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LETTER TO THE EDITOR

Geographic variation in the frequency of abdominal adiposity and metabolic syndrome in Italian adolescents with type 1 diabetes

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Dear Sir,

In line with the global obesity epidemic, a raised weight gain has been described in children and adolescents with type 1 diabetes mellitus (T1DM) [1, 2]. The waist-to-height ratio (W/h), a proxy measure of central fat distribution, has been proposed as a simple and useful tool to detecting, among overweight children, those with a higher likelihood of having cardiometabolic risk [3]. Since the distribution of overweight in the general population in Italy varies among different geographic areas and shows the highest prevalence in the south [4], we explored whether the frequency of abdominal adiposity and consequently of metabolic syndrome (MetSy) also varied across the different geographic areas in Italian adolescents with T1DM.

This cross-sectional study included a total of 412 Italian adolescents of Caucasian origin (219 males) with T1DM, aged 16–19 years, with a duration of diabetes of 8.4 ± 3.9 years. They were recruited from 18 care referral centers for diabetes in childhood affiliated to the Study Group on Diabetes of the Italian Society of Paediatric Endocrinology and Diabetology. Anthropometry, blood pressure, and venous fasting blood samples tested for triglycerides and HDL cholesterol were measured; HbA1c values (mean of four determinations during the previous year) were mathematically standardized to the DCCT normal range. All patients were on multi-injection or pump insulin treatment; the daily insulin dose (ID) per body surface area was calculated. MetSy was defined according to the IDF criteria; all patients were considered to fulfill the criterion of hyperglycemia.

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The study was conducted on behalf of Study Group on Diabetes of the Italian Society of Paediatric Endocrinology and Diabetology (ISPED).

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Table 1 Clinical features of T1DM patients stratified across the three Italian geographic areas

	North ($n = 123$)	Center ($n = 129$)	South ($n = 160$)	p
Age (years)	17.4 ± 1.0	17.3 ± 0.9	17.3 ± 0.8	0.903
BMI (kg/m^2)	23.1 ± 3.6	22.8 ± 2.8	23.2 ± 3.4	0.850
Waist-to-height ratio	0.45 ± 0.06	0.45 ± 0.04	0.49 ± 0.06	<0.01*
Insulin dose (U/m^2/day)	33.9 ± 9.0	32.1 ± 10.4	33.2 ± 8.6	0.278
HbA1c (%)	9.4 ± 1.8	8.6 ± 1.4	8.9 ± 1.7	<0.01**
Waist-to-height ratio ≥0.5, *N* (%)	19 (15.4)	22 (17.1)	75 (46.9)	<0.01*
MetSy, *N* (%)	7 (5.7)	9 (6.9)	23 (14.4)	0.024

* South versus North and Center

** North versus Center

Abdominal adiposity (W/h ≥0.5) was found in 116 patients (28.1 %) and MetSy in 39 patients (9.5 %). The highest frequencies of both abdominal adiposity and MetSy were found in patients living in southern Italy (Table 1). No difference in BMI and daily ID was found among patients living in the three geographic areas, while HbA1c levels differed between patients living in the northern and central regions. In addition, patients with MetSy living in the North had not only significantly higher ID and worse HbA1c than patients without MetSy, but also higher ID ($p = 0.022$) and worse HbA1c ($p = 0.012$) than patients with MetSy living in the south (Table 2).

After adjustment for HbA1c, the differences between T1DM patients from the south and those from the northern and central regions remained significant when the presence of high W/h (South vs North: odds ratio (OR) 6.1, 95 % confidence interval (CI) 3.3–11.1, $p < 0.001$; South vs Center: OR 5.8, 95 % CI 3.2–10.6, $p < 0.001$; Center vs North: OR 1.1, 95 % CI 0.5–2.2, $p = 0.874$) or the prevalence of MetSy (South vs North: OR 3.5, 95 % CI 1.4–8.5, $p < 0.01$; South vs Center OR 3.3, 95 % CI 1.3–8.3, $p = 0.013$; Center vs North: OR 1.1, 95 % CI 0.3–3.4, $p = 0.872$) were considered.

In line with recent data on the North–South gradient in the prevalence of overweight in Italy, a higher frequency of abdominal adiposity associated with cardiometabolic risk factors has been found in adolescents with T1DM from southern Italy. Our data confirm and extend previous findings on the epidemiology of MetSy in Italian T1DM adults [5]. Whether a difference in the genetic background might play a role is currently unknown. Since an opposite gradient in socioeconomic status exists in Italy, the influence of lifestyle factors, socioeconomic and socio-environmental effects could play a role in the cross-country differences in abdominal fat and MetSy frequency. Intensified insulin therapy may promote weight gain in T1DM patients; however, ID did not differ by geographic area. Indeed, the higher ID and the worse HbA1c found in patients living in the North suggest that despite their "leaner" phenotype, at least when compared in terms of W/h to patients from southern Italy, they exhibited higher insulin resistance, leading to worse metabolic control and consequently higher ID. Therefore, the weight of the various components of the MetSy could be different across the different geographic areas. The finding of a worse metabolic control in adolescents from the northern regions is unique, since no national study has previously analyzed the geographic or regional differences in HbA1c levels in T1DM adolescents. It is difficult to explain the reasons of this surprising result. The care of type 1 diabetes in Italy is

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Table 2 Insulin dose and HbA1c levels in patients with and without MetSy stratified across the three Italian geographic areas

	ID (U/m^2/day)			HbA1c (%)		
	MetSy$^-$	MetSy$^+$	p	MetSy$^-$	MetSy$^+$	p
North	33.2 ± 8.4	46.2 ± 10.9*	<0.001	9.3 ± 1.7**	11.4 ± 1.7***	0.002
Center	31.9 ± 10.1	35.1 ± 14.5	0.373	8.5 ± 1.5	9.1 ± 0.9	0.373
South	32.9 ± 8.2	34.7 ± 10.9	0.367	8.8 ± 1.7	9.3 ± 1.7	0.192

ID, insulin dose; MetSy$^-$, patients without metabolic syndrome; MetSy$^+$, patients with metabolic syndrome

* $p = 0.022$ North versus South (within MetSy$^+$ patients)

** $p = 0.050$ North versus South and $p = 0.001$ North versus Center (within MetSy$^-$ patients)

*** $p = 0.012$ North versus South and $p = 0.014$ North versus Center (within MetSy$^+$ patients)

provided by the National Health Service; consequently, all patients have equal access to the treatment of this chronic disease. Moreover, all patients were caucasians of Italian origin; therefore, racial/ethnic disparities can be excluded, neither the differences were related to insulin treatment (multi-injection vs pump). Diet composition and physical activity, important contributing factors to insulin sensitivity, were not assessed in this study, and their potential role should be investigated in future studies.

Descriptive studies linking health issues and geography can be useful to search relationships between distribution of disease and some factor of interest, such as genetics or lifestyle exposure. More detailed studies on nutritional habits, physical activity, and lifestyle in T1DM patients are needed in order to explore the determinants for cardiovascular risk in T1DM adolescents, providing new possibilities for personalized prevention and treatment.

Conflict of interest None.

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