Cardiovascular Risk Profile in Caribbean Youth with Diabetes Mellitus
MK Tulloch-Reid, MS Boyne, MF Smikle, EG Choo-Kang, RH Parkes, RA Wright-Pascoe, EN Barton, RJ Wilks, DE Williams

ABSTRACT

Objective: To assess the effect of diabetes mellitus type on conventional and novel cardiovascular risk factors in patients, diagnosed with diabetes from two major referral hospitals in Jamaica, before age 25 years and with diabetes duration < 6 years.

Methods: Participants were classified based on the presence of GAD-65 and IA-2 autoantibodies, C-peptide, leptin and clinical phenotype. Trained observers obtained anthropometric measurements and sitting blood pressure. Fasting blood was taken for glucose, A1c, lipids, high sensitivity C-reactive protein and lipoprotein profile.

Results: Fifty-eight participants (21M; 37F, age 20 ± 8 [Mean ± SD] years, diabetes duration 2.6 ± 2 years) were enrolled. Thirty-six had Type 1 diabetes (T1D), thirteen Type 2 diabetes (T2D), six were not typed and three had lipoatrophic diabetes. Patients with Type 2 diabetes (T2D) were more obese with a higher systolic blood pressure but a lower A1c than those with Type 1 diabetes (T1D). Total cholesterol, LDL-cholesterol, triglycerides, VLDL, LDL and HDL particle numbers were similar in patients with T1D and T2D. HDL-cholesterol and LDL and HDL particle sizes were lower in patients with T2D but differences were no longer significant after adjusting for BMI.

Conclusions: Risk factors for cardiovascular disease are common in patients with all forms of youth onset diabetes. Clinicians should therefore investigate these risk factors in their patients regardless of diabetes type.

Perfil de Riesgo Cardiovascular entre la Yuventud Caribeña con Diabetes Mellitus
MK Tulloch-Reid, MS Boyne, MF Smikle, EG Choo-Kang, RH Parkes, RA Wright-Pascoe, EN Barton, RJ Wilks, DE Williams

RESUMEN

Objetivo: Evaluar el efecto del tipo de diabetes (DM) sobre los factores de riesgo cardiovasculares en pacientes diagnosticados con diabetes antes de los 25 años de edad, con una duración de la DM < 6 años, y remitidos de dos hospitales principales de Jamaica.

Métodos: Los participantes fueron clasificados a partir de la presencia de anticuerpos GAD-65 y IA-2, péptido C, leptina y fenotipo clínico. Observadores entrenados obtuvieron mediciones antropométricas y datos sobre la presión sanguínea en posición sentada. Se utilizó sangre en ayunas para los perfiles de glucosa, A1c, lipidos, proteína C de alta sensibilidad, y lipoproteína.

Resultados: Cincuenta y ocho participantes (21M; 37F, edad 20 ± 8 [Media ± SD] años, duración de la diabetes 2.6 ± 2 años) fueron enrolados. Treinta y seis tenían diabetes tipo 1 (DT1), 13 de ellos tenían diabetes tipo 2 (DT2), 6 no estaban clasificados, y 3 padecían de diabetes lipoatrópica. Los pacientes con diabetes de tipo 2 eran más obesos y su presión arterial sistólica era más alta, pero presentaban un perfil A1c más bajo que los de la diabetes tipo 1. El colesterol total, el colesterol LDL, los triglicéridos, y el número de partículas VLDL, LDL, y HDL fueron similares en los pacientes con diabetes tipo 1 y 2.

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INTRODUCTION

Diabetes mellitus is associated with an increased risk of cardiovascular disease (CVD), a result of poor glucose control and insulin resistance. For young patients, while the absolute risk of cardiovascular events is very low, the presence of cardiovascular risk factors at an early age has been associated with an increased risk of subclinical cardiac disease in early adulthood (1, 2). In addition, the Epidemiology of Diabetes Interventions and Complications (EDIC) study has demonstrated that intensive management of hyperglycaemia at a young age can reduce the risk of atherosclerotic disease and cardiovascular events in later adulthood (3, 4).

