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# Metabolic syndrome in adult patients with Prader–Willi syndrome

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**Abstract** *Background and aims:* Prader–Willi syndrome (PWS), the most common genetic cause of obesity, is characterized by elevated morbility and mortality in all ages. In this context, non-obese PWS children showed low frequency of metabolic syndrome (MetS), while a comparable prevalence was observed in obese PWS and obese controls. Aim of this study was to estimate the occurrence of MetS and its components in a large group of PWS adults, according to obesity status.
*Methods and results:* A cross-sectional study was performed in 108 PWS aged 18.0–43.2 years (87 obese and 21 non-obese) and in 85 controls with nonsyndromic obesity matched for age, gender, and BMI with obese PWS.

*Abbreviations:* PWS, Prader–Willi syndrome; T2DM, type 2 diabetes mellitus; MetS, metabolic syndrome; BMI, body mass index; DELETED, interstitial deletion of the proximal long arm of chromosome 15 (del15q11–q13); UPD15, uniparental maternal disomy for chromosome 15; WC, waist circumference; BP, blood pressure; HDL-C, high density lipoprotein cholesterol; HOMA-index, homeostasis model assessment index.

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Non-obese PWS showed lower waist circumference, insulin, HOMA-index, triglycerides, diastolic blood pressure, and higher HDL-C than both obese PWS and obese controls ($p < 0.017$). Obese PWS showed higher glucose and systolic blood pressure than both non-obese PWS and obese controls ($p < 0.017$). MetS was found in 1/21 (4.8%) non-obese PWS, 36/87 (41.4%) obese PWS and 39/85 (45.9%) obese controls. Non-obese PWS showed lower frequency for each MetS component as compared with obese PWS and obese controls. PWS patients with deletion of the chromosome 15q11—13 showed a lower risk for low HDL-C ($p < 0.01$) and a trend towards a lower MetS risk ($p < 0.06$) compared to subjects without deletion.
*Conclusion:* Our findings suggest the main role that obesity status plays on the individual metabolic risk clustering in PWS adults. Early identification of MetS could be helpful to improve morbidity and prevent mortality in such patients.


## Introduction

Prader—Willi syndrome (PWS) is a contiguous gene syndrome caused by the non-expression of the paternal alleles in the PWS region of chromosome 15q11—13 [1]. PWS is the single most common known genetic cause of obesity with an estimated population prevalence varying from 1:49,911 up to 1:91,802 [2]. The clinical picture of PWS includes muscular hypotonicity, early childhood-onset obesity, characteristic appearance, hypogonadism, impaired growth hormone secretion, mild or severe mental retardation, and behavioral disturbance [3]. Some of the typical features of PWS seem to reflect a hypothalamic dysfunction [4]. In the early period of life, PWS is characterized by severe neonatal hypotonia, feeding problems and a failure to thrive. In absence of intervention, weight excess typically begins after 2—3 years of age and is later exacerbated by hyperphagia with lack of satiety. Consequently, a disproportionate accumulation of body fat develops as early as in childhood [5] and leads progressively to severe obesity by the adult age [3].

Retrospective studies estimated that yearly mortality rates was 7% in PWS patients older than 30 years [6]. Reduced life expectancy seems to be due to the complications conventionally related to obesity, including cardiovascular and respiratory problems as well as disorders associated with type 2 diabetes mellitus (T2DM) [7]. Nevertheless, the factors determining the evolution to cardiovascular disease and metabolic complications remains to be still elucidated. In non-PWS populations, several studies have shown that individuals with metabolic syndrome (MetS) have an increased risk of T2DM and coronary heart disease or are at a greater risk of developing them [8]. In this light, MetS might be one of the risk factors responsible for excessive mortality in PWS. The metabolic profile of PWS adults, however, is usually characterised by a healthier lipid profile and by a higher insulin sensitivity, compared with matched nonsyndromic obese subjects [9]. These findings seem to be due to an atypically reduced visceral fat depot, which is not common in nonsyndromic obesity [10]. Nevertheless, data on fat distribution in PWS are still conflicting [9,11]. In addition, impaired microvascular function and subnormal exercise capacity have been observed in young adults without ischemic symptoms [12], and several cardiovascular risk factors are already present in pre-pubertal children with PWS [13]. In this context, we have recently demonstrated that non-obese PWS children showed low MetS frequency, while a comparable prevalence was found in obese PWS and obese controls [14].

Since there are no data about the frequency of MetS in adult patients with PWS, the aim of our study was to estimate the occurrence of MetS in a large group of adults with genetically confirmed PWS. We also looked for metabolic differences between obese PWS and non-obese PWS subjects, and between obese PWS and a control group of patients with nonsyndromic obesity, matched for age-, gender- and body mass index (BMI).

