UTILITY OF ESTIMATED GLUCOSE DISPOSAL RATE AND FAT MASS PERCENTAGE FOR PREDICTING METABOLIC SYNDROME IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES

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Introduction and Objectives

Today, the leading cause of death in patients with type 1 diabetes (T1D), as in T2D, are reported to be cardiovascular diseases associated with obesity and metabolic syndrome (MetS). But, there is no study that reports the prevalence of obesity and MetS in children and adolescents with T1D in Turkey. The methods used for T2D population to determine insulin resistance (IR) that plays a key role in the pathophysiology of MetS are invalid for the patients with T1D, which is characterized by absolute absence of insulin. Estimated glucose disposal rate (eGDR) is a formula developed by the euglycemic hyperinsulinemic clamp method and used to determine IR in the patients with T1D. Therefore, the objectives of our study were to determine the prevalence and related factors of obesity and MetS in our T1D cohort and to evaluate the clinical utility of eGDR and body fat mass percentage (fat%) for predicting MetS.

Methods

Patients: We conducted a descriptive, cross sectional study including a total of 200 patients (52% male) between 8-18 years of age. All patients were followed at least six months with the diagnosis of T1D. Clinical and laboratory data were obtained from medical records of patients.

Measures: The patients' height, weight and waist circumference (WC) were measured and body mass index (BMI) was calculated. BMI between 85-94 percentile and ≥95th percentile were defined as overweight and obesity, respectively. Modified criteria of IDF, WHO and NCEP were used to determine the prevalence of MetS. A fat% was measured by bioelectrical impedance analysis (BIA). eGDR, of which the lower values indicate IR, was calculated in two separate formula using presence of hypertension (HT), HbA1c and WC, or waist-hip ratio (WHR):

$eGDR_{WC}$ = 21,158- (0,090xWC)-(3,407xHT)- (0,551xHbA1c)

$eGDR_{WHR}$ = 24,31- (12,22xWHR)- (3,29x HT)- (0,57XHbA1c)

Statistical analysis: According to the IDF criteria, the patients were divided into two subgroups with and without MetS. eGDR and %fat cut off values were determined by ROC analysis. For the diagnostic accuracy of the cut off values, sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios (LR) were calculated using cross table statistics. Diagnostic odds ratio (DOR) was calculated in order to compare the diagnostic effectiveness of evaluation methods by the formula shown in equation.

DOR = Positive LR / Negative LR

Results

The characteristics of the 200 patients with T1D are presented in Table 1. Of the cohort, 9.5% were overweight and 8.5% were obese. In whole group, MetS prevalence were %10,5, %8,5, %13,5 according to IDF, WHO and NCEP criteria, respectively. There were no statistically significant difference in age, gender, family history of T2D, pubertal stage, duration of diabetes, A1c levels and daily insulin doses between patients with or without MetS. LDL-cholesterol and triglyceride concentrations are higher in patients with than without MetS (p<0,001) (Table 2). As compared to the patients without MetS, the patients with MetS had lower values of $eGDR_{WC}$ and $eGDR_{WHR}$ [6.4 ± 2.2 vs. 9.5 ± 1.3 mg/kg/min and 6.7 ± 1.8 vs. 10.2 ± 1.2 mg/kg/min, respectively (p<0,001)]. Fat mass percentage was significantly higher in the MetS group (29.7±7.8%) than in the other group (21.3±7.9%) (p<0,001). ROC analysis results are presented in Table 3. While the measurement of fat% has the lowest statistical power, the statistical analyses of the two methods of eGDR did not show superiority to each other. Upon this, diagnostic efficacy was assessed by DOR. DOR of $eGDR_{WC}$ [37.7 (10.8 to 140.8)] was higher than that of $eGDR_{WHR}$ [28.6 (7.3 to 131.0)].

Conclusion

Overweight and obesity prevalence of our group with T1D was similar in the population of same age group in our country, but prevalence of MetS is higher than the community. Except the components of metabolic syndrome, the other clinical and laboratory parameters were not helpful for predicting metabolic syndrome. Compared with other clinical variables, eGDR is a good indicator for diagnosing MetS. Our study supports the utility of eGDR for predicting the diagnosis of MetS in children and adolescents with T1D as a simple and practical method. BIA measurement is time consuming, causes additional costs and a weaker process for diagnosis . $eGDR_{WC}$ seems more convenient to use because only WC measurement is sufficient for the formula and DOR is higher than $eGDR_{WHR}$. The 8,16 cut off value of $eGDR_{WC}$ has a higher specificity and negative predictive value for ruling out diagnosis of MetS so it seems more useful in clinical practice.