Type 1 diabetes is the predominant form of youth onset diabetes, accounting for most cases of diabetes with an onset before 20 years old. However, changing diets and low physical activity levels have resulted in increasing rates of obesity in youth and Type 2 diabetes, once considered a disease of middle and old age, now occurs more frequently in the young (5, 6). In Type 1 diabetes, beta cell failure/destruction results in hyperglycaemia while in Type 2 diabetes, hyperglycaemia results from both beta cell failure and insulin resistance (7). One might therefore expect patients with Type 2 diabetes to have a more adverse cardiovascular risk profile, since both insulin resistance and hyperglycaemia are typically present.

It has been suggested that the lipoprotein measurements used in clinical care are only able to explain a small proportion of CVD risk (8). This is because the standard density based classification of lipoproteins results in heterogenous categories that contain particles of differing diameter, composition and atherogenicity. A more detailed atherosclerotic profile that includes lipoprotein particle size and number and markers of inflammation might better predict adverse events and aid in identifying those who may need more immediate intervention (9). The Quebec Cardiovascular Study has demonstrated that small dense LDL particles in the setting of a high LDL particle number are associated with an increased cardiovascular risk and is a better indicator of risk than LDL cholesterol alone (10, 11). Large VLDL particles might indicate delayed chylomicron clearance, a risk factor for CVD (9, 12). Larger HDL particle subclasses may protect against atherosclerosis while the smaller subclasses are more atherogenic (9). Elevated high sensitivity C-reactive protein (hsCRP), an inflammatory marker, has also been shown to be an important cardiovascular disease risk factor that is independent of the lipid profile or the Framingham Risk Score (13).

The aim of this study was to determine the prevalence of traditional and novel cardiovascular risk factors in young patients with diabetes and evaluate the effect of diabetes type on the cardiovascular risk profile.

METHODS

The study was conducted in Jamaica, a multi-ethnic, predominantly black, middle income developing country in the Caribbean. A list of hospital admissions and clinic records for diabetes at the island’s two largest referral hospitals over a 5-year period (1999–2004) was obtained. Patients diagnosed with diabetes mellitus after January 1, 1998, 25 years old or younger at the time of diagnosis and living in the south-east section of the island (within 2 hours commute of the Tropical Medicine Research Institute) were invited to participate in this study to develop classification criteria for youth onset diabetes and estimate the proportion of recently diagnosed youth who had Type 2 diabetes. Additional patients who met the inclusion criteria were referred at the time of diagnosis or admission to hospital – between September 2004 and May 2006 – while the study was being conducted. Patients with gestational diabetes (that resolved after pregnancy) who were pregnant or less than 10 years old at the time of the study (as they were unlikely to have Type 2 diabetes) were excluded. The study was approved by The University of the West Indies/University Hospital of the West Indies, and the Kingston Public Hospital Ethics Committees and informed consent was obtained from each participant prior to enrolment.

Medical History

Each study participant was invited to attend a research clinic at the Tropical Medicine Research Institute. During the visit, the participants (and, for younger participants, their parents/guardians) completed an interviewer administered questionnaire to determine details about their history such as symptoms of diabetes at diagnosis, hospitalizations, diabetes-related complications, medications, co-morbid illnesses, social habits and family medical history.

Anthropometric Measurements

Trained observers used a standardized protocol to measure height, weight and waist circumference (14). Height was measured to the nearest centimetre using a portable stadiometer and weight was measured to the nearest 0.1kg with an electronic digital scale. The body mass index (BMI) – weight in kilograms divided by the square of the height in
metres – was calculated. Waist circumference was measured midway between the anterior-superior iliac spine and the lowest rib. Blood pressure was measured using an appropriately sized cuff and a mercury sphygmomanometer to the nearest 2 mmHg using the first (systolic) and fifth (diastolic) Korotkoff phases (15). Three measurements were taken at 1-minute intervals in the sitting position after the participant had been seated for 5 minutes. The mean of the last two blood pressure readings was used for the analysis.

