Section: Medicine

Original Research Article

STUDY OF THE CLINICAL, BIOCHEMICAL, AND ASSOCIATED COMPLICATIONS AMONG EARLY- AND LATE-ONSET TYPE 2 DIABETES MELLITUS IN NORTH INDIAN POPULATION

Khwaja Saifullah Zafar[1], Md Maaz Uddin[2], Ruhi Khan[3], Reda Alam[4]

[1]Professor, Department of Medicine, Jawaharlal Nehru Medical College, Aligarh Muslim University, India
[2]Junior Resident, Department of Medicine, Jawaharlal Nehru Medical College, Aligarh Muslim University, India
[3]Assistant Professor, Department of Medicine, Jawaharlal Nehru Medical College, Aligarh Muslim University, India
[4]Junior Resident, Department of Radiodiagnosis, Jawaharlal Nehru Medical College, Aligarh Muslim University, India

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Corresponding Author:
Dr. Md Maaz Uddin,
Email: maaz.md100@gmail.com

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a chronic disorder characterized by insulin resistance, β-cell dysfunction, and persistent hyperglycemia that leads to micro- and macrovascular complications. Formerly considered typical of middle age, T2DM is now increasingly diagnosed in younger adults. Early-onset T2DM (<40 years) often shows more aggressive metabolic derangement and a higher lifetime risk of complications, however Indian data directly comparing early- and late-onset disease remain limited. **Materials and Methods:** This hospital-based cross-sectional study was conducted at J.N. Medical College, Aligarh after ethics approval. 280 confirmed T2DM patients were enrolled and classified as early-onset or late-onset Clinical and anthropometric data were recorded, and fasting blood glucose, HbA1c, lipid profile, renal parameters, and inflammatory cytokines were measured. Microvascular complications were assessed. Statistical analysis used t-tests, chi-square tests, and multivariable regression. **Result:** Early-onset patients had significantly higher BMI (30.4 ± 3.7 kg/m² vs 26.7 ± 3.1; p<0.01), FBG (184 ± 45 mg/dL vs 158 ± 39; p=0.003), and HbA1c (9.2 ± 1.3 % vs 7.8 ± 1.1 %; p<0.001). Dyslipidemia was more severe, with higher triglycerides and LDL-C and lower HDL-C. Despite shorter disease duration, early-onset T2DM showed more neuropathy (42 % vs 28 %; p=0.03) and microalbuminuria (38 % vs 24 %; p=0.04). Insulin use was greater (28 % vs 14 %; p=0.04). **Conclusion:** Early-onset T2DM in this North Indian cohort demonstrates more severe metabolic disturbance, poorer glycemic and lipid profiles, and a greater burden of microvascular complication rates than late-onset disease. Early, intensive screening and age-specific management are essential to reduce long-term morbidity and mortality.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic progressive disease characterised by insulin resistance, beta cell dysfunction, and persistent hyperglycemia, leading to microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (cardio-, cerebro-, and peripheral vascular) complications. Over the past two decades, its epidemiology has shifted towards younger populations , including adolescents.[1] Urbanization, sedentary lifestyle, and genetic predisposition have driven a rise in early onset T2DM(<40 years), especially in south Asian countries such as India. [2]

Compared to late-onset diabetes, early-onset T2DM usually exhibits more aggressive metabolic derangement, poorer glycaemic control, and faster progression of insulin resistance and β-cell failure. These factors lead to increased lifetime morbidity and mortality as well as earlier and more severe micro- and macrovascular complications. The illness has significant psychological and financial consequences since it strikes during a person's prime working years.However, there is still a dearth of information from India comparing the clinical, biochemical, and inflammatory characteristics of early- and late-onset type 2 diabetes, underscoring the necessity of country-specific studies to inform treatment.[3]

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Objective of the Study

To compare the clinical and biochemical profile between early-onset and late-onset T2DM patients and highlight the the need for age-specific diagnostic and therapeutic strategies.

MATERIALS AND METHODS

Study Design and Setting

This observational cross-sectional study was conducted in the Department of Medicine and the Rajiv Gandhi Centre for Diabetes and Endocrinology, J.N. Medical College, AMU, Aligarh, over a 18-month period (April 2023 – May 2025), after obtaining approval from the Institutional Ethics Committee(IEC JNMC 1053) .Patients with type 2 diabetes mellitus (T2DM) attending the outpatient clinic were recruited after obtaining written informed consent.

