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A New Insulin Sensitivity Index Derived From Fat Mass Index and Quantitative Insulin Sensitivity Check Index

Yağ Kütle ve Kantitatif İnsulin Sensitivite Kontrol İndekslerinden Türetilmiş Yeni Bir İnsulin Sensitivite İndeksi

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Abstract

Aim

Obesity has recently become one of the most important health problems throughout the world. This fact led to the controversies on the clinical use of insulin sensitivity indices. Indices previously described or introduced in this study have been evaluated to choose one, which is capable of exhibiting significant distinctions between healthy children and those involved in the classes of childhood obesity.

Material and Methods

A total of 179 girls; 81 morbidly obese(MO), 42 obese(O), 16 overweight(OW) and 40 normal(N) participated in the study. Groups were constituted based upon age- and sex-specific body mass index percentiles tabulated by World Health Organization. Homeostasis Model Assessment of Insulin Resistance(HOMA-IR), HOMA-IR/BMI, log HOMA-IR, fasting glucose/fasting insulin ratio(FGIR), quantitative insulin sensitivity check index(QUICKI), Raynaud, reciprocal insulin indices and also new indices HOMA-IR*BMI, HOMA-IR*fat mass index(FMI), QUICKI*BMI, QUICKI*FMI were calculated. The cut-offs 3.16 and 2.5 for HOMA-IR, 7 and 6 for FGIR, 0.357 and 0.328 for QUICKI were evaluated to estimate insulin resistance. Statistical analyses were performed with Predictive Analytics SoftWare(PASW) Statistics 18.

Results and Conclusion

QUICKI*FMI was able to make a clear-cut separation between the groups. A new trilogy for cut-offs (HOMA>2.5, FGIR<7, QUICKI<0.328); each giving the similar results, has been suggested. Multifaceted character of QUICKI was also introduced. QUICKI was capable of discriminating MO from O when 0.328 cut-off was used, and O from OW when 0.357 cut-off was used. QUICKI*FMI index, a new one, was unique in detecting the advanced level of differences($p \leq 0.005$) between N-OW, OW-O and O-MO groups during childhood obesity.

Key words: Obesity, childhood, insulin sensitivity index

Özet

Amaç

Obezite, dünya çapında en önemli sağlık sorunlarından biridir. Bu gerçek, insülin sensitivite indekslerinin klinik kullanımı konusunda tartışmalara yol açmaktadır. Sağlıklı çocuklar ve çocukluk çağı obezitesi gruplarına dahil olanlar arasındaki belirgin farklılıkları ortaya koyabilen bir indeksin seçilebilmesi amacıyla bu çalışmada ortaya konmuş ya da daha önce tanımlanmış indeksler değerlendirildi.

Materyal ve Metod

81 morbid obez (MO), 42 obez (O), 16 kilolu (OW) and 40 normal (N) toplam 179 kız çocuk çalışma kapsamında değerlendirildi. Gruplar, Dünya Sağlık Örgütü tarafından belirlenen yaş- ve cinsiyet- parametrelerine dayalı olarak hesaplanmış vücut kitle indeksi persentillerine göre oluşturuldu. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), HOMA-IR/BMI, log HOMA-IR, fasting glucose/fasting insulin ratio (FGIR), quantitative insulin sensitivity check index (QUICKI), Raynaud, reciprocal insulin indeksleri ve yeni geliştirilen HOMA-IR*BMI, HOMA-IR*fat mass index(FMI), QUICKI*BMI, QUICKI*FMI indekslerine ilişkin değerler hesaplandı. İnsülin direncinin belirlenmesi için 3.16 ve 2.5 (HOMA-IR), 7 ve 6 (FGIR), 0.357 ve 0.328 (QUICKI) cut-off değerleri esas alındı. İstatistiksel analizler Predictive Analytics SoftWare (PASW) Statistics 18 ile gerçekleştirildi.

