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Research Article

Cross-sectional observational study on correlation of obesity and overweight in children with insulin resistance based on HOMA-IR score

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Abstract

With improvements in lifestyle and healthcare throughout the world, there has been an increasing incidence of obesity among adults and children. It is important that obesity and its adverse effects be recognized in childhood and measures be taken right from childhood to tackle the long-term outcomes of the same. We have studied the correlation of scores like Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) and its relation with Insulin resistance in children. Which helps as a tool in early recognition of lifestyle diseases in children. It was seen that of a total of 50 children of which 40 children were obese (BMI greater than 95th centile) and 10 children were overweight (BMI greater than 85th centile), 43 children had insulin resistance based on HOMA-IR score (cut-off=2.5) and 7 were non-insulin resistant. From our study, it has been concluded that HOMA-IR has a strong correlation with BMI and can be used as a surrogate marker of Insulin resistance.

Introduction

Obesity is a global public health problem associated with complications in childhood as well as increased morbidity and mortality later on in life. Increasing trends have been reported in many low and middle-income countries, particularly in urban areas [1]. In a study conducted by Anoop Mishra, et al. to study the high burden of obesity and abdominal obesity in urban Indian school children, the prevalence of overweight and obesity in 8 to 18-year-old children was 14.4% and 2.8%. The prevalence of abdominal obesity in urban Indian schoolchildren was 4.5%. Thus there is a substantial high in the burden of childhood obesity in India [2].

Obese children have a greater tendency to remain obese throughout adulthood, thus increasing the likelihood of non-communicable diseases like Diabetes, Hypertension, and Cardiovascular diseases. Parental obesity is associated with a higher risk of obesity in offspring. Other factors that predispose include intrauterine growth restriction with early catch-up growth, high birth weight, and maternal smoking [3].

Insulin resistance in obesity

Insulin plays a pivotal role in the regulation of blood sugar levels, it determines how the body stores glucose and fat. It is also responsible for allowing glucose entry to cells for energy use. Insulin resistance happens when body cells become resistant to insulin, as cells can show resistance against insulin and prevent excess glucose entry, thus increasing the amount is required to have the same effect on the body cells [4,5].

'Insulin resistance' is the resistance to the effects of insulin including glucose uptake, metabolism, or storage. It is known to be influenced by obesity, other factors like growth hormone therapy, steroids, and genetic disease may also affect insulin sensitivity [6]. Insulin resistance is due to genetic and lifestyle factors leading to an inflammatory process in the body [7], combined with the lipolytic effect of adipocytes, which leads to the production of free fatty acids in large amounts, leading to impaired secretion of adipokines, both of which have an influence on insulin resistance. Insulin resistance is the first sign of impaired glucose tolerance. If there is insulin resistance, there is an increased production of insulin by the beta cells of

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the pancreas to make glucose available to cells by overcoming the resistance. Failure of this compensatory mechanism leads to impaired glucose tolerance, in turn resulting in Type 2 Diabetes Mellitus. Metabolic syndrome – characterized by central obesity, hypertension, increased triglycerides, low HDL, and impaired glucose tolerance is associated with insulin resistance. Insulin resistance is also a risk factor for cardiovascular diseases [1,7,8].

Definition

Body mass index (BMI) = Weight (in Kg)/ Height ^{2} (in m ^{2}) [3,5]

BMI changes with age in children, hence Overweight is defined as a BMI greater than the 85th percentile for age and gender-specific BMI WHO charts.

Obesity is defined as a BMI greater than 95th percentile for age and gender-specific BMI WHO charts [3,5]. Insulin Resistance was defined by HOMA-IR score (greater than 2.5) [9-11].

Yaser Mirzaalian studied 80 adolescents aged 12-13 years in Iran. There was a significant correlation between anthropometric indicators including BMI and HOMA-IR. Both our studies demonstrated that the higher the BMI, the higher is the HOMA-IR score [9].

To evaluate the presence of insulin resistance and its association with metabolic syndrome in obese children and adolescents, Romualdo, et al. included 220 children and adolescents aged 5-14. Insulin resistance was found in 33.20% of the sample. The highest frequencies were observed among adolescents (65.8%) and pubertal (54.8%), there also exists a relation between insulin resistance and increased waist circumference [10].

Mihai, et al. studied 56 obese children to determine the association of BMI with HOMA-IR, the average level of HOMA-IR in obese children was 6.79, and in non-obese children it was 1.79, thus demonstrating that HOMA-IR may be used as a tool for insulin resistance in children [12].

