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Comparative Analysis of Cardio Metabolic Risk Factors in Context of Insulin Resistance among South Indian Obese and Non-obese Adolescents

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Authors' contributions

Author SMG designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of manuscript. Authors MBG and SMG managed the analyses of the study. Author SMG managed the literature searches. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Background: Presently, it is of an utmost importance to know the prevalence of cardio metabolic risk factors and insulin resistance among obese adolescents in south Indian population, where genetic predisposition to obesity is high. This knowledge would enable us to take preventive measures as well as health education that can be implemented much early in school going adolescents.
Aim and Objectives: To study the prevalence of cardio metabolic risk factors in obese adolescent age group (11-18 years) and to correlate these cardio metabolic risk factors with insulin resistance among them.
Materials and Methods: A total of 120 adolescents (two groups: obese versus non-obese healthy controls) were selected for this cross-sectional study. Obesity was defined as per BMI at 95th percentile. Both groups were analysed for anthropometric parameters: body mass index (BMI), blood pressure (BP), waist circumference (WC), hip circumference

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(HC), waist-hip ratio (WHR) and other relevant biochemical parameters viz. glucose (fasting), insulin (fasting), lipid profile and insulin resistance by Homeostasis model assessment of insulin resistance ($HOMA_{IR}$). Statistical analysis was performed by Pearson's correlation analysis using SPSS 16.0.

Results: The data depicts the prevalence of three or more than three cardio metabolic risk factors among obese adolescents **(**36.7%). BMI and WC were significantly higher among obese as compared to non-obese adolescents ($P<0.001$). Similarly, fasting glucose ($P<0.05$), insulin, insulin resistance ($HOMA_{IR}$) were significantly increased among obese adolescents ($P<0.001$). Insulin resistance was having better correlation with BMI, WHR and mean arterial BP.

Conclusion: The result of the study clearly suggested a high prevalence of cardio metabolic risk factors among obese adolescents with elevation in insulin level and insulin resistance.

Keywords: $HOMA_{IR}$; BMI; obesity; WHR; metabolic syndrome.

1. INTRODUCTION

The prevalence and magnitude of adolescent obesity are increasing dramatically in India as well as globally during the last few decades [1,2]. It is the issue of grave concern in India. The prevalence of insulin resistance and cardio metabolic risk factors are high among obese adolescents, and it increases with worsening abdominal obesity [3]. Metabolic syndrome is a clustering of cardio metabolic risk factors that include poor glucose tolerance, hypertension, elevated triacylglycerols, low HDL cholesterol and obesity [4]. This clustering of different abnormal parameters has been shown to occur not only in adults, but also in adolescents.

Overweight and obesity cast adverse metabolic effects on blood pressure, cholesterol, triacylglycerol and insulin resistance. The more life-threatening problems are those concerned with cardio metabolic risk factors which will eventually lead to all future complications such as stroke, coronary arterial disease and Type 2 Diabetes mellitus (T2DM) [5].

Adolescents undergo a number of physical and psychological changes including changes in their social interactions and relationships combined with poor nutrition, sedentary lifestyle, lack of immunisation, adoption of unhealthy eating habits and addictions [6].

Evaluation of adolescents for obesity and cardio metabolic risk factors could thus identify adolescents at an increased risk of metabolic syndrome, T2DM and coronary artery disease (CAD) in adulthood.

The association between insulin resistance and cardio metabolic risk factors is often a matter of deliberation, once the disease sets in. The ideal population for examining these associations in depth would be one that is: 1) At high risk of insulin resistance 2) young and has not yet acquired clinical disease and 3) undergoing rapid environmental and lifestyle changes.

The emerging epidemic of obesity in adolescents underlines the importance of studying the cardio metabolic risk factors in south Indian adolescents. Very few studies have been

undertaken in Puducherry, which have depicted the association of insulin resistance with cardio metabolic risk factors among obese adolescents.

2. MATERIALS AND METHODS

This was a cross sectional study performed in a semi urban school population of Puducherry region following the approval of the Institutional Human Ethics Committee. The procedure was explained to the subjects (adolescent students)/parents in their local language and written informed consent was obtained from parents and assent from adolescents. A total of 120 students in the age group of 11-18 years (divided into two groups: sixty obese versus sixty non-obese healthy controls) were selected for this study. Sixty obese adolescents were selected as per BMI criteria (95^{th} percentile as obese) [7].

2.1 Physiological Parameters of Obesity

Both groups were analysed for physiological parameters: weight, height, BMI, BP, waist circumference (WC), hip circumference (HC) and waist-hip ratio (WHR) to assess general and central obesity.

