Type 2 Diabetes in Asian-Indian Urban Children

Ambady Ramachandran, MD, PHD, DSC, FRCP1
Chamukuttan Snehalatha, MSC, DSC2
Kumpatla Satyavani, MSC, MTECH2
Selvaraj Sivasankari, MSC2
Viswanathan Vijay, MD, PHD1

OBJECTIVE — Due to a background of high prevalence of type 2 diabetes and the increasing rate of obesity occurring in relatively young urban children, we felt the need to look for type 2 diabetes in children.

RESEARCH DESIGN AND METHODS — A study of cases of type 2 diabetes with age at diagnosis of ≤15 years seen at a diabetes specialty center in Chennai, India, is reported. A total of 18 children (5 boys and 13 girls) aged 9–13 years with insidious onset of diabetes responding to oral antidiabetic agents (ODAs) for periods from 2 months to 12 years were studied. Clinical details, anthropometry, and details of family history of diabetes were elicited. All of them were tested for the presence of anti-GAD65 antibodies and for pancreatic β-cell reserve by measuring serum C-peptide response (radioimmunoassay procedures).

RESULTS — All children showed a response to ODAs, had good β-cell reserve (≥0.6 pmol/ml on stimulation), and negligible GAD65 antibodies indicating the presence of type 2 diabetes. The children were nonketotic; nine were obese, four had acanthosis nigricans, and one had polycystic ovary syndrome. Positive family history of diabetes was present in all cases.

CONCLUSIONS — The clinical, immunological, and biochemical profile showed that the children had type 2 diabetes. The profile of type 2 diabetes was similar to that described in children in many other countries. Although less common than type 1 diabetes, type 2 diabetes in children is a condition that needs to be recognized and looked for in Asian-Indians.

Diabetes Care 26:1022–1025, 2003

Type 2 diabetes poses a major health problem globally, especially in many developing countries (1). In urban India, type 2 diabetes is reaching epidemic proportions (2–5). Diabetes develops at a younger age in Indians, i.e., at least a decade or two earlier than in the Western population (4,6). We have reported a high prevalence of maturity-onset diabetes of the young (MODY) in our population (7). Reports from different parts of the world, especially from the U.K. (8–10) and the U.S. (11–13), show an increasing occurrence of type 2 diabetes in children, particularly in the minority populations, including Asians. The American Diabetes Association has highlighted a high prevalence of type 2 diabetes in children in ethnic minority populations such as the American and Canadian Indians, Hispanics, African Americans, Japanese, Pacific Islanders, and Asian and Middle-Eastern populations (14). Obesity has been on the rise in the adolescent age, which might have a causative role for the rising prevalence of diabetes in the young (8–13,15).

A recent survey in southern India has shown that obesity among adolescent school children was related to decreased physical activity (16). It is likely that with the emerging epidemic of diabetes and obesity, type 2 diabetes could occur in children in India. This report highlights the need to look for type 2 diabetes in children in India.

RESEARCH DESIGN AND METHODS — Children with diabetes diagnosed ≤15 years who had features of type 2 diabetes (n = 18) are reported here. They were seen at the Diabetes Research Centre and M.V. Hospital for Diabetes, Madras, India. Among them, three cases were diagnosed within the last 3 months. The other 15 cases were diagnosed by us at least 1 year ago and patients had come for follow-up from January to June 2002. All of them satisfied the criteria given below.

1. Insidious onset of diabetes at age of ≤15 years
2. Response to treatment with ODAs
3. Presence of insulin secretory capacity comparable to type 2 diabetes in adults, as indicated by serum C-peptide concentrations (stimulated response ≥ 0.6 pmol/ml)
4. Lack of evidence of autoimmune process indicated by the absence of circulating GAD65 antibodies

Informed consent was obtained from the parents to use the data of the probands and the family members for scientific purposes. The study protocol was also approved by the ethics committee of the Diabetes Research Centre and M.V. Hospital for Diabetes.

Details of clinical history with emphasis on presence of symptoms were recorded. Blood pressure was measured, the details of dietary habits were noted, and waist-to-hip ratio was calculated. Anthropometric measurements included height, weight, and waist and hip circumferences. For each child, the percentage of body weight for the height was calculated using the table for normal height and weight for Indian children (17). Family history of diabetes was noted. We looked...
for skin manifestation of acanthosis nigri-
cans. A total of 18 parents without known
history of diabetes were invited to un-
dergo a standard oral glucose tolerance
test. Among them, diabetes was diag-
nosed in four fathers and five mothers. All
children had measurements of fasting and
2-h postprandial plasma glucose (glucose
oxidase–peroxidase method), HbA1c (im-
munoturbidimetry method; Roche Diag-
nostics, Mannheim, Germany; normal
value <6.1%), fasting total cholesterol,
and triglycerides (enzymatic methods; Roche
Diagnostics). A total cholesterol
value of ≥200 mg/dl (5.2 mmol/l) and a
triglyceride value of ≥150 mg/dl (1.7
mmol/l) were considered abnormal.