Participants were classified into two groups based on age at diagnosis which were Early-onset T2DM; diagnosed before 40 years and Late-onset T2DM; diagnosed at or after 40 years Sample Size was calculated Using the formula 4 pq / d^2 (p = prevalence; 95% confidence limit), the required sample size is 280 patients. A convenience sampling technique was applied.

Diagnostic Criteria

As per American Diabetes Association (ADA) 2023 guidelines:

Fasting plasma glucose (FPG) ≥ 126 mg/dL (7 mmol/L) after ≥ 8 h fasting, or

2-hour plasma glucose (2hPG) ≥ 200 mg/dL (11.1 mmol/L) during a WHO-standard oral glucose tolerance test (75 g glucose), or

HbA1c ≥ 6.5% (48 mmol/mol).

Results were confirmed on repeat testing if hyperglycemia was not unequivocal.

Clinical and Anthropometric Assessment

A detailed history and physical examination were performed. Measurements were include-Height measured with stadiometer, recorded to nearest 0.1 cm. Weight measured with digital scale, minimal clothing, recorded in kilograms Body Mass Index (BMI),calculated as weight (kg) / height $(m)^2$. Waist circumference measured at midpoint between lower rib margin and iliac crest. Neck circumference measured at mid-neck level in upright position. Blood pressure, two readings 5 min apart, averaged

Laboratory and Other Investigations

All participants underwent FPG, post-prandial glucose (PPG), HbA1c, Blood urea, serum creatinine, estimated glomerular filtration rate (eGFR), Lipid profile through Total cholesterol, HDL-C, LDL-C, triglycerides. Renal Function Tests, Serum urea, creatinine, estimated GFR and Liver Function Tests like ALT, AST, ALP, Urinary albumin-to-creatinine ratio (UACR), Electrocardiogram (ECG), Fundus examination for proliferative diabetic retinopathy(PDR) and non proliferative diabetic retinopathy(NPDR)

Results were recorded in a structured proforma for analysis.

Inclusion criteria was Confirmed diagnosis of T2DM as per ADA 2022 guidelines and Age ≥18 years.

Exclusion criteria were Type 1 diabetes mellitus, gestational diabetes, or secondary diabetes. Presence of autoimmune or infectious diseases, cancer, or chronic inflammatory conditions.

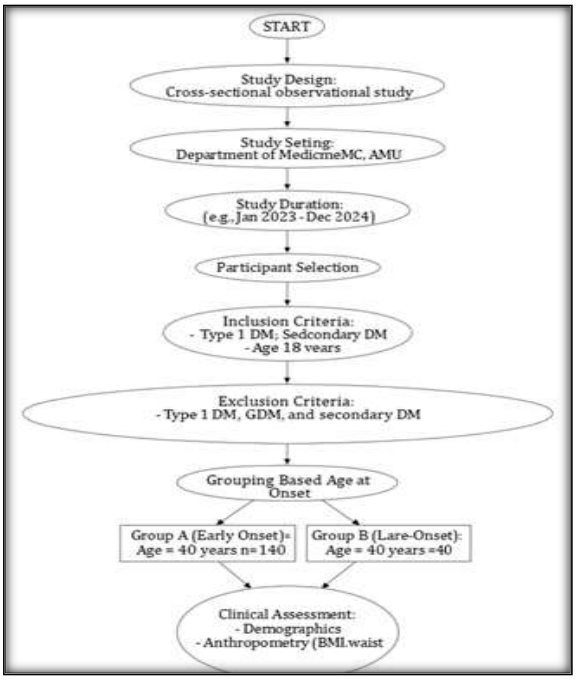

Figure 1: A flowchart showing a cross-sectional diabetes study design: recruitment, inclusion/exclusion criteria, sample size, group allocation, and clinical assessments.

Statistical Analysis

Data were analyzed using SPSS software. Categorical variables were compared using chi-square tests, while continuous variables were compared using unpaired t-tests or Mann-Whitney U tests, as appropriate. A p-value <0.05 was considered statistically significant.

RESULTS

The present study involved a total of 280 patients with type 2 diabetes mellitus (T2DM), divided into two groups based on the age of onset. Group A (Early-Onset T2DM) consist of patients with age at diagnosis < 40 years (n = 140) and Group B (Late-Onset T2DM) with patients age at diagnosis >40 years (n = 140)

A comparative evaluation was conducted between the two groups across multiple domains: demographic variables, clinical parameters, biochemical profiles, inflammatory cytokines, and microvascular complication rates.

