Introduction and objectives. Numerous clinical and epidemiological studies have highlighted the fact that metabolic syndrome is an important precursor of cardiovascular disease. Metabolic syndrome is generally associated with type-2 diabetes, and few data exist on its occurrence in type-1 diabetes. The aims of this study were to determine the prevalence of metabolic syndrome in patients with type-1 diabetes and to identify associated factors.

Methods. This cross-sectional study included consecutive patients aged over 18 years with autoimmune type-1 diabetes of more than 6 months’ duration who were treated during 2008 at the Outpatient Endocrinology Clinic of the Hospital del Mar, Barcelona, Spain. The presence of metabolic syndrome was determined using the modified criteria proposed by the National Cholesterol Education Program–Adult Treatment Panel III.

Results. Overall, 31.9% (95% confidence interval [CI], 22.3%-41.5%) of patients with type-1 diabetes had metabolic syndrome. The following factors were significantly and independently associated with the presence of metabolic syndrome in patients with type-1 diabetes: age (odds ratio [OR] = 1.09; 95% CI, 1.029-1.154), body mass index (OR = 1.389; 95% CI, 1.134-1.702) and glycosylated hemoglobin level (OR = 1.745; 95% CI, 1.081-2.815). In addition, there was a direct relationship between the number of components of metabolic syndrome present and prevalence of microangiopathy, which reached 100% in patients who satisfied all diagnostic criteria.

Conclusions. Metabolic syndrome was common in patients with type-1 diabetes and was associated with microvascular complications.

Key words: Diabetes mellitus. Microvascular complications. Metabolic syndrome. Insulin resistance.
hypothesis that mitochondrial dysfunction, possibly related to the metabolic syndrome, may be the cause of insulin resistance and type 2 diabetes.

Patients

We undertook a cross-sectional study of patients with DM1 seen consecutively between January and December 2008 at the Outpatient Endocrinology Clinic of the Hospital del Mar in Barcelona, Spain. DM1 was considered to be autoimmune when it fulfilled the diagnostic criteria for diabetes mellitus together with positive tests for anti-GAD/65 Ks or anti-IA2 antibodies at the start and a concentration of free C-peptide <1.1 ng/mL 6 min after intravenous administration of 1 mg of glucagon. Non-Caucasian patients were excluded, as were patients with variations in the concentration of glycosylated hemoglobin >1% at 3 bimonthly determinations, pregnant women, patients who had an excessive consumption of alcohol, patients with chronic end-stage kidney failure, kidney transplant recipients or those on hemodialysis. No patient was being treated with insulin sensitizing drugs, such as thiazolidinediones or metformin. The study protocol, approved by the hospital Ethics Committee, included a physical examination and a blood test. All the participants were aged 18 years or over and had had diabetes for longer than 6 months.

Data were recorded for each patient on age, sex, time since the diagnosis of diabetes, history of major cardiovascular events (acute myocardial infarction, coronary revascularization procedures, angioplasty, stroke, transient ischemic attack, and peripheral vascular disease, defined as the presence of intermittent claudication or amputation), as well as the presence of chronic microangiopathic complications of the diabetes (microalbuminuria or macroalbuminuria, retinopathy, peripheral or autonomic neuropathy). The presence of complications was evaluated by an expert diabetologist (JJC), except for retinopathy, which was assessed by an ophthalmologist. The criteria of the American Diabetes Association were used for the clinical diagnosis of complications, and the insulin requirements were estimated in units per kilogram of body weight (U/kg/d). The physical examination included measurements of weight, height and abdominal waist circumference, as well as the blood pressure using standardized methods.