Naglaa Fathy Barseem, et al. evaluated insulin resistance based on HOMA-IR score in 60 obese children and adolescents with and without metabolic syndrome, metabolic syndrome was found in 42 subjects (70%). On comparing metabolic syndrome-related parameters between groups with and without metabolic syndrome, mean BMI, waist circumference, and waist/height ratio were significantly higher in those with metabolic syndrome. The presence of insulin resistance according to the HOMA-IR score was identified in 53% of obese children and adolescents [13].

In a study conducted by Consuelo Chang Rueda to study the correlation of BMI with HOMA-IR, it was found that HOMA-IR values correlated positively with BMI percentile (r = 0.198). In our study, HOMA-IR was found to have a significant correlation with BMI (r = .452) and (p = 0.001). Both in our study and in the study conducted by Consuelo Chang HOMA-IR values showed homogeneity between sexes [14].

Diagnosis of insulin resistance

The gold standard for measuring insulin resistance is a hyperinsulinemic-euglycemic clamp, during which insulin is administered intravenously at a steady rate, which increases and maintains systemic insulinemia, and glucose infusion occurs at a steady rate to maintain blood glucose levels [15,16]. The rate of glucose infusion during a steady-state corresponds to insulin resistance. This method is invasive and expensive. Other surrogate markers used include fasting plasma insulin, homeostasis model assessment of insulin resistance (HOMA-IR), triglyceride, HDL ratio (TG/ HDL ratio), and quantitative insulin sensitivity check index (QUICKI), of which HOMA-IR is a commonly used index in adults. Although several studies have been conducted to determine its cut-off value in children and adolescents, there is no reliable cut-off value obtained. The reliability of these indices requires further research [17-19]. Acanthosis Nigricans is considered a physical marker of Insulin resistance. This helps in early identification of children who are at risk [20].

Aims and objectives

To determine the relation between obesity and overweight with insulin resistance in children and adolescents between 3 and 18 years of age based on the Homeostasis model assessment- Insulin resistance (HOMA-IR) index.

Materials and methods

Study design and study area

A cross-sectional, observational, randomized study conducted in the Outpatient and inpatient department of Aster CMI Hospital, Bangalore.

Study duration

From October 2020 to August 2021

Sample Size – 50

Based on the formula

N=

r -correlation coefficient,

= Desired confidence level

1-β -Power

Based on study by Yaser Mirzaalian, et al. [9]

Correlation coefficient -0.5

Power (1-B) % -90

Error (%) - 5

required sample size-32 (round off-50).

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Inclusion criteria

Children and adolescents aged 3-18 years who fulfilled the criteria for obesity and overweight based on BMI charts [21].

Consent to participate in the study.

Exclusion criteria

Children below 3 years of age and above 18 years of age

Children below the 85th percentile for BMI

Syndromal obesity

Children with proven endocrine disorders such as Hypothyroidism, Cushing's

Syndrome, Type I Diabetes Mellitus, Renal and Liver diseases

Children on medications causing obesity

Children unwilling to participate.

Measurement

After collecting consent to participate in the study from children or their parents, anthropometric indices were measured using the following methods. Height was measured using a stadiometer with a precision of 0.1 cm, by making the child stand straight, keeping heels together and without shoes. Weight was measured by asking the child to stand on a digital weighing scale.

BMI is calculated as Weight/ Height 2[22] Insulin resistance (IR) is calculated using the HOMA-IR score (Homeostasis model assessment- Insulin resistance) = Fasting insulin (µU/ L) x Fasting glucose (m mol/L)/22.5 or Fasting Insulin (µU/ ml) x fasting glucose (mg/dl)/405 [9,14,19].

Blood samples were collected from the participants after overnight fasting for 8-10 hrs. Four ml of peripheral venous blood was collected Two ml was transferred to a sodium fluoride and potassium oxalate anticoagulant-containing bottle for glucose estimation and 2ml transferred to a serum vacutainer. Glucose estimation is done by Hexokinase method using a COBAS 6000 Analyzer.

Fasting Insulin using ECLIA (Electrochemiluminescence immunoassay) using COBAS 6000 Analyzer (Roch).

Statistical analysis

The data collected was stored and processed. The analysis in this study was conducted using SPSS (Statistical Package for the Social Sciences) software for Pearson's Correlation test. The significance was defined using a two-tailed p-value of 0.001 (Table 1).

Ethical considerations

The study was approved by the Aster CMI Hospital Scientific Research Committee (Aster/RC/059/2020-21). The participants provided their consent to participate in the study.

Results

In Table 2 we can see that there was not much difference in HOMA-IR based on gender. Hence, gender does not cause much variation in the values of HOMA-IR.

