance. *Indian J Endocrinol Metab*. 2015;19:160-4.
15. Zhu Y, Zheng H, Zou Z, Jing J, Ma Y, Wang H, et al. Metabolic Syndrome and Related Factors in Chinese Children and Adolescents: Analysis from a Chinese National Study. *J Atheroscler Thromb*. 2020;27:534-44.
16. Organization WH. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. 2006. World Health Organization: Geneva, Switzerland. 2020.
17. Wilkin TJ. The accelerator hypothesis: weight gain as the missing link between Type I and Type II diabetes. *Diabetologia*. 2001;44:914-

- 22.
18. Tulloch-Reid MK, Boyne MS, Smikle MF, Choo-Kang EG, Parkes RH, Wright-Pascoe RA, et al. Clinical and laboratory features of youth onset type 2 diabetes in Jamaica. *West Indian Med J.* 2010;59:131-8.
19. Erbey JR, Kuller LH, Becker DJ, Orchard TJ. The association between a family history of type 2 diabetes and coronary artery disease in a type 1 diabetes population. *Diabetes Care.* 1998;21:610-4.
20. Hawa MI, Kolb H, Schloot N, Beyan H, Paschou SA, Buzzetti R, et al. Adult-onset autoimmune diabetes in Europe is prevalent with a broad clinical phenotype: Action LADA 7. *Diabetes Care.* 2013;36:908-13.
21. Cantley NW, Lonnen K, Kyrou I, Tahrani AA, Kahal H. The association between overweight/obesity and double diabetes in adults with type 1 diabetes; a cross-sectional study. *BMC Endocr Disord.* 2021;21:187.
22. Conway B, Miller RG, Costacou T, Fried L, Kelsey S, Evans RW, et al. Temporal patterns in overweight and obesity in Type 1 diabetes. *Diabet Med.* 2010;27:398-404.
23. Hummel K, McFann KK, Realsen J, Messer LH, Klingensmith GJ, Chase HP. The increasing onset of type 1 diabetes in children. *J Pediatr.* 2012;161:652-7.e1.
24. Palomo Atance E, Giralt Muiña P, Ballester Herrera MJ, Ruiz Cano R, León Martín A, Giralt Muiña J. [Prevalence of obesity and cardiovascular risk factors in a group of paediatric patients with type 1 diabetes]. *An Pediatr (Barc).* 2013;78:382-8.
25. Zhang M, Mao J, Tuerdi A, Zeng X, Quan L, Xiao S, et al. The Constellation of Macrovascular Risk Factors in Early Onset T2DM: A Cross-Sectional Study in Xinjiang Province, China. *J Diabetes Res.* 2018;2018:3089317.
26. Tuomi T, Santoro N, Caprio S, Cai M, Weng J, Groop L. The many faces of diabetes: a disease with increasing heterogeneity. *Lancet.* 2014;383:1084-94.
27. Kilpatrick ES, Rigby AS, Atkin SL. Insulin resistance, the metabolic syndrome, and complication risk in type 1 diabetes: "double diabetes" in the Diabetes Control and Complications Trial. *Diabetes Care.* 2007;30:707-12.

To cite this article: Amina M. Ahmed, Mohamed S. Saleh, Ayman M. El Badawy, Amira M. Elsayed, Walaa M. Ibrahim. prevalence of double diabetes in Benha city, Egypt hospital based cross sectional study. *BMFJ* 2025;42(4):674-686.