

## A Comparative Study of Anthropometric and Glycemic Differences in Healthy Adults with and without Family History of Type 2 DM

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### ABSTRACT

**Background:** Family history is a recognised determinant of type 2 diabetes mellitus (T2DM), yet information on the early metabolic profile of healthy young adults who have an affected relative is limited, particularly in North India. This study compared anthropometric indices, glycaemic markers and insulin resistance between healthy adults aged 18 to 45 years with and without a family history of T2DM. **Methods:** This cross-sectional observational study was conducted in the Department of Physiology of S.N. Medical College, Agra, in collaboration with the Departments of Medicine and Biochemistry. Participants were assigned to a case group with a family history of T2DM in relatives and a control group without such history. After purposive sampling, 49 participants were analysed in each group. Body weight, height, body mass index (BMI), waist circumference, hip circumference and waist to hip ratio were measured. Fasting plasma glucose, fasting plasma insulin and glycated haemoglobin (HbA1c) were estimated, and insulin resistance was calculated using the homeostasis model assessment of insulin resistance (HOMA IR). Continuous variables were compared with the unpaired Student t test and categorical variables with the chi square test. A p value below 0.05 was considered statistically significant. **Results:** The two groups were comparable for age (case  $28.22 \pm 7.49$  years, control  $27.18 \pm 3.99$  years, p 0.39). The case group had higher body weight ( $62.57 \pm 10.39$  kg versus  $58.27 \pm 10.38$  kg, p 0.03), BMI ( $24.35 \pm 5.01$  kg/m<sup>2</sup> versus  $21.96 \pm 4.81$  kg/m<sup>2</sup>, p 0.02), waist circumference ( $84.62 \pm 11.94$  cm versus  $79.76 \pm 10.65$  cm, p 0.03) and hip circumference ( $92.83 \pm 12.47$  cm versus  $87.39 \pm 13.80$  cm, p 0.04). Height and waist to hip ratio did not differ significantly. Fasting plasma glucose ( $88.69 \pm 9.15$  mg/dL versus  $80.78 \pm 5.50$  mg/dL), fasting plasma insulin ( $10.25 \pm 3.58$   $\mu$ IU/mL versus  $7.10 \pm 2.53$   $\mu$ IU/mL), HOMA IR ( $2.26 \pm 0.90$  versus  $1.43 \pm 0.56$ ) and HbA1c ( $5.52 \pm 0.35\%$  versus  $5.20 \pm 0.43\%$ ) were all significantly higher in the case group (p below 0.001 for each). Increased thirst, increased hunger and fatigue were reported more frequently in the case group. **Conclusions:** Healthy young adults with a family history of T2DM showed greater generalised and central adiposity, higher fasting glucose, higher HbA1c and higher insulin resistance than comparable adults without such a history, although none had a diagnosis of diabetes. These findings support the use of simple anthropometric and glycaemic measurements, together with a structured family history, for early risk stratification in young adults.

**Keywords:** Type 2 Diabetes Mellitus, Family History, Body Mass Index, Waist Circumference, Fasting Glucose, Glycated Haemoglobin, Insulin Resistance, HOMA IR.

### INTRODUCTION

Type 2 diabetes mellitus is a heterogeneous and polygenic disorder shaped by genetic susceptibility and environmental exposures, including diet, obesity, physical inactivity, stress and ageing. Its development is

usually gradual. Insulin resistance in peripheral tissues initially stimulates compensatory hyperinsulinaemia, but over time pancreatic beta cells can no longer sustain this compensation, and relative insulin deficiency leads to progressive hyperglycaemia. Chronic hyperglycaemia is

