

EVALUATION OF HOMA-IR(HOMEOSTATIC MODEL ASSESSMENT INSULIN RESISTENCE) AND ITS CORRELATION WITH ANTHROPOMETRY IN THE OBESE OR OVERWEIGHT CHILDREN AND ADOLESCENT

Ajmariya M.*, Ghanghoriya P., Agrawal G. and Mittal P.,

¹Dr. Manish Ajmariya, Senior Resident, Department of Pediatrics, Nscb Medical College, Jabalpur.

²Dr.Pawan Ghanghoriya, Associate Professor, Department of Pediatrics, Nscb Medical College, Jabalpur.

³Dr.Gaurav Agarwal, Post Graduate Resident, Department of Pediatrics, Nscb Medical College, Jabalpur.

⁴Dr Preeti Mittal, Post Graduate Resident Department of Pediatrics, Nscb Medical College, Jabalpur.

*Corresponding Author: Ajmariya M.

Dr. Manish Ajmariya, Senior Resident, Department of Pediatrics, Nscb Medical College, Jabalpur.

Article Received on 04/04/2017

Article Revised on 24/04/2017

Article Accepted on 14/05/2017

ABSTRACT

Objective-evaluation of HOMA-IR(homeostatic model assessment insulin resistance) and its correlation with anthropometry in the obese or overweight children and adolescent. Methodology: Study was approved by the ethical committee and subjects were enrolled after written consent of parents/subjects. Various Anthropometric measurements were taken.

1. Weight: weight was recorded using the electronic weighing machine to nearest 1000 gram. Subjects were made to stand barefoot without touching anything else.

2. Height: it was measured to the nearest 1 cm using stadiometer. Subjects were made to stand barefoot on the foot board heel, buttocks, shoulders and occiput touching against the vertical plank, looking straight ahead with the head held in a way that it lies in the Frankfurt plane (i.e. lower border of orbital fossa on the same horizontal plane as the upper border of external auditory meatus in parallel to the ground). Height was measured to the nearest 1 cm using the scale mounted on vertical plank.

3.Body mass index (BMI): following formula was used to compute the BMI-

$$\text{BMI (kg/m}^2\text{)} = \text{weight (kg)/height (m)}^2$$

Each BMI value was converted into corresponding BMI percentile (age & sex specific). Than subjects were classified into 3 categories as follow

- i. <85th centile – normal
- ii. 85 – 95th centile – overweight
- iii. >95th centile –obese^[1]

Beyond 18 years

- i. 18.5 – 22.9 kg/m² – normal
- ii. 23.0 – 26.9 – overweight
- iii. > 27 – obese^[2]

4.Waist circumference: measured using a non stretchable tape at the mid-point of the lowest rib-cage and the iliac crest to the nearest 1 cm in the standing position during end tidal expiration. It was measured twice and if the difference between the two readings was 0.4 cm a 3rd reading was taken and mean was calculated using the two closet values. Waist circumference percentiles were generated using age and sex specific Kuriyan chart of waist measurements for Indian children and based these percentiles subjects were categorized into three groups

1. <75th centile – normal
2. 75 – 90th centile – overweight
3. >90th centile – obese^[3]

Beyond 16 years, based on sex following values were taken as cut off^[4]

Girls <80cm – normal
>80 cm – obese

Boys <90 cm – normal
>90 cm – obese.

5. Hip circumference: recorded to the nearest 0.1 cm at the level of greater trochanter in the standing position. It was measured twice and if the agreement between 2 repeats was >0.4 cm, than a 3rd measurement was taken and the mean was calculated using the 2 closet values.