**Laboratory Measurements**

After verifying an overnight fast and determining time of the last insulin dose, a fasting blood sample was obtained. A C-peptide stimulation test was performed using Boost (7 mls/kg up to maximum of 400 mls) given at 0 minutes and blood samples for glucose and C-peptide were collected from an indwelling catheter every 30 minutes for 2 hours. Samples were stored in ice where appropriate and all specimens were processed at the Institute’s laboratory within 4 hours of collection and stored at -70°C. Specimens that were sent abroad were shipped by courier using a cold pack.

Serum glucose was measured using a glucose oxidase enzymatic method. Total cholesterol, HDL-cholesterol and triglycerides were measured directly (Abbot® Spectrum) and LDL-cholesterol calculated using the Friedwald Equation (16). The glycosylated haemoglobin (A1c) was measured by affinity chromatography on a Primus® Automated Analyzer. Lipoprotein particle size and number were measured by nuclear magnetic resonance spectroscopy (9) and high sensitivity C-reactive protein (hsCRP) by immunometric assay (IMMULITE Diagnostic Products Cooperation, Los Angeles, CA) at Liposcience Laboratories (North Carolina, USA).

Serum C-peptide concentration was measured using commercially prepared reagents with a lower detection limit of 165 pmol/L. (IMMULITE Diagnostic Products Cooperation, Los Angeles, CA) at the University Hospital Chemical Pathology Laboratory. Glutamic acid decarboxylase (GAD65) and tyrosine phosphate IA-2 autoantibodies were measured at Northwest Lipid Laboratory (University of Washington, Seattle, WA) using a radioligant binding assay (17). Patients with a GAD65 Index > 0.085 or an IA-2 Index > 0.017 were considered diabetes antibody positive. Serum leptin levels were determined by immunoassay with the use of a commercial kit (Linco Research, St Charles, MO).

**Definitions**

**Diabetes Classification**

Subjects were classified into five groups by two endocrinologists (MTR and MB):

(i) Type 1A diabetes – GAD65 or IA-2 positive
(ii) Type 1B diabetes – GAD65 and IA-2 negative and fasting C-peptide < 230 pmol/L and/or stimulated C-peptide < 660 pmol/L
(iii) Type 2 diabetes – GAD65 and/IA-2 negative and fasting C-peptide > 500 pmol/L and/or stimulated C-peptide > 1160 pmol/L
(iv) Lipotrophic diabetes – distribution of subcutaneous fat with or without a low serum leptin (< 5 ng/ml)
(v) Untypeable diabetes – GAD65 and IA-2 negative with fasting C-peptide between 230–500 pmol/L and/or stimulated C-peptide 660–1160 pmol/L

**Overweight and Obesity**

The CDC age and gender specific BMI distribution was used to classify patients under 18 years old as overweight (CDC at risk for overweight – 85–94th percentile) or obese [CDC overweight – ? 95th percentile] (18). Patients 18 years and older with a BMI between 25 and 29.9 kg/m² were classified as overweight and those with a BMI > 30kg/m² were considered obese.

**Hypertension**

The National Heart Lung and Blood Institute (NHLBI) age, gender and height specific blood pressure tables were used to assess blood pressure in patients under 18 years old and those ? 95th percentile for blood pressure were classified as hypertensive (19). Participants at any age with a systolic blood pressure > 140 mmHg or a diastolic blood pressure > 90 mmHg and those who were on medications for treatment of high blood pressure were also classified as hypertensive (19, 20).

**Dyslipidaemia**

American Diabetes Association (ADA) guidelines were used to define patients as having dyslipidaemia (21). A LDL-cholesterol > 2.5 mmol/L, triglycerides > 1.7 mmol/L and a HDL-cholesterol < 1.1 mmol/L were considered abnormal.

**Poor glucose control**

An A1c > 7%, regardless of age, was considered elevated (21).

