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# Association with Metabolic Syndrome in Children Diagnosed with Type 1 Diabetes Mellitus: A Cross-Sectional Study

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## ABSTRACT

**Objective:** To evaluate the prevalence of metabolic syndrome (MetS) in children with type 1 diabetes mellitus (T1DM) and to determine the predictive value of simple anthropometric measurements, in particular neck circumference (NC) and waist circumference (WC), for identifying MetS.

**Methods:** Children (aged 6-18 years) and diagnosed with T1DM were included in this cross-sectional study. Anthropometric [NC, WC, hip circumference (HC), body mass index (BMI), tri-ponderal mass index (TMI)] and laboratory parameters, including lipid profile and hemoglobin A1c (HbA1c) were recorded. MetS diagnosis was established using the International Diabetes Federation criteria. Receiver operating characteristic (ROC) curve analysis and Least Absolute Shrinkage and Selection Operator (LASSO) regression were employed to identify key predictors.

**Results:** A total of 168 children with T1DM participated, among whom the prevalence of MetS was 8.9%. Children with MetS had significantly higher BMI, WC, NC, HC, and TMI values compared to non-MetS counterparts. ROC analysis identified WC Z-score having the highest discriminative power [area under the curve (AUC)=0.954], followed by NC Z-score (AUC=0.906). LASSO regression identified NC Z-score and BMI percentile as the most robust predictors. A strong positive correlation was observed between NC and WC ($r=0.812$, $p<0.001$), and there was a mild inverse correlation between NC and high-density lipoprotein cholesterol.

**Conclusion:** NC and WC are simple, non-invasive, and reliable tools for early detection of MetS risk in pediatric T1DM patients. Their routine measurement may enhance risk stratification and guide preventive interventions targeting obesity and dyslipidemia. These findings support incorporating NC and WC into standard clinical assessments to improve long-term cardiometabolic outcomes in children with T1DM, with NC $z>1.04$ or WC $z>1.41$ as actionable thresholds.

**Keywords:** Anthropometric measurements, metabolic syndrome, neck circumference, type 1 diabetes mellitus

### What is already known on this topic?

Cardiovascular risk is increased by metabolic syndrome (MetS) in children with type 1 diabetes mellitus (T1DM) but further studies are needed to determine its prevalence and predictors among these children. Neck circumference (NC) shows promise as an anthropometric indicator of central obesity and metabolic risk in T1DM but is not routinely used in T1DM care.

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**What this study adds?**

Based on International Diabetes Federation criteria, the study found MetS in 8.9% of a Turkish cohort of children with T1DM. A strong correlation was found between NC, waist circumference (WC), and body mass index and NC emerged as an independent predictor of MetS predictor. The strong discriminatory ability of NC and WC Z-scores suggests their inclusion in standard pediatric T1DM evaluations for early cardiometabolic risk detection may be warranted.

## Introduction

Recent decades have witnessed a dramatic shift in the management of type 1 diabetes mellitus (T1DM) in children, from an acute, life-threatening disease to a chronic condition characterized by long-term complications and metabolic complications (1,2). Despite improvements in survival because of widespread availability of insulin therapy and self-monitoring, pediatric T1DM patients are experiencing increased rates of overweight, obesity, and related cardiovascular risks (3,4,5). These trends parallel the global childhood obesity epidemic, contributing to a higher risk of metabolic syndrome (MetS), a cluster of metabolic issues that increase the risk of type 2 DM (T2DM), cardiovascular disease, and early mortality (3,6,7).

MetS in children is diagnosed with central obesity and at least two of these: elevated triglycerides, low high-density lipoprotein (HDL) cholesterol, hypertension, and/or impaired fasting glucose (1,2). The International Diabetes Federation (IDF) criteria are widely used in pediatrics because of pragmatic cut-off values for waist circumference (WC) based on age and sex (2). T1DM children experience worsened MetS risk due to poor glycemic control, insulin-related weight gain, and a proinflammatory state (4,6,8,9). MetS prevalence in this group shows variability, ranging from 3.2% to 29.9%, with IDF criteria-based rates of 8-10% (4,10). The extent of this variability emphasizes the requirement for practical, early screening tools in identifying cardiometabolic risk.

Anthropometric indices provide readily available alternatives to assess adiposity and cardiovascular risk in children. Body mass index (BMI) is most commonly employed to classify overweight and obesity. However, BMI does not distinguish between lean and fat mass or capture fat distribution (11). Measurements of central adiposity, such as WC and waist-to-height ratio (WHtR), more accurately reflect visceral fat and its metabolic effects, despite needing standardized methods and age/sex-specific references (12,13).

A simple anthropometric marker, neck circumference (NC), indicates upper-body subcutaneous adiposity and its metabolic implications (14,15,16). In contrast to WC, NC measurement shows less sensitivity to respiration and posture changes, proving more socially suitable in specific contexts. ACFIES (Association between Cardiorespiratory Fitness, Muscular Strength and Body Composition with Metabolic Risk Factors in Colombian Children) study data (14) revealed that NC levels in school-aged children correlated positively with fasting glucose, triglycerides, blood pressure, insulin, and Homeostatic Model Assessment for Insulin Resistance, but inversely with HDL (14). These findings suggest that using NC alongside current methods could enhance pediatric MetS screening, especially in situations requiring rapid assessment or where WC measurement is difficult.

