

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

Albayrak S et al. Metabolic Syndrome in Type 1 DM Children

Serpil Albayrak, Murat Karaoglan, Mehmet Keskin, Ahmet Yildirim
Gaziantep University Faculty of Medicine, Department of Pediatric Endocrinology, Gaziantep, Türkiye

What is already known on this topic?

- Cardiovascular risk is increased by MetS in children with T1DM; however, further studies are needed to determine its prevalence and predictors among these children.
- NC shows promise as an anthropometric indicator of central obesity and metabolic risk in T1DM, but is not routinely used in T1DM care.

What this study adds?

- Based on IDF criteria, the study found MetS in 8.9% of children with T1DM.
- A strong correlation exists between NC, WC, and BMI; NC is an independent 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.

ABSTRACT

Objective: This study aimed 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—particularly neck circumference (NC) and waist circumference (WC)—in identifying MetS.

Methods: A total of 168 children (aged 6–18 years) with T1DM were included in this cross-sectional study. Anthropometric (NC, WC, BMI, TMI) and laboratory parameters (lipid profile, HbA1c) were recorded. MetS diagnosis was established according to the International Diabetes Federation (IDF) criteria. Receiver operating characteristic (ROC) curve analysis and LASSO regression were employed to identify key predictors.

Results: 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 revealed WC z-score had the highest discriminative power (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 NC showed a mild inverse correlation with HDL cholesterol.

Conclusion: NC and WC are simple, non-invasive, and reliable tools for early detection of MetS in pediatric T1DM patients. Their routine measurement could 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 (i.e., $NC z > 1.04$ or $WC z > 1.41$ as actionable thresholds).

Keywords: Anthropometric Measurements, Anthropometry, Metabolic Syndrome, Neck Circumference, Pediatric, Type 1 Diabetes Mellitu

Serpil Albayrak,
Gaziantep University Faculty of Medicine, Department of Pediatric Endocrinology, Gaziantep, Türkiye
drserpilalbayrak@gmail.com
0000-0003-3368-6451

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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 issues (1,2). Despite improvements in survival due to 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 diabetes mellitus (T2DM), cardiovascular disease (CVD), 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 impaired fasting glucose (1,2). The International Diabetes Federation (IDF) criteria are widely used in pediatrics because of pragmatic cutoff 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-based rates near 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, it 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 study data (14) revealed that NC levels in school-aged children correlated positively with fasting glucose, triglycerides, blood pressure, insulin, and HOMA-IR, but inversely with HDL (14). This data implies 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—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 stresses the importance of integrating simple, reliable physical measurements into routine healthcare for early detection and prompt intervention.

This study aimed to examine the connections between NC, WC, BMI, and MetS markers in Turkish children with T1DM. Our goal was to give clinicians easy-to-use, evidence-based tools for early cardiometabolic risk detection in children with T1DM by elucidating the contributions of various anthropometric measures to MetS risk stratification.

MATERIALS AND METHODS

Study Design and Population

The study, a cross-sectional one, 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 under the same IRB approval (Decision No: 356, 03.11.2021). The study included 168 participants, all of whom 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 6 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 in 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 HC in cm. All measurements were taken with the subjects standing upright, facing forward, and shoulders relaxed.

- **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 head in an upright position, with the eyes forward and the neck in a horizontal plane.

- **WC (cm):** Measured with a non-elastic 150 cm tape measure. The measurement is 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 it was 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 issues.

- **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 resting. Hypertension was identified when systolic or diastolic blood pressure exceeded the 95th percentile for age, sex, and height, based on international guidelines (21).

Height (cm), weight (kg), blood pressure and BMI standard deviation 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 <5th percentile
- Normal weight: BMI between the 5th and 85th percentiles
- Overweight: BMI between the 85th and 95th percentiles
- Obesity: BMI \geq 95th percentile

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

- **WHtR :** A WHtR \geq 0.5 was also considered a marker of central obesity, in line with guidelines.