Demographic and Anthropometric Characteristics

Participants in Group A were 33.2 ± 4.1 years old on average, whereas those in Group B were 54.7 ± 5.8

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years old. With a male-to-female ratio of 1.5:1 in Group A and 1.3:1 in Group B, males were somewhat more prevalent in both groups. But ($p = 0.18$), this difference was not statistically significant.

There was a significant difference in the body mass index (BMI), with the average BMI of early-onset diabetics being higher (30.4 ± 3.7 kg/m²) than that of the late-onset group (26.7 ± 3.1 kg/m²), $p < 0.01$. Similarly, early-onset individuals had greater waist circumferences, which is indicative of central adiposity, which is known to contribute to insulin resistance.

These findings support the link between central obesity/metabolic syndrome and early-onset T2DM.

Table 1: Comparison of mean age, sex and BMI in Early vs Late onset T2DM groups.

Parameter	Group A (Early-onset T2DM)	Group B (Late-onset T2DM)	p-value	Statistical Significance
Mean Age (years)	33.2 ± 4.1	54.7 ± 5.8	—	—
Sex (Male : Female)	1.5 : 1	1.3 : 1	0.18	Not significant
Body Mass Index (kg/m²)	30.4 ± 3.7	26.7 ± 3.1	<0.01	Significant

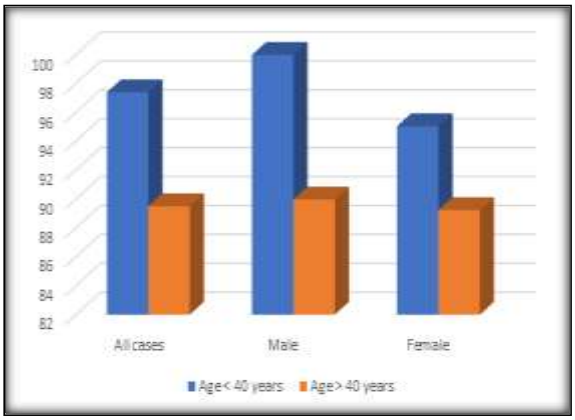

Figure 2: Comparison of mean waist circumference according to age of patient. Glycemic Control and Glucose Parameters

The fasting blood glucose (FBG) levels of Group A were significantly higher than those of Group B (184 ± 45 mg/dL vs. 158 ± 39 mg/dL; $p = 0.003$). Furthermore, glycated haemoglobin (HbA1c), a measure of chronic glycaemic control, was higher in the early-onset group ($9.2 \pm 1.3\%$) than in the late-onset group ($7.8 \pm 1.1\%$), and the difference was highly statistically significant ($p < 0.001$).

Even though their disease duration is shorter, younger people have poorer glycaemic control, as this data highlights. It may indicate accelerated β-cell exhaustion and/or increased insulin resistance in people with early-onset diabetes. Moreover, elevated HbA1c values within this age range suggest either a postponed diagnosis or insufficient adherence to treatment.

Table 2. Comparison of HbA1c in Early vs Late onset T2DM groups.

HbA1c	Age < 40 yearsMean ± SD	Age > 40 yearsMean ± SD	p-value
Baseline	10.62 ± 1.84	9.55 ± 1.44	<0.001
p-value (within group)	<0.001	<0.001	—

Lipid Profile: Early-onset diabetics exhibited noticeably greater atherogenic lipid patterns, according to a thorough examination of lipid profiles: Triglycerides and LDL cholesterol were considerably higher in the early-onset group, while HDL cholesterol was lower. These abnormalities increase the risk of cardiovascular disease in this younger cohort and are consistent with dyslipidemia linked to insulin resistance.

Table 3: Comparison of Lipid parameters in Early vs Late onset T2DM groups.

Lipid Parameter	Group A (Early-Onset)	Group B (Late-Onset)	p-value
Triglycerides (mg/dL)	206 ± 38	172 ± 34	0.002
HDL-C (mg/dL)	34 ± 6	42 ± 7	<0.001
LDL-C (mg/dL)	118 ± 25	102 ± 22	0.006
Total Cholesterol	204 ± 32	192 ± 28	0.04

Renal and Hepatic Function: There were no statistically significant variations between the two groups' levels of liver enzymes or serum creatinine. Despite similar creatinine levels, Group A had a higher prevalence of microalbuminuria, one of the early indicators of diabetic nephropathy (38% vs. 24%; $p = 0.04$).