GAD<sub>65</sub> antibodies were measured in
fasting serum by radioimmunoassay pro-
cedure using a commercial reagent kit that
used <sup>125</sup>I-labeled human recombi-
nant GAD<sub>65</sub> (RSR, Cardiff, U.K.). The
performance of the assay had been evaluated
using <sup>35</sup>S-labeled human recombinant
GAD<sub>65</sub> as a reference method (18), and it
was found to have a significant correlation
(r = 0.93) with the standard assay (19). It
had a sensitivity very similar to the stan-
dard assay, at specificities of 97.5 and
99%. The lowest titer detected was 0.02
units/ml. The intra- and interassay coeffi-
cient of variations were <10%. The cutoff
value (&lt;1.1 unit/ml) for the normal titer
was 0.003 pmol/ml. Stimulated C-
peptide value ≥0.6 pmol/ml indicated
good β-cell reserve (22). Mean and SDs of
the numerical variables are given.

**RESULTS** — Details of 18 children (5
males and 13 females), belonging to 17
families and identified as having type 2
diabetes, are reported. Among them, 15
had been treated with ODAs for durations
ranging from 1 to 12 years; the remaining
3 recently diagnosed girls were being
treated with ODAs for 2–3 months. All of
the children showed good glycemic con-
trol with treatment. The clinical details
are shown in Table 1. Monotherapy with
metformin or sulfonylureas or a combina-
tion of both were prescribed. The age at
diagnosis was 9–12 years in seven chil-
dren, 13–14 years in six children, and 15
years in the other five subjects. All chil-
dren had a positive family history of type
2 diabetes; parental history was present in
16, and the other 2 children had second-

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Age at diagnosis (years)/Sex</th>
<th>% of ideal body weight</th>
<th>WHR</th>
<th>Family history of diabetes</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16/F</td>
<td>14</td>
<td>90</td>
<td>0.98</td>
<td>Both parents, maternal and paternal grandparents</td>
</tr>
<tr>
<td>2</td>
<td>14/F*</td>
<td>13</td>
<td>102</td>
<td>0.94</td>
<td>Father</td>
</tr>
<tr>
<td>3</td>
<td>16/F†</td>
<td>15</td>
<td>139</td>
<td>0.91</td>
<td>Mother</td>
</tr>
<tr>
<td>4</td>
<td>15/F‡</td>
<td>15</td>
<td>110</td>
<td>0.94</td>
<td>Mother, sibling, grandparents</td>
</tr>
<tr>
<td>5</td>
<td>16/M</td>
<td>12</td>
<td>122</td>
<td>0.93</td>
<td>Both parents, grandparents</td>
</tr>
<tr>
<td>6</td>
<td>18/M</td>
<td>14</td>
<td>83</td>
<td>0.94</td>
<td>Mother, paternal grandparents</td>
</tr>
<tr>
<td>7</td>
<td>21/M</td>
<td>15</td>
<td>143</td>
<td>0.95</td>
<td>Mother, maternal grandparents</td>
</tr>
<tr>
<td>8</td>
<td>20/M</td>
<td>14</td>
<td>81</td>
<td>0.97</td>
<td>Both parents, paternal grandparents</td>
</tr>
<tr>
<td>9</td>
<td>21/F*</td>
<td>15</td>
<td>135</td>
<td>0.89</td>
<td>Father, maternal grandmother</td>
</tr>
<tr>
<td>10</td>
<td>25/F</td>
<td>14</td>
<td>106</td>
<td>0.96</td>
<td>Both parents</td>
</tr>
<tr>
<td>11</td>
<td>25/F</td>
<td>15</td>
<td>146</td>
<td>—</td>
<td>Mother, maternal and paternal grandmother, sibling</td>
</tr>
<tr>
<td>12</td>
<td>12/F*</td>
<td>12</td>
<td>126</td>
<td>—</td>
<td>Mother</td>
</tr>
<tr>
<td>13</td>
<td>15/F</td>
<td>11</td>
<td>113</td>
<td>0.94</td>
<td>Both parents, maternal and paternal grandparents</td>
</tr>
<tr>
<td>14</td>
<td>24/F</td>
<td>11</td>
<td>125</td>
<td>—</td>
<td>Mother, maternal grandparents, sibling</td>
</tr>
<tr>
<td>15</td>
<td>20/F</td>
<td>11</td>
<td>102</td>
<td>—</td>
<td>Mother</td>
</tr>
<tr>
<td>16</td>
<td>14/M*</td>
<td>13</td>
<td>130</td>
<td>0.94</td>
<td>Grandparents</td>
</tr>
<tr>
<td>17</td>
<td>9/F</td>
<td>9</td>
<td>106</td>
<td>—</td>
<td>Paternal grandparents</td>
</tr>
<tr>
<td>18</td>
<td>12/F‡</td>
<td>11</td>
<td>120</td>
<td>0.94</td>
<td>Mother, grandparents, sibling</td>
</tr>
</tbody>
</table>