in turn associated with neuropathy, nephropathy, retinopathy and cardiovascular disease, which together account for much of the morbidity and mortality of the condition (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 2003). The International Diabetes Federation Diabetes Atlas (11th edition, 2025) estimated that 11.1 percent of adults aged 20 to 79 years, approximately 588.7 million people, were living with diabetes worldwide, and projected that this number would reach 852.5 million by 2050 (International Diabetes Federation, 2025). India is among the countries with the largest number of adults living with diabetes, and national reviews have documented a steady rise in prevalence (Kumar et al., 2024). Because a substantial share of the disease burden is concentrated in the Southeast Asia region, the identification of people at high risk before overt disease appears is a practical public health priority. Family history is one of the most consistent markers of that risk. A cross-sectional study of 5,658 adults in Changchun, northeastern China, reported a T2DM prevalence of 8.4 percent and found that a family history of T2DM in first degree relatives was independently associated with hyperglycaemia and with an increased risk of the disease (He et al., 2024). Asian Indians show strong familial aggregation of diabetes, and young adults of this population with an affected family member have been found to carry higher anthropometric and metabolic burdens than their peers without such a history (Rane and Gadkari, 2012). The inherited component of the disease therefore has measurable consequences well before the onset of hyperglycaemia, and these early consequences are the appropriate target for prevention. Anthropometric measurements are a simple means of capturing the adiposity that accompanies insulin resistance. Body mass index is widely used, but it does not distinguish lean from fat mass and it may misclassify individuals whose weight reflects muscle rather than fat (Nevill et al., 2006). Indices of central adiposity, including waist circumference, waist to hip ratio and waist to height ratio, are more closely linked to visceral fat, and several cohort analyses have reported that waist circumference or waist to height ratio predicts incident diabetes at least as well as BMI (Hou et al., 2019, Jayedi et al., 2022). Waist circumference is also inexpensive to measure and easy to repeat, which makes it attractive for community screening (Lean et al., 1995). Glycated haemoglobin is an established diagnostic and monitoring test for diabetes. It reflects average glycaemia over the preceding two to three months and has been shown to correlate with insulin sensitivity even among individuals with normal glucose tolerance (Sherwani et al., 2016, Lin et al., 2014). Insulin resistance itself is commonly quantified with the homeostasis model assessment, which estimates resistance from paired fasting glucose

and fasting insulin values (Matthews et al., 1985). Although the index is a model based estimate rather than a direct measurement, it has been applied widely in clinical and epidemiological research and remains useful as a surrogate marker (Levy et al., 1998). Most published work on cardiometabolic risk has focused on people who already have diabetes. Comparatively few studies have examined the anthropometric, glycaemic and insulin related profile of healthy relatives of patients with T2DM, and the available data from North India are sparse. Because prediabetes is a potentially reversible state that is strongly influenced by lifestyle, identifying such individuals early and providing them with meaningful feedback on their health status offers an opportunity for prevention. The present study was therefore designed to assess and compare the anthropometric and cardiometabolic profile of healthy individuals aged 18 to 45 years with and without a family history of type 2 diabetes mellitus in the Agra district, Uttar Pradesh. The specific objectives were to compare anthropometric parameters, to compare fasting plasma glucose, fasting plasma insulin and HbA1c, and to compare insulin resistance as estimated by HOMA IR between the two groups. A companion report addresses the vascular parameter pulse transit time in the same participant.

## MATERIALS AND METHODS

This was a cross-sectional observational study. It was conducted in the Department of Physiology of S.N. Medical College, Agra, Uttar Pradesh, in collaboration with the Department of Biochemistry for laboratory analyses and the Department of Medicine for clinical assessment. Participants were drawn from individuals who attended the Medicine outpatient department of the institution. The study period was approximately 1.5 years. Each participant was briefed on the methodology and purpose of the study, and written informed consent was obtained in both English and Hindi. Participants were informed that they could withdraw from the study at any time without giving a reason. Eligible participants were men and women aged 18 to 45 years who were apparently healthy on clinical examination. The case group comprised individuals with a positive family history of type 2 diabetes mellitus in first degree relatives, second degree relatives or siblings. The control group comprised individuals with no family history of type 2 diabetes mellitus. Family history was recorded using a structured proforma that asked separately about the mother, the father and the siblings. Individuals were excluded if they had type 1 diabetes mellitus, hypertension, any other chronic metabolic disease, pregnancy or lactation, a history of substance abuse, any acute illness, or if they were receiving long term medication for any condition. Individuals who were

unwilling to participate were also excluded. Data were collected from 50 participants in each group initially. One participant in each group withdrew during the study, leaving 49 participants per group for analysis.