6. Waist/Hip ratio: it signifies the ratio of the truncal and extremity fat distribution. In male >0.9 and in female >0.8 were taken off as cut off.^[5]

7. Neck circumference: measured in the standing position, head held erect at the level of thyroid cartilage. In the absence of data on the cut off values for neck circumference in Indian children we adopted the corresponding values from the US counterpart^[6]

Result-total 30 subjects participated in the study. 17(57%) were male and 13(43%) were female. 6(20%) subjects were in 6-<10 year age group, 15(50%) were in 10-<15 year, and 09(30%) were in 15-19 year age group. Total 25 subjects had abnormal neck circumference. Out of 17% had normal neck circumference and 83% had higher neck circumference. it was found tha no significant correlation between neck circumference and insulin resistance (p value = 0.24) **Conclusion:** Insulin resistance is significantly associated with marker of adiposity like neck circumference.it association was significant.nc on application chi square trends the association between the bmi and homa-ir was found to be not significant.Our study show that the insulin resistance of adult disease erupt in childhood itself and therefore control of weight should be aim from early childhood so as to prevent complication of obesity in future.

INTRODUCTION

Diabetes is most common endocrinological disorder characterised by chronic hyperglycemia due to an absolute or relative deficiency of insulin.^[7] around the globe news on diabetes 366 million people have diabetes in 2011 by 2030 this will have risen to 552 million. it is fourth leading cause of death globally. at least 50% of all people with diabetes are unaware of their condition in some countries this figure may reach 80%. in Indian scenario and 61.3 million in 2011 and this will have risen to 101.2 million in 2030.^[8] Indian develop diabetes at an earlier age with lower level of obesity. until recently predominant form of diabetes in children type 1 however during past 2 decades an increased frequency of type 2 dm. has been reported in children especially in adolescents. this increased frequency of type 2 dm seems to parallel with increased prevalence and severity of obesity in children and adolescents. type 2 dm hand in hand with childhood obesity represent an emerging health problem of 21st century. (9) insulin resistance is key factor leading to type 2 dm. insulin resistance usually denotes resistance to the effect of insulin on glucose uptake, metabolism and storage. insulin resistance is associated with obesity, type 2 dm cardiovascular disease and cardiometabolic risk marker such as dyslipidemia, hypertension and central obesity.

Need for the study- risk factor of type 2 dm 2 types- 1- modifiable, and type 2 non modifiable. this study aim to evaluating insulin resistance and establish a correlation with certain modifiable factor and anthropometry. as a sequel to this study, the aim is to target these modifiable factor on their established correlation. and thereby decreased risk of type 2 dm in this high risk group.

AIMS AND OBJECTIVE

To evaluate insulin resistance by HOMA-IR in these obese, overweight children and adolescents, association of insulin resistance with BMI, neck circumference and waist hip ratio. *Materials and methods*

Study design: cross sectional observational study
Study period: 1st sept. 2012 to 31st august 2013.

Study setting: Endocrinological clinic, Department of pediatrics, NSCB Medical College Jabalpur Madhya Pradesh

Sample size: 30 overweight and obese children and adolescents.

INCLUSION CRITERIA

1. Obese children BMI $\geq 85\%$ for the particular age and sex
2. Age 06-19 years
3. Free of any systemic or metabolic disorder and free of medications

Exclusion criteria

1. Subjects who refused to give consent

2. Subjects with any metabolic and systemic disorder or any medication known to affect energy metabolism or body weight.

METHODOLOGY

Study was approved by the ethical committee and subjects were enrolled after written consent of parents/subjects. Various Anthropometric measurements were taken.

1. Weight

Weight was recorded using the electronic weighing machine to nearest 10 gram. Subjects were made to stand barefoot without touching anything else.

2. Height

It was measured to the nearest 1 cm using stadiometer. Subjects were made to stand barefoot on the foot board heel, buttocks, shoulders and occiput touching against the vertical plank, looking straight ahead with the head held in a way that it lies in the Frankfurt plane (i.e. lower border of orbital fossa on the same horizontal plane as the upper border of external auditory meatus in parallel to the ground). Height was measured to the nearest 1 cm using the scale mounted on vertical plank.