Bulgular ve Sonuç

QUICKI*FMI nın gruplar arasında kesin ayırım yapabilen bir indeks olduğu saptandı. Cut-off değerleri ile ilgili olarak, her biri benzer sonuçlar verebilen yeni bir üçlü (HOMA>2.5, FGIR<7, QUICKI<0.328) ortaya kondu. QUICKI nin çok yönlü özelliği gözlendi. QUICKI nin, 0.328 cut-off noktası kullanıldığında MO i O den, 0.357 cut-off noktası kullanıldığında ise O i OW den ayırt edebildiği belirlendi. QUICKI*FMI indeksinin, çocukluk çağı obezitesi bağlamında N-OW, OW-O ve O-MO gruplar arasındaki farklılıkların ileri düzeyde ($p \leq 0.005$) tanımlanmasında eşsiz bir indeks olduğu sonucuna varıldı.

Anahtar kelimeler: Obezite, çocukluk çağı, insulin sensitivite indeksi

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Introduction

Obesity has recently become one of the most important health problems with a high prevalence in both developed and developing countries[1]. World Health Organization (WHO) reports that childhood overweight and obesity are on the rise[2]. Childhood obesity has more than doubled in children and tripled in adolescents in the past 30 years[3,4]. There are increasing data related to the fact that obesity must be prevented to be able to avoid chronic diseases. The most significant health consequences of childhood overweight and obesity include diabetes, metabolic syndrome, certain types of cancer, cardiovascular diseases, which take the first place among the causes of death worldwide, and musculoskeletal disorders such as osteoarthritis[2,5,6]. The money spent for the treatment of such chronic diseases and the medicines consumed so much, unfortunately, have not been sufficient to be able to reach the desired well-being target.

Insulin resistance (IR) has a key role in metabolic changes in overweight and obese children[7]. It constitutes a link between obesity and the associated disease risk. Insulin sensitivity (IS) may pose an important target to regulate neural responses to food cues in the prevention of excessive weight gain[8].

The gold standard method for measuring IS is the hyperinsulinemic-euglycemic clamp (HEC) test[9]. It measures IS in a controlled, fixed state at a given insulin concentration, and reflects mainly the peripheral aspects of IS. Frequently-sampled intravenous glucose tolerance test (FSIVGTT) is an alternative procedure to the clamp technique. However, both are invasive and impractical. Fasting indices have the advantage of simplicity and they reflect IS in a fasting steady-state predominantly determined by hepatic IS. It is strongly suggested that fasting-derived indices provide a valid assessment of IS in youth[10].

Most of the information about ISI indices is derived from studies on the adult population. It has been focused on the parameters e.g. weight, height, body mass index (BMI), IR for the evaluation of obesity in children and for this purpose, various simple fasting-based IS indices, which may help the pediatrician identify patients at risk of developing IR have been taken into consideration. The importance of this health problem has led to the diversity and controversies on the availability and clinical use of these indices[11]. For example, homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI) are commonly used proxy measures for IS[12-14]. Despite this knowledge, comparisons between the methods continue[11,14]. The aim of this study is to evaluate a total of eleven different IS indices; seven previously described as well as four introduced in this study to be able to choose the best informing about the clear-cut distinctions between the classes of the childhood obesity as well as normal. In this study, we tried to put a stop to the ambiguity on the use of IS indices, to enable the comparability of the studies by simply using one index, which is capable of exhibiting statistically significant distinctions between normal and overweight, overweight and obese as well as obese and morbid obese groups of children and finally, to contribute to the preventive measures related to obesity during childhood.

Materials and Methods

Patients:

A total of 179 girls aged 06-18 years; 81 morbidly obese (MO) (Group I), 42 obese (O) (Group II), 16 overweight (OW) (Group III) and 40 normal (N) (Group IV), who were admitted with feeding problems to Namik Kemal University, Faculty of Medicine, Department of Practice and Research Hospital, Clinics of Pediatrics, participated in this study. Participants were screened by history, physical exam, and routine hematological and biochemical tests. Groups were constituted based upon age and sex-specific BMI percentiles tabulated by WHO[15]. Children, whose percentiles are >99th were grouped as MO, those between the 99-95th percentiles were considered O, those between the 95-85th percenttiles were considered OW and those between 85-15th percentiles were considered N.

