Glycosuria as a screening tool for diabetes mellitus in school children in Port Harcourt, Nigeria

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Abstract
Diabetes mellitus (DM) is the most common endocrine disorder of childhood and adolescence. Urine testing for glycosuria is an important screening tool for DM, especially in mass screening programmes. The screening of secondary school children in Port Harcourt for DM was done using glycosuria as a screening tool. Also, the relationship between risk factors for DM and glycosuria was determined. In November 2008, a cross sectional study of 1008 students aged 10 to 18 years from 12 secondary schools in Port Harcourt was carried out. Structured questionnaires were completed by the investigators. Urine glucose was determined using a dipstick urinary multistix strip. The prevalence of glycosuria was 0.7% with males having a higher prevalence (1.2%) than females (0.2%). Glycosuria was found more amongst children aged 16 to 17 years (1.1%), children from private schools (0.9%) and children in social class IV (3.3%). The relationship between elevated blood pressure and glycosuria was statistically significant. There was no statistically significant relationship between glycosuria and body mass index categories, waist hip ratio, acanthosis nigricans and family history of diabetes. Glycosuria occurs in apparently healthy secondary school children. As such, regular screening of secondary school children for DM using urine glucose testing should be incorporated into the school health programme.

Keywords: Glycosuria, diabetes, screening, secondary school children, Port Harcourt

INTRODUCTION
Diabetes mellitus (DM) is a common, chronic metabolic syndrome characterized by hyperglycemia as a cardinal biochemical feature (Alemzadeh et al., 2007). The major forms of diabetes are divided into those caused by deficiency of insulin secretion due to pancreatic β-cell damage (type 1 DM), and those that are consequences of insulin resistance occurring at the level of skeletal muscle, liver and adipose tissue, with various degrees of β-cell impairment (type 2 DM) (Alemzadeh et al., 2007). Type 1 DM is the most common endocrine-metabolic disorder of childhood and adolescence, with important consequences for physical and emotional development (Alemzadeh et al., 2007). Type 2 DM was previously thought to occur only in adults. However, there are increasing reports of type 2 DM in children globally (Rosenbloom et al., 1999). The onset of type 2 DM is often insidious, without symptoms to alert the patient or clinician about the illness. Risk factors for childhood type 2 DM include obesity, overweight, family history, evidence of insulin resistance such as acanthosis nigricans, hypertension, dyslipidaemia and polycystic ovarian syndrome (American Diabetes Association, 1997). DM may cause life threatening metabolic complications like diabetic ketoacidosis (Alemzadeh et al., 2007) which contributes to death in 1 out of 200 children presenting with DM (Schober et al., 1997). Diabetes is also an important risk factor for other leading causes of death such as coronary heart disease, congestive heart failure and cerebrovascular disease in adults. World Health Organization. Definition, diagnosis, and classification of diabetes mellitus and its complications

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Individuals with DM confront lifestyle alterations that include an absolute daily requirement for exogenous insulin or oral hypoglycaemic drugs, the need to monitor their own glucose control, to pay attention to dietary intake and good hygiene (Alemzadeh et al., 2007). Diabetes mellitus is a major challenge to public health in the 21st century because of the cost of care of the increasing number of people with diabetes (Zimmet et al., 2001).

Currently, majority of the asymptomatic people who have diabetes mellitus have not been diagnosed and may remain undiagnosed for many years (Davis et al., 1997). The progression of the complications is worse when the illness starts from childhood. Identifying asymptomatic children early in the disease process will allow early institution of lifestyle changes and medical therapy of this disease to reduce its cost as well as to avoid enormous consumption of resources.