**Statistical Methods**

For continuous variables, comparisons were made between patients according to diabetes type using the Wilcoxon Rank Sum Test and the Kruskal Wallis Test while comparisons between dichotomous variables were made using the Fishers Exact Test. Skewed variables were log transformed and regression analysis was used to adjust for possible confounders that might have explained differences in cardiovascular risk by diabetes type. We considered results significant if p < 0.05. Analysis was performed using Stata 8.0 (Stata Corporation, TX).
RESULTS
Of the 65 patients identified, two refused to participate in the study, two could not be located, two had died and one on repeat testing was not found to have diabetes. Most of the participants had Type 1 diabetes –18 (31%) Type 1A and 18 (31%) Type 1B, 13 (22%) had Type 2 diabetes, 3(6%) had lipoatrophic diabetes (a rare form of diabetes associated with severe insulin resistance) and 6 (10%) patients could not be typed after evaluation. As we found no significant difference in clinical characteristics and cardiovascular risk profiles between patients with Type 1A and Type 1B diabetes apart from a longer duration of diabetes in patients with Type 1B diabetes (4 ± 2 [Mean ± SE] years vs 2 ± 1 years), these patients were combined into one group (Type 1 diabetes) for comparisons with other groups.

The characteristics of the study participants according to diabetes type – except for those with lipoatrophic diabetes – appear in Table 1. The participants with Type 2 diabetes were more likely to be female ($p < 0.01$) and were usually diagnosed with diabetes at an older age than those with Type 1 diabetes ($p = 0.04$). Diabetes duration was not significantly different in those patients classified as having Type 1 or Type 2 diabetes.

Traditional Cardiovascular Risk Factors
Table 1 shows the cardiovascular risk factors according to diabetes type. In comparing patients with Type 1 and Type 2 diabetes, patients with Type 2 diabetes had a greater mean BMI and waist circumference than those with Type 1 diabetes. Patients with Type 2 diabetes also had a higher mean systolic blood pressure ($p < 0.01$) but not diastolic blood pressure ($p = 0.06$). The mean A1c was lower in patients with Type 2 diabetes ($p < 0.01$). There were no significant differences in mean total cholesterol, HDL-cholesterol or triglycerides between these groups; however, patients with Type 2 diabetes had a lower mean HDL cholesterol ($p < 0.01$).

Table 1: Demographic characteristics and cardiovascular risk factors (Mean ± SD) in the study participants by diabetes type