Children with chronic disorders of especially gastrointestinal tract, cardiovascular, respiratory, renal, hepatic, neurologic/neuromuscular, hematological, immunelogical and endocrine systems, children with growth retardation and children using regular drug due to a chronic disease were excluded from the study.

Study protocol was approved by The Ethics Committee of Namik Kemal University, Faculty of Medicine. Informed consent forms were obtained from the parents prior to the study. Procedures were carried out in accordance with Declaration of Helsinki.

Measurements:

Each child was anthropometrically measured following the physical examination and a detailed history taken from the parents. Head circumference (C), neck C, mid-Cs of left and right upper and lower limbs and ankle C of each child were measured in addition to weight, height, waist C and hip C. Shoeless children with thin issued clothing were measured for their weights by an electronic weighing instrument sensitive to 0.1 kg intervals. Shoeless children were measured for their heights by a portable stadiometer designed in 0.1 cm intervals, in a position that child looks at completely in the horizontal plane and in a position that her occiput, back, hip and heels are in contact with the vertical posterior plane. Measurements were performed by a flexible, non-elastic tape. All the measurements were carried out by pediatricians. Each measurement was taken twice and the mean was recorded.

After the measurements and the routine laboratory tests including fasting blood glucose and insulin analyses, each girl was sent to the diet clinic. Following the evaluation of the girls, nutrition and physical activity recommendations as well as treatment regimens were given. No specific protocol was required. Consecutive fasting samples were taken and glucose and insulin concentrations were measured.

Fasting blood glucose levels were measured by spectrophotometric hexokinase assay, fasting insulin values were detected by electrochemiluminescence immunoassay (ECLIA).

Measurements of body fat were performed following the detailed nutritional evaluation of the children. The analyses of the body fat were performed by TANITA ® “MC 980 multi frequency segmental body composition analysis” (bio-electrical impedance analysis-BIA). Then, follow-up monitoring was undertaken at regular intervals.

Ratio calculations:

Anamnesis, physical examinations, anthropometric measurements, biochemical values and body fat ratios of the girls participated in the study were evaluated. BMI [body weight (kg)/height (m) * height (m)] was calculated for each patient. In order to evaluate body fat amount and BMI groups together, upper, lower extremities and trunk fat ratio, whole body fat ratio [total body fat (kg)/body weight (kg)], fat mass index (FMI) [total body fat (kg)/height (m) * height (m)], trunk to appendicular fat ratio [trunk fat (kg)/upper + lower extremities fat (kg) ratio] were calculated.

Insulin sensitivity indices and insulin resistance:

The following IS indices were calculated using fasting plasma glucose and insulin values:

Homeostasis Model Assessment of Insulin Resistance [HOMA-IR= fasting glucose (mg/dL)* fasting insulin (μIU/ml)/ 22,5*0,0555)][12], fasting glucose/fasting insulin ratio (FGIR) [(fasting glucose(mg/dL)/fasting insulin (mU/L) [16], quantitative insulin sensitivity check index {QUICKI=1/[log (fasting insulin(μIU/ml)+log (fasting glucose(mg/dL)]} [13] were calculated accordingly.

The formulae used to calculate Raynaud index[17] and reciprocal insulin index[18] were described as [40/Fasting insulin (mU/L)] and [1/ Fasting insulin (mU/L)], respectively. HOMA/BMI, log HOMA-IR, HOMA-IR*BMI, HOMA-IR*FMI, QUICKI*BMI and QUICKI*FMI values were also added to the list.

To estimate IR, the cut-offs 3.16, 7, and 0.357 were used for HOMA-IR, FGIR, and QUCKI, respectively [19-21]. IR was also evaluated according to the second set of criteria; HOMA-IR>2.5, FGIR<6, QUICKI<0.328 [22-25].

