Gender diversity of insulin sensitivity markers among patients of type 2 diabetes mellitus in northern India: A cross-sectional analytical study

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ABSTRACT

Background: Diabetes mellitus is a worldwide health problem with more than 80% diabetics living in LMIC. Biological and psychosocial factors are also responsible for gender diversity in T2DM which highlights the need for action to combat T2DM in India. The current study was undertaken to evaluate the gender diversity of insulin sensitivity markers among patients of T2DM in northern India and secondly, to assess and compare the quality of life among T2DM patients in northern India.

Material and Methods: It was a cross-sectional analytical study enrolling 78 patients from tertiary care teaching hospital, India. Inclusion criteria was patients within the age group of 18–60 years, diagnosed with T2DM and on insulin therapy. Case reporting form, anthropometric measures, laboratory investigations, and diabetes quality of life (DQoL) instruments were used for data collection for the period of 3 months.

Results: The mean age of T2DM patients for males was 48.00 ± 9.92 years and for females was 49.96 ± 10.39 years. Male and female patients were 50% and 50%, respectively. WHR (P = 0.032), DBP (P = 0.000), body fat % (P = 0.04), and duration of diabetes (P = 0.001) had statistically significant association with insulin resistance (binary logistic regression analysis (P-value <0.05). Results show the statistically significant difference between means of WHR (t value = 4.702, P = 0.000) and body fat % (t value = 3.035, P = 0.000) in male and female T2DM patients (Independent 't'-test) (P-value <0.05).

Conclusions: The study concludes that WHR, DBP, body fat %, and duration of diabetes were significant markers of insulin sensitivity. WHR and body fat % were the differential insulin sensitivity markers in male and female patients of T2DM in northern India. Diabetes adversely affects the quality of life in a nearly similar pattern in both male and female patients.

Keywords: C-peptide, diabetes, diversity, female, gender, insulin, markers, male, quality of life, sensitivity

Introduction

Diabetes mellitus (DM) is a worldwide health problem with more than 80% diabetics living in low and middle-income countries (LMIC). It is a metabolic disorder and along with that, it is a source of macrovascular and microvascular complications. According to WHO, DM affects millions of people globally. In India, DM results in nearly 1 million deaths per year. DM results from inadequate insulin secretion and resistance. It is well-known evidence that the prevalence of DM has increased in the world during the last four decades. It is a result of the consequent changes in our dietary habits and the lack of exercise. Hence, the American Diabetes Association (ADA) guidelines suggest early treatment and lifestyle measures for hyperglycemia in type 2 DM (T2DM) directed to individualized targets. Insulin initiation is affected by many factors and is
variable from individual to individual. However, with the start of insulin therapy, some changes occur in the quality of life (QoL) of diabetic patients.\(^7\) Diabetes is a chronic disease so it can cause many short-term and long-term sequelae that affect the QoL of diabetic patients.\(^8\) The only presence of DM may worsen the QoL of diabetic patients. Therefore, age and gender differences should also be examined for the QoL of diabetic patients.\(^9\) There are biological and psychosocial factors that are also responsible for gender diversity in T2DM and highlights the need for action to combat T2DM in India.\(^10\) As insulin and C-peptide are secreted in an equimolar amount from the pancreatic beta cells,\(^11\) Hence, in the homeostatic model assessment, fasting C-peptide can be replaced with serum insulin to assess insulin resistance.\(^12\) Hence, identification of gender diversity of predictors of insulin efficacy may provide necessary evidence on the best available treatment plan for the management of DM. The current study aims to evaluate the gender diversity of insulin sensitivity markers among patients of T2DM in northern India and secondly, to assess and compare the quality of life among T2DM patients in northern India.

**Material and Methods**

It was a cross-sectional analytical study involving 78 patients of T2DM on insulin therapy. Purposive sampling technique was chosen to recruit the study subjects. Data was collected for the period of 3 months from the endocrine and general medicine ward at AIIMS, Rishikesh, India.

**Inclusion criteria**

1. We included the patients aged 18–60 years, who were diagnosed with T2DM and were undergoing treatment with insulin therapy.
2. Patients who provided informed consent to participate in the study.

**Ethical permission**

Ethical permission has been taken from the Institutional Ethics Committee.