Screening for diabetes mellitus is an important measure in detecting the pre-diabetic stages and undiagnosed diabetes in order to avert pernicious effects of hyperglycaemia and associated complications (American Diabetes Association, 2003). Fasting plasma glucose is the preferred method of screening and World Health Organization’s gold standard for confirmation of DM (Alemzadeh et al., 2007; American Diabetes Association, 2003). However, it is not favourable for non-hospital studies and not recommended for routine use. Urine testing for glycosuria is an important screening tool for DM. Glucose is usually detected when the renal threshold for blood glucose is exceeded (180 mg/dL; 10 mmol/L) (Alemzadeh et al., 2007). It is highly specific but less sensitive than most blood tests for DM. In population-based screening using quantitative urine dipstick in the USA, a “trace positive” dipstick result or greater has a reported sensitivity of 23-64% and specificity of 98-99% for DM (Modan and Harris 1994). In a high-risk adult population, quantitative assays of urine glucose achieved high sensitivity (81%) with high specificity (98%), comparable to both fasting plasma glucose and glycosylated protein assays (Modan and Harris 1994). It has been shown that screening for diabetes mellitus using urine glucose is invaluable in some clinical settings and has been utilized in mass screening of school children for DM (Afoke et al., 1992). It is particularly useful in resource poor countries in Sub Saharan Africa because it is simple, affordable, reliable, safe, feasible and requires less sophisticated technique and manpower (Van der Sande et al., 1999). In Japan, mass urine screening programme (for both type1 and 2 DM,) for school children has been mandatory since 1994. (Yokota et al., 2004). A study by Afoke et al (Afoke et al., 1992) on the prevalence and clinical picture of type1 DM in Nigerian Igbo school children aged 7-15 years was able to identify 12 new diabetic cases with a crude prevalence rate of 0.33/1000 following screening with urine glucose. There is however no available information about screening for DM in children using glycosuria in Port Harcourt and other parts of Nigeria.

This study was carried out to raise awareness of DM especially type 2 DM and the risk factors for DM in children and also serve as a basis for developing health education and control programmes for prevention and treatment of DM as well as controlling the risk factors. Data generated from the study can serve as a reference standard for prevalence of glycosuria and other risk factors for DM in Nigerian adolescents using Port-Harcourt as a case study.

OBJECTIVES

To determine the prevalence of glycosuria in secondary school children aged 10-19 years in Port Harcourt City Local government Area, Nigeria. Also to determine the relationship between various risk factors for diabetes mellitus and glycosuria these children.

METHODS

In November 2008, a cross sectional study of 1008 students aged 10 to 19 years from 12 secondary schools in Port Harcourt was carried out. A total of 84 children were recruited from each secondary school. In each school, one arm per class was selected by simple random sampling. In the selected arm, 14 children were recruited by the simple random sampling of balloting. Structured questionnaires were completed by the investigators. Measurement of weight, height, waist-hip circumference and blood pressure was done and the school children were examined for acanthosis nigricans. The Body Mass index (BMI) was calculated using the formula weight (kg)/height (m)$^2$ Urine glucose was determined using a dipstick urinary multistix strip.

Children with glycosuria, risk factors for DM (obesity/overweight, family history, hypertension and acanthosis nigricans) and any abnormal findings in the urine were referred to Paediatric Endocrine Clinic of UPTH for follow up and management.

The data obtained were analysed using the Statistical Package for Social Sciences (SPSS) software version 14 and Epi Info version 6.04.

The approval of the Ethics and Research Committee of the UPTH was obtained before proceeding with the study. Permission was also obtained from the, Rivers State Ministry of Education and the Principals of the selected schools. Informed written consent was obtained...
from the parents /or guardians of the children recruited for the study.

RESULTS

General characteristics of study subjects

A total of 1008 children were recruited for the study. They comprised of 672 (66.7%) from private school and 336 (33.3%) from public school. There were equal number of males and females (50%) in both public and private schools (Table 1). More than half 443(65.9%) of the children in private schools and 174 (51.8%) in the public schools belonged to the upper socio economic class (Social Classes I and II). Forty(6%) of the children in private schools and 37(11%) of those in public schools belonged to the lower socio economic class.

Distribution of study population by age group and gender

The ages of the children ranged from 10 to 19 years with a mean of 14.25 ± 2.23 years. The mean age of males was 14.23 ±2.32 years, while that of females was 14.27 ± 2.13 years. The mean age difference between sexes was not statistically significant. t = -value= -.283,  P>0.05. Table 2 shows the distribution of the subjects by age group and gender. The subjects were divided into 5 groups, 10-11, 12-13, 14-15, 16-17, and 18-19 years respectively. The highest number of the subjects belonged to the 14-15 year age group (31.9 %) while 18-19 age group had the least number of subjects (6.7 %). Male subjects were found more in the 10-11 and 18 -1 9 age groups while females were more in the 12-13, 14 -15 and16-17 age groups. The sex difference in the various age groups was not statistically significant $\chi^2 = 4.56, \ P > 0.05$.