The relationship between NC, WC, BMI, and MetS prediction in T1DM children, especially within the Turkish pediatric population, is understudied, despite a growing body of work on general pediatric anthropometric indices. Children with T1DM face unique metabolic challenges, including insulin-induced weight gain, autoimmune-related inflammation, and glycemic variability, that increase susceptibility to dyslipidemia, hypertension, and central obesity (2,10,17,18). In Türkiye, about 10.5% of children with T1DM meet the IDF criteria for MetS, a rate higher than that in age-matched healthy peers (19). This increased rate highlights the importance of integrating simple, reliable physical measurements into routine healthcare for early detection and prompt intervention in children with T1DM.

The aim of this study was to examine the connections between NC, WC, BMI, and MetS markers in Turkish children with T1DM. Our ultimate goal was to identify easy-to-use, evidence-based tools for early cardiometabolic risk detection in children with T1DM by investigating the contributions of various anthropometric measures to MetS risk stratification.

## Methods

### Study Design and Population

The study was cross-sectional and investigated the relationships between physical measurements, laboratory results, and MetS in children with T1DM. Written informed consent was obtained from all participants and their parents or guardians, and ethical approval was obtained from the Gaziantep University Clinical Research Ethics Committee approval (approval no.: 2021/356, date: 03.11.2021). The study included participants who were between 6 and 18 years old. Inclusion criteria were a confirmed diagnosis of T1DM for at least one-year, regular follow-up for at least six months in a pediatric endocrinology clinic, evaluated and monitored for MetS components and the availability of complete clinical and laboratory data. Participants with T2DM, monogenic DM, syndromic obesity, other secondary causes of

obesity, incomplete anthropometric data, or missing laboratory records were excluded.

The presence of MetS was the key outcome. Secondary outcomes included the evaluation of risk factors, such as obesity, dyslipidemia, and distortion of anthropometric measurements associated with MetS, focusing on anthropometric and laboratory markers. Predictor variables included NC, WC, BMI, tri-ponderal mass index (TMI), and lipid profile components.

## Data Collection

Demographic, clinical, and anthropometric data were collected during routine clinic visits and recorded.

### 1. Anthropometric Measurements

An experienced individual took anthropometric measurements, including weight in kilograms (kg), height in centimeters (cm), WC in cm, NC in cm, and hip circumference (HC) in cm. All measurements were taken with the subjects standing upright, facing forward, and shoulders relaxed. Further anthropometric parameters were derived from these measurements, including waist-to-hip ratio (WHR) and WHtR.

• **NC (cm):** Measured with a non-elastic tape at the level of the thyroid cartilage, which is the most prominent part of the subject's neck in an upright position, with the eyes forward and the head in a horizontal plane.

• **WC (cm):** Measured with a non-elastic 150 cm tape measure. The measurement was taken with the patient standing in anatomical position, midway between the iliac crest and lowest rib.

• **HC (cm):** Measured by circling the hips at their widest point with a tape, ensuring the tape remained level and parallel to the ground.

• **WHR:** Calculated by dividing WC (cm) by HC (cm). A higher WHR signifies greater central obesity and has been connected to elevated risks of cardiovascular and metabolic complications.

• **WHtR:** Derived by dividing WC (cm) by height (cm).

• **BMI:** Calculated as weight in kg divided by height in m squared ($kg/m^2$).

• **TMI:** Computed using the formula: weight (kg) divided by height cubed ($kg/m^3$). TMI has established cutoff values of 16.0 $kg/m^3$ for overweight boys and 16.8 $kg/m^3$ for overweight girls (20).

• **Blood pressure:** Measured in a seated position using an automated sphygmomanometer after 10 minutes of rest. Hypertension was identified when systolic or diastolic blood pressure exceeded the 95$^{th}$ percentile for age, sex, and height, based on international guidelines (21).

Height (cm), weight (kg), blood pressure and BMI standard deviation (SD) score (SDS) were calculated according to Turkish Pediatric Endocrinology and Diabetes Association official formula list 2017: ÇEDD Çözüm/Child Metrics (www.ceddcozum.com, www.childmetrics.org data) (21).

### 2. Obesity Definitions (4)

• **BMI Percentiles**

- Underweight=BMI<5$^{th}$ percentile

- Normal weight=BMI between the 5$^{th}$ and 85$^{th}$ percentiles

- Overweight=BMI between the 85$^{th}$ and 95$^{th}$ percentiles

- Obesity=BMI≥95$^{th}$ percentile

• **WC classification:** The WC classification for abdominal obesity was determined using population-specific standards, where a WC at or above the 90$^{th}$ percentile for age and sex was obese.

• **WHtR:** A WHtR≥0.5 was also considered a marker of central obesity, in line with guidelines.