3. Body mass index (BMI)

following formula was used to compute the BMI-
$$\text{BMI (kg/m}^2\text{)} = \text{weight (kg)/height (m)}^2$$

Each BMI value was converted into corresponding BMI percentile (age & sex specific). Then subjects were classified into 3 categories as follow

- i. <85th centile – normal
- ii. 85 – 95th centile – overweight
- iii. >95th centile – obese

Beyond 18 years

- i. 18.5 – 22.9 kg/m² – normal
- ii. 23.0 – 26.9 – overweight
- iii. > 27 – obese

1. Waist circumference: measured using a non stretchable tape at the mid-point of the lowest rib-cage and the iliac crest to the nearest 1 cm in the standing position during end tidal expiration. It was measured twice and if the difference between the two readings was 0.4 cm a 3rd reading was taken and mean was calculated using the two closest values. Waist circumference percentiles were generated using age and sex specific Kuriyan chart of waist measurements for Indian children and based these percentiles subjects were categorized into three groups
2. <75th centile – normal
3. 75 – 90th centile – overweight
4. >90th centile – obese

Beyond 16 years, based on sex following values were taken as cut off

Girls <80cm – normal
 >80 cm – obese
 Boys <90 cm – normal
 >90 cm – obese.

5. Hip circumference: recorded to the nearest 0.1 cm at the level of greater trochanter in the standing position. It was measured twice and if the agreement between 2 repeats was >0.4 cm, than a 3rd measurement was taken and the mean was calculated using the 2 closet values.

6. Waist/Hip ratio: it signifies the ratio of the truncal and extremity fat distribution. In male >0.9 and in female >0.8 were taken off as cut off.

7. Neck circumference: measured in the standing position, head held erect at the level of thyroid cartilage. In the absence of data on the cut off values for neck circumference in Indian children we adopted the corresponding values from the US counterpart.

SMR

Tanner's staging was done in all the subjects. Fasting blood sample were obtained after a minimum fasting of 8 hours and were transported to the laboratory on ice (4-8°C) for estimating plasma glucose by glucose oxidase

peroxidase method. Fasting serum insulin was estimated by "enhanced pulse" – chemiluminescence system (Monobind– USA).

HOMA-IR (Homeostatic Model assessment of insulin Resistance) was estimated as

$HOMA-IR = \text{Fasting glucose (mmol/L)} \times \text{Fasting insulin}(\mu\text{U/ml})/22.5$

HOMA-IR centiles based on sex and pubertal staging were generated based on insulin resistance indexed in healthy children. (10) HOMA-IR >90th centile.

Observation

Total 30 subjects participated in the study. 17(57%) were male and 13(43%) were female. 6(20%) subjects were in 6-<10 year age group, 15(50%) were in 10-<15 year, and 09(30%) were in 15-19 year age group. Clinical, Anthropometric & Biochemical characteristics of the subjects are shown in table 1.

Table: 1 Clinical, anthropometric, and Biochemical characteristics of the subjects

Parameters	Mean \pm SD (Range)
Age	12.7 \pm 3.3 (7-19)
BMI kg/m ²	27.7 \pm 4.2 (20-35.9)
Waist circumference (cm)	92.3 \pm 12.7 (67-116)
Waist/Hip ratio	0.93 \pm 0.09 (0.77-1.17)
Neck circumference (cm)	34.1 \pm 2.8 (28-40)
Fasting sugar	87.1 \pm 7.6 (73.1-107)
Fasting insulin	17.4 \pm 13.5 (1.6-61)
HOMA-IR	6.7 \pm 3.07 (0.4-14.5)

HOMA-IR was correlated with neck circumference. Total 25 subjects had abnormal neck circumference. Out of these 13 had normal HOMA-IR while 12 had insulin resistance (HOMA-IR>90%).on statistical analysis it was found that abnormal neck circumference was statistically

not significantly associated with insulin resistance (p value = 0.24) as shown in table 2.