3. MetS Diagnosis: According to IDF criteria (2), MetS diagnosis involved abdominal obesity (WC \geq 90th percentile) and at least two of these:

- Elevated triglycerides (TG) [\geq 150 milligram (mg)/deciliter (dL)]
- Low high-density lipoproteins (HDL) cholesterol (<40 mg/dL)
- Elevated blood pressure (above the 95th percentile for age, sex, and heights)
- Fasting glucose \geq 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 Analysis and others

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 from Beckman Coulter in Brea, CA, USA.

- **Fasting glucose and glycated hemoglobin (HbA1c) levels:** High-performance liquid chromatography (HPLC) is used to measure fasting glucose and HbA1c levels. Poor T1DM control was defined as HbA1c levels greater than 8% (22).

Dyslipidaemia was defined as one of the following (4): 1) TC >200 mg/dL, 2) TG \geq 100 mg/dL between the ages of 0-9 years, 3) TG: \geq 130 mg/dL between the ages of 10-19 years, 4) LDL \geq 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 dosage (expressed as units/kg/day), co-morbidities, and current therapeutic regimens.

Statistical Analysis

All data analysis was conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Based on their distribution, continuous variables were presented either as the mean with standard deviation (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, neck circumference (NC) and waist circumference (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:

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

The predictive value of both raw and standardized NC and WC measures for metabolic syndrome (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). Because of the 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: λ_{\min} , which minimizes cross-validated binomial deviance, and λ_{1SE} , the most parsimonious model within one standard error of the minimum. Variables included in the penalized model were age, sex, NC z-score, BMI percentile, and triglyceride levels. At λ_{\min} , NC z-score ($\beta = 0.589$) and BMI percentile ($\beta = 0.038$) 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%, Table 1). The mean age of participants was 12.5 ± 2.9 years, and the median T1DM duration was 4 years (0–15 years). Participants' mean NC and WC were 30.8 ± 3.2 cm and 68.6 ± 8.3 cm. The mean BMI (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 mg/dL (95–314); LDL cholesterol 108.5 mg/dL (47–214); HDL cholesterol 57.0 mg/dL (26–132); and TG 92.0 mg/dL (27–544). The IDF definition identified MetS in 15 (8.9%) of the sample.

Comparing Children with and without Metabolic Syndrome

Table 2 shows that children with MetS differed from those without. Median daily insulin dose was 0.94 (0.31 – 1.58) units/kg/day, with no significant difference between MetS and non-MetS groups ($p = 0.391$). MetS-positive children had significantly greater weight (43.0 vs. 55.6), BMI (18.7 vs. 22.7 kg/m^2), BMI SDS (-0.34 vs. 1.10), NC (30.5 vs. 33.1 cm), WC (67.6 vs. 78.6 cm), and HC (83.6 vs. 94.3 cm) than those without ($p < 0.050$ for all). HDL levels were significantly lower (51.0 mg/dL vs 58.0 mg/dL, $p = 0.038$) in MetS participants.

Anthropometric Measurement of Participants

Anthropometric variables and their connections with MetS are illustrated in Table 2. High 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 high NC (93.3%) compared to the non-MetS group (34%), a statistically significant difference ($p < 0.001$). Elevated WHtRs were also significantly associated with MetS ($p < 0.001$).

Correlations Between Anthropometric and Laboratory Variables

As Table 3 demonstrates, significant correlations were found between various anthropometric measures. Strong positive correlations between NC and WC ($r = 0.812$, $p < 0.001$), and NC and HC ($r = 0.786$, $p < 0.001$) show that NC effectively measures central obesity. Moderate 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 inversely correlated with NC ($r = -0.190$, $p = 0.015$), possibly suggesting higher NC is associated with less favorable lipid profiles.

ROC-Based Comparison of Neck and Waist Circumference Metrics in 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 cutoff 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 of 0.906 is reached by the NC z-score (SE = 0.032; $p < 0.001$; 95% CI: 0.854–0.959) at a threshold of 1.041, giving 93.3% sensitivity and 80.0% specificity, while the WC z-score achieves an AUC of 0.954 (SE = 0.019; $p < 0.001$; 95% CI: 0.915–0.992) at a 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. Because of the low number of outcome events, LASSO penalized logistic regression ($\alpha = 1$) was employed to prevent model overfitting. The model exhibiting optimal performance, identified via minimization of the penalty parameter (λ_{\min}), indicated that neck circumference z-score ($\beta = 0.589$) and BMI percentile ($\beta = 0.038$) 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, demonstrate superior predictive validity for MetS within this cohort compared to conventional demographic or biochemical markers. Supplemental Figure 1 provides further elucidation of these findings by illustrating the coefficient shrinkage path across λ values.