**Steps of data collection**

Informed consent was obtained from the study participants. Data were collected from the patients of T2DM on insulin therapy admitted at the endocrine ward and general medicine at tertiary care hospital. Study tools such as case reporting form, biophysiologic measures (anthropometric and laboratory measurements), diabetes quality of life (DQoL) instrument were used to collect data from participants.

**Anthropometric measurements and laboratory investigations**

Anthropometric measurements and laboratory investigation of the patient were measured. Anthropometric measures included height, weight, body mass index (BMI), weight, waist circumference (WC), hip circumference (HC), neck circumference (NC), waist to hip ratio (WHR), body fat %, and blood pressures (BP). Stadiometer was used to measure the height of the patients while the weight of the patients was measured using a digital weighing machine. The measuring tape was used to measure the WC at a level midway between the iliac crest and the lower edge of the 12th rib. The BMI was calculated with this formula (kg/m\(^2\)). A digital BP recording machine was used to measure BP. Body fat percentage was calculated by combining WC and HC and deducting the NC from it. For laboratory investigations, participants were advised to fast for 12 h, then venous blood samples of patients were withdrawn between 7 and 10 AM, and sent to biochemistry laboratory for testing of fasting plasma glucose, fasting C-peptide, HbA1C, and lipid profile (high-density lipoprotein cholesterol, low-density lipoprotein, triglyceride, and total cholesterol).

**Revised version of diabetes quality of life instrument**

The revised instrument for DQoL includes an assessment of the three main domains as “satisfaction,” “impact,” and “worry.”

The validity of this instrument was based on exploratory factor analysis, confirmatory factor analysis, and Rasch analysis. The reliability of items was better with 0.92 and 0.84, 0.98 and 0.60, and 0.99 and 0.57 for “satisfaction” domain, “worry” domain, and “impact” domain, respectively. Composite reliability of this tool was for “satisfaction” domain (0.92; 95% CI: 0.909–0.936), “worry” domain (0.794; 95% CI: 0.755–0.832), and “impact” domain (0.781; 95% CI: 0.745–0.818). The satisfaction domain includes 6 items, the impact domain includes 4 items, and the worry domain includes 3 items. The range of scores for each item was 1 to 5. The range of score for the satisfaction domain was 6 to 30, for the impact domain was 4 to 20 and for worry domain was 3 to 15. The score converted to percentage was 30/100, 20/100, and 15/100 for satisfaction domain, impact domain, and worry domain, respectively: The total percentage score was 65/100. This tool was used to measure the QoL of T2DM patients comparing the QoL of male and female patients.

**Definition of insulin resistance**

Insulin resistance was measured by HOMA-IR. In inclusion criteria, we recruited the patients who were on insulin therapy. Hence, in the HOMA model, we replaced the value of serum insulin with fasting C-peptide and calculated using the following formula:

\[
\text{Homeostatic model assessment - Insulin Resistance (HOMA-IR)} = \frac{\text{FPG} \times \text{fasting c-peptide}}{22.5}
\]

**Results**

The data were collected from 78 patients with case reporting form, anthropometric measures, laboratory investigations, and DQoL instruments. The analysis was done with a focus on the objective of the study using SPSS software version 23. Data were described using descriptive statistics in tabular and graphical form. Statistical test Chi-square, binary logistic regression,
and independent ‘t’-test were applied considering a significant P value <0.05.

Table 1 described the frequency and percentage of demographic variables. The mean age of T2DM patients for males 48.00 ± 9.92 years and for females 49.96 ± 10.39. Male and female patients were 50% and 50%, respectively. Around 60% of patients were from rural backgrounds. The majority of patients 39 (50%) had a duration of DM for 1-5 years.

Table 2 described the mean and standard deviation of continuous variables separately for males and females. The duration of diabetes was 7.43 ± 4.87 years and 7.90 ± 5.57 for male and female patients, respectively. Mean BMI was 23.17 ± 6.57 kg/m² and 22.84 ± 5.64, respectively for male and female patients. Mean body fat % was 27.90 ± 12.90 and 31.41 ± 17.54 for male and female patients, respectively. Mean WHR 1.03 ± 0.11 and 0.89 ± 0.10 for male and female patients, respectively.

Table 3 Chi-square test was applied for analysis with P value <0.05. It showed a statistically significant association of BMI (P-value 0.002), body fat% (P-value 0.008), C-peptide (P-value 0.000), duration of diabetes (0.002), systolic blood pressure (0.010), diastolic blood pressure (0.04), duration of diabetes (0.002), body fat%, C-peptide (P-value 0.000), duration of diabetes (0.002), systolic blood pressure (0.010), diastolic blood pressure (0.04), WHR (0.04) with insulin resistance.