TABLE=2

	HOMA-IR <90 th percentile	HOMA-IR >90 th percentile
NC normal(n=5)	4 (80%)	1 (20%)
NC > normal(n=25)	13(52%)	12 (48%)
Total	17(57%)	13(43%)

$X^2 = 1.33$, p value = 0.24

HOMA-IR was correlated with waist-hip ratio. Total 23 subjects had abnormal abnormal waist hip ratio. Out of these 13 had normal HOMA-IR while 10 had insulin resistance (HOMA-IR>90%).on statistical analysis it was found that abnormal waist hip ratio was statistically not significantly associated with insulin resistance (p value = 0.97)as shown in table 3.

TABLE=3

	HOMA-IR< 90 th percentile	HOMA-IR >90 th percentile
W/H <0.9 OR <0.8	4 (57%)	3(43%)
W/H >0.9 OR >0.8	13(56%)	10(44%)
Total	17(56%)	13(44%)

Pvalue=0.97

HOMA-IR>90TH Percentile vs BMI percentile respectively males and females p value 0.06and 0.83this difference was found to be statistically insignificant=TABLE=4 and 5

TABLE=4

	HOMA-IR (<90 TH percentile)	HOMA-IR (>90 TH percentile)
Bmi%tile	86.4	97.1
	89.8	97.5
	93.4	98.1
	96.5	98.2
	97.4	98.5
	98.4	98.6
	99.5	98.9
		99.4
		99.4
		99.5
Mean	94.4±4.85	98.5±0.81

P value=0.06

HOMA-IR (>90th percentile)vs BMI percentile males.

TABLE: 5

	HOMA-IR (<90 TH percentile)	HOMA-IR (>90 th percentile)
Bmi%tile	91.3	
	91.8	
	91.8	
	93.6	
	94.2	92.6
	95.2	95.8
	95.9	97.6
	97.8	
	98.0	
	99.8	
Mean	94.92. ±9	95.4±2. 5

P value=0.83.

DISCUSSION

G shrinivasa rao at al^[11] found prevalence of the insulin resistance obesity dyslipidemia among children and adolescent is increasing rapidly in india and it is well established that obesity is risk factor for metabolic syndrome type 2 diabetes and can adult and children.^[12,13,14] the goal of study to evaluated the IR in children and its relation with several anthropometric indices.in current study we found that IR is high in both obese and overweight children and statistically significant association could be demonstrated with one of the anthropometric marker neck circumference but in our study statistically significant association it could not be

established with other anthropometric parameter BMI and WHR IR and BMI in our study mean value with HOMA-IR value less than 90th percentile and value more than 90th percentile in both males and females gender was found to be statistically insignificant. murdock at al^[15] found the high prevalence of IR among overweight and obese children as seen in current study. Also found another study significantly elevated BMI, WHR in both obese and overweight children and adolescents than controls and our observations strongly suggest the association between adiposity and insulin resistance^[16,17] adequate proxy measure for monitoring the underlying increases in health risk due to excess weight at