DISCUSSION

This research investigates the complex relationships among anthropometric measures, MetS, and laboratory findings in children with T1DM. Using IDF criteria, MetS was found in 8.9% of participants with T1DM. Anthropometric measures (NC, WC, HC, BMI, and TMI) and lipid profiles were significantly higher among participants with MetS. WC z-score showed the highest power to discriminate, followed by NC z-score, according to ROC analysis. NC z-score and BMI percentile as strong predictors of MetS. This study emphasizes the significance of straightforward anthropometric measures—mainly NC and WC—for detecting cardiometabolic risks in T1DM children.

Early identification and evaluation of MetS in individuals with T1DM is vital to stopping the development of both major and minor complications. Despite limited research, studies on MetS in T1DM patients indicate a variable incidence 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 obesity/overweight prevalence.

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. Additionally, chronic hyperglycemia and oxidative stress contribute to dyslipidemia and hypertension (9). These metabolic abnormalities are further complicated by diet/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 (coefficients at $\lambda_{\min} = 0.589$; at $\lambda_{1SE} = 0.296$) and BMI percentile (coefficients at $\lambda_{\min} = 0.038$; at $\lambda_{1SE} = 0.018$) emerged as a robust predictor (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—therefore showing disease processes BMI ignores (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 dyslipidemic and inflammatory processes. Lower HDL cholesterol was observed in MetS children in our study, aligning 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 HDL association highlights central adiposity's importance (33). These moderate correlations are consistent with Ma et al. (12), whose findings showed an inverse relationship between WHtR and HDL in adolescents. Besides, the strong 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, underscoring 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 behaviors, 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 WC z score's superior discriminative power ($AUC = 0.954$) versus the NC z score ($AUC = 0.906$). The optimal WC z-score threshold of 0.10 yielded 73.3% sensitivity and 74.2% specificity, whereas an NC z-score cutoff of 0.12 achieved 80% sensitivity but only 54% specificity. The acceptable WC AUCs and moderate NC performance in predicting pediatric MetS, reported by Masquio (13) and Formisano (35), are consistent with our results. The rise in childhood obesity, particularly in insulin-treated children, suggests that combining NC and WC measurements 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 are clinically advocated by these results to identify T1DM children at heightened MetS risk. Given Lasso's 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 guidelines could receive tailored counseling, such as dietary and physical activity promotion. Moreover, the observed inverse correlation between HDL and anthropometric measures suggests that comprehensive cardiometabolic evaluations, like fasting lipid panels, are necessary for high-risk children. Collaborative, interdisciplinary teams (endocrinologists, dietitians, and exercise physiologists) are vital in integrating weight and cardiometabolic risk management into standard T1DM care, personalizing interventions to minimize obesity-related complications (34). 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 threshold

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 MetS-positive participants. While Lasso regression promotes 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 threshold.

CONCLUSION

Simple anthropometric indices, especially NC and WC, are shown by our study 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, mean that adding NC and WC measurements to regular checkups may help spot children with a higher chance of cardiovascular problems sooner. Early 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 readily available anthropometric markers to improve long-term health.

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	Total (n=168) n (%)		Total (n=168) n (%)
Age*	12.5 ± 2.9	Mets (based on IDF) No Yes	153 (91.1) 15 (8.9)
Sex Female Male	84 (50) 84 (50)	NC (cm)*	30.8 ± 3.2
T1DM duration (years)	4.0 (0-15)	NC classification † Normal High	96 (57.1) 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 High	143 (85.1) 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/m ³)*	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/m ²)*	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 Normal Overweight Obese	21 (12.5) 122 (72.6) 21 (12.5) 4 (2.4)	Puberty No Pubertal	100 (59.5) 68 (40.5)

Notes: Numeric variables were presented as median (minimum-maximum) or mean ± SD. † NC measurements could not be made in 4 patients in the MetS negative group.
BMI and TMI are calculated as weight in kilograms divided by height in meters squared and weight in kilograms divided by height in meters cubed, respectively.
Abbreviation: 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.

