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Original Research Article

Prevalence of prediabetes in children and its association with risk factors

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ABSTRACT

Background: Type 2 Diabetes is becoming more common at younger age group. It is important to screen children and adolescents for prediabetes to prevent long-term complications of diabetes. This study was conducted to study the prevalence of prediabetes in children and its association with risk factors
Methods: It is a Prospective hospital-based study. Children aged 6 to 18 years admitted in the Pediatric ward of tertiary care hospital were included. Study was done over a period of 2 years November 2015-October 2017. Participants were screened to find out the prevalence of prediabetes. Prediabetes was defined as fasting glucose concentration (FBS)of 100-125 mg/dl or a HbA1c value of between 5.7% and 6.4%, or a two-hour post-glucose tolerance concentration (OGTT) of 140-199mg/dl.
Results: 607 children participated in the study.56.3% were males. Prevalence of Prediabetes was 20.4% with a combination of OGTT, FBS and HbA1c tests. Prevalence by OGTT was 5.9%, HbA1c 4.1% and by FBS was 17.1%. Higher prevalence of prediabetes was associated with male gender, frequent consumption of junk foods, decreased physical activities, overweight, obesity and high waist to hip ratio. Combination of FBS with GTT and FBS with HbA1c had better sensitivity and specificity when compared to combination of OGTT with HbA1c .
Conclusion: Screening of children for prediabetes at younger age especially those with risk factors and intervention with lifestyle modification may help in delaying the progression of the disease.

Keywords: Glycosylated hemoglobin, Fasting blood sugar, Obesity, Oral Glucose tolerance test, Prediabetes, Waist to hip ratio

INTRODUCTION

Diabetes mellitus poses a major public health problem worldwide and India ranks 2nd in the list. India currently represents 49% of the world's diabetes burden with an estimated 72 million cases in 2017, expected to double to 134 million by 2045.[1] Around 58% of diabetic population are unaware of their disease. Although Type 1 diabetes is common in children, prevalence of type 2 Diabetes is on the rise due to various factors. Type 2 diabetes is a lifestyle disease common in adults but is increasingly seen in children and adolescents due to rising levels of obesity, physical inactivity and poor diet. The clinical manifestations are preceded by an asymptomatic prediabetic period and hence may be underdiagnosed. Prediabetes is an intermediate state of hyperglycemia with glycemic parameters above normal but below diabetic threshold.[2] Prediabetes is defined by the American Diabetes Association (ADA) as a fasting glucose concentration of 100-125 mg/dl or a HbA1c value of between 5.7% and 6.4%, or a two-hour plasma glucose tolerance concentration after 75gm oral glucose

tolerance test of 140–199 mg/dl.[3] The World Health Organization (WHO) has defined prediabetes as a state of intermediate hyperglycemia using two specific parameters, impaired fasting glucose (IFG) defined as fasting plasma glucose of 110 to 125 mg/dL and impaired glucose tolerance (IGT) defined as 2 h plasma glucose of 140-200 mg/dl after ingestion of 75 g of oral glucose load.[4] In India 24 million people have impaired glucose tolerance and is expected to increase to 41 million by 2045.[1] Early identification of prediabetes helps in appropriate management including diet modification and healthy life style, thereby reducing the progression to diabetes and its complications.

The data on prevalence of diabetes in children is scanty and only few studies have been conducted. The present study aims to study the prevalence of prediabetes in apparently healthy children and its association with various risk factors.

METHODS

A Prospective Hospital based study design conducted in a tertiary care teaching hospital. Study was conducted for the period of November 2015 - July 2017.

Study population

Children of age group between 6 to 18 years admitted in Paediatric ward for minor illness. Informed consent was obtained prior to participation and study was approved by the ethical committee.

Inclusion criteria

Children in the above-mentioned age group who have recovered from the illness. Children were on their normal diet at least for 48hrs prior to the test.

Exclusion criteria

Those with Acute diarrhoea Disease, underlying chronic illness, on drugs which are known to cause elevated blood glucose levels and those who were not taking their routine normal diet.

Criteria used for diagnosis of prediabetes

Fasting plasma glucose level of 100 to 125 mg/dL, a 2 - hour plasma glucose level after oral glucose tolerance test (OGTT) of 140 to 199 mg/dL, hemoglobin A1c(HbA1c) 5.7 to 6.4% as defined by the American Diabetes Association.