Statistical evaluation:

All statistical analyses were performed with Statistical Package for Social Sciences (SPSS) [Predictive Analytics SoftWare (PASW) Version 18] for Windows statistical package program. Variance analysis (ANOVA) was used to determine the differences between the groups. Post Hoc Tests Multiple Comparisons Tukey HSD test was used to compare the binary groups. Also Kruskall-Wallis variance analysis was used in case normality could not be maintained. A p value less than 0.05 was considered statistically significant.

Results

Based upon age and gender characteristics tabulated by WHO, 45.3%, 23.5%, 8.9% and 22.3% of 179 girls were identified as MO, O, OW and N, respectively. Mean age ± standard deviation (SD) calculated for MO group was 10.9 ± 3.0 year (yr). Corresponding values for O, OW and N groups were 11.9 ± 2.2 yr, 10.8 ± 2.7 yr, and 8.9 ± 1.9 yr. There were no statistically significant differences between the groups ($p \geq 0.05$).

Physical and metabolic characteristics of the study population (n=179) were tabulated in Table I and Table II, respectively.

In Table I, there were statistically significant differences among four groups for Ponderal indices at birth as well as BMIs ($p \leq 0.05$), and even more remarkably, for fat mass indices (FMIs) ($p \leq 0.001$). There were also tendency to increase towards OW, O and MO groups in comparison with N in terms of parental BMI values. The differences among the four groups were not significant for age, parental ages, breast feeding, formula feeding, fast food consumption, television (TV)/personal computer (PC)/play station (PS), outdoor activities. However, it was interesting to note

that fast food consumption in normal weight children almost doubled in the weekly diets of MO children. On the contrary, durations of TV/PC/PS use subtracted from outdoor activities greatly increased (more than double) in MO children when compared to those in N group (1.6 *vs* 3.6 hours). Differences among the groups in terms of waist, hip, head and neck circumferences as well as fat percentages of trunk, upper, lower extremities were statistically significant ($p \leq 0.001$). Differences in terms of hip, head and neck circumferences between MO and O groups were not significant. Waist circumference was the only parameter, which significantly differs between MO and O groups. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) values among the groups were significantly different ($p \leq 0.001$). Blood pressures showed a progressive increase starting from N to MO children. However, only blood pressures in N group differed from those measured in O and MO groups. There were no statistically significant difference between MO-O, O-OW and OW-N.

Upon evaluation of the lipid fractions in Table II, any significant difference was not detected among the groups for total cholesterol and low density lipoprotein (LDL)-cholesterol. However, it was interesting to observe statistically significant differences for triglycerides ($p \leq 0.05$) as well as high density lipoprotein (HDL) cholesterol ($p \leq 0.001$), which are the determinants of metabolic syndrome. Fasting insulin levels differed significantly among the groups ($p \leq 0.001$) and particularly between MO-O ($p \leq 0.05$), as well as N-O and MO ($p \leq 0.001$). Fasting glucose, glycated hemoglobin values of the groups were similar. Almost twice the values of C-reactive protein (CRP) observed in O, OW and N groups were detected in MO children. This suggested that inflammation started during this stage.

The values for the laboratory indices of the groups were shown in Table III.

Two sets of cut-offs were evaluated. As far as the values calculated for the first set (HOMA>3.16, FGIR<7, QUICKI<0.357) were evaluated, the percentage of cases that fulfill the criterias were 35.8 %, 42 % and 63% in MO group, 19.1 %, 26.2 % and 62 % in O group, 18.8%, 25% and 43.8% in OW group, 2.5%, 5%, 7.5% in N group, respectively. The corresponding values obtained for the second set (HOMA>2.5, FGIR<6, QUICKI<0.328) were calculated as 44.4%, 37%, 43.2% in MO group, 28.6%, 19%, 26.2% in O group, and 25%, 19%, 25% in OW group, 2.5%, 5%, 2.5% in N group.

HOMA-IR/BMI ratio was capable of differentiating only the MO and N groups ($p \leq 0.05$). There were no statistically significant differences between MO-O, O-OW and OW-N ($p \geq 0.05$). Therefore, it was concluded that a much more sensitive index was needed for a better discrimination.