**3. MetS Diagnosis:** Based on IDF criteria (2), MetS diagnosis involved abdominal obesity (WC≥90$^{th}$ percentile) and at least two of the following:

• Elevated triglycerides (TG) [≥150 milligram (mg)/deciliter (dL)]

• Decreased HDL cholesterol (<40 mg/dL)

• Elevated blood pressure (above the 95$^{th}$ percentile for age, sex, and height)

• Fasting glucose≥100 mg/dL or pre-existing diabetes diagnosis.

Individuals in this study were classified as having MetS if they met the criteria set by the IDF, while those who met none or only some criteria were considered not to have MetS.

## Laboratory and Other Analyses

Venous blood samples, drawn after an overnight fast, were analyzed for:

• **Lipid profile:** The lipid profile included measurements of total cholesterol (TC), low-density lipoproteins (LDL) cholesterol, HDL cholesterol, and TG. Plasma TG, HDL, LDL, and TC were analyzed using standard enzymatic methods on the AU 5800 Series AU model biochemistry analyzers (Beckman Coulter, Brea, CA, USA).

• **Fasting glucose and glycated hemoglobin A1c (HbA1c) levels:** High-performance liquid chromatography was used to measure

fasting glucose and HbA1c levels. Poor T1DM control was defined as HbA1c levels greater than 8% (22).

Dyslipidemia was defined as one of the following (4): 1) TC>200 mg/dL, 2) TG≥100 mg/dL between the ages of 0-9 years, 3) TG: ≥130 mg/dL between the ages of 10-19 years, 4) LDL≥130 mg/dL increase, and 5) HDL<40 mg/dL decrease (4).

Patient medical records were reviewed to extract clinical and demographic data, including age, sex, duration of diabetes, daily insulin dose (expressed as units/kg/day), co-morbidities, and current therapeutic regimens.

### Statistical Analysis

All data analysis was conducted using R version 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria). Data management and visualization were performed using R packages. Based on their distribution, continuous variables are presented either as the mean with SD or the median and range (minimum to maximum). Frequencies and percentages were used to represent categorical variables.

Continuous data were analyzed using Independent Samples t-tests (normal distribution) or Mann-Whitney U tests (non-normal distribution), while categorical data were analyzed using chi-square tests. The associations between anthropometric measurements and laboratory parameters were assessed using Pearson or Spearman correlation coefficients, depending on data distribution. To account for age- and sex-related variability, NC and WC values were standardized into Z-scores using reference LMS parameters derived from Turkish pediatric populations (16,23). Z-scores were calculated using the LMS method formula:

$Z=((X/M)^{L}-1)/(L\times S)$ when $L\neq 0$, or $Z=\ln(X/M)/S$ when $L=0$.

The predictive value of both raw and standardized NC and WC measures for MetS was examined through receiver operating characteristic (ROC) curve analysis. Optimal cut-off points were identified using the Youden index, and corresponding sensitivity, specificity, and area under the curve (AUC) values were reported at 95% confidence intervals (CIs). As there were a limited number of outcome events (n=15), to prevent overfitting, a penalized logistic regression model using the Least Absolute Shrinkage and Selection Operator (LASSO) was employed for variable selection. The optimal penalty parameter (λ) was determined using 10-fold cross-validation with the glmnet package in R. Two models were considered: λmin, which minimizes cross-validated binomial deviance, and λ1 standard error (SE), the most parsimonious model within one SE of the minimum. Variables included in the penalized model were age, sex, NC Z-score, BMI percentile, and TG levels. At λmin, NC Z-score (β=0.589) and BMI percentile (β=0.038) were retained as predictors, while age, sex, and triglycerides were shrunk to zero. The final model thus included the most significant predictors, addressing multicollinearity and accounting for the limited number of events per variable. Two-tailed tests were used, with $p<0.05$, signifying statistical significance.

## Results

### Demographic and Anthropometric Characteristics of Participants

The study included 168 children with T1DM, 84 male and 84 female (50% each) (Table 1). The mean age of participants was 12.5±2.9 years, and the median T1DM duration was 4 (0-15) years. Participants' mean NC and WC were 30.8±3.2 cm and 68.6±8.3 cm. The mean BMI [SD score (SDS)] of participants was -0.24 (-3.43-2.63) kg/m$^2$, with 12.5% (n=21) being overweight and 2.4% (n=4) being obese. The laboratory results showed a median HbA1c level of 9.4% (5.7-16.5%), while median lipid values were: TC 180.0 (95-314) mg/dL; LDL cholesterol 108.5 (47-214) mg/dL; HDL cholesterol 57.0 (26-132) mg/dL; and TG 92.0 (27-544) mg/dL. The IDF definition identified MetS in 15 (8.9%) of the sample.

### Comparing Children with and without MetS

Median daily insulin dose was 0.94 (0.31-1.58) units/kg/day, with no significant difference between MetS and non-MetS groups (p=0.391). Table 2 compares anthropometric and clinical parameters between children with MetS and children without MetS. Children with MetS had significantly greater weight, BMI, BMI SDS, NC, WC, and HC than those without MetS ($p<0.05$ for all). HDL levels were significantly lower (p=0.038) in children with MetS. Anthropometric variables and their connections with MetS are illustrated in Table 2. Increased WC was present in all participants with MetS, but only 6.5% of those without MetS ($p<0.001$). Similarly, the MetS group showed a considerably higher prevalence of increased NC compared to the non-MetS group (93.3% vs. 34%, respectively; $p<0.001$). Elevated WHtRs were also significantly associated with MetS ($p<0.001$).