This reinforces the notion that early-onset patients have a faster trajectory toward complications.

Figure 3: Comparison of hematological parameters according to the age of the patient

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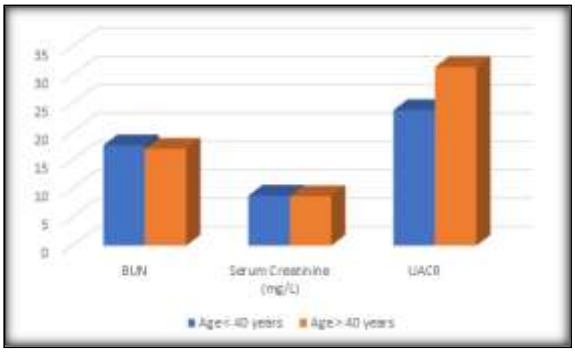

Figure 4: Comparison of renal parameters according to the age of the patient

Microvascular Complications: Despite a shorter disease duration, early-onset patients had a higher prevalence of microvascular complications:

Table 4. Comparison of Complication rate in Early vs Late onset T2DM groups.

Complication	Group A (Early-Onset)	Group B (Late-Onset)	p-value
Retinopathy	34%	26%	0.21
Neuropathy	42%	28%	0.03
Nephropathy	38%	24%	0.04

Patients with early onset are most likely to have diabetic neuropathy. Many reported experiencing numbness, tingling, and burning in their feet. One out of three early-onset patients had retinopathy discovered by fundoscopy; however, the difference was not statistically significant. Microalbuminuria: Even when serum creatinine is normal, this condition, which is more common in patients with early onset, suggests early glomerular impairment. These findings imply that the early-onset group experienced a greater burden of illness and a faster progression of complications, most likely as a result of a combination of metabolic dysregulation and poor glycaemic control.

Correlation Analysis: Pearson correlation coefficients showed: These relationships highlight the link between systemic inflammation, glycemic control, obesity, and lipid derangements in T2DM pathogenesis.

Table 5: Regression analysis among outcome parameters in Early vs Late onset T2DM groups.

Outcome	Model Type	β / OR	p-value	Age Significant Predictor?	95% CI
HbA1c (Follow-up)	Linear Regression	–1.36	<0.001	Yes ✓	(–1.81 to –0.91)
UACR	Linear Regression	+7.57	<0.001	Yes ✓	(+5.12 to +10.02)
Diabetic Foot (Yes/No)	Logistic Regression	4.17	0.073	No ✗	(0.85 to 20.4)
Grade ≥1 NPDR (vs Normal)	Logistic Regression	1.66	0.08	No ✗	(0.94 to 3.15)
Deranged Triglycerides	Logistic Regression	3.36	<0.001	Yes ✓	(1.89 to 5.98)

Medication and Insulin Use: It is interesting to note that, despite having shorter duration of the disease, early-onset diabetics used insulin more frequently (28%) than late-onset patients (14%; p = 0.04). This could be a result of earlier β-cell failure that necessitates insulin therapy and a more aggressive disease phenotypes.

The two groups use of statins, sulfonylureas, and metformin was similar.

An overview of the main conclusions: Individuals with early onset Diabetes had worse dyslipidaemia, a higher incidence of microvascular complications, and poorer glycaemic control. They also had significantly higher BMI, FBG, HbA1c, triglycerides, and inflammatory cytokines. More patients with early onset needed insulin therapy, suggesting that their condition was more severe and needed more intensive care. Patients with early-onset type 2 diabetes had worse dyslipidaemia, a higher incidence of microvascular complications, and poorer glycaemic control. They also had significantly higher BMI, FBG, HbA1c, triglycerides, and inflammatory cytokines. More patients with early onset needed insulin therapy, suggesting that their condition was more severe and needed more intensive care.

DISCUSSION

The goal of the current study was to examine the clinical, biochemical, and inflammatory cytokine profiles of individuals with Type 2 Diabetes Mellitus (T2DM) who developed the disease early (less than 40 years of age) and those who developed it later (more than 40 years of age). Based on the age of onset, this comparative analysis highlights significant differences in metabolic behaviour, illness load, and inflammatory condition. In addition to providing

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particular insights into the diabetic community in India, our findings support earlier research.