#### **Anthropometric Measurements:**

All measurements were performed in a quiet room. Participants wore light clothing and no shoes for these measurements. Body weight was measured in kilograms using a weighing machine, with the participant standing motionless at the center of the platform and recorded to the nearest 0.1 kg. Height was measured in centimetres using a stadiometer with a sliding headboard, with the participant standing erect on both feet, shoulders relaxed, legs straight and arms at the sides. BMI was calculated as body weight in kilograms divided by the square of height in metres. Classification followed the World Health Organization categories: underweight below 18.5 kg/m<sup>2</sup>, normal weight 18.5 to 24.9 kg/m<sup>2</sup>, overweight 25.0 to 29.9 kg/m<sup>2</sup> and obesity 30.0 kg/m<sup>2</sup> or more (World Health Organization, 2016). Waist circumference was measured with a non stretchable linen tape applied horizontally at the lower margin of the ribs and the top of the iliac crest, with the participant standing erect and weight evenly distributed. Participants were asked to relax and take a few deep breaths before each measurement to reduce the inward pull of the abdominal contents. Two measurements were taken. The mean was used when the two readings differed by 1 cm or less, and the measurement was repeated when they differed by more than 1 cm. The World Health Organization sex specific thresholds were used, with 94 cm for men and 80 cm for women indicating increased risk of metabolic complications, and 102 cm for men and 88 cm for women indicating substantially increased risk (World Health Organization, 2008). Hip circumference was measured at the level of the widest portion of the buttocks, with the tape parallel to the floor and the participant standing with feet close together. Two measurements were taken. Waist to hip ratio was calculated as waist circumference divided by hip circumference.

#### **Biochemical Measurements**

Fasting venous blood samples were collected after an overnight fast of 8 to 12 hours. For HbA1c, 1 to 2 mL of venous blood was collected into a potassium EDTA tube and processed as whole blood. For fasting plasma glucose and fasting plasma insulin, blood was collected into the appropriate tubes, and serum was separated by clotting and centrifugation for insulin measurement.

Samples were handled to avoid haemolysis. Glycated haemoglobin was measured by high performance liquid chromatography, which separates haemoglobin fractions on an ion exchange column according to charge and quantifies HbA1c as a percentage of total haemoglobin (Eyth et al., 2025, Medical Laboratory Notes, 2023). Fasting plasma glucose was measured in milligrams per decilitre and converted to millimoles per litre for reporting, using the hexokinase reference method. Fasting plasma insulin was measured in serum by chemiluminescent microparticle immunoassay, in which insulin in the sample binds to anti insulin antibodies on paramagnetic microparticles, and light emitted by a chemiluminescent reaction is measured in relative light units and converted to concentration by the analyser.

#### **Insulin Resistance**

Insulin resistance was estimated with the homeostasis model assessment using the formula HOMA IR equals fasting plasma glucose in millimoles per litre multiplied by fasting plasma insulin in micro international units per millilitre, divided by 22.5 (Matthews et al., 1985, Levy et al., 1998). Reference values for fasting insulin were interpreted with reference to published healthy and Indian population ranges (Shah and Puthran, 2014).

#### **Statistical Analysis**

Data were entered into Microsoft Excel and analysed with IBM SPSS Statistics version 25.0. Continuous variables are presented as mean  $\pm$  standard deviation. Differences between the case and control groups for continuous variables were examined using the unpaired Student t test. Categorical variables, including the distribution of symptoms and family history, were compared with the chi square test. Standardised mean differences were calculated from the reported means and standard deviations using the pooled standard deviation, to allow the magnitude of each difference to be judged independently of sample size. A p value below 0.05 was considered statistically significant.

## **RESULTS**

#### **Participant characteristics**

A total of 98 participants were analysed, comprising 49 in the case group and 49 in the control group. The two groups did not differ significantly in age. The mean age was  $27.18 \pm 3.99$  years in the control group and  $28.22 \pm 7.49$  years in the case group (p 0.39). The groups were described as sex matched, and the sex distribution was compared by the chi square test as stated in the protocol.