### Correlations Between Anthropometric and Laboratory Variables

Significant correlations were found between various anthropometric measures (Table 3). Strong positive correlations between NC and WC (r=0.812, $p<0.001$), and NC and HC (r=0.786, $p<0.001$) suggest that NC is an effective measure of central obesity. Moderate positive correlations were found between WHtR and WC (r=0.482, $p<0.001$) and TMI and WC (r=0.321, $p<0.001$). HDL levels were weakly inversely correlated with NC (r=-0.190, p=0.015), suggesting higher NC may be associated with a less favorable lipid profile.

**Table 1. Demographic variables of participants (n=168)**

| | Total (n=168) n (%) | | Total (n=168) n (%) |
|---|---|---|---|
| | | **MetS (based on IDF)** | |
| **Age*** | 12.5±2.9 | No | 153 (91.1) |
| | | Yes | 15 (8.9) |
| **Sex** | | | |
| Female | 84 (50) | **NC (cm)*** | 30.8±3.2 |
| Male | 84 (50) | | |
| **T1DM duration (years)** | 4.0 (0-15) | **NC classification¥** | |
| | | Normal | 96 (57.1) |
| | | High | 66 (39.3) |
| **Median insulin dose (units/kg/day)*** | 0.94 (0.31-1.58) | **WC (cm)*** | 68.6±8.3 |
| **Median insulin dose (units/kg)*** | 41.0 (9.0-105.0) | **WC classification** | |
| | | Normal | 143 (85.1) |
| | | High | 25 (14.9) |
| **Family T1DM history** | 22 (13.1) | **HC (cm)*** | 85.6±11.4 |
| **Family T2DM history** | 51 (30.4) | **WHR*** | 0.81 (0.65-1.15) |
| **Height (cm)*** | 150.3±16.6 | **WHtR*** | 0.45 (0.38-0.60) |
| **Height (SDS)*** | -0.21 (-3.78-2.65) | **TMI (kg/m³)*** | 12.8±2.2 |
| **Weight (kg)*** | 44.1±14.3 | **HbA1c (%)** | 9.4 (5.7-16.5) |
| **Weight (SDS)*** | -0.37 (-3.77-2.63) | **Total cholesterol (mg/dL)*** | 180.0 (95-314) |
| **BMI (kg/m²)*** | 19.0±3.3 | **LDL (mg/dL)*** | 108.5 (47-214) |
| **BMI (SDS)*** | -0.24 (-3.43-2.63) | **HDL (mg/dL)*** | 57.0 (26-132) |
| **BMI percentile** | 40.5 (0.03-98.64) | **Triglyceride (mg/dL)*** | 92.0 (27-544) |
| **BMI percentile classification** | | | |
| Underweight | 21 (12.5) | **Puberty** | |
| Normal | 122 (72.6) | | |
| Overweight | 21 (12.5) | **No** | 100 (59.5) |
| Obese | 4 (2.4) | **Pubertal** | 68 (40.5) |

Numeric variables are presented as median (minimum-maximum) or mean±SD. ¥NC measurements could not be made in four patients in the MetS negative group.
BMI: body mass index; cm: centimeter; dL: deciliter; HbA1c: glycated hemoglobin A1c; HC: hip circumference; HDL: High-density lipoproteins; kg: kilogram; IDF: International Diabetes Federation; LDL: low-density lipoproteins; m: meter; MetS: metabolic syndrome; mg: milligram; NC: neck circumference; SD: standard deviation; SDS: standard deviation score; TMI: tri-ponderal mass index; WC: waist circumference; WHR: waist-to-hip ratio; WHtR: waist-to-height ratio.

**Table 2. Components of metabolic syndrome according to International Diabetes Federation (IDF) criteria in children with type 1 diabetes mellitus**

| | Based on the IDF criteria | | |
|---|---|---|---|
| | MetS (-) n=153 | Mets (+) n=15 | p value |
| Age (years)* | 12.6±2.9 | 11.9±2.8 | 0.363 |
| **Sex** | | | |
| Female | 75 (49.0) | 9 (15.0) | 0.416 |
| Male | 78 (51.0) | 6 (40.0) | |
| T1DM duration (years) | 4.0 (0-15) | 4.0 (1-12) | 0.905 |
| Median insulin dose (units/kg/day)* | 0.94 (0.31-1.58) | 1.01 (0.43-1.28) | 0.391 |
| Median insulin dose (units/kg)* | 40.0 (9.0-90.0) | 49.0 (30.0-105.0) | ***0.026*** |
| Family T1DM history | 20 (13.1) | 2 (13.3) | 0.977 |