population level. it is attractive and cheap and non invasive means of assessing excess body fat. although BMI not gold standard measure of overweight or obesity (national obesity observatory june 2009). Its advantage in term of ease of measurement, established cut offs and existing published statistics make it only currently variable option for high level of summary figure of population level. BMI not provided any indication of the distribution of body fat. low sensitivity for screening of obese individual. children and adolescent grow both in weight and height and gain lean body mass and adipose tissue throughout childhood and adolescent and there are large between population inter and intra individual variation.^[18] Waist circumference the measurement of waist circumference is an attempt to capture information regarding the distribution of body fat. visceral adipose tissue that has been linked to increased health risk and metabolic disorder in children and adults. in adult measurement of WC as an indicators of intra abdominal fat mass more directly correlate with CVD risk than overall obesity determined by BMI.^[19] but health risk associated with an excessive abdominal fat distribution in children is unclear. wc is highly sensitive and specific measure of upper body fat and has been shown to correlate with insulin resistance in adults. measurement of WC in children good correlation in IR-syndrome shown that various studies.^[20] but adiposity for children will change with age so it is not possible to use of fixed set of threshold as used in adults. in current study we have used these charts as reference with cutoff 75th percentile for overweight and 90th for obesity. waist circumference help to identifying the obese children who are at high risk for developing insulin resistance syndrome. WAIST TO HIP RATIO--in current study no association was found between insulin resistance and this ratio. Several study dr kusum and kalker et al study also found no correlation between insulin resistance and W/H ratio. The use of ratio such as WHR to assess obesity may not be appropriate because they are highly age dependent and may obscure stronger relation that may be present with separate circumference measurements. kalker et al^[21] study but not found correlation between percentage overweight and. thus WHR is not a good marker of adiposity and cardiovascular health in children. NC and IR-in current study, neck circumference is found to be closely associated with insulin resistance (more close in females, p value 0.096 as compared to males. p value 0.118) but statistically significant association could not be established in individual sexes. however statistically significant value is established when neck circumference of both the sexes simultaneously was taken into account. while not significant association was found when homa-ir 90th percentile was taken as cut off earlier. framington sarah et al upper body sc fat as estimated by neck circumference may confirm risk above and beyond the visceral abdominal fat. anatomically upper body s/c fat is unique fat depot located in a separate compartment compared with VAT. this fat depot may play important role in risk factor for free fatty acid concentration. and elevated free fatty acid concentration associated with

IR.⁽²²⁾ some studies indicated that neck circumference may be independent correlate of metabolic risk factor above and beyond BMI and WC in adults. very few paediatrician investigators have explored the potential value of NC as an index of high BMI. and its association with metabolic profile-elevated IR (23,24,25) thus NC could be useful screening instrument for identifying overweight or obese children, who are at high risk of having insulin resistance.

CONCLUSION

Insulin resistance is significantly associated with marker of adiposity like neck circumference. its association was significant. nc on application chi square trends the association between the BMI and HOMA-IR was found to be not significant. Our study shows that the insulin resistance of adult disease erupts in childhood itself and therefore control of weight should be aimed from early childhood so as to prevent complication of obesity in future.

REFERENCES

1. BMI FOR AGE NATIONAL health and nutrition survey (NHANES) CDC/national center for health statistic.
2. Government the health ministry has reduced the diagnostic cutoff for body mass index (BMI) to 23kg/m² the standard waist circumference to deal obesity submitted on 11/26/2008-www.igovernment.in health.
3. Kurian R, Thomas T, Lokesh DP, Sheth NR, Mahendra A. Waist circumference and waist for height percentile in urban south Indian children aged 3-16 years. Indian pediatric, 2011 Mar 15. pii: S09747559100381-1.
4. Weiss R, Dziura J, Bugert TS, Tamborlane WV et al obesity and the metabolic syndrome in children and adolescent, New England journal of Medicine, 2004; 350: 2362-2374.
5. Huxley R, Barzi F, Lee C, Lear S, Shaw J, Lam TH, Patel J et al. waist circumference thresholds provide an accurate, simple and widely applicable method for the discrimination of diabetes. diabetes care, 30: 3116-8.
6. Hales CN, Barker DJ. TYPE 2 DIABETES MELLITUS THE THRIFTY PHENOTYPE HYPOTHESIS DIABETOLOGIA, 1992; 35: 595-601.
7. Daniel E, Hale and Stuart. weinzimer. type-2 DM in children and adolescent. jr. moshang. pediatric endocrinology-the requisites in pediatric. mosby publication.
8. http://www.idf.org/diabetesatlas/5e/the_global_burden
9. Barbara B. Kahn and Jeffrey S. Flier. obesity and insulin resistance. j clin invest, 2000; 106(4): 473-481.
10. Giuseppe D Annunzio, Maurizio et al. insulin resistance and secretion indexes in healthy Italian children and adolescent a multicentre study, ACTA BIOMED, 2009; 80: 21-28.