Glycosuria

Prevalence of Glycosuria according to Gender

Table 3 shows the incidence of glycosuria. Seven (0.7%) subjects had glycosuria. These were 6 males (1.2%) and one female (0.2%). However, gender difference was not statistically significant. $\chi^2 = 2.302, P>0.05$. Four (66.7%) out of the 6 males with glycosuria had 50mg of glucose in
the urine while 2(37.3%) had 100mg of glucose in the urine. The only female subject with glycosuria had 50mg of glucose in the urine.

### Age characteristics of subjects with glycosuria

The mean age of the male subjects with glycosuria was higher (14.50±2.35years) than those without glycosuria (14.23±2.32years). In the females, the mean age of the subjects without glycosuria was (14.27±2.14 years) while the only female with glycosuria was 13.00 years. Overall the total mean age for those with glycosuria (14.29±2.22years) was higher than the subjects without glycosuria (14.25±2.22years). This age difference was however not statistically significant t-value=. 045, P>0.05

### Relationship between type of school, socio economic class and glycosuria

As shown in table 4, none of the subjects within the age group 18-19 years had glycosuria. Glycosuria was seen more among subjects 16-17 years (1.1%). The relationship between age and glycosuria was not statistically significant \( \chi^2=0.145, P > 0.05 \).

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### Relationship between type of school, socio economic class and glycosuria

Table 5 shows the relationship between the type of school, Social Class of subjects and glycosuria. Out of the 7 subjects with glycosuria 6 (0.9%) were from 5 private schools while 1 (0.3%) was from a public school. This difference was however not statistically significant \( \chi^2 \)
Table 6. Mean Weight, Height and BMI of subjects with glycosuria

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Male Positive Mean(±SD)</th>
<th>Female Positive Mean*</th>
<th>Male Negative Mean(±SD)</th>
<th>Female Negative Mean(±SD)</th>
<th>Total Positive Mean(±SD)</th>
<th>Total Negative Mean(±SD)</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight(kg)</td>
<td>55.50±13.08</td>
<td>47.38±11.36</td>
<td>49.16±10.8</td>
<td>55.71±11.95</td>
<td>48.33±14.14</td>
<td>48.33±14.14</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Height(m)</td>
<td>1.65±0.11</td>
<td>1.57±0.12</td>
<td>1.65±0.10</td>
<td>1.57±0.10</td>
<td>1.65±0.10</td>
<td>1.57±0.10</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BMI(kg/m²)</td>
<td>20.26±3.19</td>
<td>18.95±2.78</td>
<td>20.00±3.67</td>
<td>20.36±2.93</td>
<td>19.49±3.30</td>
<td>19.49±3.30</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

* One female had no standard deviation

Table 7. Mean WC, HC & WHR of subjects with glycosuria

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Male Positive Mean(±SD)</th>
<th>Female Positive Mean*</th>
<th>Male Negative Mean(±SD)</th>
<th>Female Negative Mean(±SD)</th>
<th>Total Positive Mean(±SD)</th>
<th>Total Negative Mean(±SD)</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>WC(cm)</td>
<td>71.00±5.87</td>
<td>67.68±7.16</td>
<td>70.33±8.11</td>
<td>72.71±7.02</td>
<td>69.04±7.76</td>
<td>69.04±7.76</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>HC(cm)</td>
<td>75.00±3.46</td>
<td>73.45±8.95</td>
<td>78.59±10.76</td>
<td>77.00±6.16</td>
<td>76.04±10.20</td>
<td>76.04±10.20</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>WHR</td>
<td>0.95±0.05</td>
<td>0.93</td>
<td>0.90±0.08</td>
<td>0.94±0.05</td>
<td>0.91±0.74</td>
<td>0.91±0.74</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Relative frequency of risk factors for DM in subjects with glycosuria

Table 8 shows the relative frequency of risk factors for DM in subjects with glycosuria. Glycosuria was found more in subjects with elevated blood pressure (3(4.1%) followed by subjects with positive family history of DM (2(1.7%). The only subject with acanthosis nigricans had no glycosuria.

DISCUSSION

This study showed that the incidence of glycosuria among secondary school children in Port Harcourt was 0.7%. The incidence of glycosuria noted in this study was higher than that reported by Bai et al., (Bai et al., 1991) in their study of glycosuria and diabetes mellitus in children and adolescents in South India. They reported an incidence rate of 0.038% in 10,513 children aged between 3 and 20 years. This difference could be due to
the larger sample size studied with age groups including children below 5 years who are less likely to develop diabetes unlike in the present study that involved only adolescents. Racial difference could also play a part in the difference in the prevalence rate of glycosuria noted in the Indian study. A similar incidence of 0.8% was however reported by Yang et al (Yang et al., 2004) in China among women aged 40-70 years although, the study involved only females that are older who are more likely to have type 2 DM than the subjects in the present study.