**Table 2. Continued**

| | Based on the IDF criteria | | |
|---|---|---|---|
| | **MetS (-) n=153** | **Mets (+) n=15** | **p value** |
| Family T2DM history | 46 (30.1) | 5 (33.3) | 0.794 |
| Height (cm)* | 149.8 ±16.5 | 155.5±17.1 | 0.209 |
| Height (SDS)* | -0.26 (-3.78-2.17) | 0.49 (-2.90-2.65) | 0.068 |
| Weight (kg)* | 43.0±13.3 | 55.6±19.1 | **0.001** |
| Weight (SDS)* | -0.43 (-3.77-2.244) | 1.15 (-1.37-2.63) | **<0.001** |
| BMI (kg/m$^2$)* | 18.7±3.1 | 22.7±3.6 | **<0.001** |
| BMI (SDS)* | -0.34 (-3.43-1.92) | 1.10 (-1.07-2.21) | **<0.001** |
| BMI percentile | 36.7 (0.03-97.3) | 86.4 (14.23-98.64) | **<0.001** |
| **BMI percentile classification** | | | |
| Underweight | 21 (13.7) | 0 (0.0) | **<0.001** |
| Normal | 117 (76.5) | 5 (33.3) | |
| Overweight | 3 (8.5) | 8 (53.3) | |
| Obese | 2 (1.3) | 2 (13.3) | |
| NC (cm)* | 30.5±3.1 | 33.1±3.3 | **0.002** |
| **NC classification**¥ | | | |
| Normal | 95 (62.1) | 1 (6.7) | **<0.001** |
| Increased | 52 (34.0) | 14 (93.3) | |
| WC (cm)* | 67.6±7.6 | 78.6±9.2 | **<0.001** |
| **WC classification** | | | |
| Normal | 143 (93.5) | 0 (0.0) | **<0.001** |
| Increased | 10 (6.5) | 15 (100.0) | |
| HC (cm)* | 83.6±11.0 | 94.3±11.4 | |
| **WC classification** | | | |
| Normal | 143 (93.5) | 0 (0.0) | **<0.001** |
| Increased | 10 (6.5) | 15 (100.0) | |
| WHR* | 0.80 (0.65-1.5) | 0.83 (0.71-0.97) | 0.195 |
| WHtR* | 0.45 (0.38-0.59) | 0.51 (0.42-0.60) | 0.186 |
| **WHtR** | | | |
| Normal | 128 (83.7) | 4 (26.7) | <0.001* |
| Increased | 25 (16.3) | 11 (73.3) | |
| TMI (kg/m$^3$)* | 12.7±2.1 | 14.4±1.9 | **0.004** |
| **TMI (kg/m$^3$)** | | | |
| Normal | 147 (96.1) | 13 (86.7) | 0.102 |
| Increased | 6 (3.9) | 2 (13.3) | |
| **Dyslipidemia + HT** | 36 (25.3) | 5 (33.3) | 0.414 |
| HbA1c (%) | 9.2 (5.7-15.8) | 9.7 (6.4-16.5) | 0.332 |
| Total cholesterol (mg/dL)* | 180.0 (95-314) | 171.5 (100-294) | 0.416 |
| LDL (mg/dL)* | 109.0 (47-211) | 107.0 (59-214) | 0.791 |
| HDL (mg/dL)* | 58.0 (26-132) | 51.0 (36-79) | **0.038** |
| Triglyceride (mg/dL)* | 88.0 (27-544) | 119.0 (44-289) | 0.248 |

**Table 2. Continued**

| | Based on the IDF criteria | | |
|---|---|---|---|
| | MetS (-) n=153 | Mets (+) n=15 | p value |
| **Puberty** | | | |
| Prepubertal | 91 (59.5) | 9 (60.0) | 0.969 |
| Pubertal | 62 (40.5) | 6 (40.0) | |

Numeric variables are presented as median (minimum-maximum) or mean±SD. ¥NC measurements could not be made in four patients in the MetS negative group.
BMI: body mass index; cm: centimeter; dL: deciliter; HbA1c: glycated hemoglobin; HC: hip circumference; HDL: high-density lipoproteins; kg: kilogram; IDF: International Diabetes Federation; LDL: low-density lipoproteins; m: meter; MetS: metabolic syndrome; mg: milligram; NC: neck circumference; SD: standard deviation. SDS: standard deviation score; TMI: tri-ponderal mass index; WC: waist circumference; WHR: waist-to-hip ratio; WHtR: waist-to-height ratio.

## ROC-Based Comparison of Neck and WC Metrics for Predicting MetS

To determine the ability of raw and Z-scored anthropometric measures to identify MetS, ROC curve analysis was performed (Figure 1, Table 4). For NC (cm), the AUC was 0.718 (SE=0.063; p=0.005; 95% CI, 0.595-0.841), with an optimal cut-off of 30.25 cm yielding 80.0% sensitivity and 52.4% specificity. The AUC for WC (cm) was 0.809 (SE=0.065; p<0.001; 95% CI, 0.682-0.935), with an optimal cutoff of 73.5 cm corresponding to 73.3% sensitivity and 74.2% specificity. The AUC was 0.906 for the NC Z-score (SE=0.032; p<0.001; 95% CI: 0.854-0.959) with an optimal threshold of 1.041, giving 93.3% sensitivity and 80.0% specificity, while the WC Z-score achieved an AUC of 0.954 (SE=0.019; p<0.001; 95% CI: 0.915-0.992) at an optimal threshold of 1.408, with 100% sensitivity and 80.0% specificity.