1. Anthropometric and Demographic Findings

A significant portion of individuals with early-onset T2DM in our cohort were overweight or obese, with a notably higher BMI and waist circumference than their late-onset counterparts.

This supports the global finding that insulin resistance and the early onset of type 2 diabetes are significantly influenced by obesity, especially visceral adiposity.

Several studies, including those by Lascar et al. and Twig et al., have shown a strong association between obesity in adolescence or early adulthood and the onset of type 2 diabetes before the age of 40. Our findings support this connection, showing that a major contributing factor to the onset of disease in young adults is central adiposity-driven metabolic syndrome.[4] The late-onset group, on the other hand, had a far lower average BMI even though they were also overweight. This implies that age-related β-cell function decline and increasing insulin resistance might be more important factors in late-onset type 2 diabetes than obesity alone.[5]

2. β-cell function and glucose regulation: Despite a shorter duration of the disease, our study revealed that the early-onset type 2 diabetes group had significantly worse glycaemic control, with significantly higher fasting blood glucose and HbA1c levels. Due to faster β-cell exhaustion and an earlier need for insulin, nearly 28% of patients with early onset were already on insulin therapy, compared to 14% of patients with late onset. This lends credence to the idea that β-cell decline is accelerated and the course of early-onset diabetes is more aggressive.

These findings are consistent with previous reports. According to Hatunic et al. and Mingqi Wang et al., younger-onset patients had higher HbA1c levels at diagnosis and during follow-up, and their insulin dependence progressed more quickly. Delays in diagnosis, stress in lifestyle, and severe metabolic dysfunction in younger people are all mentioned as contributing factors. Collectively, these findings emphasize the need for early, intensive glycemic management and patient education in early-onset type 2 diabetes.[6]

3. Risk for Cardiovascular Disease and Lipid Profile: Additionally, our results demonstrated that the early-onset group's lipid profiles were significantly worse, with higher levels of triglycerides and LDL-C and lower levels of HDL-C. These atherogenic patterns, which are indicative of insulin-resistant states, increase the risk of prematurely developing cardiovascular disease (CVD).

Early in the course of the disease, prolonged exposure to dyslipidaemia and hyperglycemia exacerbates vascular inflammation and endothelial damage. Young diabetics often have more dysregulated metabolisms. Since early-onset diabetics are likely to have the disease for several decades, they are at a significant lifetime risk for peripheral vascular disease, myocardial infarction, and stroke. This is really concerning.

The findings of Can Hou et al. and Gunathilake et al., who stressed the importance of early and aggressive cardiovascular risk management in young T2DM patients, support this. Even before overt cardiovascular events occur, our data supports the need for early statin use and lifestyle changes in this population.[7]

5. Complications of the Microvascular System

Despite having a shorter disease duration, early-onset diabetics in our study had a higher prevalence of microvascular sequelae, including retinopathy, nephropathy, and neuropathy, than late-onset patients. This study highlights the aggressive nature of early-onset diabetes, which is very concerning. Peripheral neuropathy was the most common side effect, occurring in 28% of group A and 42% of group BThese processes include cytokine-mediated nerve damage, ischaemia caused by microvascular dysfunction, and direct neuronal glucose toxicity. This is consistent with research demonstrating that diabetic neuropathy, particularly in patients with inadequate management, can develop early in the course of the disease.

Nephropathy: Microalbuminuria, a surrogate marker for early diabetic nephropathy, was substantially more common in patients with early onset. Retinopathy: The prevalence of diabetic retinopathy was higher in the early-onset group, albeit not statistically significant. Because of the extended duration of disease that lies ahead, early detection and retinal screening become extremely important in this group.

Severe outcomes are in line with the findings of the UKPDS and ACCORD trials, which demonstrated the importance of rigorous glycaemic control in preventing or delaying serious issues. However, because younger patients have a higher inflammatory load and metabolic dysfunction, more potent medication may be required to attain and sustain control.[8]

6. Therapeutic Consequences and Insulin Utilization: One important practical finding was that a significantly higher proportion of group b individuals were already taking insulin. This may be due to accelerated β-cell failure, more severe hyperglycemia at diagnosis, or the aggressive course of the disease leading to therapeutic resistance to oral medications. Even though insulin is an effective blood sugar regulator, its early use may indicate a disease that is progressing quickly.