* Acanthosis nigricons; †polycystic ovary syndrome; ‡sisters. F, female; M, male; WHR, waist-to-hip ratio.
Type 2 diabetes in children

Table 2—Anthropometric and biochemical details of the study subjects: basal values

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Fasting/2-h postprandial plasma glucose (mmol/l)</th>
<th>HbA1c (%)</th>
<th>Total cholesterol (mmol/l)</th>
<th>Triglycerides (mmol/l)</th>
<th>HDL cholesterol (mmol/l)</th>
<th>LDL cholesterol (mmol/l)</th>
<th>Stimulated C-peptide (pmol/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14.1/18.6</td>
<td>9.3</td>
<td>4.24</td>
<td>1.7</td>
<td>0.85</td>
<td>2.64</td>
<td>1.4</td>
</tr>
<tr>
<td>2</td>
<td>13.3/24.0</td>
<td>9.0</td>
<td>3.85</td>
<td>0.79</td>
<td>0.90</td>
<td>2.45</td>
<td>0.9</td>
</tr>
<tr>
<td>3</td>
<td>7.8/17.3</td>
<td>8.0</td>
<td>4.50</td>
<td>1.22</td>
<td>0.90</td>
<td>3.02</td>
<td>1.6</td>
</tr>
<tr>
<td>4</td>
<td>10.8/13.0</td>
<td>12.4</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>6.4/11.1</td>
<td>9.0</td>
<td>4.37</td>
<td>1.21</td>
<td>0.90</td>
<td>2.69</td>
<td>1.4</td>
</tr>
<tr>
<td>6</td>
<td>6.9/11.8</td>
<td>9.3</td>
<td>3.70</td>
<td>0.86</td>
<td>—</td>
<td>—</td>
<td>1.1</td>
</tr>
<tr>
<td>7</td>
<td>9.4/15.6</td>
<td>9.9</td>
<td>4.01</td>
<td>1.15</td>
<td>0.25</td>
<td>2.64</td>
<td>1.4</td>
</tr>
<tr>
<td>8</td>
<td>7.3/10.6</td>
<td>8.1</td>
<td>6.12</td>
<td>3.66</td>
<td>1.21</td>
<td>3.22</td>
<td>1.1</td>
</tr>
<tr>
<td>9</td>
<td>10.3/12.4</td>
<td>9.3</td>
<td>4.26</td>
<td>2.39</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>10</td>
<td>9.1/13.9</td>
<td>9.2</td>
<td>3.72</td>
<td>1.05</td>
<td>0.90</td>
<td>2.35</td>
<td>0.6</td>
</tr>
<tr>
<td>11</td>
<td>8.5/11.1</td>
<td>10.0</td>
<td>5.3</td>
<td>0.90</td>
<td>0.88</td>
<td>3.95</td>
<td>1.4</td>
</tr>
<tr>
<td>12</td>
<td>8.1/14.7</td>
<td>13.8</td>
<td>2.64</td>
<td>2.58</td>
<td>—</td>
<td>—</td>
<td>1.4</td>
</tr>
<tr>
<td>13</td>
<td>11.7/15.3</td>
<td>13.7</td>
<td>5.50</td>
<td>1.31</td>
<td>1.63</td>
<td>3.28</td>
<td>1.9</td>
</tr>
<tr>
<td>14</td>
<td>7.9/19.8</td>
<td>9.3</td>
<td>7.16</td>
<td>0.49</td>
<td>1.34</td>
<td>5.58</td>
<td>2.0</td>
</tr>
<tr>
<td>15</td>
<td>9.1/20.2</td>
<td>10.5</td>
<td>4.26</td>
<td>2.47</td>
<td>—</td>
<td>—</td>
<td>1.6</td>
</tr>
<tr>
<td>16</td>
<td>14.3/19.4</td>
<td>15.2</td>
<td>3.49</td>
<td>1.28</td>
<td>1.03</td>
<td>1.86</td>
<td>2.2</td>
</tr>
<tr>
<td>17</td>
<td>7.6/16.9</td>
<td>9.5</td>
<td>5.56</td>
<td>1.92</td>
<td>—</td>
<td>—</td>
<td>2.0</td>
</tr>
<tr>
<td>18</td>
<td>15.6/19.6</td>
<td>10.8</td>
<td>4.86</td>
<td>2.02</td>
<td>—</td>
<td>—</td>
<td>1.1</td>
</tr>
</tbody>
</table>

degree family history (grandparents with type 2 diabetes).

