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Anthropometric and Metabolic Parameters to Detect Insulin Resistance in Children

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ABSTRACT

Background: The pathological state of insulin resistance (IR) is closely related to obesity. Insulin sensitivity, therefore, could be permanently impacted by genetic disorders, steroids, or growth hormonal treatment.

Objective: Measuring the specificity and sensitivity of several cutoff points in order to determine insulin resistance in pediatric community depending on anthropometric and metabolic characteristics.

Methods: 107 children between the ages of seven to eleven years participated in this cross-sectional survey, of whom 53 had obesity, 22 had overweight, and 32 had adequate nutrition as determined by body mass index (BMI) for age. BMI, hip and waist circumference measurements, the conicity index, and the percent of body fat were all measured. Fasting samples of blood had been used to assess the levels of triglyceridemia, glycemia, and insulinemia. Using the 90^{th} percentage as the cutoff point, the glycemic homeostatic approach was used to assess insulin resistance.

Results: For such entire sample, the values were: insulinemia = 0.97 (0.97-0.98), 18.5 μUmL^{-1}; fat mass proportion = 0.86 (0.79-0.93), 41.1%; BMI = 0.88 (0.81-0.95), 23.67 kgm^{2-1}; waist circumference = 0.86 (0.77-0.94), 76.0 cm; glycemia = 0.69 (0.52-0.86), 86.0 $mgdL^{-1}$; triglyceridemia = 0.76 (0.64-0.88). For the entire sample, triglyceridemia was 114.0 mg/dL^{-1} and conicity index was 0.67 (0.48-0.85), 1.21; for the obese subgroup, these values were insulinemia of 0.97 (0.96-0.98), 19.52 μUmL^{-1}, body fat percentage of 0.74 (0.62-0.87), 42.0%, BMI of 0.76 (0.62-0.90), 24.51 kg/m^{2-1}, waist circumference of 0.75 (0.59-0.90).

Conclusions: Utilizing the cutoff points with the optimal specificity and sensitivity for the prediction method, anthropometric and metabolic markers seem to have strong predictive potential for insulin resistance in children aged between seven to eleven years old.

Keywords: Anthropometric, Insulin resistance, Metabolic parameters, Pediatrics.

INTRODUCTION

Reduced cellular glucose absorption as responding to a specific level of insulin characterizes the clinical condition known as insulin resistance that has recently been recognized as a public health issue [(1)], whereas the disease has also received attention in demographics including children and teenagers. A problem in the insulin signaling pathways post-receptors is linked towards the illness. This hinders the muscle glucose transporter's (GLUT-4) translocation mechanism, which in turn plays a crucial role in glucose absorption [(2, 3)]. Recently, numerous researchers have developed this initial notion and put up a lipocentric theory to explain why there is insulin resistance, how the translocations of GLUT-4 to the plasma levels membranes may be inhibited by a buildup of intramuscular lipids resulting from long-chain fatty acid derivatives perforating cells, hence also providing a potential alternative strategy of identifying insulin resistance by use of markers connected to the level of body fat [(4-6)].

Euglycemic-hyperinsulinemic clamp measurement, which examines glucose metabolism throughout mediated hyperinsulinemia, and other methods for identifying insulin resistance depending on biomolecular assessment of insulin receptors and postreceptors are pricy and, for several medical practitioners, are challenging to access [(7, 8)]. Once opposed to the gold standard, ***Huang et al.*** validation's study of Homeostasis Model Assessment (HOMA) for the detection of insulin resistance in pediatrics showed it to be an intriguing idea. However, the HOMA estimates need the fasting glycemia and insulinemia readings, which need invasive data gathering. These techniques make it difficult to apply this index, particularly when evaluating large population sampling for diagnostic purposes [(9)].

It is evident that the development of diagnostics with the goals of anticipating insulin resistance depending on risk variables necessitates their development. These tests must be simple to use, accurate, and affordable. It is a proven truth that juvenile obesity has detrimental effects on kids' health, and over the past few years, its incidence has been steadily rising [(10, 11)].

In this situation, having too much body fat is a factor that may be capable of predicting a child's insulin resistance. For instance, it has been demonstrated that waist circumference (WC) is a reliable indicator of hemodynamic and metabolic problems. The 90^{th} percentile for a particular population was used in these studies to determine cutoff points for the parameter; moreover, more researches are needed to imply diagnostic tests and their benefits, as well as to include information depending on how sensitive and specific the offered methods are [(12-14)].

In context of the above, the objective of this research was to assess the sensitivity and specificity of cutoff points as well as the accuracy of predicted insulin

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resistance in pediatric community using anthropometric and metabolic indicators.