Out of 50 children, Acanthosis was seen in 42 children, of which 85% of children who are obese and 80% of children who are overweight have acanthosis (Table 3).

An ROC curve (receiver operating characteristic curve) was obtained after analysis. The sensitivity of the test was found to be 72%, specificity of 57.1%, the area under the curve was 0.746 and was statistically significant with p value of 0.039. (Figure 1, Table 4)

Of a total of 50 children, 40 were obese (BMI greater than 95th percentile) and 10 children were overweight (BMI greater than 85th percentile), 43 children had insulin resistance based on HOMA-IR score (cut-off=2.5) and 7 were non-insulin resistant (Table 2). Hence, Insulin resistance was found in 86% of the sample size. HOMA-IR was found to have a significant correlation with BMI (r = .452) and (p = 0.001) (Table 1). Out of 10 children who were overweight, 9 had insulin resistance based on HOMA-IR score (cut-off greater than/=2.5), and 1 was noninsulin resistant (Table 2). Out of 40 children who were obese, 34 had insulin resistance based on the HOMA-IR score (Table 5). According to Figure 2, HOMA-IR and BMI showed a positive correlation with Pearson's correlation index R^2 = 0.204.

Table 1: Correlation of BMI with HOMA-IR showed a moderately significant correlation with (r = 0.452), (p = 0.001)

		HOMA-IR
BMI	Pearson Correlation	.452**
	Sig. (2-tailed)	.001
	N	50

Table 2: HOMA-IR and BMI based on gender.

Sex		N	Mean	Std. Deviation	Std. Error Mean
BMI	Male	22	27.5532	5.52294	1.17750
	Female	28	27.3829	5.66313	1.07023
HOMA-IR	Male	22	4.49773	2.062389	.439703
	Female	28	4.68168	2.286396	.432088

Table 3: Prevalence of Acanthosis in children who are obese and overweight.

Crosstab					
			Overweight/Obese		Total
			Overweight	Obese	
ACANTHOSIS	A	Count	2	6	8
		% within ACANTHOSIS	25.0%	75.0%	100.0%
		% within OverweightObese	20.0%	15.0%	16.0%
	P	Count	8	34	42
		% within ACANTHOSIS	19.0%	81.0%	100.0%
		% within OverweightObese	80.0%	85.0%	84.0%
Total		Count	10	40	50
		% within ACANTHOSIS	20.0%	80.0%	100.0%
		% within OverweightObese	100.0%	100.0%	100.0%

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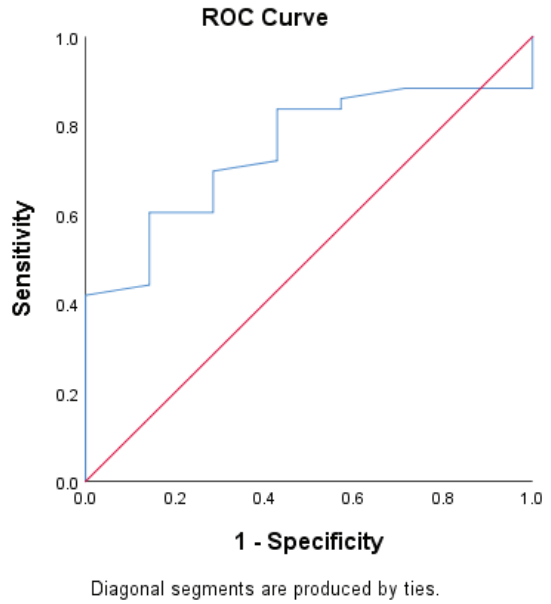

Figure 1: ROC Analysis.

Table 4: Area under the curve (AUC) analysis.

Area Under the Curve							
Area	Std. Error	p value	Asymptotic 95% Confidence Interval		Cut Off	Sensitivity	Specificity
			Lower Bound	Upper Bound			
0.746	0.080	0.039	0.589	0.902	24.75	72%	57.1%

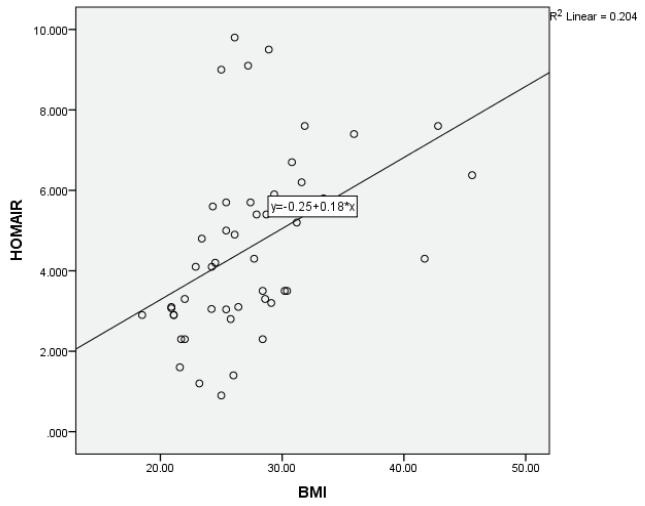

Figure 2: Scatter Diagram to determine the correlation of HOMA-IR with BMI, where Pearson's correlation index R2 is 0.204.