<table>
<thead>
<tr>
<th>Characteristics (Mean ± SE)</th>
<th>Type 1 (n = 36)</th>
<th>Type 2 (n = 13)</th>
<th>Untyped (n = 6)</th>
<th>p value T1D vs T2D*</th>
<th>p value All groups**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>18 ± 5</td>
<td>20 ± 5</td>
<td>23 ± 4</td>
<td>0.10</td>
<td>0.04</td>
</tr>
<tr>
<td>Onset age (years)</td>
<td>15 ± 5</td>
<td>19 ± 5</td>
<td>20 ± 3</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td>Male (n)</td>
<td>15</td>
<td>2</td>
<td>2</td>
<td>&lt; 0.01†</td>
<td>0.01†</td>
</tr>
<tr>
<td>Black Ancestry (n)</td>
<td>33</td>
<td>13</td>
<td>6</td>
<td>0.39†</td>
<td>0.12†</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>3 ± 2</td>
<td>2 ± 2</td>
<td>4 ± 2</td>
<td>0.20</td>
<td>0.17</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>75 ± 10</td>
<td>104 ± 17</td>
<td>89 ± 11</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>22.3 ± 4.2</td>
<td>36.0 ± 8.6</td>
<td>27.9 ± 7.0</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>105 ± 8</td>
<td>114 ± 12</td>
<td>114 ± 17</td>
<td>0.01</td>
<td>0.03</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>59 ± 15</td>
<td>72 ± 19</td>
<td>64 ± 14</td>
<td>0.06</td>
<td>0.14</td>
</tr>
<tr>
<td>A1c (%)</td>
<td>11.1 ± 3.5</td>
<td>7.5 ± 2.0</td>
<td>10.4 ± 2.2</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/l)</td>
<td>4.5 ± 0.8</td>
<td>4.3 ± 0.7</td>
<td>6.2 ± 1.1</td>
<td>0.32</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>HDL- Cholesterol (mmol/l)</td>
<td>1.2 ± 0.4</td>
<td>0.9 ± 0.3</td>
<td>1.0 ± 0.4</td>
<td>0.93</td>
<td>0.01</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>0.8 ± 0.3</td>
<td>0.9 ± 0.4</td>
<td>1.5 ± 0.8</td>
<td>&lt; 0.01</td>
<td>&lt; 0.07</td>
</tr>
<tr>
<td>LDL-Cholesterol (mmol/l)</td>
<td>2.9 ± 0.6</td>
<td>3.1 ± 0.7</td>
<td>4.5 ± 0.8</td>
<td>0.60</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>VLDL Particle Number (nmol/l)</td>
<td>36.1 ± 18.1</td>
<td>42.5 ± 16.2</td>
<td>65.1 ± 36.1</td>
<td>0.19</td>
<td>&lt; 0.10</td>
</tr>
<tr>
<td>LDL Particle Number (nmol/l)</td>
<td>1025 ± 309</td>
<td>1173 ± 357</td>
<td>1533 ± 392</td>
<td>0.17</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>HDL Particle Number (nmol/l)</td>
<td>25.7 ± 5.5</td>
<td>22.6 ± 4.9</td>
<td>24.3 ± 7.6</td>
<td>0.06</td>
<td>0.13</td>
</tr>
<tr>
<td>VLDL Particle Size (nm)</td>
<td>46.1 ± 7.5</td>
<td>45.2 ± 2.9</td>
<td>46.2 ± 10.0</td>
<td>0.70</td>
<td>0.94</td>
</tr>
<tr>
<td>LDL Particle Size (nm)</td>
<td>21.2 ± 0.5</td>
<td>20.6 ± 0.6</td>
<td>21.0 ± 0.9</td>
<td>0.02</td>
<td>0.03</td>
</tr>
<tr>
<td>HDL Particle Size (nm)</td>
<td>9.3 ± 0.5</td>
<td>8.7 ± 0.4</td>
<td>8.9 ± 0.3</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>High Sensitivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-Reactive Protein (nmol/l)</td>
<td>0.5 (0.2,1.2)</td>
<td>7.0 (2.9,10.0)</td>
<td>2.1 (0.6,2.5)</td>
<td>0.02</td>
<td>0.01</td>
</tr>
</tbody>
</table>

T1D- Type 1 diabetes, T2D- Type 2 diabetes * Wilcoxon Rank Sum Test ** Kruskal-Wallis Test †- Fishers Exact Test ‡Median (25th and 75th percentiles)
The three patients with lipoatrophic diabetes had the highest total cholesterol and triglycerides (results not shown). The patients who remained untyped also had a high total and LDL cholesterol and a more adverse lipid profile than those participants with Types 1 diabetes (Table 1).

Table 2 presents the proportion of patients with adverse cardiovascular risk factors by diabetes type after excluding diabetes and all the patients who remained untyped had three or more CVD risk factors.

**Novel Cardiovascular Risk Factors**

Table 1 presents the distribution of novel risk factors in the patients studied according to diabetes type. When the patients with Type 1 and Type 2 diabetes were compared, the

<table>
<thead>
<tr>
<th>Cardiovascular Risk Factor</th>
<th>Diabetes Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type 1 (n = 36)</td>
</tr>
<tr>
<td>Hypertension (&gt; 95th percentile or &gt; 140/90 mmHg)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Overweight (&gt; 85th - 94th percentile or BMI 25 – 29.9 kg/m²)</td>
<td>8 (22)</td>
</tr>
<tr>
<td>Obese (&gt; 95th percentile or BMI &gt; 30 kg/m²)</td>
<td>3 (8)</td>
</tr>
<tr>
<td>Poor HbA1c (&gt; 7%)</td>
<td>33 (91)</td>
</tr>
<tr>
<td>High LDL-Cholesterol (&gt; 2.5 mmol/L)</td>
<td>24 (67)</td>
</tr>
<tr>
<td>High Triglycerides (&gt; 1.7mmol/L)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Low HDL-Cholesterol (&lt; 1.1 mmol/L)</td>
<td>12 (33)</td>
</tr>
</tbody>
</table>

Figure: Proportion of subjects with 0, 1, 2 and 3 or more cardiovascular risk factors by diabetes type.