Statistically significant differences were detected between MO-N ($p \leq 0.01$) as well as O-N ($p \leq 0.05$) upon examination of HOMA-IR index. For this reason, this was more preferable than the previous ratio. Actually, ever-increasing values were observed between N-OW, OW-O and O-MO groups, however, due to the high SD values, the differences between these groups were not significant ($p \geq 0.05$). The mean HOMA-IR index value calculated for MO group was found as 2.87, which is above 2.5; the critical threshold.

A statistically significant difference was detected with both log HOMA-IR and FGIR between N-OW groups (p≤0.05). The differences between MO-O as well as O-OW appeared as if they were significant, however, high SD values prevented their statistical significance. Also, statistically significant differences were noted between N-O (p≤0.01), N-MO (p≤0.01) and OW-MO (p≤0.05).

Much more meaningful differences were observed with Raynaud and reciprocal insulin indices when they are compared with those obtained with log HOMA-IR and FGIR indices. High SD values also interfered with the statistically significance levels. Statistically significant differences were detected between OW-MO (p≤0.05), N-OW (p≤0.01), N-O (p≤0.01) and N-MO (p≤0.01).

The results obtained with QUICKI index were the same as those obtained with Raynaud and reciprocal insulin indices. However, QUICKI was more preferable than the other two because of relatively low SD values.

Table I. Physical characteristics of the study population (n=179)

Physical characteristics	Morbid Obese Mean ± SE	Obese Mean ± SE	Overweight Mean ± SE	Normal Mean ± SE	p value
Age (years)	10.9 ± 0.3	11.8 ± 0.3	10.7 ± 0.6	9.0 ± 0.3	p≥0.05
Mother age (years)	36.6 ± 0.7	38.4 ± 0.7	35.6 ± 1.4	35.6 ± 0.8	p≥0.05
Father age (years)	40.3 ± 0.6	41.9 ± 0.8	40.1 ± 1.5	39.5 ± 0.8	p≥0.05
Birth weight (g)	3342 ± 56	3452 ± 95	3268 ± 183	3085 ± 119	p≤0.01
Ponderal index (g/cm^3)	2.7 ± 0.1	2.7 ± 0.1	2.8 ±0.1	2.6 ± 0.1	p≤0.05
BMI (kg/m^2)	29.1 ± 0.6	25.2 ± 0.4	21.2 ± 0.6	15.5 ± 0.2	p≤0.05
BMI category, n (%)	81 (45.3)	42 (23.5)	16 (8.9)	40 (22.3)	
Mother BMI (kg/m^2)	35.0 ± 3.8	28.4 ± 1.0	27.0 ± 1.4	27.7 ± 1.0	p≤0.05
Father BMI (kg/m^2)	32.1 ± 2.6	34.6 ± 6.3	29.3 ± 2.2	25.3 ± 0.6	p≤0.05
Breast feeding (months)	11.7 ± 1.1	12.1 ± 1.5	10.8 ± 2.5	14.9 ± 1.6	p≥0.05
Formula feeding (months)	3.7 ± 0.7	4.7 ± 1.2	6.8 ± 2.0	4.7 ± 1.1	p≥0.05
Fast food (portion/week)	10.3 ± 1.0	8.8 ± 1.1	6.5 ± 1.1	5.8 ± 0.8	p≥0.05
TV/PC/PS (hours/day)	4.4 ± 1.3	3.5 ± 0.4	3.7 ± 0.4	2.9 ± 0.3	p≥0.05
Outdoor activity (minutes/day)	46.6 ± 7.4	49.0 ± 10.4	71.9 ± 16.8	78.4 ± 12.8	p≥0.05
Waist circumference (cm)	89.5 ± 1.7	82.7 ± 1.2	72.7 ± 2.3	54.2 ± 0.8	p≤0.001
Hip circumference (cm)	96.9 ± 1.8	90.1 ± 1.6	80.6 ± 2.6	62.7 ± 1.1	p≤0.001
Head circumference (cm)	54.1 ± 0.2	53.3 ± 0.3	52.9 ± 0.3	50.2 ± 0.2	p≤0.001
Neck circumference (cm)	33.1 ± 0.4	31.9 ± 0.7	29.5 ± 0.5	25.5 ± 0.2	p≤0.001
Upper extremities (% fat)	5.1 ± 0.1	4.3 ± 0.1	3.5 ± 0.1	2.5 ± 0.1	p≤0.001
Lower extremities (% fat)	15.5 ± 0.3	14.0 ± 0.2	11.6 ± 0.3	8.8 ± 0.2	p≤0.001
Trunk (% fat)	16.0 ± 0.4	14.8 ± 0.3	11.2 ± 0.5	7.1 ± 0.3	p≤0.001
Fat mass (% fat)	37.0 ± 0.8	33.1 ± 0.5	26.4 ± 0.9	18.4 ± 0.5	p≤0.001
FMI	11.0 ± 0.4	8.5 ± 0.2	5.7 ± 0.3	2.9 ± 0.1	p≤0.001
Systolic BP (mm Hg)	114.0 ± 1.4	111.0 ±1.6	105.0 ± 2.4	103.0 ± 1.2	p≤0.001
Diastolic BP (mm Hg)	75.0 ± 1.0	74.0 ± 1.2	68.0 ± 1.7	67.0 ± 1.3	p≤0.001