11. G.SRINIVASA Nageswara Rao. Gurumurthy prema, gururajan priya. sarasa barathi. comparison between serum insulin levels and its resistance with biochemical, clinical and anthropometric parameters in south Indian children and adolescent. *Ind j clinbiochem*, jan-mar, 2011; 26(1): 22-27.
12. Castelli WP. Epidemiology of coronary heart disease: the Framingham study. *Am J Med.*, 1984; 76: 4–12. doi: 10.1016/0002-9343(84)90952-5. [PubMed] [Cross Ref].
13. Despres JP, Lamarche B, Mauriege P, Cantin B, Dangenias GR, Moor Jani S, Lupin PJ. Hyperinsulinemia as an independent risk factor for ischemic heart disease. *N Eng J Med.*, 1996; 334(15): 952–957. doi: 10.1056/NEJM199604113341504. [PubMed] [Cross Ref].
14. Freedman DS, Dietz WH, Srinivasan SR, Berenson GS. The relation of overweight to cardiovascular risk factors among children and adolescents; the Bogalusa Heart Study. *Pediatrics*, 1999; 103: 1175–1182. doi: 10.1542/peds.103.6.1175.
15. murdock DK, OLSON KJ, Juza RM, Hendrick BL. effect of body mass index on insulin resistance and lipid in prepubertal and postpubertal children. *school observation.j cardiometabolic syndr*, 2006; 1(4): 242-7.].
16. Arslanian S, Suprasongsin C. Insulin sensitivity, lipids, body composition in childhood: is “syndromex” present? *J Clin Endocrinol Metab*, 1996; 81: 1058–1062. doi: 10.1210/jc.81.3.1058. [PubMed] [Cross Ref].
17. Caprio S, Bronson M, Sherwin RS, Rife F, Tamborlane WV. Co-existence of severe insulin resistance and hyperinsulinemia in pre-adolescent obese children. *Diabetologia*, 1996; 39: 1489–1497. doi: 10.1007/s001250050603.
18. Y Wang epidemiology of childhood obesity–methadological aspect and guidelines what is new. *international journal of obesity*, 2004; 28: s21-s28.
19. Valeria hirschler, MD, Cludio aranda MS, can waist circumference identify children with the metabolic syndrome. *Arch pediatr adolesc med.*, 2005; 159: 740-744.
20. freedom DS, Dietz WH. Shrinivasan SR. Berenson GS. The relation of overweight to cardiovascular risk factor among children And adolescent the Bogalusa heart study, *pediatric*, 1999; 103: 1175-1182.
21. Kalker u.O Kolbe-Saborowski. obese children and adolescent. waist hip ratio and cardiovascular risk. *Montasschr Kinderheilkd*, jan, 1993; 14(1): 36-41.
22. Preis, josheph M. Massaro, Udo Hoffmann. neck circumference as a novel measure of cardiometabolic risk; Framingham heart study. *j clin endocrinolo metab*, august, 2010; 95(8); 3701-3710.
23. OLubukola O. Nafiu, Constance Burke, Joyce Lee. terri voepellewis, shobha malviya. kevin k. tremper. neck circumference as a screening measure for identifying children with high body mass index. *pediatric aug*, 2010; 126(2): e306-e310.
24. Hetipoglu N. Mazicioglu MM. Kurtoglu s. neck circumference an additional tool of screening overweight and obesity in childhood. *Eur j pediatr jun*, 2010; 169(6): 733-9.
25. LaBerge RC, Vaccani JP, Gow RM, Gaboury I, Hoey L, Katz SL. Inter- and intra-rater reliability of neck circumference measurements in children. *Pediatr Pulmonol*, 2009; 44(1): 64–69.