METHODS

Type and setting of study

This was a population-based cross-sectional survey of an initial randomly selected chosen sample from the public outpatients attending Damietta General Hospital Pediatric Department Ministry of Health, Damietta, Egypt, from June 2021 to August 2022 in conformance with a sampling size calculation with a confidence interval (CI) of 95%.

Study population

According to the samples collected, 107 children were required to reach a sample size that was representative of all children attending the outpatient clinic at Damiette general hospital (p = 0.05). In order to ensure a more revealing percentage, the preliminary evaluation included 956 children from Damietta General Hospital Pediatric Department outpatients (p = 0.03), finding an incidence of obesity of 7.5% (n = 72) and overweight of 10.6% (n = 100).

This meant that 18.3% of the total children population sample were overweight. Following assessment of the 956 initial participants, 107 kids of both sexes, ranging in age between seven to eleven years old, and with different nutritional condition groups, were selected. Body mass index/age (BMI/age) was used to categorize the sample under study [(15)], identifying 53 kids as obese (above the 95th percentile), 32 children as well-nourished, 22 children as overweight (within percentile rank 85 and 95), and (between percentiles 5 and 75) respectively. Depending on the incidence of overweight and obesity (18.3%) experimentally demonstrated previously, it was estimated that 71 children (p = 0.05) might be adequate to stand for the community of obese and overweight children registered in Damietta General Hospital Pediatric Department outpatients.

The control group, made up of a further subgroup of 32 kids who were deemed to be in good nutritional condition, completed the entire sample under investigation.

Data collection and analysis

Every child's weight, height, and BMI were calculated using a stadiometer made by Seca and a Plena branded balancing with a digital indicator (Starrett 2900, USA). The hip circumference (HC) and the waist circumference/ (WC) [(16)] were assessed by using a tape measure (Seca, USA). After that calculations were carried out to acquire the conicity index (C index) [(17)] and waist-to-hip ratio (WHR) [(18)], as follows:

$$C\ index = \frac{waist\ circumstance\ (m)}{0.109\sqrt{\frac{Body\ weight\ (kg)}{Height\ (m)}}}$$

Dual emission X-ray absorptiometry (DEXA) was used to measure body fat using a Lunar DPX-IQ equipment (Lunar Corporation, Madison, WI, United States) and software version 4.6A. The participants were instructed to take off any metal items they could be holding or wearing. According to the manufacturer's instructions, every participant was then placed in decubitus dorsal on the DEXA device for a total body scanning with the pediatric analysis option chosen. Prior to usage, the equipment has been properly calibrated. Every child's relative fat mass (%F) was measured, and the same investigator conducted all analyses [(19)].

Venous blood was obtained for bioassay around 7:45 and 9:00 am at the Damietta General Hospital Pediatric Department after a 12-hour fast. The samples were stored in vacuum tubes (JJ Electronic, Slovak Republic) without anticoagulation and separating gel. The serum was extracted from the blood after collecting and centrifuged for ten minutes at 3,000 rpm to isolate it from the other ingredients. An enzymatic colorimetric kit (Randox Laboratories, United Kingdom) was used to measure triglycerides and blood sugar, which was then analyzed in an Autohumalyzer A5 (Human-2004). The Automation Chemiluminescence Solution ACS-180 was used to measure insulin (Ciba-Corning Diagnostic Corp., 1995, United States).

The HOMA method was used to determine insulin resistance, as shown by the formula below [(9)]:

$$HOMA = \frac{Insulinemia\ \left(\mu\frac{UI}{mL}\right) X\ Glycemia\ (\frac{mmol}{L})}{22.5}$$

Huang et al. verified the HOMA index for use in paediatric patients in comparison to the euglycemic-hyperinsulinemic clamping method [(9)]. As previously suggested, the criteria used here for the identification of insulin resistance were a HOMA index over the 90th percentile (p. 90) [(20-22)].

Ethical approval

A free and informed consent form was submitted by those in charge of the survey respondents' families, approving the participation of the chosen youngsters in the investigation. This work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. Damiette general hospital also approved the current study.

Statistical analysis

The cutoff thresholds that accurately indicated insulin resistance for all the parameters under study were chosen using the receiver operating characteristic (ROC) evaluation. For this method, the samples were divided into a larger group (n = 107; 9.22 ± 1.36 years) and a smaller group (n = 53; 9.18 ± 1.14 years) that only

included the obese children. Furthermore, the associations between each of the testable markers and insulin resistance were examined using Pearson's linear correlation test, with a level of significance of $p< 0.05$. The software packages Statistica® version 5.1 and Statatm® version 9.1 were used to statistically analyze the data.