2.2 General Obesity

Height was measured to the nearest 0.1 cm, while the subject was standing in an erect position with foot bare on flat floor, against a vertical scale and with heels touching the wall and head straight. The body weight was measured using weighing scale, while the subject was minimally clothed and without shoes, standing motionless on a weighing scale and it was recorded nearest to 0.1 kg. Body mass index (BMI) was calculated using the formula BMI=weight (kg)/height (m^2). The cut off value for obesity was more than 95^{th} percentile in adolescents [8].

2.3 Central Obesity

Waist-Hip ratio (WHR) was calculated to assess central obesity. Waist circumference (in cm) was measured at a point mid-way between the lower rib and iliac crest with the measuring tape centrally positioned at the level of umbilicus. Hip circumference was measured (in cm) at trochanter major of the head of femur. WHR was calculated using the following formula to assess central obesity. WHR=Waist (cm)/Hip (cm).

2.4 Biochemical Analysis of Cardio Metabolic Risk Factors

Three ml of venous blood sample (fasting) was collected under aseptic precautions from adolescents, following 10 hours of overnight fast. Biochemical parameters were analysed as follows: fasting plasma glucose (analysed by glucose oxidase and peroxidase method GOD-POD), plasma insulin fasting (analysed by automated electrochemiluminiscence), serum total Cholesterol (CHOD-PAP method), high density lipoprotein (Polyanion precipitation) and low density lipoprotein (Direct homogenous method) and serum triacylglycerol (Glycerol kinase method). All the above mentioned biochemical parameters estimated using IFCC approved procedures. The internal quality control was evaluated based on QC samples provided by M/s Biorad USA. The external quality assessment was based on the QC samples provided by Clinical Biochemistry Lab, CMC Vellore.

2.5 Homeostasis Model Assessment of Insulin Resistance ($HOMA_{IR}$)

Insulin resistance was calculated by $HOMA_{IR}$ (homeostasis model assessment of insulin resistance) using the following formula [9].

$$HOMA_{IR} = \frac{\text{fasting glucose x insulin}}{22.5}$$

Insulin concentration is reported as µU/ml and glucose in mmol/L.

2.6 Statistical Analysis

The statistically significant mean difference in the obese adolescents and non obese healthy adolescents was calculated using the unpaired student's t test. All statistical analysis was performed using SPSS 16. Correlation between insulin resistance with all cardio metabolic risk factors and anthropometric measurements such as BMI and waist circumference were assessed by two-tailed Pearson's correlation. A significant level of 95% was chosen for all tests. The level of significance was taken as ($P<0.05$).

3. RESULTS

3.1 Anthropometric Parameters among Obese Adolescents

Demographic, physical and biochemical characteristics of sixty obese adolescents are shown in Table 1. Systolic and diastolic blood pressure measurements were normal in all obese adolescents. Twenty two obese adolescents (36.7%) had three or more criteria of cardio metabolic risk factors.

Table 1. Demographic and physiological characteristics of obese adolescents

Characteristics	Subjects	Number of obese adolescents with abnormal results (%)
Demographic		
Sex (Male: female)	1:1	22(36.7%)
Age	14.5+3.5	
Overweight and obese	60	
Physiological characteristics		
Waist circumference(cm)	79.92±5.95	60(100%)
Body mass index(Kg/m2)	27.73±1.87	60(100%)

3.2 Lipid Profile and Insulin Level among Obese Adolescents

Out of total sixty obese adolescents, 30% had hypertriacylglycerolemia (TAG≥130mg/dl), 13.3% had high LDL level (LDL≥100mg/dl) and 10% possessed low HDL-c (HDL≤40mg/dl in boys and ≤50mg/dl in girls) and 16.6% had high fasting blood glucose level or (can be called as impaired fasting glucose IFG) (Fasting plasma glucose≥100mg/dl &<126 mg/dl). These results are shown in Table 2. IR (Insulin resistance) was present in 24 obese adolescents (40%) ($HOMA_{IR}$ score ≥3.5).