At diagnosis, nine children (50%) had ≥120% of ideal body weight and only three children were <100% of ideal body weight. The waist-to-hip ratio was high in 12 of 13 children who had their circumferences measured (normal values males = 0.88, females = 0.80) (Table 1).

At presentation, five children had polyuria and polydypsia, one had ketonuria, one girl had polycystic ovary syndrome, and three children had pruritis. Acanthosis nigricans was present in four children. Asymptomatic children (n = 9) were tested because of the strong family history of diabetes and/or because of obesity.

Before reporting to the center, one girl and one boy were being treated with insulin for >1 month and another three girls and one boy were treated with insulin for <10 days. All of them had symptoms suggestive of hypoglycemia, even with minimum doses of insulin, and responded to ODAs.

The biochemical parameters at the time of registration at the center are shown in Table 2. Isolated hypertriglyceridemia (n = 5), hypercholesterolemia (n = 3), and a combined hyperlipidemia (n = 2) were seen in some children. The C-peptide values ranged from 0.6 to 2.2 pmol/ml with a mean of 1.46 ± 0.4 pmol/ml. Table 2 also shows the fasting and 2-h postprandial plasma glucose values and HbA1c values.

One 15-year-old girl (subject no. 9) had not attained menarche. One patient was hypertensive and was treated with enalapril. All other children had normal blood pressure. The diets of all study subjects were almost similar, with calories varying from 1,200 to 2,000. They were all consuming the regular Indian diet containing 60–65% of carbohydrate and 20–25% of fat. Physical activity was sedentary in 17 of 18 children; one girl (subject no. 15) previously played tennis regularly.

CONCLUSIONS — Type 2 diabetes in children has been reported from developed countries such as the U.K. (8–10), the U.S. (11–13), and Japan (23). Its rising occurrence has been attributed to the increasing rate of obesity in children (24).

The susceptibility to the disorder was more common in ethnic minorities such as the Pima Indians in the U.S. (13,14) and Asian-Indians and Arabs in the U.K. (9). The highest prevalence of type 2 diabetes in children has been reported from Japan (23). Childhood obesity has increased enormously in parallel with rapid westernization of lifestyle in Japan. A high prevalence of glucose intolerance was observed in obese Japanese children. Impaired glucose tolerance/impaired fasting glucose and type 2 diabetes were found in 19.2 and 3.9%, respectively, of 280 children who were overweight by ≥30% of the standard weight. They had high insulin resistance that resulted in subsequent diabetes (23).

The present article highlights the fact that type 2 diabetes in children occurs even in developing countries. In concurrence with the reports from the developed countries (8–14,23,24), obesity, female sex, parental history of type 2 diabetes, and pubertal age appeared to be strongly associated with the disease in Asian children. Unlike in the children with type 1 diabetes who had acute onset of the disease with severe symptoms and ketonuria, lean body weight, and lack of familial aggregation, the type 2 diabetic children showed features similar to classic adult-onset type 2 diabetes. Obesity was present in only half of the probands seen by us. The profile is similar to that observed in adult type 2 diabetes in India—nearly half of type 2 diabetic patients are not obese. Insulin resistance is a common feature even in nonobese Asian-Indian subjects (25).
the U.S. (14). The mean age at onset of the disease was peripubertal coinciding with the relative insulin resistance occurring during puberty. Strong familial inheritance, presence of obesity, nonautoimmune nature as indicated by the absence of GAD antibodies, and good response to ODAs favored the diagnosis of type 2 diabetes in our study group as well as in the reports from other ethnic groups (8–14,23).

The longest duration of diabetes in two probands was 12 years, and both were continuing to show good glycemic control with ODAs. In obese children with diabetes, metformin was found to be effective. Sulfonylureas were also effective with diabetes, metformin was found to be effective. Sulfonylureas were also effective in other children. The possible presence of the metabolic syndrome and the long duration of diabetes could favor development of vascular complications at a young age in these subjects.

It is difficult to have a clear cut demarcation of MODY and type 2 diabetes in the young. Although the prevalence of type 2 diabetes in children is not known at present, type 2 diabetes in children is an entity that needs to be recognized and looked for, especially in obese children of diabetic parents in India. Asymptomatic nature may delay the diagnosis in many as it usually does in adult type 2 diabetic subjects.

Acknowledgments—We thank the secretarial assistance of Karvesseri Vettath Bindhu in preparation of the manuscript.

References