Table 1. General Characteristics of the study group (n=200)

Age, years	13,81±2,81
Gender: Boys, n (%)	104 (52)
Pubertal stage: Tanner II-V, n (%)	174 (87)
Family History	
type 1 diabetes, n (%)	35 (17.5)
type 2 diabetes, n (%)	88 (44.0)
Duration of diabetes, months	55,20±39,79
Daily insulin dosage, IU/kg/day	0.87±0,26
HbA1c, %	8.40±1.63
BMI z-score	0.02±1.16
Waist Circumference z-score	0.48±1.10
Obesity, n (%)	17 (8.5)
Overweight, n (%)	19 (9.5)
Fat mass percentage, %	22.14±8.34
$eGDR_{WHR,}$ mg/kg/min	9.17±1.69
$eGDR_{WC,}$ mg/kg/min	9.80±1.75

Table 2 Anthropometric. clinic and laboratory features of T1D patients with or without metabolic syndrome

	With MetS (n:21)	Without MetS (n:179)	P
Age, years	13.75±3.28	13.82±2.76	0.995
Weight, kg	63.44±18.53	48.81±12.6	<0.001
Weight, z-score	1.37±0.77	-0.4±1.07	<0.001
Height, cm	158.5±16.7	154.5±14.4	0.126
Height, z-score	0.33±0.82	-0.52±1.21	0.001
BMI, kg/m^2	24.69±3.64	20.11±3.18	<0.001
BMI z score	1.34±0.84	-0.13±1.1	<0.001
Waist circumference (cm)	82.88±10.78	67.97±7.73	<0.001
Waist circumference SDS	2.16±0.6	0.29±0.97	<0.001
Fat mass percentage (%)	29.7±7.8	21.3±7.9	<0.001
Gender			
Boys	10 (47.6)	94 (52.5)	0.671
Girls	11 (52.4)	85 (47.5)	0.488
Pubertal Stage			
Prepubertal	4 (19)	22 (12.3)	1
Pubertal	17 (81)	157 (87.5)	0.081
Family History			
T1D	3 (14.3)	32 (17.9)	0.076
T2D	13 (61.9)	75 (41.8)	0.054
Level of metabolic control (HbA1c %)			
Good (≤7.5)	4 (19)	49 (27.4)	0.684
Moderate (7.5-9.0)	8 (38.1)	66 (36.9)	0.758
Poor (≥9.0)	9 (42.9)	64 (35.8)	1.000
Acantozis Nigricans	5 (23.8)	6 (3.4)	0.002
Prehypertension	2 (9.5)	5 (2.8)	<0.001
Hypertension	14 (66.7)	10 (5.6)	<0.001
Dyslipidemia	12 (21.1)	45 (78.9)	0.004
Microalbuminuria	-	8 (4.5)	1.0000
Duration of diabetes (month)	57.33±45.82	54.95±39.16	0.949
Daily insülin dose (U/kg/day)	0.86±0.25	0.88±0.27	0.932
HbA1c (%)			
Last one year	8.87±1.45	8.59±1.51	0.374
Last control	8.59±1.55	8.38±1.65	0.439
Lipid Profile			
Trig (mg/dL)	130.1±60.4	85.16±42.02	<0.001
HDL-ch (mg/dL)	55.36±15.43	62.13±15.61	0.050
LDL-ch (mg/dL)	106.22±20.35	77.02±24.67	<0.001
eGDR			
Waist/hip ratio	6.41±1.87	9.5±1.34	<0.001
Waist circumference	6.7±2.25	10.17±1.26	

Table-3: ROC analysis

	$eGDR_{WHR}$	$eGDR_{WC}$	%fat
Area Under the Curve (AUC)	0,906757	0,908885	0,779064
P	<0,0001	<0,0001	<0,0001
Youden İndeks J	0,6840	0,6837	0,5608
Cut-off	**≤ 8,44**	**≤ 8,16**	**>27,9**
Sensitivity [%95 CI]	85,71 [63,7-97,0]	76,19 [52,8-91,8]	76,19 [52,8-91,8]
Specificity [%95 CI]	82,68 [76,3-87,9]	92,18 [87,2-95,7]	79,89 [73,3-85,5]
Positive Likelihood Ratio [%95 CI]	4,95 [3,4-7,1]	9,74 [5,6-17,0]	3,79 [2,6-5,5]
Negative Likelihood Ratio [%95 CI]	0,17 [0,06-0,5]	0,26 [0,1-0,6]	0,3 [0,1-0,6]
Positive Predictive Value [%95 CI]	36,7 [23,4-51,7]	53,3 [34,3-71,7]	30,8 [18,7-45,1]
Negative Predictive Value [%95 CI]	98 [94,3-99,6]	97,1 [93,3-99,0]	96,6 [92,3 -98,9]
Diagnostic Odds Ratio [%95 CI]	28.6 [7.3 -131.0]	37.7 [10.8 -140.8]	12.6 [3.7-52.4]

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