Statistical test binary logistic regression was used for analysis with P value significant <0.05 [Table 4]. It showed statistically significant association of WHR (odds ratio: 12.3, 95% CI: 1.240, 12.260; P value 0.032), DBP (odds ratio: 2.978, 95% CI: 1.629, 5.445; P value 0.000), body fat% (odds ratio: 2.525, 95% CI: 0.910, 7.011; P value 0.04), duration of diabetes (odds ratio: 2.479, 95% CI: 1.487, 4.134; P value 0.001), with insulin resistance.

Independent ‘t’-test was applied for analysis and P value <0.05 [Table 5]. It shows a statistically significant difference between means of WHR (t = 4.702, P value 0.000) and body fat % (t = 3.035, P value 0.000) in male and female T2DM patients.

The graph shows a nearly similar pattern of QoL in male and female patients [Figure 1]. For the satisfaction domain, the score was 13% and 11%, for impact domain 38% and 41%, and domain impact 49% and 48% among male and female patients, respectively.

**Discussion**

Fasting C-peptide can replace serum insulin in the homeostasis model assessment index to assess insulin resistance and islet beta-cell function. A previous study supported that fasting C-peptide levels are helpful to assess the endogenous insulin level and to change the type of treatment in T2DM. The present study was conducted taking fasting C-peptide into consideration in place of fasting serum insulin. As the previous study suggested

| S. No. | Variables               | Categories                           | Frequency % |
|--------|-------------------------|--------------------------------------|-------------|
| 1.     | Age                     | Male - 48.11±9.6                     | 49 (50%)    |
|        |                         | Female - 49.64±10.26                 | 51 (50%)    |
| 2.     | Gender                  | Male                                 | 39 (50%)    |
|        |                         | Female                               | 39 (50%)    |
| 3.     | Marital status          | Married                              | 43 (55%)    |
|        |                         | Single /widow/ divorced              | 35 (45%)    |
| 4.     | Education               | Uneducated                           | 43 (55%)    |
|        |                         | Primary school                       | 19 (25%)    |
|        |                         | Secondary school                     | 8 (10%)     |
| 5.     | Occupation              | Unemployed                           | 23 (30%)    |
|        |                         | Private job                          | 12 (15%)    |
|        |                         | Government job                       | 20 (25%)    |
|        |                         | Farmer                               | 23 (30%)    |
| 6.     | Family income per month | <INR 5,000-20,000                    | 55 (70%)    |
|        |                         | INR 20,000-35,000                    | 19 (25%)    |
|        |                         | INR 35,000-50,000                    | 2 (3%)      |
| 7.     | Habitat                 | Urban                                | 31 (40%)    |
|        |                         | Rural                                | 49 (60%)    |
| 8.     | Number of a family member | 4-6                               | 62 (80%)    |
|        |                         | 7-9                                  | 12 (15%)    |
|        |                         | 10-12                                | 4 (5%)      |
| 9.     | Family history          | Yes                                  | 44 (57%)    |
|        |                         | No                                   | 34 (43%)    |
| 10.    | Physical activity       | Sedentary                            | 8 (10%)     |
|        |                         | Moderate                             | 66 (85%)    |
|        |                         | Severe                               | 4 (5%)      |
| 11.    | Use of insulin          | Acute                                | 4 (5%)      |
|        |                         | Chronic                              | 74 (95%)    |
| 12.    | Duration of diabetes    | 1-5 years                            | 39 (50%)    |
|        |                         | 5-10 years                           | 16 (20%)    |
|        |                         | 10-15 years                          | 12 (15%)    |
|        |                         | 15-20 years                          | 12 (15%)    |