The prevalence of glycosuria was higher in males (1.2%) than females (0.2%) with a ratio of 6:1. The higher prevalence of glycosuria in males in this study supports previous studies that noted a higher prevalence of DM in males (Wild et al., 2000; Nyenwe et al., 2003; Dahiru et al., 2008). Nyenwe and colleagues in Port Harcourt reported a crude prevalence rate of type 2 DM in adults as 6.8% with male and female rates of 7.7 and 5.7% respectively. Similarly, Dahiru et al., in their study of the prevalence of diabetes in a semi urban community in Northern Nigeria reported a prevalence rate of 2.0% with all the diabetic cases being males. No obvious explanation has been given for the higher rate of diabetes in males in Nigeria and it may be assumed that genetic and hormonal differences between the males and females may be contributing factors. Other studies in Asia have however reported a higher incidence of DM in females (Urakami et al., 2005; Wei et al., 2003). In Japan, the overall annual incidence of 2.63/100,000 of type 2 DM was reported in school children in Tokyo Metropolitan area from 1972 to 2002 with a male-to-female ratio of 1.0:1.2 (Urakami et al., 2005). Wei et al in Taiwan, reported that the overall rates of newly identified DM were 9/100,000 boys, and 15.3/100,000 girls. The higher female preponderance reported in their studies was attributed to higher prevalence of obesity among the females. These children were all identified through urine glucose screening (Urakami et al., 2005; Wei et al., 2003). The prevalence of glycosuria has been noted to be highly predictive of development of DM and hence its comparison with the present study.

The mean age of the males with glycosuria was 14.5±2.35 years while the only female with glycosuria was 13 years. Glycosuria was found more in subjects aged 16-17 years. Although there is paucity of data to compare with this finding, (Wei et al., 2003) in Taiwan however noted that the highest rate of new cases of DM in school children identified through screening for glycosuria occurred within 13-18 years which is the peak of adolescence. During this period, there is heightened sex steroids and growth hormone which are antagonistic to insulin production and action (Alemzadeh et al., 2007). Children in private schools had more subjects with glycosuria than those in public schools, although this difference was not statistically significant. Generally, children in private school are more likely to come from higher socio economic class but this trend is not apparent in this study area where both low and high social classes attend private schools. The highest prevalence of glycosuria in this study was from lower social class IV. The finding that glycosuria was more in children from lower socio class IV supports previous studies that found a higher incidence of diabetes and its complications among people in lower socio economic classes than people from higher economic classes (Koskinen et al., 1996; Pill et al.,1995). Lack of healthy diet, high prevalence of infections which may trigger pathogenesis of type I DM is more apparent in children in lower socio economic class. Also in the USA, obesity a risk factor for type 2 DM, is reported more in poor black Americans due to poor dietary habit (Olson 1999).

In this study, subjects with glycosuria were observed to have higher mean weight than those without glycosuria. This finding is comparable with previous reports that increasing weight is a risk factor for hyperglycaemia and diabetes because of its predisposition to obesity and insulin resistance (Alemzadeh et al., 2007; Chang et al., 2006; Unwin et al., 1997). The mean height of the subjects with glycosuria was significantly higher than the subjects without glycosuria. This finding is similar to other studies which have also shown that children who became diabetic were considerably taller than non-diabetic children. In some children this increase in height was evident up to three years before diagnosed diabetes. It was assumed that the height increase may be caused by changes in metabolism that occur before the onset of diabetes (John et al., 2002; Price and Burden, 1992). Increased stature may represent an phenomenon of the islet-cell hyperplasia and hyperinsulinaemia, which characterize the preclinical stages of diabetes. (Price and Burden, 1992).
Obese and overweight children are more likely to have abnormalities in glucose homeostasis in obesity. This finding is similar to studies that found a higher prevalence of hyperglycaemia and diabetes among those with higher BMI (Chang et al., 2006; Unwin et al., 1997). BMI is directly related to obesity which is a major risk factor for type 2 DM due to insulin resistance leading to hyperinsulinaemia and finally to type 2 DM (Alemzadeh et al., 2007). The mean waist circumference, Waist Hip Ratio (WHR) of all the subjects with glycosuria was higher than those without glycosuria. Studies have also shown (Caro, 2009) that these variables like the BMI are also directly related to obesity, a major risk factor for type 2 DM (Unwin et al., 1997).