Method: Information about physical activity and frequency of dietary intake of fast food, sweets, soft drinks were obtained using a preformed pretested questionnaire. Anthropometry measurements taken included weight, height, hip circumference, waist circumference, waist to hip ratio and body mass index (BMI). Weight was taken using electric weighing machine and height using a stadiometer. Hip circumference was measured with the child standing erect with arms at the sides and feet together, the measurer sitting at the side of the subject so that the level of the maximum extension of buttocks was seen. The measuring tape was placed around the buttocks in the horizontal plane snuggly and the reading was made to the nearest 0.1 cm. The waist circumference was taken with measuring tape placed snugly at the midpoint between the lowest rib and the anterior superior iliac spine and the reading was made to the nearest 0.1cm. BMI was calculated using the formula weight(kg)/ height in meter^2 BMI values were plotted on the IAP chart for BMI. BMI value >95th percentile for age and sex was taken as obesity and values between 85th to 95th percentile was taken as overweight. Waist to Hip ratio was calculated and value >0.90 for males and >0.85 for females was taken as high values.

Blood glucose measurement

All participants in the study were asked to fast overnight. Sample for Fasting Blood Sugar (FBS) and glycosylated Hb (HbA1C) was taken. The samples were collected in tubes containing sodium fluoride and delivered to the laboratory within 10 minutes of collection. Oral glucose tolerance test (OGTT) was performed by giving 1.75gm/kg(max-75gm) of oral glucose in 250ml water and blood sample was collected after 2 hours for plasma glucose. Biochemical analysis of blood sugar was performed on fresh samples by glucose oxidase method and HbA1C by high performance liquid chromatography.

Statistical analysis

With 95% confidence level and 80% power with respect to prevalence of 13% in previous reported study, the calculated sample size was 560 children. Data was collected in Microsoft Excel Spread sheet. SPSS software version 17 was used for data analysis. Collected data was analyzed by frequency, percentage, mean, SD. Comparison of variables was done by chi square test, logistic regression and ROC curve. P value <0.05 was considered as significant.

RESULTS

The total number of study subjects was 607 aged 6-18yrs with a mean age of 10.7$\pm$2.6 years. Maximum number of subjects (71.3%) belonged to 9 to 14years age group. 342 were males and 265 were females.

Most of the study population were from lower socio economic classes 258 (42.5%) Class 5, 286 (47.1%) class 4 and 63 (10.4%) class 3 of modified Kuppuswamy classification. 7.8% of the population had family history of diabetes in one of the parents,74.5% parents were not evaluated and 17.7% did not have family history of diabetes.

Dietary habits of the study population revealed that maximum number of them consumed fast food, sweets and soft drinks occasionally. Also 38.6% played outdoor games only occasionally whereas 53.5% played thrice or more than thrice a week (Figure 1).