RESULTS

The CIs for the regions below the ROC curves for anthropometric and metabolic insulin resistance indicators (LL-CI 0.50) are shown in table 1.

None of the WHR for the total group, the C index, the glycemia for the obese subgroup, or the WHR for the obese subgroup demonstrated any observable discriminating significance for insulin resistance. The anthropometric measurements %F, WC, BMI, and C index for the entire group as well as %F, WC, and BMI for the obese subgroup could, however, show to be important predictor of insulin resistance (LL-CI ≥ 0.50) following analysis of the areas underneath the ROC curves.

Additionally, the metabolic markers, insulinemia, triglyceridemia and glycemia for the entire group as well as triglyceridemia and insulinemia for the sample of obese kids all showed considerable discriminating the level for insulin resistance predictions (LL-CI ≥ 0.50).

Table (1) Area underneath the receiver operating characteristic curve and 95% confidence intervals for the associations between anthropometric, metabolic, and insulin resistance for the total sample, as well as the obese sample

Insulin resistance (Glycemic Homeostasis Index)	**Area underneath the curve receiver operating characteristic (95% confidence interval)**	
	Total (n = 107)	**Obese (n = 53)**
Metabolic		
Insulinemia ($\mu U \cdot mL^{-1}$)	0.97 (0.97-0.98)*	0.97 (0.96-0.98)*
Triglyceridemia ($mg \cdot dL^{-1}$)	0.76 (0.64-0.88)* x 2 = 0.000	0.70 (0.54-0.85)* x 2 = 0.000
Glycemia ($mg \cdot dL^{-1}$)	0.69 (0.52-0.86)*	0.64 (0.45-0.82)
Anthropometric		
Waist circumference (cm)	0.86 (0.77-0.94)*	0.75 (0.59-0.90)*
Body fat percentage (Dual emission X-ray absorptiometry)	0.88 (0.79-0.93)* x 2 = 0.055	0.74 (0.62-0.87)* x 2 = 0.029
Conicity index	0.67 (0.48-0.85)*	0.54 (0.32-0.77)
Waist-to-hip ratio	0.65 (0.44-0.85)	0.53 (0.30-0.76)
Body mass index (kg/m^2)	0.88 (0.81-0.95)*	0.76 (0.62-0.90)*

*Area underneath the curve ROC displaying the ability to distinguish between insulin resistance (Lowest value of the CI (LL-CI) ≥ 0.50).

The cutoff values, specificity, and sensitivity are provided in table 2. Additionally, table 2 provides relationships between these variables and insulin resistance.

Table (2) Cutoff points, correlations, specificity, and sensitivity of metabolic as well as anthropometric markers for determining insulin resistance across the board (n = 107) and in the obese sample (n = 53)

Insulin resistance (Glycemic Homeostasis Index)	Cutoff points		Specificity (%)		Sensitivity (%)	
	Total	**Obese group**	Total	Obese group	Total	Obese group
Metabolic						
Triglyceridemia ($mg \cdot dL^{-1}$)	114.00 (r = 0.45)*	125.00 (r = 0.44)*	67.28	63.62	63.58	63.62
Insulinemia ($\mu U \cdot mL^{-1}$)	17.68 (r = 0.97)*	18.52 (r = 0.97)*	95.88	92.16	98.00	89.89
Glycemia ($mg \cdot dL^{-1}$)	86.00 (r = 0.35)*	Indicator not predictive	73.48	Indicator not predictive	72.68	Indicator not predictive
Anthropometric						
Body fat percentage (Dual emission X-ray absorptiometry)	40.28 (r = 0.55)*	41.18 (r = 0.41)*	83.65	72.71	89.89	72.71
Conicity index	1.21 (r = 0.37)*	Indicator not predictive	63.25	Indicator not predictive	63.62	Indicator not predictive
Body mass index (kg/m^2)	22.67 (r = 0.64)*	23.51 (r = 0.52)*	78.57	71.71	80.80	71.71
Waist circumference (cm)	76.0 (r = 0.65)*	77.0 (r = 0.55)*	77.53	63.62	81.80	63.62

r: correlation coefficient, *: p< 0.05 for the relationship between the predictors and insulin levels

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DISCUSSION

The main results of this study indicate that anthropometric and metabolic markers may be used to identify insulin resistance in children. As illustrated in table 1, the cutoff values with the highest resemblance between specificity and sensitivity are suggested by assessment of the ROC curves, a technique never before utilized for this goal and providing details about the validity level of the indicator employed in the predictions. For the entire sample, as suggested by table 2, the indicators of insulin resistance thusly suggested were: the C index, BMI, %F, WC, triglyceridemia, glycemia, and insulinemia; and for the subgroup made up of obese children, insulinemia, and %F, BMI, WC, and triglyceridemia.

