

Pre-diabetes and Type 2 Diabetes Status in Overweight and Obese Children in a Tertiary Care Hospital of Bangladesh

MONIRA HOSSAIN¹, SURAIYA BEGUM², SHAHANAA RAHMAN³

Abstract:

Introduction: Obesity in childhood is associated with many co-morbid conditions; one of them is alteration of glucose metabolism.

Materials and Methods: This cross-sectional study was conducted among 100 overweight and obese children aged 5-16 years to determine the status of pre-diabetes (IFG and IGT) and type 2 diabetes mellitus (T2DM), attending the OPD, BSMMU, Dhaka. All overweight/obese children were included according to BMI for age and sex using CDC growth chart. Children taking steroid for any cause or having any endocrine disorder or syndrome was excluded from the study. Anthropometry and blood pressure measurement were done and skin manifestations of insulin resistance were looked for. Fasting lipid profile and oral glucose tolerance test (OGTT) was done for each child.

Result: Among the studied children 62% were male and 38% female, 77% were obese and 23% were over weight. Evidence of insulin resistance were found among most of the children and most common evidence was dyslipidemia (80%) followed by acanthosis nigricans (76%). Skin manifestation of polycystic ovary syndrome (PCOS) was found in 3% of children. Impaired fasting glucose (IFG) was found in 4% and Impaired Glucose Tolerance (IGT) was found in 7% of children among them 4% had both IGT and IFT. No child was found diabetic in this study.

Conclusion: Altered glucose metabolism was present in overweight and obese children of our children, so screening is recommended.

Keywords: Overweight, Childhood Obesity, Impaired Fasting Glucose (IFG), Impaired glucose tolerance (IGT), Pre-diabetes, Type 2 Diabetes Mellitus (T2DM).

Introduction

Prevalence of childhood obesity is gradually increasing. The burden of overweight and obesity is high in high-income countries while the low- and middle-income countries are also showing the same trend with no significant difference between the sexes.¹ Earlier the complications of obesity were mainly seen in elderly people but are now appearing in childhood also. The common major complications are hypertension, impaired glucose metabolism, dyslipidemia and nonalcoholic fatty liver disease. Childhood obesity has a substantial influence on the increasing diagnosis in Type 2 Diabetes (T2DM). Obese children and

adolescent have four times greater risk of developing T2DM than their non-obese peers.² A strong association is found between childhood obesity and insulin resistance, where obesity is considered as a precursor of T2DM.³ In childhood obesity T2DM occurs when insulin secretion fails to meet the increased demand of the body that occurs due to insulin resistance, consequently creating to a state of relative insulin deficiency.⁴ Among obese children the prevalence of altered glucose metabolism is reported to be between 10-30% in different countries.⁵⁻⁸ The prevalence of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) among obese adolescents were reported to be 6.5% and 5.5% respectively.⁹ The development of normal glucose tolerance (NGT) to T2DM comprises a transitional phase of IFG or IGT which is also recognized as prediabetes.¹⁰ Aim of this study was to assess the status of IFG, IGT and T2DM in overweight and obese children and adolescents in Bangladesh.

1. Consultant, Department of Paediatrics, Shaheed Suhrawardy Medical College Hospital

2. Professor of Paediatrics, BSMMU

3. Pro-VC(Academic) & Professor of Paediatrics, BSMMU

Correspondence: Dr. Monira Hossain, Consultant, Department of Paediatrics, Shaheed Suhrawardy Medical College Hospital, Sher-e-bangla Nagar, Dhaka, Mobile no: 01712084725, E-mail: moniradr@gmail.com

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Materials and Methods:

It was a cross sectional study conducted in paediatric endocrine clinic and paediatric OPD (outpatient department), Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from February, 2016 to July, 2017. Children aged 5 to 16 years attending in OPD for overweight or obesity were included in this study. Total 100 children were enrolled after considering inclusion criteria. Children who were taking systemic steroid for any cause and children suffering from genetic, endocrine disease that might cause obesity were excluded from the study. Ethical clearance was taken from Institutional Review Board, BSMMU. Informed written consent was obtained from children or their guardians after explaining to them the objectives as well as the method of the study. A structured questionnaire was used to collect data regarding socio-demographic status including position of index case, family members, family structure, family income level and educational status of parents. Physical examination consisted of a detailed evaluation of skin for clinical sign of insulin resistance including acanthosis nigricans, hirsutism, androgenic alopecia, acne etc. Weight was measured by using electronic weighing machine (Omron HN 286, Japan) to a nearest 100g and height was recorded on upright position and bare footed by using locally made height board. After measuring height and weight, BMI was calculated and categorized as overweight and obese according to Centers for disease control (CDC) and prevention criteria.¹¹ Here children having BMI for age and sex $\geq 85^{th}$ to $< 95^{th}$ centile were classified as overweight and $\geq 95^{th}$ percentile were classified as obese. By using a mercury sphygmomanometer three blood pressure determinations were obtained by standard methods on the right arm. BP was measured 3 times at 60 second intervals. The average of the second and third measurements was used in our analysis. Diagnosis of hypertension was made on the basis of national high blood pressure education programme (NHBPEP) guidelines.¹²

After clinical evaluation patient was advised to do fasting lipid profile and oral glucose tolerance test. National heart lung and blood institute (NHLBI) panel definition of dyslipidemia in 2011 was used in this study.¹³ So in this study dyslipidemia was defined as total cholesterol level 200 mg/dl or more, LDL over 130 mg/dl or more, HDL less than 40 mg/dl, triglyceride 100 mg/dl or more (0-9 years) and 130 mg/dl or more (10-19 years). Oral glucose tolerance test was performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water or 1.75 g/kg of body weight to a maximum of 75 g.

Then blood sugar was measured after 2 hours. In this study International society for paediatric and adolescent diabetes (ISPAD) clinical practice consensus guidelines 2018 was used to diagnose diabetes.¹⁴

The criteria for the diagnosis of diabetes mellitus (DM):¹⁴

Fasting plasma glucose	Interpretation
<5.6mmol/L (100mg/dl)	Normal glucose tolerance
5.6 to 6.9mmol/L (100-125mg/dl)	Impaired glucose tolerance
≥ 7.0 mmol/L (≥ 126 mg/dl)	Provisional diagnosis of diabetes

The corresponding categories for IGT when the OGTT was used¹⁴:

2 hour post load plasma glucose	Interpretation
100-125mg/dl (140mg/dl)	Normal glucose tolerance
7.8 to < 11.1 mmol/L (140-200mg/dl)	Impaired glucose tolerance
≥ 11.1 mmol/L (≥ 200 mg/dl)	Provisional diagnosis of diabetes

Statistical analysis was performed by using IBM SPSS Statistics for Windows, version 21.0. Armonk NY: IBM Corp. Data was analyzed by proportion test or frequency distribution table.

Results

Among the total number of 100 children 62% were male and 38% were female. Among them 23% were overweight and 77% obese (Table I). Most common evidence of insulin resistance was dyslipidemia (80%) followed by acanthosis nigricans (76%). Seven percent of children presented with either impaired fasting glucose or impaired glucose tolerance and 5% had hypertension. Three percent of study children presented with physical signs of polycystic ovary syndrome which was evident by hirsutism or acne but no child presented with male pattern of baldness (Table II). Impaired fasting glucose (IFG) was observed among 4% and impaired glucose tolerance (IGT) was observed among 7% of study population (Table III & Table IV). Among the children 4% had both IFG and IGT.

Table I*Distribution of the study children by body mass index (n=100)*

Body mass index (kg/m ²)	No. of patients
≥85th-<95 percentile (Overweight)	23
≥95th percentile (Obese)	77

Table II*Distribution of study children by evidence of Insulin Resistance (n=100)*

Sign of Insulin Resistance	Number (%)
Acanthosis Nigricans	76 (76%)
Hypertension	05 (5%)
Dyslipidemia	80 (80%)
IFG	04(4%)
IGT	07(7%)
Skin manifestation of PCOS:	
Hirsutism/Hypertrichosis	03(03%)
Acne	03(03%)
Male pattern of baldness	00(0%)

Table III*Distribution of study children by Fasting Plasma Glucose(n=100)*

Fasting Plasma Glucose	No. (%)
<5.6 mmol/L(<100mg/dl)	96(96%)
5.6 – 6.9 mmol/L(100 - 125mg/dl)	04 (4%)
≥7 mmol/L(≥126mg/dl)	00 (0%)