VLDL, LDL and HDL particle numbers were similar. Patients with Type 2 diabetes however had lower LDL and HDL particle sizes (p < 0.01 for both). These measurements are known to vary according to age and gender; however, these differences remained significant after adjustment for these variables. After adjustment for BMI, the effect of having Type 1 or Type 2 diabetes on the particle size and number was no longer significant. High sensitivity C-reactive protein
(hsCRP) was highest in the patients with Type 2 diabetes but differences between patients with Type 1 and 2 diabetes were also no longer significant after adjustment for BMI.

Patients who remained untyped had the highest LDL particle number with a HDL and LDL particle size similar to that of patients with Type 2 diabetes (Table 1). As expected, patients with lipoatrophic diabetes had the highest VLDL particle size and lowest LDL and HDL particle sizes – findings consistent with severe insulin resistance (results not shown).

**DISCUSSION**

There was a high prevalence of CVD risk factors in Jamaican youth with diabetes regardless of diabetes type, with most participants having two or more CVD risk factors. Despite having a lower mean A1c, patients with Type 2 diabetes were more obese and had a higher hsCRP than those with Type 1 diabetes. The expected difference in total cholesterol, LDL cholesterol and triglycerides between patients with Type 1 and Type 2 diabetes was not found, though patients with Type 2 diabetes had a lower HDL-cholesterol. We found no differences in the proportion of subjects with elevated LDL-cholesterol or triglycerides. Despite similarities in the lipid subfractions, the lipoprotein analysis demonstrated that patients with Type 2 diabetes had a smaller LDL and HDL particle size, consistent with a more atherogenic lipid profile. Patients who remained untyped also had a severe risk factor profile. Differences by diabetes type were no longer significant after adjusting for BMI.

There are few studies of cardiovascular risk factors in youth with diabetes. The Search for Diabetes in Youth study (SEARCH) is a population-based study conducted in the United States of America to assess the prevalence and incidence of diabetes in youth under 20 years old (17). The prevalence of CVD risk factors was highest in the adolescent population 10 to 19 years old (22). Hypertension was present in 30%, hyperlipidaemia in 23%, low HDL-cholesterol in 16% and increased waist circumference in 23%. Two or more of these risk factors were present in 25% of the sample. Girls had a higher prevalence of obesity (increased waist circumference) and boys were more likely to have a low HDL. Among minority youth, African-American children had the lowest prevalence of CVD risk factors [39% high blood pressure, 20% elevated triglycerides, 14% low HDL, 36% elevated waist circumference and 32% with two or more risk factors] (22). As in the present study, children with Type 2 diabetes had a higher prevalence of CVD risk factors with two or more of these being present in 92% of patients; obesity was particularly common.

In this study, the proportion of patients with an adverse lipid profile was higher in the patients with Type 1 diabetes than in the SEARCH study. In two analyses from the SEARCH cohort, an elevated A1c was associated with a more adverse lipid profile (23, 24). The very high A1c in the study population of patients with Type 1 diabetes may account for the more adverse lipid profile in this group.

Type 2 diabetes typically occurs in older persons and is usually associated with insulin resistance. Accordingly, CVD risk factors in adults with Type 2 diabetes are treated aggressively, often from diagnosis. Type 1 diabetes is also associated with increased cardiovascular risk. When diabetes occurs in youth as the absolute risk of a CVD event is low, aggressive management of CVD risk factors at diagnosis with pharmacotherapy may be delayed until mid to late adulthood because of concerns about the risks associated with medications. These young patients are therefore encouraged to make lifestyle changes; however, given the adverse CVD risk profile at this age, consideration should be given to identifying effective and safe pharmacotherapy for earlier treatment.