Table 2. Biochemical characteristic of obese adolescents

Biochemical parameters	Mean±std. deviation	Number of obese adolescents with abnormal results (%)
TAG≥130mg/dl	134.02±57.11	18(30)
LDL	89±30	8(13.3)
HDL≤40mg/dl	54.4±15	6(10)
IFG(impaired fasting glucose in range of 100-125mg/dl)	90.1±7.55	10(16.6)
Insulin resistance ($HOMA_{IR}$)	3.12±1.00	24(40)

3.3 Correlation among Insulin Levels, Insulin Resistance and General Obesity Parameter Namely Body Mass Index (BMI)

A positive correlation was observed between $HOMA_{IR}$ (insulin resistance) and the anthropometric measurement BMI ($r=0.788$, $p<0.01$) and with mean arterial BP($r=0.740$, $p<0.01$). A positive correlation was seen between fasting plasma insulin and BMI ($r=0.811$, $p<0.01$), and with mean BP($r=0.751$, $p<0.01$) (Table 3)

Table 3. Correlation between insulin and HOMAIR with other parameters in obese adolescents

	r value	P value
BMI with fasting plasma insulin	0.811**	P<0.001
Mean BP with fasting plasma insulin	0.751**	P<0.001
BMI with $HOMA_{IR}$	0.788**	P<0.001
$HOMA_{IR}$ with mean arterial BP	0.740**	P<0.001
Waist circumference with insulin level	0.491*	P<0.05
Waist circumference with $HOMA_{IR}$	0.460*	P<0.05
Waist-hip ratio with insulin level	0.93**	P<0.001
Waist-hip ratio(WHR) with $HOMA_{IR}$	0.845**	P<0.001

***Correlation is significant at the 0.01 level (2-tailed).*
**Correlation is significant at the 0.05 level (2-tailed)*

3.4 Correlation between Insulin Level, Insulin Resistance and Waist Circumference (Central Obesity), Waist Hip Ratio (WHR)

Correlation was seen between fasting plasma insulin with waist circumference ($r=0.49$, $p<0.05$), and with WHR ($r=0.93$, $p<0.01$) (Table 3).

Correlation was seen between HOMAIR (insulin resistance) and central obesity estimated by waist circumference ($r=0.46$, $p<0.05$) and with WHR($r=0.845$, $p<0.01$). There was no correlation that was observed between lipid profile and insulin level as well as insulin resistance ($HOMA_{IR}$).

3.5 Prevalence of Cardio Metabolic Risk Factors among Obese Adolescents

Among our study population, obese adolescents presenting with cardio metabolic risk factors was 36.7% and met three or more criteria for metabolic syndrome. This fact also accounts for the higher percentage of hypertriacylglycerolemia (30%) observed in our studied group of

obese adolescents. One more study reported the prevalence of metabolic syndrome from 1.2% to 22.6% and reaching up to 60% in obese adolescents [10,11].

In obese adolescents, insulin (fasting) and insulin resistance were significantly higher as compared to healthy and non-obese adolescents ($P<0.001$). Obese adolescents had significantly higher body mass index (BMI), waist circumference, mean arterial blood pressure, triacylglycerol (TAG), low high density lipoprotein and total cholesterol.

4. DISCUSSION

The first proposal of definition of metabolic syndrome was established in 2003. It was elaborated based on assessment of adolescents from 12 to 19 years old using modified criteria and also based on the criteria of National Cholesterol Education Program and Adult treatment Panel III definition modified for age (NCEP/ATP-III), including abdominal circumference over percentile 85 to 90, blood pressure over limits established by the National Blood pressure Education program, lipids over the limit established by the NCEP, and glycemia over the values for adolescents [17].

According to ATP III, a diagnosis of the metabolic syndrome is made when three or more of the risk factors shown above are present [18].

In adolescents, the prevalence and magnitude of the cardio metabolic risk factors are relatively low (3.7 to 4.2%) when compared to adult population, excepting among overweight and obese adolescents where there is an increase in prevalence of the metabolic syndrome up to 32% [12,13]. The prevalence of overweight/obesity among adolescents is higher (17.8 in boys of 13-18 years of age group and 15.8% in girls of the same age group) drawn from Tamil Nadu (BMI>=25) even though the studies from Delhi have used a lower criteria (BMI>=23) [14]. Prevalence in five major cities of India was 18% whereas Augustine *et al*. have reported 24% prevalence of overweight/obesity (BMI>23) among urban college going girls aged between seventeen and eighteen in Ernakulum, Kerala [14,15,16].

4.1 Insulin Level, Insulin Resistance ($HOMA_{IR}$) and BMI

In our study, it was found out that adolescents with insulin resistance and enhanced insulin level were obese. Also significant correlation was found to exist between insulin resistance and body mass index in obese adolescents. Similar findings were reported previously by Ramchandran A et al. [19].

This clearly shows an association between insulin resistance and insulin level with reference to general obesity [20]. In obesity, fat cells secrete adipokines namely leptin, adiponectin, resistin and TNF alpha which increase insulin resistance eventually leading to hyperinsulinaemia [21].