## Penalized Regression Model for Risk Factors

Table 5 presents penalized logistic regression analysis revealing several independent predictors of MetS. The model exhibiting optimal performance, identified via minimization of the penalty parameter (λ_min), indicated that NC Z-score (β=0.589) and BMI percentile (β=0.038) significantly predicted MetS. In contrast, age, sex, and triglyceride levels were penalized to zero, showing minimal additional predictive value. Anthropometric indicators, especially the NC Z-score, demonstrated superior predictive validity for MetS within this cohort compared to conventional demographic or biochemical markers. Supplementary Figure 1 provides further elucidation of these findings by illustrating the coefficient shrinkage path across λ values.

**Table 3. Correlation analysis of anthropometric measurements and laboratory values**

| | NC (cm) | WC (cm) | HC (cm) | WHR | WHR | TMI (kg/m³) | HbA1c (%) | HDL (mg/dL) |
|---|---|---|---|---|---|---|---|---|
| **NC (cm)** | 1 | 0.812 | 0.786 | -0.102 | 0.174 | 0.184 | 0.034 | -0.190 |
| **WC (cm)** | 0.812 | 1 | 0.823 | 0.111 | 0.482 | 0.321 | 0.075 | -0.125 |
| **HC (cm)** | 0.786 | 0.823 | 1 | -0.466 | 0.139 | 0.254 | -0.015 | -0.140 |
| **WHR** | -0.102 | 0.111 | -0.466 | 1 | 0.487 | 0.071 | 0.122 | 0.050 |
| **WHtR** | 0.174 | 0.482 | 0.139 | 0.487 | 1 | 0.643 | 0.086 | -0.053 |
| **TMI (kg/m³)** | 0.184 | 0.321 | 0.254 | 0.071 | 0.643 | 1 | -0.064 | -0.094 |
| **HbA1c (%)** | 0.034 | 0.075 | -0.015 | 0.122 | 0.086 | -0.064 | 1 | 0.131 |
| **HDL (mg/dL)** | -0.190 | -0.125 | -0.140 | 0.050 | -0.053 | -0.094 | 0.091 | 1 |

NC: neck circumference; WC: waist circumference; HC: hip circumference; WHR: waist-to-hip ratio; TMI: tri-ponderal mass index; HbA1c: glycated hemoglobin; HDL: high-density lipoproteins; WHtR: waist-to-height ratio.

**Table 4. Diagnostic performance of anthropometric measurements in predicting MetS in children with type 1 diabetes mellitus**

| Variable | AUC | p value | 95% CI | Optimal cut-off | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|---|---|
| **NC** | 0.718 | **0.005** | 0.595-0.841 | 30.25 | 80.00 | 52.38 |
| **WC** | 0.809 | **<0.001** | 0.682-0.935 | 73.50 | 73.33 | 74.15 |
| **NC Z-score** | 0.906 | **<0.001** | 0.854-0.959 | 1.041 | 93.33 | 80.00 |
| **WC Z-score** | 0.954 | **<0.001** | 0.915-0.992 | 1.408 | 100.00 | 80.00 |

AUC: area under the curve; CI: confidence intervals; MetS: metabolic syndrome; NC: neck circumference; WC: waist circumference.

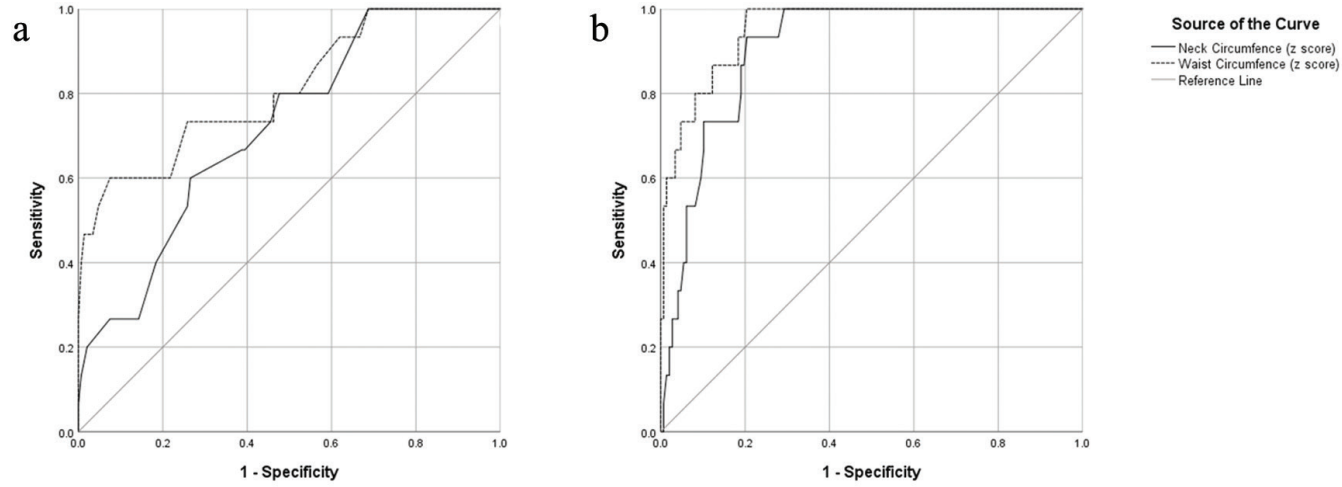


**Figure 1.** ROC analysis of the NC, WC, NC (Z-score), and WC (Z-score). a) ROC analysis of the NC and WC. b) ROC analysis of the NC (Z-score) and WC (Z-score)