The renal status was classified from the urinary albumin excretion (UAE): a) absence of kidney disease was defined as normoalbuminuria (UAE<30 mg/24 h); b) incipient kidney disease as microalbuminuria (UAE 30-300 mg/24 h); and c) established kidney disease as macroalbuminuria (UAE>300 mg/24 h). The UAE was expressed as the mean of three 24 h urine samples taken at the patient’s home during a period of normal activity on 2 separate occasions, at least 1 month apart.
Criteria for the Metabolic Syndrome

In accordance with the modified criteria of the National Cholesterol Education Program -Adult Treatment Panel III (NCEP-ATP III),21 the metabolic syndrome was diagnosed if the patient had 3 or more of the following conditions: fasting plasma glucose ≥100 mg/dL or treatment with glucose lowering drugs, arterial blood pressure ≥130/85 mmHg or treatment with antihypertensive medication, fasting plasma triglycerides ≥150 mg/dL (1.7 mmol/L) or treatment for hypertriglyceridemia, HDL-C <40 mg/dL (1.03 mmol/L) in men and <50 mg/dL (1.3 mmol/L) in women or drug therapy to raise the HDL-C concentration, and an abdominal waist circumference ≥102 cm in men and ≥88 cm in women.

Statistical Analysis

For an alpha risk of .05 and precision of ±10% in a bilateral contrast for an estimated 40% rate of the metabolic syndrome and assuming a population of 100,000, we required a random sample of 93 persons.

The Student t test was used to compare means and the χ² test for categorical variables, as well as the Mann-Whitney U test for variables that did not follow a normal distribution, and Pearson’s correlation coefficient to establish relations between quantitative variables. To evaluate the factors associated with the presence of the metabolic syndrome (dependent variable), a multiple logistic regression model was applied that included as independent variables those which had a P<.1 in the univariate analysis. The results were analyzed using the statistical program SPSS, version 12.0 for Windows.

RESULTS

Of the 165 patients seen at the Outpatient Endocrinology Clinic during 2008, 56 were excluded due to lack of confirmation of the diagnosis of autoimmune DM1, variations in the glycosylated hemoglobin concentration, excessive consumption of alcohol or end-stage renal failure. Of the 109 patients eligible, 91 (83.5%) completed the study protocol and composed the definitive sample. The age (mean [standard deviation]) of the patients was 39.7 (13.2) years; 53 were men and 38 women, with a mean duration of DM1 of 16.7 (12.9) years and a mean glycosylated hemoglobin concentration of 7.29% (1.4%).

All the patients fulfilled the criterion of high fasting plasma glucose; 57 (62.6%) fulfilled 2 or more criteria; 29 (31.9%), 3 or more; 11 (12.1%), 4 or more; and 2 (2.2%) fulfilled all the criteria for the metabolic syndrome. Thus, 29 patients (17 men, 12 women) had the metabolic syndrome according to the NCEP-ATP III modified criteria,21 giving an overall prevalence of 31.9% (95% confidence interval [CI], 22.3-41.5). Table 1 shows the prevalence of each of the components of the metabolic syndrome in the whole group of patients with DM1.

The most frequent criterion among the patients with the metabolic syndrome, besides glycemia, was the HDL-C concentration, present in 93.1% of the cases, followed by hypertension (72.4%), abdominal obesity (58.6%) and hypertriglyceridemia (20.7%). These percentages contrast with those seen in the patients with DM1 but without the metabolic syndrome (Figure 1).

TABLE 1. Components of the Metabolic Syndrome in the 91 Patients With Type 1 Diabetes Mellitus

<table>
<thead>
<tr>
<th>Variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal circumference</td>
<td></td>
</tr>
<tr>
<td>≥102 cm in men</td>
<td>9/53 (16.9)</td>
</tr>
<tr>
<td>≥88 cm in women</td>
<td>15/38 (39.5)</td>
</tr>
<tr>
<td>HDL-C</td>
<td></td>
</tr>
<tr>
<td>&lt;40 mg/dL in men</td>
<td>9/53 (16.9)</td>
</tr>
<tr>
<td>&lt;50 mg/dL in women</td>
<td>15/38 (39.5)</td>
</tr>
<tr>
<td>Triglycerides ≥150 mg/dL</td>
<td>6 (6.6)</td>
</tr>
<tr>
<td>Blood pressure ≥130/85 mmHg</td>
<td>33 (36.3)</td>
</tr>
</tbody>
</table>