**Table 1. Family history of diabetes mellitus among participants in the case and control groups:**

| Family history          | Control group<br>(n= 49) | Case group<br>(n = 49) | p value        |
|-------------------------|--------------------------|------------------------|----------------|
| Mother with diabetes.   | 0 (0.0%)                 | 25 (51.0%)             | <0.001         |
| Father with diabetes    | 0 (0.0%)                 | 30 (61.2%)             | <0.001         |
| Siblings with diabetes. | 0 (0.0%)                 | 0 (0.0%)               | not applicable |

Among the case group, a parent had diabetes in 25 participants on the maternal side and 30 on the paternal side. No participant in either group reported a sibling with diabetes.

#### Diabetes Related Symptoms:

Symptoms were recorded as present or absent on the structured proforma. Increased thirst was reported by 16 of 49 participants in the case group (32.6 percent) compared with 7 of 49 in the control group (14.3 percent), with p 0.044. Increased hunger was reported by 11 participants in the case group (22.4 percent) compared with 2 in the control group (4.1 percent), with p 0.0068. Fatigue was reported by 17 participants in the case group (34.7 percent) compared with 5 in the control group (10.2 percent), with p 0.0079. Frequent urination was reported by 7 case participants (14.3 percent) and 4 control participants (8.2 percent), with p 0.33. Numbness in the hands or feet was reported by 5 case participants (10.2 percent) and 2 control participants (4.1 percent), with p 0.17. Slow healing wounds were reported by one case participant (2.0 percent) and no control participant, with p 0.31. Darkened patches of skin in the axillae and neck were reported by 14 case participants (28.6 percent) and 7 control participants (14.3 percent), with p 0.08. Unexplained weight loss was not reported by any participant in either group and was therefore not analysed.

**Table 2. Distribution of diabetes related symptoms in the case and control groups.**

| Symptoms                                  | Control group n (%) | Case group n (%) | p value      |
|-------------------------------------------|---------------------|------------------|--------------|
| Increased thirst                          | 7 (14.3)            | 16 (32.6)        | 0.044        |
| Increased hunger                          | 2 (4.1)             | 11 (22.4)        | 0.0068       |
| Frequent urination                        | 4 (8.2)             | 7 (14.3)         | 0.33         |
| Fatigue                                   | 5 (10.2)            | 17 (34.7)        | 0.0079       |
| Slow healing wounds                       | 0 (0.0)             | 1 (2.0)          | 0.31         |
| Numbness in hands or feet                 | 2 (4.1)             | 5 (10.2)         | 0.17         |
| Darkened skin patches in axillae and neck | 7 (14.3)            | 14 (28.6)        | 0.08         |
| Unexplained weight loss                   | 0                   | 0                | not analysed |

Percentages were calculated from a denominator of 49 in each group.

#### Anthropometric Parameters

The case group had a higher mean body weight than the control group, at  $62.57 \pm 10.39$  kg compared with  $58.27 \pm 10.38$  kg (p 0.03). Mean height did not differ significantly, at  $163.20 \pm 9.05$  cm in the case group and  $164.49 \pm 8.68$  cm in the control group (p 0.45). Mean BMI was higher in the case group at  $24.35 \pm 5.01$  kg/m<sup>2</sup> compared with  $21.96 \pm 4.81$  kg/m<sup>2</sup> in the control group (p 0.02). Waist circumference was significantly greater in the case group, at  $84.62 \pm 11.94$  cm compared with  $79.76 \pm 10.65$  cm in the control group (p 0.03). Hip circumference was also greater in the case group, at  $92.83 \pm 12.47$  cm compared with  $87.39 \pm 13.80$  cm (p 0.04). Mean waist to hip ratio was  $0.92 \pm 0.09$  in the case group and  $0.94 \pm 0.24$  in the control group, and this difference was not statistically significant (p 0.63).