Table 5: Tabular representation of data collected.

OverweightObese * HOMAIR_C Crosstabulation					
			HOMAIR_C		Total
			>= 2.5	< 2.5	
Overweight/ Obese	Overweight	Count	9	1	10
		% within Overweight	90.0%	10.0%	100.0%
	Obese	Count	34	6	40
		% within Obese	85.0%	15.0%	100.0%
Total		Count	43	7	50

Discussion

In our study, 50 children were selected and fulfilled the inclusion criteria. Of the 50 children, 28 were females and 22 were males. 43 children had insulin resistance based on a HOMA-IR score cut-off of 2.5. Based on our statistical analysis, there was a positive correlation between BMI and HOMA-IR.

A study conducted by Consuelo Chang Rueda to understand the correlation of BMI with HOMA-IR found that HOMA-IR values correlated positively with BMI percentile (r = 0.198). In our study, HOMA-IR was found to have a significant correlation with BMI (r = .452) and (p = 0.001). Both in our study and in the study conducted by Consuelo Chang HOMA-IR values showed homogeneity between sexes [22].

Rashmi Ranjan Das, et al. studied the prevalence of insulin resistance in urban Indian school children who were overweight/ obese. As a total of 545 children were included as subjects, the male-to-female ratio was 1:1.27. Around 32.3% of children had a HOMA-IR >2.5 and 22% had a HOMA-IR>3.16. The mean HOMA-IR was found to be 5.46 in children with MS, as compared to 2.18 in those without insulin resistance. The overall prevalence of metabolic syndrome in children who were overweight or obese was 21.8%. The physical indicator of insulin resistance, acanthosis nigricans was found in 46.4% of children, in our study acanthosis was seen in 84% (42 children out of 50). There was a positive correlation between HOMA-IR and TG, waist circumference and obesity [23].

Sun Min Lim, et al. investigated if indices of obesity were associated with insulin resistance. 817 children with no prior history of diabetes were included in the study. Of the 817 children, 418 males and 399 females were included. It was noted that as BMI increased the HOMA-IR values showed an increasing trend, a similar finding was noted in our study as well. HOMA-IR was shown to have a positive and strong association with BMI. This study validated the use of the HOMA-IR score as a surrogate marker of Insulin resistance [24].

It is documented that insulin resistance is more evident during adolescence, it has been considered secondarily due to rapid elevation of sex hormones or changes in the growth hormone levels [25,26]. Thus it becomes important to screen adolescents who are obese for Insulin resistance. So that preventive measures can be initiated at the latest.

Limitations

As much of the data collection was during the COVID period, there were constraints in the attainment of adequate sample size. A larger sample size would have ensured a more reliable representation. HOMA-IR cut-off of 2.5 has been used in several studies in adults, but its reliability in children requires further evaluation.

Conclusion

Childhood obesity has significantly increased all over the world, due to the Westernization of food and the increasing

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popularity of junk food. Childhood obesity is also associated with an increased risk of several metabolic complications like insulin resistance, glucose intolerance, and Type 2 diabetes.

'Insulin resistance' is the resistance to the effects of insulin including glucose uptake, metabolism, or storage. It is known to be influenced by obesity, other factors like growth hormone therapy, steroids, and genetic disease may also affect insulin sensitivity.

Acanthosis Nigricans is considered a physical marker of Insulin resistance. In our study, there is a positive correlation between HOMA-IR and Insulin resistance. This helps in early identification of children who are at risk.

HOMA-IR is a commonly used marker of insulin resistance in adults. Although several studies have been conducted to determine its cut-off value in children and adolescents, there is no reliable cut-off value obtained. The reliability of these indices in Indian children requires further research [27,28].

From our study, it has shown that HOMA-IR has a strong correlation with BMI and can be used as a surrogate marker of Insulin resistance.

With early diagnosis and identification of insulin resistance in childhood, lifestyle modifications can be brought about. This will not only increase awareness among the general population about lifestyle diseases but also decrease the incidence of diabetes and metabolic syndrome in the long run.

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