Table IV*Distribution of study children by 2 hour post load plasma glucose (n=100)*

2 hour post load plasma glucose	Number
<7.8 mmol/L(<140mg/dl)	93
7.8 – <11.1 mmol/L(140 - 200mg/dl)	07
≥11.1 mmol/L(≥200mg/dl)	00

Discussion:

Childhood obesity is strongly related to insulin resistance which is thought to be a fore runner of type 2 diabetes.³ Acanthosis nigricans is a very common finding of hyperinsulinemia and childhood obesity. It

is characterized by a dark velvety rash around the neck or under arm and is a physical marker for underlying endocrine dysfunction.¹⁵ This condition occurs due to excess insulin resulting from insulin resistance and is present in up to 90% of type 2 diabetic children.¹⁶ Several international studies reported that the prevalence of acanthosis nigricans was between 49.2% to 58.2% among overweight and obese children.^{17,18} In the current study 76% of obese and overweight children presented with acanthosis nigricans which is much higher than previous studies.

Obesity is frequently accompanied with hypertension, which is a significant risk factor for cardiovascular disease. The pathophysiological mechanism that is supposed to play the vital role in development of hypertension in obesity is activation of sympathetic nervous system and renin angiotensin aldosterone system.¹⁹ Anjan et al. found that prevalence of both the systolic hypertension(22%) and diastolic hypertension (33.8%) were much higher among obese children.²⁰ Two other Indian studies showed similar findings where the prevalence of hypertension were 25% and 34.43% among the obese children.^{21,22} Present study is not consistent with above studies as we found that only 5% of our children were hypertensive.

It has been hypothesized that insulin resistance plays a major role in the development of dyslipidemia. Obesity plays the principal role in insulin resistance syndrome which comprises of hyperinsulinemia, hyperlipidemia, hypertension and type 2 diabetes.²³ Deeb et al. found 55.3% of obese children having dyslipidemia while Inalhan et al. found 62.6% abnormal lipid profile among obese children.^{24,25} In the current study dyslipidemia was found in 80% of overweight and obese children.

Obesity increases the risk of PCOS through insulin resistance and subsequent compensatory hyperinsulinemia. This changes enhance the ovarian/adrenal androgen production and also suppress sex hormone binding globulin, thus increasing the androgen bio-availability.²⁶ The clinical manifestations of PCOS are oligoanovulation, acanthosis nigricans, acne, hirsutism, alopecia and increased body fat mass.²⁷ Previous study showed that the prevalence of PCOS was 1.18% in overweight, 2.58% in moderately obese and 5.69% in extremely obese girls.²⁸ In our study we found that 76% had acanthosis

nigricans, 3% had hirsutism and 3% had acne but no patient had alopecia or male pattern of baldness.

In obese children, the amount of non-esterified fatty acid, glycerol, cytokines, pro-inflammatory substances, hormones, and other elements are increased which lead to the development of insulin resistance. Insulin resistance along with β -cell dysfunction lead to the development of diabetes in the obesity. Non esterified fatty acid is the key grounding factor for the development of insulin resistance and for the impairment of α -cell function.²⁹ Two nationwide large cohort study done in Germany and Sweden revealed that the prevalence of IFG among obese children in the Germany was 5.7% and in Sweden was 17.1%.³⁰ Another Iranian study found that the prevalence of IFG was 4.61% in the 6-10 year age group and 5% in aged 10.1-19 year while the prevalence of T2D was 0.1%.³¹ A Bangladeshi study done by Mohsin et al. found that IGT was present in 16.9% of obese children and adolescents and diabetes mellitus was detected in 2.1% of obese subjects.³² In the present study IFG and IGT was found in 4% and 7% of study children respectively and among them 4% had both IGT and IFT. No patient was found to have diabetes in our study.

Limitations of the study were firstly the number of study children was small to reach an appropriate inference; further studies are needed on large sample size to give definite result. Also it needs to be mentioned here that insulin resistance index (HOMA-IR) was not done in the current study which was required to diagnose insulin resistance.

Conclusion:

A number of overweight/obese children and adolescents were being affected by dysregulation of glucose homeostasis. Therefore, it is very important to identify obese children and adolescents who may be at risk for development of altered glucose metabolism which ultimately can progress to type 2 diabetes.

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Conflicts of interest: Nothing to declare

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