This raises the question of whether anti-inflammatory medications or other complementary therapies could be tried early in the treatment paradigm for this group.

Metformin, the first-line drug, has a mild anti-inflammatory effect. However, newer drugs may offer additional cardiovascular and renal protection and may be considered earlier in younger patients who show signs of poor control and systemic inflammation.[9]

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7. Social Consequences and Public Health

Early onset of type 2 diabetes has major socioeconomic consequences, especially in countries with high disease burdens like India. Type 2 diabetes in people in their 20s or 30s increases the risk of complications, medical costs, lost productivity, and a decades-long decline in quality of life.

Additionally, younger patients may exhibit poorer treatment adherence due to psychosocial stress, a lack of symptoms, or denial. This highlights the importance of regular screenings, systematic diabetes control programs, and targeted health education for youth. Our findings suggest that early-onset type 2 diabetes is more aggressive in its physiological, metabolic, and social manifestations, rather than merely being a "younger" form of the disease.[10]

Why This Research Is Superior

New Indian-specific Evidence of Western or East Asian cohorts provide the majority of published data on early-onset type 2 diabetes. Comprehensive Multidimensional Assessment Compared to traditional studies that only look at lipids or glycemia, simultaneous assessment of clinical, biochemical, and inflammatory cytokines (TNF-α, IL-6) provides a more comprehensive picture of the disease. The observed higher complication rates in patients with early onset are more biologically plausible thanks to this multidomain approach. The Age-stratified Comparative Design minimises heterogeneity and permits strong internal validity for age-related differences by directly comparing groups (less than 40 years vs. more than 40 years at diagnosis) using the same inclusion/exclusion criteria. The findings (e.g., higher HbA1c, dyslipidemia, microalbuminuria in young patients) immediately inform screening intervals, treatment intensification, and earlier statin/insulin initiation for this demographic.The findings of this study have several important implications for clinical care and public health. Guideline refinement is a priority: age-specific diagnostic and therapeutic algorithms may be needed, including lower HbA1c targets, earlier initiation of statins or GLP-1/SGLT2 therapy, and more intensive lifestyle counselling tailored for young adults. From a public health perspective, the evidence of earlier and more aggressive complications highlights the importance of school- and workplace-based screening programs and preventive education in high-risk urban Indian settings. The data also provide a basis for longitudinal and interventional research, supporting the development of cohort follow-up studies and clinical trials that evaluate early anti-inflammatory or β-cell–preserving therapies. Furthermore, the health-economics impact cannot be overlooked: earlier onset of complications predicts decades of healthcare costs and productivity loss, information that can guide national policy and resource allocation.[11]

At the same time, several key confounding factors must be considered when interpreting these results. Early-onset patients may have experienced a longer undetected hyperglycemic period, potentially exaggerating the severity of their disease at diagnosis. Lifestyle and socioeconomic variables—such as diet, physical activity, psychological stress, and access to healthcare—can differ between younger and older adults and influence outcomes. Medication adherence and previous treatment history also affect HbA1c, lipid profiles, and complication rates. A strong family history or genetic predisposition to T2DM and dyslipidemia may further confound associations if not fully adjusted for. Finally, subclinical infections or other inflammatory comorbidities could elevate cytokine levels independent of diabetes itself. Recognizing and adjusting for these factors is essential to accurately interpret the observed differences between early- and late-onset T2DM and to design effective future interventions.[12]

Limitations

Although our research provides insightful information, some limitations must be noted. It is a Cross-sectional Design,this makes it impossible to prove temporal or causal relationships. Single-Center Data is used, not all populations may be able to use the results. Lack of Longitudinal Follow-Up, the progression of long-term complications was not evaluated.

CONCLUSION

In conclusion, the metabolic profile, inflammatory burden, and complication risk of early-onset type 2 diabetes are significantly different from those of late-onset illness. In order to improve outcomes and lower the long-term disease burden in young adults with type 2 diabetes, a change in clinical approach is required. This includes early screening for complications, intensive glycemic and lipid control, anti-inflammatory measures, and rapid diagnosis. Proactive early management, encompassing medication and lifestyle modifications. Age-based care models that are tailored to enhance long-term results.

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