4.2 Insulin Level, Insulin Resistance with Waist Circumference and WHR

As per our study, there was a less significant correlation found between waist circumference and insulin resistance. This could possibly be attributed to the phased response observed in insulin resistance. Whereas, we got significant positive correlation between insulin level, insulin resistance and WHR. Hence an increase in insulin resistance could be linked to increase in waist hip ratio (WHR), which could be used as a cost effective and reliable

marker of central obesity in adolescent. Epidemiological and metabolic studies conducted over the last fifteen years have confirmed that a high proportion of abdominal fat(central obesity) is a major risk factor for coronary heart disease, T2DM and related morbidity. Epidemiological studies have mainly used the waist-to hip circumference ratio (waist: hip ratio) to compute the proportion of abdominal adipose tissue. Visceral obesity is associated with insulin resistance, hyperinsulinaemia, and poor glucose tolerance "Central obesity is often referred to as abdominal, upper body, male type, android or visceral obesity whereas, in female-type gynoid obesity, there is preferential fat accumulation in the gluteal and femoral region." This can be measured by WC and WHR. These are known to be very important risk factors in the development of metabolic syndrome. Intra abdominal fat thickness has been found to be a reliable indicator of central obesity. Androgens influence the deposition of adipocytes in areas around the waist that are different from those deposited in the gluteo-femoral region as observed in females. These endocrinal perturbations cause visceral obesity resulting in insulin resistance thereby creating poor glucose tolerance [22].

4.3 Mean Arterial BP and Insulin Level and $HOMA_{IR}$

A significant correlation was found between insulin levels with mean arterial BP in obese adolescents. Mean arterial blood pressure was significantly higher among obese adolescents as compared to non-obese adolescents. Similar results were reported citing a prevalence of 17.34% of hypertension among overweight children aged 5-16 years as against 10.1% in normal weight [23].

4.4 Insulin Level, $HOMA_{IR}$ and IFG (Impaired Fasting Glucose Level) among Obese Versus Non-obese Adolescents

Insulin resistance ($HOMA_{IR}$), high insulin level, IFG also are significant among obese adolescents in comparison to non-obese adolescents. One of the previous studies performed in urban South India, showed similar findings linked to glucose intolerance which is higher in obese adolescents (12.7%) in comparison to non-obese adolescents (3.7-4.2%) [24].

One or more cardio metabolic abnormalities and insulin resistance (i.e. low HDL cholesterol, elevated triacylglycerols, fasting plasma glucose (or) increased blood pressure) were present in 67.7% adolescent girls and 61.7% in adolescent boys as reported by a previous study [25]. However, our study has included three or more cardio metabolic risk factors which are more objective than considering only one entity. That is why it would be much safer to compare three or more cardio metabolic risk factors in comparison to one or more such factors.

Insulin resistance is associated with dyslipidemia, hypertension, diabetes mellitus, and coronary heart disease, sleep apnoea syndrome, and certain types of cancers in obese persons [26].

According to a study performed by Ramachandran et al. in an urban population of Chennai, one or more cardio metabolic abnormalities are present in nearly 67.7% of young healthy, Asian-Indian adolescent and 64.8% even among those with normal weight [27]. Insulin resistance is associated with individual cardio metabolic factors and plasma insulin showed an association with clustering of some variables.

The govt. of Puducherry has initiated noon meal scheme in all government schools. It is worth bearing in mind that the nutritious noon meal can now include low glycemic index

foodstuff and in addition the adolescent school children may be advised lifestyle modification including robust and mandatory physical exercise in the daily routine. A more comprehensive door to door survey can also be undertaken in urban, rural and semi-urban population of Puducherry to assess the prevalence of adolescent obesity as linked to their genetic makeup in South Indian population

Hence, policymakers as well as health professionals must focus on primordial/primary prevention of emerging cardio metabolic risk factors among adolescents. Effective health awareness and health education programme should be promptly initiated and sustained all parts of India keeping in view the fact that the adolescent of today are the adults of tomorrow.

5. CONCLUSION

The prevalence of cardio metabolic risk factors in obese adolescents group was 36.7%. The prevalence was more in obese than in non-obese adolescents. A significant positive association was found among insulin levels, insulin resistance and body mass index (BMI) and waist hip ratio. Hence, BMI and WHR could be used as reliable cardio metabolic risk factors (predictor variables) for the obese adolescent population. Hence, periodic assessment of BMI and WHR as a routine health check up would help enable the prevention of development of IFG and cardio metabolic disorders including T2DM and coronary arterial diseases. Early prevention measures could thus be initiated and established in obese adolescent by regular weight, BMI and WHR monitoring.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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