*Notes: For clarity in grayscale printing, NC and WC are represented with solid and dashed lines, while Z-score curves are shown with dotted lines and circle markers.*

*ROC: receiver operating characteristic; NC: neck circumference; WC: waist circumference; HC: hip circumference.*

**Table 5. Multivariate LASSO regression analysis of risk factors associated with metabolic syndrome in children with type 1 diabetes mellitus**

| Variable | Coefficient at $\lambda_{min}$ | Coefficient at $\lambda_{1SE}$ |
|---|---|---|
| (Intercept) | -5.673 | -3.886 |
| Age | 0.000 | 0.000 |
| Sex (F:M) | 0.000 | 0.000 |
| NC Z-score | **0.589** | 0.296 |
| BMI (percentile) | **0.038** | 0.018 |
| TG (mg/dL) | 0.000 | 0.000 |

BMI: body mass index; dL: deciliter; mg: milligram; F: female; M: male; NC: neck circumference; TG: triglyceride.

## Discussion

This research investigated the complex relationships between anthropometric measures, MetS, and laboratory findings in children with T1DM. Using IDF criteria, MetS was identified in 8.9% of participants with T1DM. Anthropometric measures (NC, WC, HC, BMI, and TMI) and lipid profiles were significantly elevated in children with MetS. WC Z-score showed the highest power to discriminate, followed by NC Z-score. NC Z-score and BMI percentile were strong predictors of MetS. This study highlights the utility of straightforward anthropometric measures, especially NC and WC, for detecting increased cardiometabolic risk in T1DM children.

Early identification and evaluation of MetS in individuals with T1DM is important to prevent or ameliorate the development of both major and minor complications. Despite limited research, studies into MetS in T1DM patients indicate an incidence ranging between 3.2% and 29.9% (4,5,9,10). Several factors contribute to the discrepancies observed between studies, including variations in MetS diagnostic criteria, study population characteristics, participant age, and country-specific differences in the prevalence of obesity/overweight.

Pediatric T1DM is increasingly associated with MetS, largely due to the obesity epidemic and inherent disease factors. Our cohort showed an 8.9% prevalence of MetS, consistent with previous pediatric studies (2,4,19,24). Conversely, general population rates vary between 2.1% and 11.2%, contingent on criteria and location (5). Despite limited data on T1DM prevalence, some studies report rates up to 29.9% in similar age groups (10). Weight gain and fat redistribution, especially abdominal adiposity, and increased MetS risk are potential side effects of insulin therapy, despite its essential role in glycemic control (3,25,26). Moreover, chronic hyperglycemia and oxidative stress lead to dyslipidemia and hypertension (26,27). Concurrently, T1DM-associated inflammation fosters insulin resistance, a central feature of MetS. In addition, chronic hyperglycemia and oxidative stress contribute to dyslipidemia and hypertension (9). These metabolic abnormalities are further complicated by diet and physical inactivity (28,29). According to Messiah et al. (18), early metabolic problems in T1DM may persist despite optimal glycemic control, increasing long-term cardiovascular risk.

Practical screening tools for MetS in children with T1DM now include anthropometric indices, with a focus on NC and WC measurements. We found significantly increased NC, WC, HC, BMI, and TMI in participants with MetS. This data confirms earlier studies which highlighted the significant role of overweight

and obesity in the development of MetS among adolescents with T1DM (11,20,30). In multivariate LASSO regression, NC z-score and BMI percentile emerged as a robust predictors (31). Adolescent metabolic risk showed independent associations with TMI and BMI percentile, as observed by Sun et al. (30). Notably, NC includes upper-body subcutaneous fat, an adipose tissue related to metabolic dysfunction by releasing pro-inflammatory adipokines, thus measuring anthropometric changes that are missed if only BMI is measured (11,14,15,29). Consequently, despite its minimal invasiveness and reproducibility, NC is a preferred clinical measurement, particularly when WC measurement variability is problematic (16).

The hallmarks of MetS in T1DM are dyslipidemia and inflammatory processes. Lower HDL cholesterol was observed in MetS children in our study, consistent with the effects of central adiposity on lipid metabolism (32). Although NC weakly inversely correlated with HDL and showed no significant triglyceride relationship, WC's inverse association with HDL highlights the importance of central adiposity (33). These moderate correlations are consistent with findings reported by Ma et al. (12), who showed an inverse relationship between WHtR and HDL in adolescents. Besides, the strong positive correlations between HC and NC (r=0.786) and HC and WC (r=0.823) suggest that generalized adiposity levels often change together across different body parts. Despite this, LASSO analyses identified NC and BMI percentile as independent predictors of MetS, with NC highlighting the crucial role of upper-body fat distribution in cardiometabolic risk assessment.