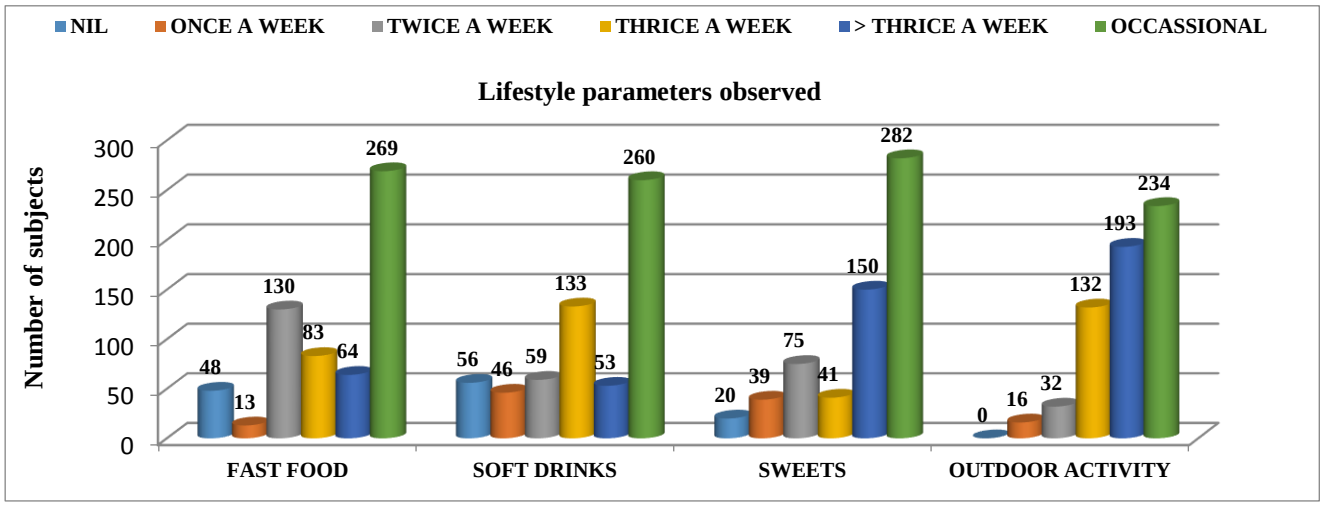

Figure 1: Diet habits and outdoor activities in the study population.

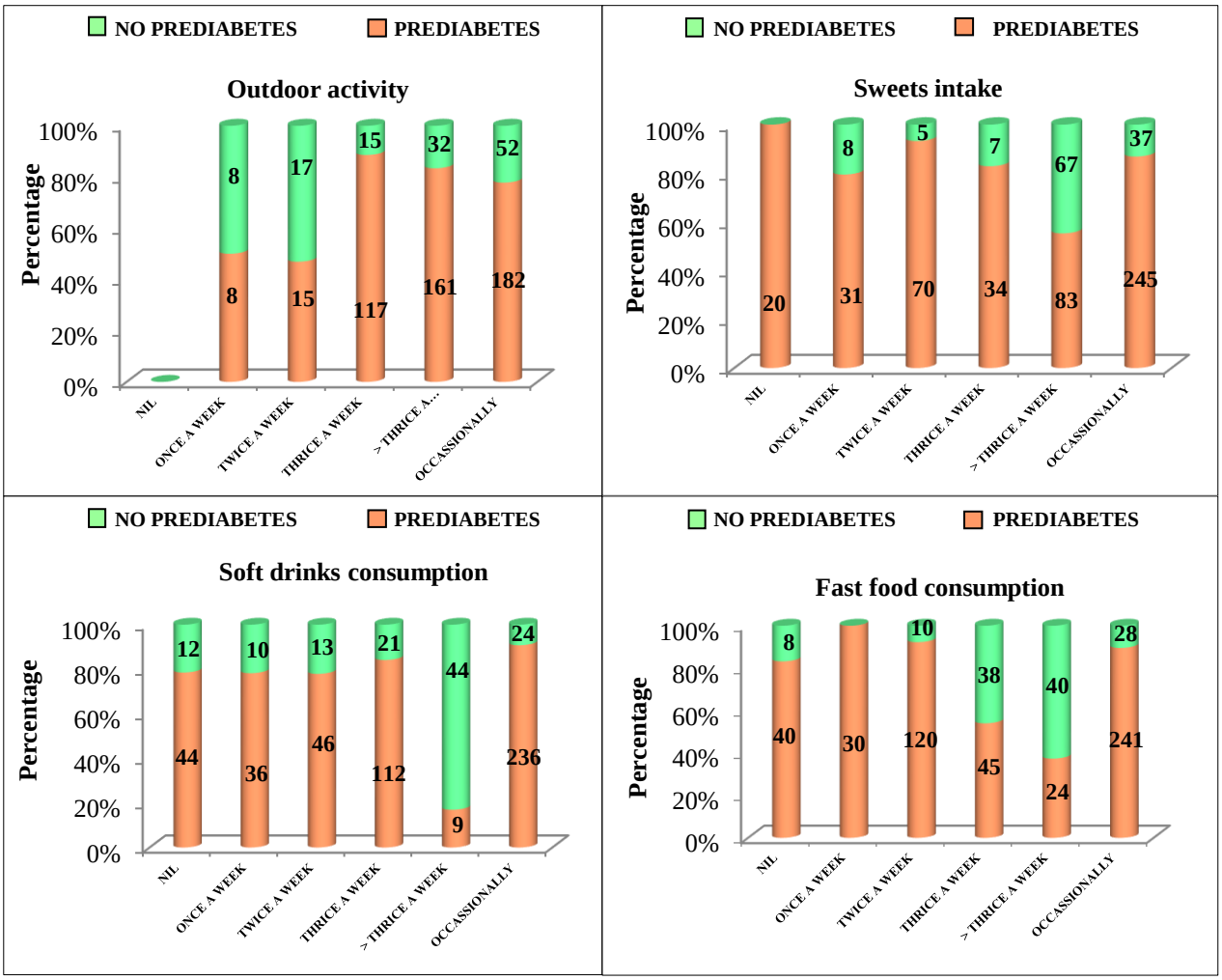

Figure 2: Fast food, sweet, soft drink intake and outdoor activity in those with normal blood glucose and in prediabetes group.