	Based on the IDF		
	MetS (-) n (%), n=153	MetS (+) n (%), n=15	p value
Age (years)*	12.6 ± 2.9	11.9 ± 2.8	0.363
Sex Female Male	75 (49.0) 78 (51.0)	9 (15.0) 6 (40.0)	0.416

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
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 [‡]			<0.001
Normal	95 (62.1)	1 (6.7)	14 (93.3)
High	52 (34.0)		
WC (cm)*	67.6 ± 7.6	78.6 ± 9.2	<0.001
WC classification			
Normal	143 (93.5)	0 (0.0)	<0.001
High	10 (6.5)	15 (100.0)	
HC (cm)*	83.6 ± 11.0	94.3 ± 11.4	<0.001
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*
High	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
High	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

Puberty			
No	91 (59.5)	9 (60.0)	0.969
Pubertal	62 (40.5)	6 (40.0)	

Notes: Numeric variables were presented as median (minimum-maximum) or mean \pm SD. * NC measurements could not be made in 4 patients in the MetS negative group.
BMI and TMI are calculated as weight in kilograms divided by height in meters squared and weight in kilograms divided by height in meters triplet, respectively.
The analysis of data showing normal distribution was done with independent sample t test, and those not showing normal distribution were done with Mann Whitney U.
Abbreviations: 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.

Table 3. Correlation analysis of anthropometric measurements and laboratory values

	NC (cm)	WC (cm)	HC (cm)	WHR	WHR	TMI (kg/m ³)	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/m ³)	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

Abbreviations: cm: centimeter, dL: deciliter; HbA1c: glycated hemoglobin, HC: Hip Circumference, HDL: High-density lipoproteins, kg: kilogram, IDF: International Diabetes Federation, mg: milligram, NC: Neck Circumference, TMI: Tri-Ponderal Mass Index, WC: Waist Circumference, WHR: Waist to hip ratio, 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 Cutoff	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

Abbreviations: AUC: Area Under the Curve, CI: Confidence Intervals, MetS: metabolic syndrome, NC: Neck Circumference, WC: Waist Circumference.

Table 5. Multivariate Lasso Regression Analysis of Risk Factors Associated with Metabolic Syndrome in children with Type 1 Diabetes Mellitus

Variable	Coefficient at λ_{min}	Coefficient at λ_{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

Abbreviations: BMI: Body Mass Index, CI, confidence interval, dL: deciliter; mg: milligram, F: female, M: male, NC: Neck Circumference, OR: odds ratio, TG: Triglyceride