Free fatty acids and inflammatory mediators released from adipose tissue underlie the pathophysiology of these anthropometric-metabolic associations (14,16,23,29,33). Upper-body subcutaneous fat, as measured by NC, releases free fatty acids into the hepatic portal vein, worsening hepatic insulin resistance and dyslipidemia (14,16,32). Increased central adiposity (WC) promotes visceral fat accumulation, leading to metabolic dysfunction due to its lipolytic and pro-inflammatory effects (29,33). Autoimmune β-cell destruction, in addition to weight gain and sedentary behavior, causes insulin resistance in T1DM, fostering a milieu in which adiposity-driven inflammation amplifies metabolic disturbances (34). In the present study, significant correlations found between NC, WC, and TMI indicate the strong relationship between adipose tissue stores, necessitating comprehensive anthropometric assessment.

ROC analysis further illustrated the superior discriminative power of the WC Z-score (AUC=0.954) versus the NC Z-score (AUC=0.906). The optimal WC z-score threshold of 1.408 yielded 100% sensitivity and 80% specificity, whereas an NC z-score cutoff of 1.041 achieved 93.3% sensitivity and 80% specificity. The acceptable WC AUCs and moderate NC performance in predicting pediatric MetS, reported by Masquio et al. (13) and Formisano et al. (35), are consistent with our results but we achieved much improved performance after conversion to Z-scores. The rise in childhood obesity, particularly in insulin-treated children, suggests that combining NC and WC measurements and converting them to Z-scores could allow for early identification of at-risk individuals, leading to prompt lifestyle interventions (11,13,14,35).

Routine NC and WC measurements during pediatric endocrinology visits may be appropriate as they are relatively easy and simple to implement in clinical settings and, especially when converted to Z-scores, are useful for identifying T1DM children at heightened MetS risk. Given the identification of NC z-score as an independent predictor and WC's excellent AUC, incorporating both measures into screening protocols could optimize risk stratification before laboratory testing. Children surpassing NC or WC cut-offs could receive tailored counseling, such as dietary and physical activity promotion. Moreover, the observed but weak inverse correlation between HDL and anthropometric measures suggests that comprehensive cardiometabolic evaluations, including fasting lipid panels, may be appropriate in high-risk children. Collaborative, interdisciplinary teams (endocrinologists, dietitians, and exercise physiologists) will be important for integrating weight and cardiometabolic risk management into standard T1DM care, personalizing interventions to minimize obesity-related complications (34).

### Study Limitations

Several limitations must be acknowledged. Our cross-sectional design precludes causal inferences; longitudinal studies are needed to confirm whether elevated NC and WC predict incident MetS in T1DM children. Generalizability and statistical power may be limited by the small sample of 168, including just 15 (9%) MetS-positive participants. While LASSO regression promoted model parsimony through penalization, the model suffered from a lack of key variables, such as physical activity levels. Predictive models should be improved in future research by including objective activity measurements (like accelerometry). Despite standardization of NC and WC measurements, precision remained susceptible to intra- and inter-observer variability. It is also important to note that cut-off values for NC and WC might differ according to sex and pubertal status. Future studies should perform stratified analyses by sex and Tanner stage to refine these thresholds and to produce robust data for calculating Z-scores.

## Conclusion

Simple anthropometric indices, especially NC and WC, were found to be useful for screening for MetS in children with T1DM. The different metabolic processes in T1DM, such as weight

changes from insulin and autoimmune inflammation, suggest that adding NC and WC measurements to regular checkups may help identify children with a higher chance of cardiovascular problems earlier. Then lifestyle interventions, thorough lipid monitoring, and including weight management in T1DM treatment plans might reduce future cardiometabolic disease. Globally, rising childhood obesity rates among those with T1DM highlight the need for preventive strategies using simple and readily available anthropometric markers with the aim of improving long-term health for children with T1DM.

**Ethics**

**Ethics Committee Approval:** The study protocol was approved by the Gaziantep University Clinical Research Ethics Committee (approval no.: 2021/356, date: 03.11.2021).

**Informed Consent:** Written informed consent was obtained from all participants and their parents or guardians.

**Footnotes**

**AI Statement:** The authors used AI and AI-assisted Technologies (Grammarly and MS Word Editor) in the writing process. These technologies improved the readability and language of the work but did not replace key authoring tasks such as producing scientific or medical insights, drawing scientific conclusions, or providing clinical recommendations. The authors are ultimately responsible and accountable for the contents of the whole work.

**Authorship Contributions**

Concept: Ahmet Yıldırım, Design: Serpil Albayrak, Mehmet Keskin, Data Collection or Processing: Serpil Albayrak, Analysis or Interpretation: Murat Karaoğlan, Writing: Serpil Albayrak.

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**Supplementary Figure:** https://d2v96fxpocvxx.cloudfront.net/beb8919b-f013-4ea1-b1c8-40332e840fe1/content-images/02ae3f9a-00c5-49b5-bc71-c33b226aaf5a.pdf

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