Table II. Metabolic characteristics of the study population (n=179)

Metabolic characteristics	Morbid Obese Mean ± SE	Obese Mean ± SE	Overweight Mean ± SE	Normal Mean ± SE	p value
Fasting glucose (mg/dl)	87.0 ± 0.8	87.0 ± 0.9	88.0 ± 2.1	87.0 ± 1.6	p≥0.05
Fasting insulin (µU/ml)	13.9 ± 1.2	9.8 ± 1.0	8.0 ± 1.7	3.3 ± 0.7	p≤0.001
CRP (mg/dl)	5.6 ± 0.8	2.9 ± 0.5	2.4 ± 0.4	3.2 ± 0.5	p≥0.05
Triglycerides (mg/dl)	111.0 ±6.5	90.0 ±7.4	101.0 ± 17.2	85.0 ± 9.8	p≤0.05
Total cholesterol (mg/dl)	163.0 ± 3.6	164 ± 4.4	163.0 ± 6.5	158 ± 4.1	p≥0.05
LDL cholesterol (mg/dl)	104.0 ± 3.6	98 ± 3.9	108 ± 6.3	94.0 ± 4.0	p≥0.05
HDL cholesterol (mg/dl)	42.0 ± 0.9	47.0 ± 1.1	44.0 ± 2.4	53.0 ± 2.2	p≤0.001
Glycated hemoglobin (%)	5.4 ± 0.1	5.3 ± 0.1	5.3 ± 0.1	5.2 ± 0.1	p≥0.05

Table III. Mean ± SD and median (min-max) values of insulin sensitivity indices calculated for the groups developed based upon their age- and sex-specific BMI percentiles.