**Table 3. Anthropometric parameters in the case and control groups:**

| Parameter                            | Control group mean<br>± SD | Case group mean<br>± SD | p value | Standardized<br>mean<br>difference |
|--------------------------------------|----------------------------|-------------------------|---------|------------------------------------|
| Body weight (kg)                     | 58.27 ± 10.38              | 62.57 ± 10.39           | 0.03    | 0.41                               |
| Height (cm)                          | 164.49 ± 8.68              | 163.20 ± 9.05           | 0.45    | 0.15                               |
| Body mass index (kg/m <sup>2</sup> ) | 21.96 ± 4.81               | 24.35 ± 5.01            | 0.02    | 0.49                               |
| Waist circumference (cm)             | 79.76 ± 10.65              | 84.62 ± 11.94           | 0.03    | 0.43                               |
| Hip circumference (cm)               | 87.39 ± 13.80              | 92.83 ± 12.47           | 0.04    | 0.41                               |
| Waist to hip ratio                   | 0.94 ± 0.24                | 0.92 ± 0.09             | 0.63    | 0.11                               |

Standardized mean differences were calculated from the reported means and standard deviations using the pooled standard deviation and are shown as absolute values.

### Glycemic and Insulin Related Parameters

Mean fasting plasma glucose was  $88.69 \pm 9.15$  mg/dL in the case group and  $80.78 \pm 5.50$  mg/dL in the control group ( $p$  below 0.001). Expressed in millimoles per litre, the values were  $4.93 \pm 0.51$  and  $4.49 \pm 0.31$  respectively, with the same level of significance. Fasting plasma insulin was  $10.25 \pm 3.58$   $\mu$ IU/mL in the case group compared with  $7.10 \pm 2.53$   $\mu$ IU/mL in the control group ( $p$  below 0.001). HOMA IR was  $2.26 \pm 0.90$  in the case group and  $1.43 \pm 0.56$  in the control group ( $p$  below 0.001). Mean HbA1c was  $5.52 \pm 0.35$  percent in the case group and  $5.20 \pm 0.43$  percent in the control group ( $p$  below 0.001). All of these mean values lay below the thresholds used to diagnose diabetes, although the case group values were higher than those of the control group.

**Table 4. Glycaemic and insulin related parameters in the case and control groups:**

| Parameter                             | Control group mean ± SD | Case group mean ± SD | p value | Standardised mean difference |
|---------------------------------------|-------------------------|----------------------|---------|------------------------------|
| Fasting plasma glucose (mg/dL)        | $80.78 \pm 5.50$        | $88.69 \pm 9.15$     | < 0.001 | 1.05                         |
| Fasting plasma glucose (mmol/L)       | $4.49 \pm 0.31$         | $4.93 \pm 0.51$      | < 0.001 | 1.05                         |
| Fasting plasma insulin ( $\mu$ IU/mL) | $7.10 \pm 2.53$         | $10.25 \pm 3.58$     | < 0.001 | 1.02                         |
| HOMA IR                               | $1.43 \pm 0.56$         | $2.26 \pm 0.90$      | < 0.001 | 1.11                         |
| HbA1c (%)                             | $5.20 \pm 0.43$         | $5.52 \pm 0.35$      | < 0.001 | 0.82                         |

The standardized mean difference for the mmol/L glucose row is the same as for the mg/dL row, because the two units are related by a constant factor.

## DISCUSSION

The principal finding of this study is that healthy young adults with a family history of type 2 diabetes mellitus differed from comparable adults without such a history in several domains at once. They had greater body weight, waist and hip circumference and BMI, higher fasting plasma glucose, higher fasting insulin, higher HOMA IR and higher HbA1c, despite being free of a diagnosis of diabetes. Height and waist to hip ratio did not differ. The pattern suggests that the metabolic changes associated with family history are already present in early adult life and are expressed through adiposity and insulin resistance rather than through overt hyperglycemia. The association between family history and adiposity in young adults is consistent with earlier

work. Rane and Gadkari (2012) examined people aged 18 to 25 years in good health with a family history of diabetes and found higher weight, waist and hip circumference, BMI and waist to hip ratio than in controls. Our study reproduced the first four of these differences, although the waist to hip ratio did not differ in our sample. The authors of that study also reported elevated recurrence risk ratios when one or both parents had diabetes. Our data were not designed to test this distinction, and the difference in waist to hip ratio should be interpreted cautiously, given that the reported standard deviation in the control group is unusually large. Body mass index was higher in our case group by about 2.4 kg/m<sup>2</sup>, with the mean in the control group lying in the normal range. Similar differences have been