HDL-C indicates high-density lipoprotein cholesterol. The values are expressed as n/N (%).
The patients with DM1 and the metabolic syndrome were older and had longer duration of diabetes, higher body mass index and a greater prevalence of overweight than those DM1 patients without the metabolic syndrome (Table 2). No differences were found in the percentage of macroangiopathic complications. However, the patients with DM1 and the metabolic syndrome had a significantly higher prevalence of microangiopathic complications (retinopathy, neuropathy and nephropathy) than the DM1 patients without the metabolic syndrome. In addition, a direct relation was detected between the number of components of the metabolic syndrome and the prevalence of microangiopathy, reaching 100% in those patients who had all the diagnostic criteria for the metabolic syndrome (Figure 2). On the other hand, the daily insulin requirements were similar in patients with and without the metabolic syndrome (0.69 [0.2] vs 0.72 [0.3] U/kg/d).

In the multiple logistic regression analysis, age, body mass index and glycated hemoglobin retained a significant and independent association with the presence of the metabolic syndrome (Table 3).

**DISCUSSION**

This study found a prevalence of the metabolic syndrome in patients with DM1 of 31.9% (31.5%...
In the present study no differences were found in the daily insulin requirements between the patients with and without abdominal obesity (0.69 [0.15] vs 0.72 [0.34] U/kg/d), which indicates that factors such as dietary habits, exercise or a family history must be intervening in the development of visceral obesity.

Concerning the repercussion of the metabolic syndrome on chronic complications, the proportion of patients with microangiopathy was clearly greater among those who had this complication. This confirms the results reported in other European series, which have found prevalence rates of the metabolic syndrome reaching 62% in patients with macroalbuminuria, and an odds ratio of 3.75 (95% CI, 2.89-4.85) for diabetic nephropathy in the case of the metabolic syndrome. In the present study, the proportion of patients with microangiopathy rose in parallel with the number of components of the metabolic syndrome, reaching 100% in those persons who had all 5 diagnostic criteria. Studies in a large number of patients with a long-term follow-up have also shown the relation between insulin resistance, the metabolic syndrome and macroangiopathy, an association that was not found in our study. The low number of cases in both groups, the mean age of the patients, the good metabolic control and the relatively short mean duration of the diabetes (16.7 years) may all have contributed to the lack of significant differences in macrovascular complications. In addition, most of these patients were diagnosed after publication of the DCCT study results, and they have therefore followed intensive insulin treatment since their diagnosis, which has been shown to reduce the incidence of severe cardiovascular events by 42% over 20 years.

Finally, strict criteria have been published for the diagnosis of autoimmune DM1, which exclude young patients with DM2, in whom...
the prevalence of macroangiopathy on diagnosis may reach 20% given the delay between the onset of the hyperglycemia and the diagnosis,\(^\text{30}\) due to the close association between DM2, the metabolic syndrome and cardiovascular disease.\(^\text{31}\)

The multiple logistic regression model showed that the degree of blood glucose control, evaluated from the glycylated hemoglobin, was the most influential variable in the development of the metabolic syndrome, followed by the body mass index and age. Earlier studies found no influence of metabolic syndrome, followed by the body mass index and age. Earlier studies found no influence of metabolic control,\(^\text{11}\) though it is worth noting that the glycylated hemoglobin in these studies was above 10%, almost 3% higher than in the present study.

**Limitations**

The limitations of this study derive from its cross-sectional design. Thus, we should recall not only the possible variations over time in the parameters studied but also that the findings only refer to associations, and do not imply causality. The sample size was the result of applying strict criteria for the diagnosis of autoimmune DM1 and excluding patients with a short disease evolution in order to avoid the effects of insulinopenia on the glycylated hemoglobin and the anthropometric variables. In any event, the baseline characteristics of the patients included in the study were those of the population with DM1 in our setting.\(^\text{32}\)

**CONCLUSIONS**

The metabolic syndrome is common in patients with DM1, and was present in one third of the patients with diabetes mellitus in our area, particularly the patients who were older, had a higher body mass index and worse metabolic control. The presence of the metabolic syndrome in this group of patients was associated with microvascular complications.

**REFERENCES**