Glycosuria was found in only 1.6% of the overweight and none of the obese subjects. The relationship of glycosuria with overweight and obesity was however not statistically significant. Only one (0.3%) subject with abnormal WHR had glycosuria. The lack of association between glycosuria and obesity may be as a result of delayed development of insulin resistance (in the presence of adequate beta cell function) which can manifest later in adult life if appropriate measures to control obesity are not instituted. A long term follow up may however determine the period between the onset of insulin resistance and glycosuria in obese and overweight children. The lack of finding of significant association between glycosuria and obesity may also indicate that although obesity is a risk factor for DM, but not all obese children may develop DM. Similarly, Feneli et al. (Feneli et al., 2008) in Greece did not find any significant relationship between obese children and hyperglycaemia or DM. The finding of approximately one third of the obese children in that study having hyperinsulinism points to the fact that insulin resistance is the earlier abnormality in glucose homeostasis in obesity. (Feneli et al., 2008) Obese and overweight children are more likely to be overweight adults and are at increased risk for type 2 DM and other cardiovascular complications as adult (Alemzadeh et al., 2007; Guo et al., 1994). Several studies have suggested that preventing obesity may be important in reducing the development of type 2 DM (American Diabetes Association, 2000; Bloomgarden, 2004). The prevention of obesity on the long term may require very early interventional strategies such as regular exercise, dietary control instituted in childhood and adolescence (Alemzadeh et al., 2007; Helmich, 1991).

Family History of DM was found in 115 (11.4%) of subjects in this study. The family history of DM was either in the father or mother but none had in both parents. This result was higher than that reported by (Puepet and Ohwovoriole, 2008) (3.5%) in a non-diabetic population aged 15 years and above in Jos. In this present study, 2 (28.6%) out of the 7 subjects with glycosuria had a positive family history of DM. Although this study was on glycosuria, it supports the finding in previous studies that family history of DM is seen in only 23.8% of diabetic probands. Puepet and Chuhwak (2002), Osuntokun et al. (Osuntokun et al., 1971) in Ibadan however, reported a lower prevalence of family history of DM even among probands of type 2 DM. Low prevalence of family history of DM in subjects with diabetic probands may suggest that genetic factor may not be an important risk factor for development of type 2 DM in these populations. Ignorance about DM and the fact that Africans are usually reluctant to reveal family history of illness may also be responsible for the low family history of diabetes (Puepet and Ohwovoriole, 2008). It has been reported that offsprings of fathers with type 1 DM are nearly three times more likely to have type 1 DM than the offsprings of affected mothers (Anochie et al., 2004). In another study, maternal and paternal DM conferred equivalent risk for occurrence of type 2 DM in offspring (Meigs et al., 2000).

Acanthosis nigricans (AN) has been considered to be a predictive marker for type 2 diabetes. It is one of the signs of insulin resistance often associated with obesity. In this study, only one (0.1%) subject, a female had AN and she was also found to be obese. Nguyen et al (Nguyen et al., 2001) in the USA, had reported AN in overweight subjects. In their study of 139 children, 35 (25%) had AN with a greater body weight than the children without AN. However, the only subject in this study with AN had no glycosuria presently, but this may precede the development of type 2 DM in future which could be prevented if properly managed. The subject with AN however, had more than one risk factors for DM (elevated BP, obesity and family history of DM) and will benefit from a follow up. There is however paucity of data on AN among children in Nigeria as well as other regions in sub-Saharan Africa to compare with this study. This paucity of data may either be due to rarity of AN in these regions, or mis-diagnosis because its characteristic appearance could be misdiagnosed as a skin disease or infection rather than a metabolic disorder. Furthermore, AN may lighten over time if the underlying insulin resistance is adequately treated making the diagnosis difficult.

This study was able to identify children with glycosuria as well as identifying those with various risk factors for DM (overweight, obesity, positive family history of diabetes, hypertension and acanthosis nigricans) and their association with glycosuria. All the children with glycosuria as well as those with risk factors for DM were referred to a paediatric endocrinologist for further evaluation.

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