The euglycemic-hyperinsulinemic clamping testing has been referred to as the golden standard for determining whether kids or adolescents exhibit insulin resistance [9, 23, 24]. This report's use of the HOMA index as an alternative to the euglycemic-hyperinsulinemic clamping approach to measure insulin resistance may be viewed as a drawback. ***Huang et al.***, though, have verified the HOMA method for detecting insulin resistance in youngsters [9], and other investigators have effectively used the indexes [20-22]. HOMA is more practicable than the gold standard, but it still requires the measurement of two factors (glucosemia and insulinemia), both of which are acquired invasively. Additionally, several various healthcare providers find it challenging to incorporate monitoring insulinemia into their everyday practices because it requires performing biochemical assays in a laboratory setting by a qualified technician.

Numerous research have looked for useful and accurate indicators for detecting disorders, such as insulin resistance [17, 21, 25, 26] which could lead to type 2 diabetes later in life at a young age [9, 24, 27, 28]. In addition to lowering healthcare expenses, knowledge about the early identification of insulin resistance could be helpful to a range of child health providers in their preventive and therapeutic practice.

A single metabolic marker, including such glycemia, triglyceridemia, or insulinemia itself, was used in this investigation to discover indicators of insulin resistance. In accordance with expectations, insulinemia had the highest area under the ROC curve regarding prediction performance (Table 1); strong correlation, and superior sensitivity and specificity when contrasted to the other markers (Table 2) [29] [29] [30]. In contrast, as shown in table 2, triglyceridemia and glycemia revealed to be significantly predictive of insulin resistance despite having smaller numbers for sensitivity and specificity when contrasted to insulinemia. It was verified that there was a substantial

predicting capacity for glycemia for the entire samples and for triglyceridemia for both the entire samples and the obese subpopulation when the area underneath the ROC curve and the CI were assessed, particularly the CI lower limits more than 0.50. (Table 1) (29). Today, it is simple to use measures of triglyceridemia and glycemia to anticipate children's insulin resistance thanks to the availability of low-cost portable analyzers.

Additionally, as shown in table 1, anthropometric measurements including %F, the C index, BMI, and WC showed a strong predictability for insulin resistance [(29)]. Despite this, %F was discovered using DEXA, a method that is expensive and difficult to apply in clinical settings. Additionally, identical results could be obtained for both the total group and the obese subgroup when the areas under the ROC curves for the markers BMI and WC are compared to the area under the ROC curve for %F as measured by DEXA (Table 1).

Additionally, in both this investigation and a trial by ***de Almeida Gomes et al.***, %F as determined by DEXA had significant moderate to high associations with BMI (r = 0.89), WC (r = 0.84), and the C index (r = 0.53) [(26)]. The ability of the parameter WC to anticipate insulin resistance, which was observed for both groups in this experiment, is consistent with previous research showing that this parameter is a reliable predictor of insulin resistance, lipids contents, and arterial blood pressure in different populations [(25, 27, 30)]. It is proposed that the anthropometric markers investigated here be used for identifying insulin resistance in pediatric patients because they are easy to measure, inexpensive, noninvasive, and have ranges associated with the level of sensitivity and specificity of the chosen cutoff point.

There is currently an increasing preponderance of children with a variety of risk factors, of which obesity is of highest emergence and is closely associated to insulin resistance at a younger age in settings under which morphophysiological, postural, and nutritional qualities are appraised, such as sporting activities, fitness centers, and physical therapy, nourishment, and pediatrics management consulting halls [(31, 32)]. Due to this, adopting the indicators suggested here is both feasible and very clinically significant for upcoming therapeutic and preventative measures [(19, 27, 33)]. These procedures are particularly important when evaluating youngsters since they allow for the prevention of issues related to insulin resistance and type 2 diabetes in later life.

CONCLUSION

In light of the observed findings, we draw the conclusion that anthropometric and metabolic markers with discriminatory capacity for the diagnosis of insulin resistance in children between the ages seven to eleven years have been identified, based on the ideal cutoff values for balancing sensitivity and specificity. For the entire sample, the determinants of insulin resistance included insulinemia, %F, BMI, WC, glycemia, triglyceridemia, and the C index. For the subgroup of obese children, the determinants included insulinemia, %F, BMI, WC, and triglyceridemia. The recommended measures are useful tools for healthcare providers to utilize in their daily work because they are simple to measure. Additional research using comparable approaches are required to explore the use of these markers in diverse demographics and to stratify them according to factors like ethnicity and family history of type 2 diabetes.

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