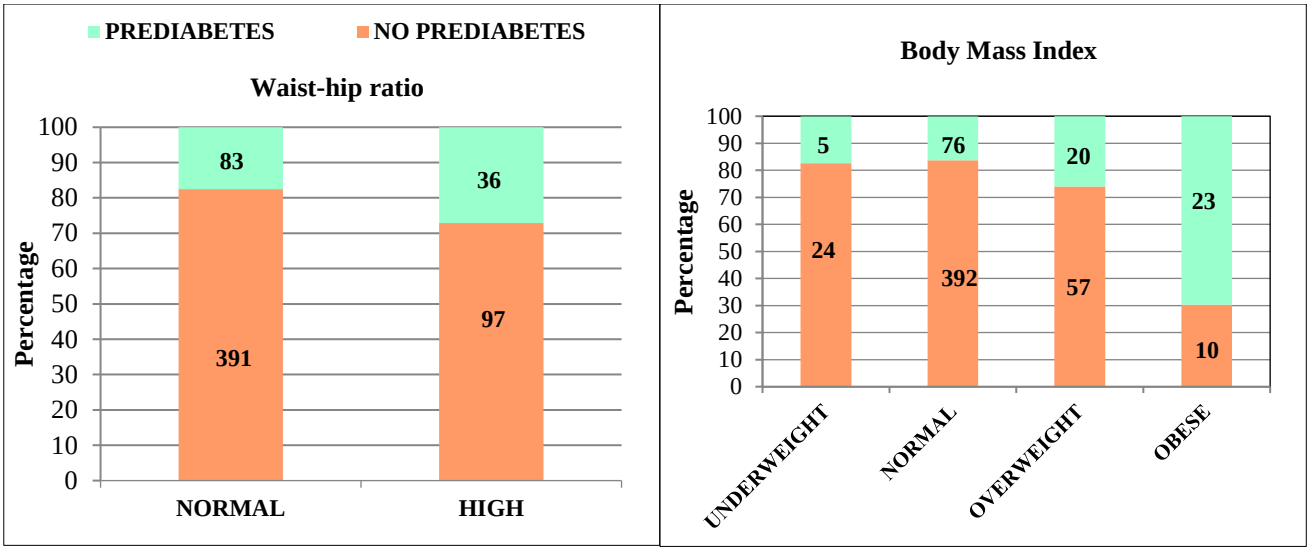

Figure 3: Waist hip ratio and BMI in the prediabetic and non-prediabetic group.