IS index	Group	Mean ± SD	Median (min-max)
HOMA-IR/BMI [a]	Morbid obese	0,09 ±0,06	0,08 (0,01-0,29)
	Obese	0,08 ± 0,04	0,07 (0,02-0,22)
	Overweight	0,08 ± 0,07	0,06 (0,02-0,24)
	Normal	0,05 ± 0,08	0,03 (0,00-0,48)
HOMA-IR [t]	Morbid obese	2,87 ± 2,23	2,47 (0,28-13,52)
	Obese	2,10 ± 1,30	1,89 (0,43-6,23)
	Overweight	1,76 ± 1,51	1,23 (0,33-4,77)
	Normal	0,75 ± 1,21	0,43 (0,03-7,58)
log.HOMA-IR [Δ b]	Morbid obese	0,32 ± 0,38	0,39 (-0,55-1,13)
	Obese	0,24 ± 0,29	0,28 (-0,37-0,79)
	Overweight	0,08 ± 0,41	0,09 (-0,48-0,68)
	Normal	- 0,30 ± 0,35	- 0,36 (-1,55-0,88)
FGIR [Δ b]	Morbid obese	12,1 ± 12,1	7,5 (0,3-51,6)
	Obese	13,8 ± 11,3	9,7 (3,1-44,5)
	Overweight	21,8 ± 16,5	18,1 (4,1-50,8)
	Normal	36,1 ± 13.0	41,7 (2,0-51,0)
Raynaud [Ω b]	Morbid obese	5,6 ± 5,6	3,4 (0,7-20,1)
	Obese	6,4 ± 5,1	4,5 (1,4-20,1)
	Overweight	10,1 ± 7,6	7,6 (1,8-20,1)
	Normal	17,5 ± 5,5	20,1 (1,5-20,1)
Reciprocal insulin [Ω b]	Morbid obese	0,14 ± 0,14	0,09 (0,02-0,50)
	Obese	0,16 ± 0,13	0,11 (0,04-0,50)
	Overweight	0,25 ± 0,19	0,19 (0,05-0,50)
	Normal	0,44 ± 0,14	0,50 (0,04-0,50)
QUICKI [Ω b]	Morbid obese	0,35 ± 0.05	0,33 (0,27-0,49)
	Obese	0,36 ± 0.04	0,35 (0,30-0,45)
	Overweight	0,38 ± 0.06	0,37 (0,30-0,47)
	Normal	0,44 ± 0.09	0,45 (0,29-0,94)
QUICKI * BMI [c d]	Morbid obese	9,9 ± 1,6	9,8 (6,8-15,1)
	Obese	8,9 ±1,2	9,2 (6,9-12,2)
	Overweight	8,0 ± 1,3	8,0 (6,0-11,2)
	Normal	6,8 ± 1,4	6,6 (4,5-14,6)
QUICKI * FMI [c d e]	Morbid obese	3,8 ± 1,1	3,6 (1,7-7,5)
	Obese	3,0 ± 0,6	3,0 (2,0-4,4)
	Overweight	2,1 ± 0,5	2,0 (1,5-3,2)
	Normal	1,3 ± 0,3	1,2 (0,7-2,5)

[Ω] p ≤ 0,05 (MO-OW), p≤0.01 (OW-N)
[t] p ≤ 0,01 (MO-N); p ≤ 0,05 (O-N)
[a] p ≤ 0,05 (MO-N)
[b] p ≤ 0,01 (MO-N, O-N)
[Δ] p ≤ 0,05 (MO-OW), (OW-N)
[c] MO-O, MO-OW, MO-N (p=0.001)
[d] O-N, OW-N (p=0.001)
[e] O-OW (p=0.002)

Upon evaluation of the combined formulas QUICKI*BMI, QUICKI*FMI, HOMA-IR*BMI and HOMA-IR-FMI, the last two indices did not exhibit statistically significant differences between the groups. Statistically significant differences were observed between N-OW and O-MO with QUICKI-BMI. On the other hand, it was concluded that the QUICKI*FMI index, a new one, was unique in detecting the advanced level of differences ($p \leq 0.005$) between N-OW, OW-O and O-MO groups.

Discussion and Conclusion

Investigators have attempts to evaluate IR during childhood obesity by way of using IS indices,-mostly formulized by fasting blood glucose and/or insulin levels-, from time to time combined with BMI values. It has been reported that the early detection of IR using homeostatic indices is important even if they do not fulfill the actual diagnostic criteria for metabolic syndrome [26]. However, any index, which is capable of setting forth the detailed distinctions among N, OW, O and MO groups have not been come into prominence yet. As one of the indices can differentiate N from OW, however, can not exhibit a significant difference between OW and O or O and MO. It is also important for the children to notice the transition from O to MO. In case of putting forward these information, that index will prevent the transition from O to MO and make possible the transfer of the child to OW group with a less effort.