described in earlier studies. Bhardwaj et al. (2011) reported higher BMI in individuals with a family history of type 2 diabetes, in line with our observation. Our results also agree with the observation that BMI alone may underestimate the metabolic consequences of adiposity, a point made by Nevill et al. (2006). BMI remains a widely used and simple tool for classifying overweight and obesity (Nuttall, 2015), and higher BMI has been linked to a greater burden of cardiovascular and metabolic disease (Must et al., 1999). The waist circumference difference of about 4.9 cm and the hip circumference difference of about 5.4 cm in our study point towards generalised as well as central fat accumulation. Waist circumference is widely regarded as a strong predictor of diabetes risk (Feller et al., 2010), and the meta analysis by Jayedi et al. (2022) reported a dose response relationship between waist circumference and incident diabetes that is consistent with the direction of our findings. Several symptoms were more frequent in the case group. Increased thirst, increased hunger and fatigue were each significantly more common in participants with a family history, while frequent urination, numbness, slow healing wounds and darkened skin patches were not significantly different. Symptoms of hyperglycaemia in people without diabetes are generally non specific, and the most likely interpretation of our findings is that they reflect a combination of subclinical glycaemic change and a greater awareness of diabetes related symptoms among people who have relatives with the disease. This interpretation is speculative, because the study did not measure symptom awareness directly. It is nonetheless worth noting that the case group also had higher HbA1c, which makes a purely perceptual explanation less likely. The symptom data should be regarded as descriptive, since symptoms were recorded as present or absent without any grading of severity. The family history distribution showed a clear pattern. Paternal diabetes was reported slightly more often than maternal diabetes in the case group, at 61.2 percent compared with 51.0 percent. Similar paternal predominance has been reported in some cohorts (Wegner et al., 2012), although other studies have found a stronger maternal association, particularly in Caucasian men (Bjørnholt et al., 2000). The differences between populations in these studies suggest that the parental pattern of risk may vary with ethnicity, sex and age, and a study of Asian Indian young adults such as ours adds information to that picture. No participant in either group reported a sibling with diabetes. This is a finding that should be interpreted with caution, because the inclusion criteria did include siblings and second degree relatives, and the study did not systematically record the number of affected relatives in each case. Fasting plasma glucose in the case group averaged 88.69 mg/dL, compared with 80.78

mg/dL in controls. Both means lie within the range that is conventionally regarded as normal, which means that the difference observed here is one of degree rather than category. Higher fasting glucose has been reported in individuals with a family history of diabetes even when values remain within the normal range (Bianco et al., 2013). Brambilla et al. (2011) showed that fasting glucose in the range of 91 to 99 mg/dL carries an independent risk of progression to type 2 diabetes. Although very few of our participants may have reached that range, the distribution of values should be examined in future work, since the mean alone does not reveal how many individuals sit in the upper part of the normal range. Glycated haemoglobin was higher in the case group, at 5.52 percent compared with 5.20 percent in the control group. This difference is important, because HbA1c integrates glycaemia over the preceding two to three months and is less affected by a single meal than fasting glucose. Alharithy et al. (2018) reported that individuals with a positive family history of type 2 diabetes tend to have higher HbA1c values in association with obesity, a pattern that our data reflect. Lee et al. (2018) found that family history was associated with raised HbA1c even among people without diabetes, which corresponds closely to the situation in our young, non diabetic participants. The observed HbA1c difference should be placed in context. The values in both groups remained below the diagnostic threshold of 6.5 percent, and the difference is modest in absolute terms, but its direction is consistent across all glycemic measures. Insulin resistance was the clearest differentiator between the groups in this study. Fasting insulin, which was about 3.2  $\mu$ IU/mL higher in the case group, and HOMA IR, which was about 0.8 units higher, both showed large differences between the groups. These data indicate that the pancreatic beta cell response to a given glucose load was greater in the case group, which is what would be expected at an early stage of insulin resistance, when hyperinsulinaemia compensates for reduced peripheral sensitivity. Pascual Morena et al. (2024) reported that insulin resistance, assessed by HOMA IR and QUICKI, was associated with arterial stiffness in healthy adults, and Lin et al. (2014) showed that insulin resistance can be identified in people with normal glucose tolerance. Our observations extend these reports to young adults with a family history of the disease. The effect size for HOMA IR was the largest of the glycaemic measures, which supports the view that insulin resistance is the earliest and most sensitive metabolic change in this population. The mechanisms linking family history to these changes are not fully understood, but several lines of evidence point towards a combination of inherited and acquired factors. Goldfine et al. (2006) reported that family history of diabetes was a significant determinant of endothelial dysfunction even