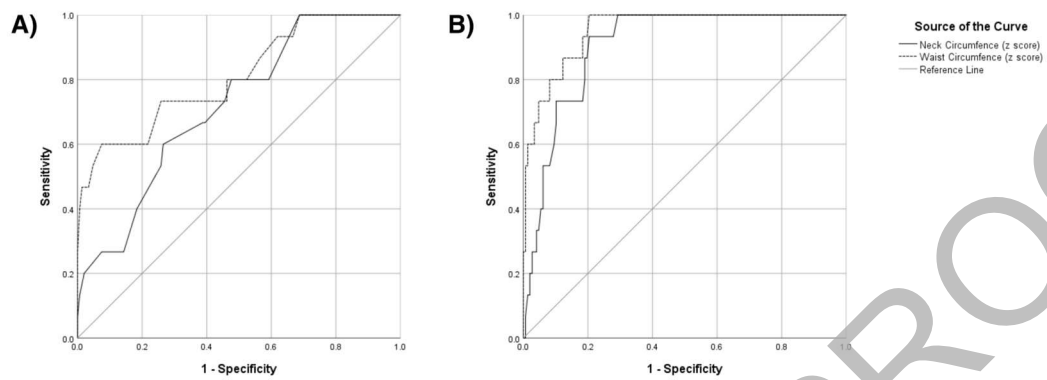


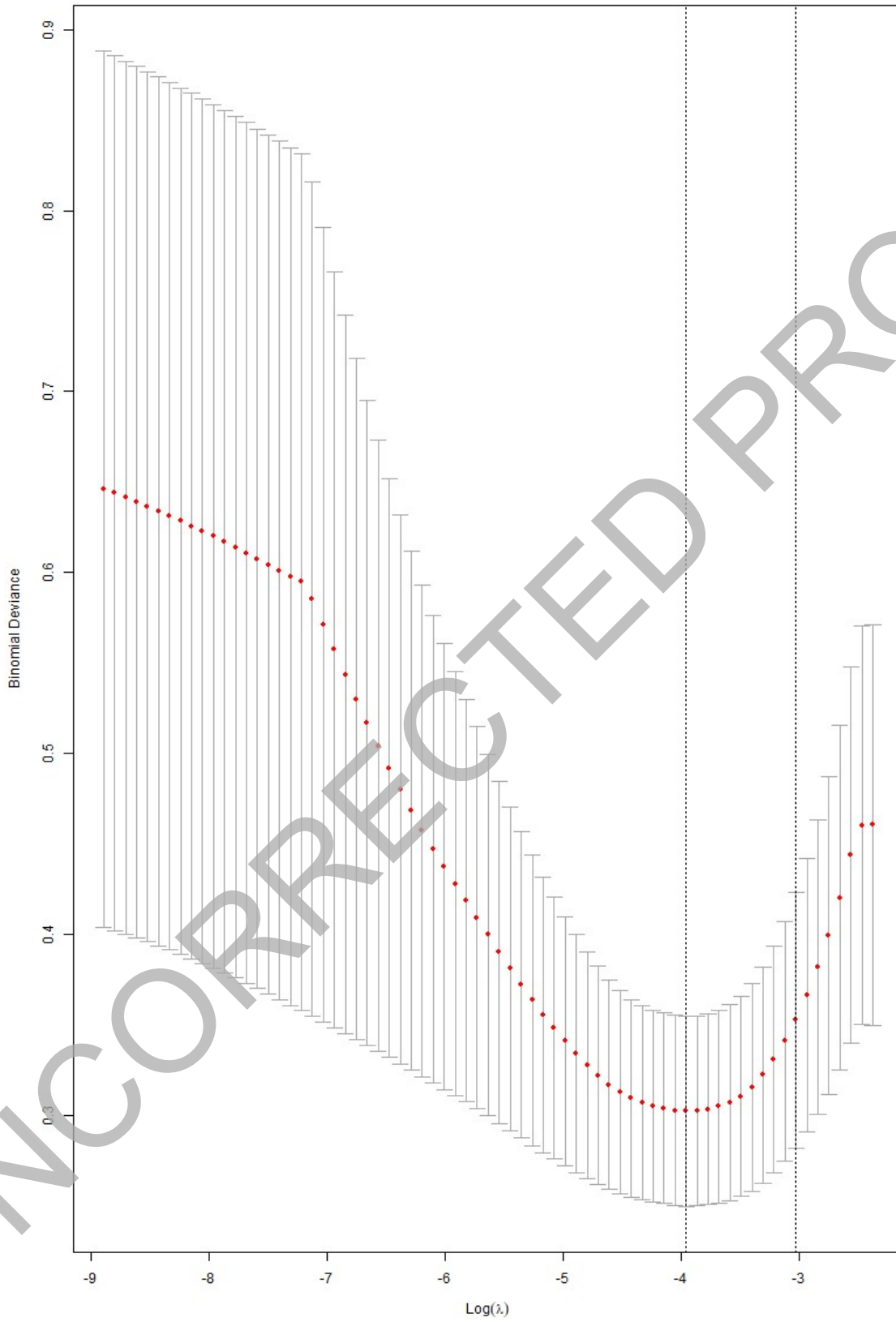
Figure 1. ROC analysis of the NC, WC, NC (z score), and WC (z score)

(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.

5 4 4 4 3 3 3 2 2 2 2 2 2 2 2 0



Supplement Figure 1. LASSO Cross-Validation Curve: Binomial Deviance vs $\text{Log}(\lambda)$