| Variables               | Male Mean±SD | Female Mean±SD |
|-------------------------|--------------|----------------|
| Age (years)             | 48.00±9.92   | 49.96±10.39    |
| Duration of diabetes    | 7.43±4.87    | 7.90±5.57      |
| (years)                 |              |                |
| BMI (kg/cm²)            | 23.17±6.57   | 22.84±5.64     |
| Waist to Hip Ratio      | 1.03±0.11    | 0.89±0.10      |
| Body Fat%               | 27.90±12.90  | 31.41±17.54    |
| Fasting Blood Sugar (mmol/L) | 8.22±3.47   | 12.09±5.51    |
| HbA1c (%)               | 10.49±3.88   | 10.33±3.41     |
| SBP (mmHg)              | 126±14.59    | 132±13         |
| DBP (mmHg)              | 77±8.4       | 81±7.14        |
| Cholesterol (mg/dL)     | 135.7±13.5   | 158.2±35.07    |
| Triglyceride (mg/dL)    | 155.06±69.26 | 202.05±163.6  |
| HDL (mg/dL)             | 27.50±11.63  | 70.71±8.89     |
| LDL (mg/dL)             | 75.11±62.42  | 83.24±18.92    |
There are few studies on insulin resistance that have been published in the past. Another previous study also concluded that the C-peptide-based index was strongly associated with comparison to the insulin-based index. There are few studies with C-peptide but considering C-peptide to calculate HOMA-IR, makes sense especially in patients receiving insulin as a part of the treatment of T2DM. We analyzed the association of insulin resistance with fasting C-peptide, HbA1c, systolic blood pressure, diastolic blood pressure, WHR, fasting plasma glucose, total cholesterol, triglyceride level, high-density lipoprotein, low-density lipoprotein, BMI, body fat %, and duration of illness among T2DM and compare the insulin sensitivity markers in male and female patients in northern India. The present study reported markers of insulin sensitivity as WHR, DBP, body fat %, and duration of diabetes. It was also found that gender diversity of insulin sensitivity markers as WHR and body fat %. Ashwell et al. reported that WHR and WC are associated with insulin resistance. However, Jablonowska-Lietz et al., reported differently that insulin resistance determined by HOMA-insulin resistance positively correlated with visceral adiposity index and WHR, followed by WC and BMI. Cheng et al., also concluded that body fat %, BMI, and WC are significantly associated with insulin resistance. However, Wang et al. observed that BMI was the predictor of metabolic syndrome for men. Kurniawan et al. supported that body weight, BMI, WC, body fat %, and visceral fat, all have a significant correlation with insulin resistance. Another study also observed that WHR is the most significant predictor for insulin resistance in polycystic ovary syndrome (PCOS) female patients. In the present study, we found WHR as a differential marker of insulin sensitivity. In another previous study, the waist was the best predictor of diabetes in females but BMI and waist were the best predictors of diabetes in males. These findings are also confirmed by studies conducted in other cohorts from different countries. However, the present study found WHR and body fat % as differential markers of insulin sensitivity. In another previous study, the waist-to-height ratio including other measures of body fat distribution was significantly associated except for BMI among men. However, in support of the present study, Benites-Zapata et al. found that WHR had an association with insulin resistance. The risk of diabetes was increased with increasing WHR at all values of BMI, while the positive association between BMI and insulin resistance was observed among women with a low WHR. The present study reported differently that association of homeostatic model assessment insulin resistance (HOMA-IR) with fasting C-peptide, SBP, DBP, WHR, body fat %, BMI, and duration of diabetes. However, the strong markers of insulin resistance were WHR, DBP, body fat %, and duration of diabetes, and differential markers of insulin resistance among males and females were WHR and body fat %. As there is not so much literature available to differentiate the quality of life among male and female diabetic patients. Therefore, in the present study, we tried to collect the data for its clinical utility. For the satisfaction domain, the score was 13% and 11%, for impact domain 38% and 41%, and for domain impact 49% and 48% among male and female patients, respectively. Xiyue Jing et al. showed that diabetes management, its treatment, and complication affect the QoL of T2DM patients. Lu et al. and Manjunath et al. observed that DM affects the quality of life of patients but not to a great extent. Rossi et al. found that not only the severity of diabetes even symptomatic hypoglycemia also adversely affects the QoL of the diabetic patient.

**Limitations**

It was a cross-sectional study with a limited sample size.
Recommendaion
The study recommends a differential weight reduction goal in male and female patients of T2DM and further research with a larger sample size.

Conclusions
In resource-limited countries, WHR, body fat %, BMI, SBP, DBP, and duration of diabetes can be utilized as independent markers of insulin sensitivity even in the absence of serum markers like c-peptide and insulin, especially in primary and secondary care hospitals. WHR and body fat % can also be taken into consideration as a differential insulin sensitivity marker in males and females. Diabetes affects the QoL of both male and female patients which suggests needing to assess the QoL of diabetic patients in diabetic clinics routinely.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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