Patients with unclassified diabetes had a CVD risk profile similar to that of patients with Type 2 diabetes. The duration of these patients’ diabetes was longer and it is possible that they could have Type 2 diabetes with waning beta cell function. Poor glucose control might also explain the severity of the lipid profile in this group of patients. However, these patients with unclassified diabetes did not have the highest mean A1c values and yet had an adverse lipid profile. The lipid profile is therefore likely to be indicative of a more severe insulin resistant state that may have resulted in premature beta-cell failure and earlier insulin replacement therapy. Reports of this form of diabetes in Jamaica are not new (25). The natural history of diabetes in these patients deserves further exploration as their overall CVD risk may actually exceed that of most patients with Type 2 diabetes. Patients with lipoatrophic diabetes had the most severe atherogenic profile.

In this study, the effect of diabetes type on new markers of atherogenesis including hsCRP and the lipoprotein particle size and number were examined. High LDL and VLDL particle number and low LDL, VLDL and HDL particle size have been associated with a more adverse cardiovascular risk profile (10,11). In cross-sectional studies, a more adverse lipoprotein particle profile has been associated with a higher triglyceride measurement and weight (26). In children and adolescents, the proportion of patients with small dense LDL particles has been found to be higher in those who are classified as insulin resistant.

In comparing the mean VLDL, LDL and HDL particle sizes in Jamaican patients with diabetes with those reported in Black adolescents in the Bogalusa Heart Study (BHS), patients with Type 1 diabetes had similar mean HDL particle sizes (BHS of 9.2 ± 0.4 nm [Mean ± SD] in boys and 9.3 ± 0.4 nm in girls) while patients with Type 2 and other forms of diabetes had a lower mean HDL particle size (27). The mean LDL particle size for patients with all forms of diabetes was similar to that reported in the Bogalusa Heart Study. However, VLDL particle size (BHS 40 ± 6.7 nm [Mean ± SD] in boys and 39.0 ± 5.6 nm in girls) was higher in patients
with all forms of diabetes perhaps as a result of chronic hyperglycaemia with delayed clearance of chylomicrons.

Serum apolipoprotein B (apoB) and LDL density are commonly utilized markers of an adverse lipid profile. Albers, in a cross-sectional analysis of these measurements in the SEARCH study, demonstrated a more adverse lipid profile in patients with Type 2 compared to Type 1 diabetes using these measurements (24). Albers found that patients with Type 2 diabetes had a higher apoB level and more dense LDL cholesterol, even after adjusting for confounding factors. In the present study, using NMR technology for lipoprotein analysis, patients with Type 2 diabetes had lower mean LDL particle size, with a higher proportion of dense/smaller LDL particles. The difference in LDL particle number, which would correspond to serum apoB, was not statistically different in patients with Type 1 and Type 2 diabetes.

Age and gender are important determinants of the lipoprotein particle profile in most studies (26–28). These factors did not explain differences in profiles between patients with Type 1 and Type 2 diabetes in the present study. Adjusting the models for BMI resulted in the loss of many of the differences by diabetes type suggesting that weight differences might explain some of the difference in the adverse lipid profiles in patients with Type 1 and Type 2 diabetes. The limited sample size did not allow for simultaneous evaluation of several risk factors.

In summary, patients with diabetes had an adverse CVD risk profile regardless of diabetes type. It is therefore important to assess overall CVD risk factors in youth with diabetes and intervene with appropriate therapy to reduce the burden of these risk factors at an early stage.

ACKNOWLEDGEMENTS

We wish to thank the participants, Margaret White, Donnahaë Rhoden-Salmon and Dominique Turnquest for their contribution to this study. We also thank the SEARCH committee for making their protocol available. This study was funded from research grants received from the Caribbean Health Research Council and The University of the West Indies New Initiative Fund.

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