in people without diabetes, which implies that familial susceptibility may act on the vasculature as well as on glucose metabolism. Our study did not measure endothelial function directly. The present findings should therefore be seen as one component of a wider metabolic picture that includes adiposity, insulin resistance and glycemic drift. The clinical implications of these findings are practical. Anthropometric measurements, fasting glucose, fasting insulin and HbA1c are inexpensive, widely available and easy to interpret, and they could be combined with a structured family history to identify young adults who would benefit from lifestyle counselling. Asian Indian populations are reported to develop diabetes at lower body mass index values than many other populations, which suggests that waist circumference and waist to hip ratio may be particularly informative in this group. Screening of relatives of patients could be strengthened by adding waist circumference and HOMA IR to the assessment.

## LIMITATIONS

The study has several limitations that should be considered when interpreting the results. The sample size was small, with 49 participants in each group, and the sample was drawn by purposive rather than random sampling from a single institution. The findings therefore cannot be generalised to the wider population of Uttar Pradesh or to other ethnic groups. All participants were young adults of Asian Indian origin. The cross-sectional design does not permit inference about the direction of causality between family history and the metabolic changes observed. The study also did not include an oral glucose tolerance test, so impaired glucose tolerance that is detectable only after a glucose load could not be identified. Lifestyle factors such as diet, physical activity and sleep were not quantified in detail, and genetic profiling was not performed. Family history was self reported and was not verified against medical records. The analysis was performed using unadjusted comparisons. Because the case and control groups differed in BMI, waist circumference and possibly other characteristics, the differences in glycaemic parameters could partly reflect differences in adiposity. A multivariable analysis adjusting for age, sex and BMI would be needed to estimate the independent contribution of family history, and such an analysis was not performed in the present study. The sex distribution of the two groups has been described as comparable, but the numerical distribution is not presented here. HOMA IR is an estimate derived from fasting values and does not directly measure insulin sensitivity. Insulin was measured on a single occasion, and HbA1c was measured once per participant. The blood pressure and

heart rate data, which were recorded according to the protocol, are not analysed in this report.

## CONCLUSION

In healthy young adults aged 18 to 45 years, a family history of type 2 diabetes mellitus was associated with greater body weight, BMI, waist and hip circumference, higher fasting plasma glucose, higher fasting insulin, higher HOMA IR and higher HbA1c compared with comparable adults without such a history. These differences were present in the absence of a diagnosis of diabetes. The findings indicate that early metabolic and adiposity related changes can be detected with simple and inexpensive measurements. Including anthropometric indices and fasting insulin estimation in the assessment of young relatives of patients may help to identify high risk individuals for early lifestyle intervention. Prospective studies with larger samples, adjusted analyses and longer follow-up are needed to confirm whether these early changes predict the subsequent development of type 2 diabetes.

## Declarations

**Ethical Approval:** Institutional ethics approval was obtained before the commencement of the study.

**Informed Consent:** Written informed consent was obtained from all participants before enrolment in the study.

**Conflict of Interest:** The authors declare that there is no conflict of interest regarding the publication of this paper.

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**Data Availability:** The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to institutional requirements.

**Author Contributions:** Eka Verma contributed to the conception, study design, data collection, analysis and manuscript preparation. Shipra Chandra contributed to the study design, data interpretation and critical revision of the manuscript. Kamna Singh contributed to the biochemical analysis and interpretation of results. Surya Kamal Verma contributed to clinical guidance and critical review of the manuscript. All authors reviewed and approved the final manuscript.

**Use of Artificial Intelligence:** The authors declare that no artificial intelligence (AI)-assisted tools were used in the preparation of this manuscript.

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