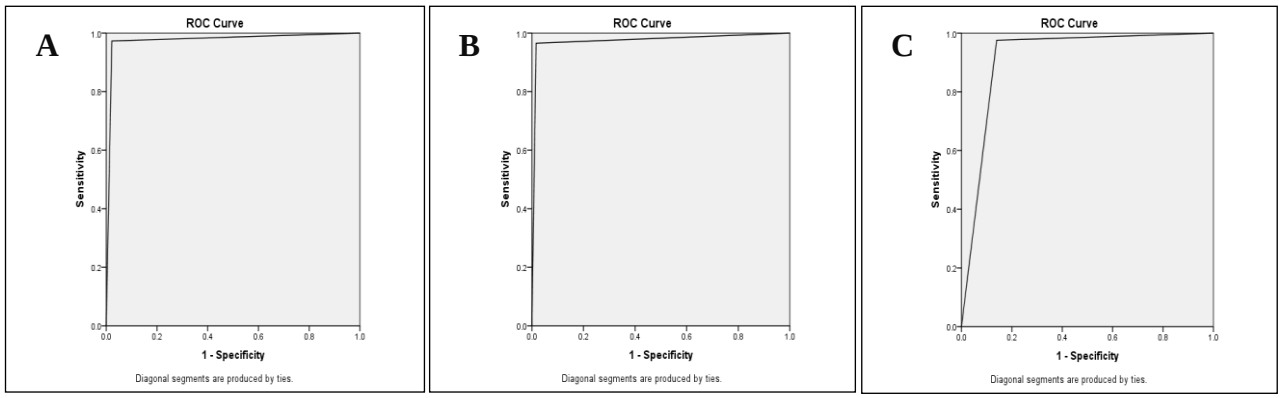

Figure 4: ROC Curves for the combination of tests. (A) FBS+OGTT: Area under the graph is 0.975, showing a high sensitivity and specificity with FBS and OGTT combination for diagnosing prediabetes. (B) FBS+GlycoHb: Area under the graph is 0.974, showing a high sensitivity and specificity with FBS and HbA1c for diagnosing Prediabetes. (C) OGTT+GlycoHb: Area under the graph is 0.918, showing lesser sensitivity and specificity in diagnosing prediabetes in children compared to combination with FBS.

Table 1: Sensitivity, Specificity and Accuracy rates of the tests.

	FBS	OGTT	HbA1C
Sensitivity	83.9%	29%	20.2%
Specificity	100%	100%	100%
PPV	100%	100%	100%
NPV	96%	84.6%	82.9%
Accuracy rate	96.7%	85.5%	83.7%

Anthropometric measurements showed normal BMI in 468 children (77.1%), underweight in 29 (4.8%), overweight in 77(12.7%) and obesity in 33(5.4%). Waist to Hip ratio was normal in 474 (78.1%) and high in 133 children (21.9%). The prevalence of prediabetes in the study population was 20.4%. Abnormal FBS values were noted in 17.1%, Abnormal GTT in 5.9% and high HbA1C in 4.1%. There was no significant difference in the prevalence among various age groups. (p-0.178) However higher prevalence was noted in boys (25.7%) in comparison to girls (13.6%) (p<0.001).

Significantly higher prevalence of prediabetes was noted in those who take fast-food, sweets or soft drinks regularly when compared to those who consume occasionally(p<0.001). Highest prevalence was noted when these food items were consumed more than thrice a week. Similarly, lower prevalence was noted in those who play outdoor games at least thrice a week(p<0.001). However lower prevalence was also noted in those playing outdoor games occasionally (Figure 2).

When the prevalence of prediabetes was compared with waist hip ratio, it was noted that prediabetes was more prevalent in those with high W/H ratio. 36 out of 133

children with high waist hip ratio had prediabetes (27.1%) compared to that of 83 out of 474 children with normal W/H ratio (17. 5%) and this difference was statistically significant (p-0.014). When correlated with BMI, statistically significant increase in the prevalence of prediabetes was noted in overweight 26% (20 out of 77) and obese 69.7% (23 out of 33) children in comparison to children with normal BMI 16.2% (76 out of 468) and underweight 17.2 % (5 out of 29). ($p<0.001$) (Figure 3).

Sensitivity, specificity, Positive and Negative predictive values for FBS, OGTT and Glyco Hb are depicted in table 1. FBS was found to be having good sensitivity (83.9%) when compared with OGTT(29%) and Glyco Hb(20.2%). All 3 tests had 100% specificity. Accuracy rate was high for FBS making it the ideal screening test. (Figure 4a,4b,4c).

DISCUSSION

The prevalence of prediabetes in our study was 20.4% by FBS, OGTT and HbA1c; A study conducted in 2013 by Madhuri Taranikanti et al in South Indian rural adolescent school students between the age group of 14 - 18 years showed lower prevalence of prediabetes of 6.8% by FBS.[5] D Narayanappa et al noted a prevalence of 3.8% by FBS in children between 5-10 years.[6] But these two studies only used FBS for the determination of prediabetes and can miss Impaired glucose tolerance after food intake. Prevalence of prediabetes in our study with FBS was 17.1% which is higher than the above mentioned studies. This may be partly explained by the wide age range selected in our study. Santosh Kumar Krishnappa et al conducted a similar screening study in 2015 in asymptomatic overweight and obese adolescent children by FBS, OGTT and HbA1c and found to have a prevalence of 13%.[7]

The prevalence in our study was much higher even with normal BMI children being included. The higher prevalence agrees with the statistics of increasing prevalence of prediabetes in India probably because of the sedentary lifestyle.

Prevalence of prediabetes with FBS was 17.1%, OGTT was 5.9% and HbA1c was 4.1% while the combination of all three in our study showed 20.4%. Santhosh Kumar Krishnappa et al study showed prevalence of prediabetes of 3% FBS,10% by OGTT,5% by HbA1c and 13% by combination of all three.[7] These findings suggest that combination of FBS, OGTT and HbA1C might have better pickup rates.