In general, validity of IS indices should be established by examining the correlation between IS measured by glucose clamp and IS indices. It has been shown that surrogate indices derived from fasting measurements are reliable and valid measures of IR [27].

There are several papers showing validity of insulin indices with glucose clamp study in children and adolescents. In a group of children, fasting indices of IS, including the HOMA-IR, QUICKI were well correlated to the clamp test [10]. In African-American and white youths, much stronger correlations were reported for the HOMA IS and QUICKI (r = 0.86–0.91) [28]. In another study, HOMA-IR and QUICKI strongly correlated with the glucose clamp M value ($p<0.0001$) [29].

The reliability of IS indices in obese adolescents were also examined by using clamp study in large number (n=188). Fasting-derived indices of IS show consistently higher correlations with clamp-derived measures of IS than oral glucose tolerance test (OGTT)-derived indices in obese youth with varying degrees of glucose tolerance. HOMA, and QUICKI had the highest correlations with clamp IS regardless of glucose tolerance group. They were the best surrogate estimates [30]. These studies demonstrated the usefulness of fasting-derived surrogate indices in estimating IS in prepubertal, pubertal lean, overweight, and obese children[28, 31].

So far, HOMA-IR and QUICKI repeatedly are being contrasted. There are reports informing that these two indices are suggested to display identical diagnostic accuracy. The confusion of using and comparing several different indices should be avoided and there is a need for a general standard on routine insulin-sensitivity assessment [14].

HOMA-IR was found to be more reliable than FGIR and QUICKI for assessing IR among obese children and adolescents [21]. Our finding of 2.87, a value above 2.5, found for HOMA-IR of MO group emphasized the importance of

this index in this group, exhibiting the highest possibility of its association with metabolic syndrome, from the laboratory evaluation point of view. On the other hand, some reports suggested that QUICKI had better reproducibility than either HOMA-IR or log HOMA-IR [32]. From time to time, some investigators have reported that fasting IS/IR surrogate indices, which include insulin values in their formulae, appeared to be more efficient in estimating IS/IR than triglycerides (TG), HDL-C based indices [33]. It has also been reported that no consensus has yet emerged regarding appropriate tools for measuring obesity [34].

In this study, to limit further comparisons between surrogate measures of IR and to identify an easily applicable and accurate formula for insulin sensitivity assessment, some comparisons between different measures have been made. However, there were some obstacles in discrimination of the groups. For most indices, it has been detected that apparently distinct values observed for the means and/or medians of the two groups, however, they have not exhibited statistically significant difference due to high SD values.

This study evaluated the relevance of four new surrogate indices of IS/IR with other indices. It was suggested that the evaluation of QUICKI in association with BMI and FMI contributed the capabilities of QUICKI index itself and using QUICKI*FMI index has made group discriminations possible in a sensitive manner. It has been concluded that QUICKI*FMI index was capable of introducing significant differences between the groups N-OW, OW-O and O-MO.

There existed also important problems related to the cut-off points. The two sets of previously used criteria have exhibited different percentages in the groups. Based upon these findings, instead of using the habitual ternary indices, it has been developed a new trilogy; HOMA>2.5, FGIR<7, QUICKI<0.328. Upon evaluation of the cut-offs, percentages were quite close to each other in all groups for three indices in question when these cut-offs were applied (44.4%, 42%, 43.2% in MO group , 28.6%, 26.2%, 26.2% in O group, and 25%, 25%, 25% in OW group).

When two sets of cut-offs were compared, HOMA-IR reflected the differences between MO-O and OW-N groups for both, however, close values were obtained for O and OW groups. FGIR index have also exhibited similar profiles. QUICKI index was capable of discriminating O from OW and OW from N groups, but not well in differentiating MO from O when the first cut-off was used. In conclusion, it was observed that QUICKI was capable of discriminating MO from O when 0.328 cut-off was used, and O from OW when 0.357 cut-off was used. These findings suggested that QUICKI can assess IR by choosing alternative cut-off points according to the composition of the group, which is defined by WHO criteria based upon percentile values-for-age.

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