In our study there is no statistically significant difference in the prevalence of prediabetes between the age groups. Similar observation was made in other studies.[5,7] This shows that prediabetes can develop at any age. Asian-Indian individuals are susceptible to insulin resistance from their early infancy.[8] Insulin resistance syndrome has been reported in children as young as 8 years in India.[9]

In our study there is a statistically significant increase in the prevalence of prediabetes in boys. Santosh Kumar Krishnappa et al study showed increased incidence of prediabetes in males than in females but was not statistically significant.[7] This higher prevalence in males may be explained because of decreased insulin sensitivity due to increased visceral fat compared to girls where fat get stored under the skin.

Lifestyle has a major impact on development of prediabetes. There is an undisputable association of diabetes with unhealthy eating habits. Authors noted significantly high prevalence of prediabetes in children with frequent consumption of fast food, soft drinks and sweets. Similar observation was made in 15yr follow up study of American women where consumption of fast food more than twice a week resulted in greater insulin resistance.[10] These foods have high glycaemic index which means they provide a quick rise in blood sugar followed by rapid fall giving rise to hunger. Carbonated drinks also contain high amounts of methyl glyoxal associated with carbonyl stress.

Exercise is known to improve responses to a 2-hour glucose tolerance test and improve insulin sensitivity even without weight loss.[11] Physical activities is thought to be inversely proportional to insulin resistance, therefore, increase in physical activity levels lead to decrease in insulin resistance. Our findings were consistent with this hypothesis. Authors noted significantly lower prevalence of prediabetes in children who played regular outdoor games.

Body mass index (BMI) has a strong relationship to diabetes and insulin resistance. In an obese individual, the amount of Non Esterified Fatty Acids, glycerol, hormones, cytokines, and proinflammatory markers involved in the development of insulin resistance are increased.[12] Though our study population consisted of predominantly lower socioeconomic class, the prevalence of overweight and obesity was comparable to those from affluent societies indicating increasing prevalence of obesity in lower socioeconomic groups.

Authors noted a statistically significant increase in the prevalence of prediabetes in overweight and obese children. Similar observation was made by Santosh Kumar Krishnappa et al study.[7] Study by Tandon N observed that obese adolescents had significantly higher prevalence of hyperinsulinemia when compared with overweight and normal weight adolescents.[13] Another study in adolescents aged 14-19 years reported that 64% of the obese adolescents in India had fasting hyperinsulinemia, a surrogate marker of insulin resistance.[14] All these studies and our study prove that obesity is a major risk factor for development of insulin resistance.

BMI measures the total adiposity and may miss central/abdominal obesity, in which the body fat

accumulates mainly around the waist. This can be measured by waist circumference (WC) and waist to hip ratio. Visceral fat or central obesity has unique metabolic effects on insulin sensitivity, with visceral fat having a greater influence on fasting insulin levels. Central obesity causes a higher risk for developing insulin resistance.[15] Authors noted a statistically significant increase in the prevalence of prediabetes in children with high waist to hip ratio.

Not many studies are available in paediatric population to correlate waist to hip ratio with prediabetes. A study on post-pubertal children in India reported a high prevalence of insulin resistance among children with adverse truncal body fat patterning, abdominal adiposity and excess body fat.[16] In a population-based study conducted in south India, the overall prevalence of glucose intolerance was 3.7%, which increased to 12.7% in girls with abdominal obesity.[17]

Limitations of the study includes, Hospital based study instead of community based study, which would have been a better representation of the population. With high prevalence noted in the study group, community based screening in schools may be considered and may be a feasible option, not separately analysed based on the pubertal status, lesser number of children in the age group of 15 years and more, hence lesser evaluation of the adolescent population.

CONCLUSION

Male gender, frequent consumption of junk foods, decreased physical activities, increased weight to hip ratio, overweight and obesity were the risk factors for prediabetes noted in our study. Though ADA recommends screening of children above 10 yrs. with risk factors, Indian children need to be screened at an earlier age.

Screening of asymptomatic children with these risk factors for prediabetes and interventions with lifestyle modification including weight loss, healthy eating habits and increasing physical activity may delay the development of overt Type 2 diabetes and its complications.

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