## Methods

### Patients

One hundred and eight patients with genetically confirmed PWS, 47 males and 61 females, aged 18.0—43.2 years, were included in the study (Table 1). All patients showed the typical PWS clinical phenotype [15]. Seventy-three subjects had interstitial deletion of the proximal long arm of chromosome 15 (del15q11—q13) (DELETED), 27 had uniparental maternal disomy for chromosome 15 (UPD15) and 2 individuals had a de novo translocation involving chromosome 15. In addition, a positive methylation test was demonstrated in the remaining 6 PWS but the underlying genetic defect was not identified. The methylation pattern analysis of the PWS region was carried out according to standard diagnostic protocols for Southern blot and bisulphite methylation polymerase chain reaction [16].

At the time of the study, 23 subjects (10 males) had T2DM (15 were treated with oral hypoglycemic agents alone, 5 with insulin, 2 with insulin plus metformin, and one was on diet only). Fifty-two patients (26 males) had hypertension: 25 subjects were taking monotherapy ($n = 9$) or a combination therapy ($n = 16$), while 27 individuals were receiving no treatment. Two individuals were treated for high triglycerides (1 male). Five subjects suffered from hypothyroidism (2 males) and were biochemically euthyroid on thyroxine substitution. Twenty-three females and 3 males were undergoing sex steroid replacement treatment. All PWS were reported to have behavioral problems, and 40 patients were treated with neuroleptics (21 males). Subjects were divided according to the presence of obesity (see below) in obese PWS and non-obese PWS.

**Table 1** Measurements of the study subjects. Abbreviations: nobPWS = non-obese PWS; obPWS = obese PWS; obCTRL = obese controls; $P_{50}$ = 50th percentile; $P_{25}$ = 25th percentile; $P_{75}$ = 75th percentile; HOMA = HOmeostasis Model Assessment index.

| | nobPWS ($n$ = 21) | | | obPWS ($n$ = 87) | | | obCTRL ($n$ = 85) | | |
|---|---|---|---|---|---|---|---|---|---|
| | $P_{50}$ | $P_{25}$ | $P_{75}$ | $P_{50}$ | $P_{25}$ | $P_{75}$ | $P_{50}$ | $P_{25}$ | $P_{75}$ |
| Age (years) | 21[a] | 20 | 29 | 26[a] | 21 | 30 | 28[a] | 23 | 31 |
| Weight (kg) | 63.6[a] | 56.8 | 68.9 | 99.0[b] | 84.8 | 118.0 | 117.0[c] | 105.9 | 138.0 |
| Height (m) | 1.50[a] | 1.50 | 1.60 | 1.50[a] | 1.40 | 1.50 | 1.70[b] | 1.60 | 1.70 |
| BMI (kg/m$^2$) | 26.2[a] | 25 | 28 | 44.6[b] | 36 | 52.9 | 42.6[b] | 39.4 | 47.7 |
| Waist (cm) | 91[a] | 81 | 95 | 121[b] | 110 | 132 | 123[b] | 113 | 138 |
| Glucose (mg/dL) | 78[a] | 69 | 87 | 85[b] | 78 | 100 | 80[a] | 74 | 88 |
| Insulin (μU/mL)[a] | 4[a] | 3 | 8 | 11[b] | 7 | 16 | 12[b] | 8 | 17 |
| HOMA[a] | 0.8[a] | 0.5 | 1.8 | 2.4[b] | 1.6 | 3.4 | 2.2[b] | 1.6 | 3.9 |
| Triglycerides (mg/dL) | 67[a] | 52 | 102 | 104[b] | 79 | 137 | 123[b] | 78 | 176 |
| HDL-C (mg/dl) | 53[a] | 49 | 63 | 48[b] | 38 | 60 | 44[b] | 37 | 50 |
| Systolic blood pressure (mm Hg) | 120[a] | 110 | 120 | 120[b] | 120 | 130 | 120[a] | 115 | 130 |
| Diastolic blood pressure (mm Hg) | 70[a] | 70 | 80 | 80[b] | 70 | 80 | 80[b] | 70 | 80 |

Figures not sharing the same superscript letters are significantly different at $p$-level $< 0.017$ (Wilcoxon–Mann–Whitney test with Bonferroni's correction for 3 groups).

[a] Available in 19 nobPWS, 72 obPWS and 83 obCTRL.

As obese control group, a sample of 85 subjects affected by nonsyndromic obesity (37 males, 48 females) was recruited among patients hospitalized at Istituto Auxologico Italiano Foundation for a multidisciplinary weight reduction program for obesity and its complications, and matched to obese PWS for gender (same), age (+/− 1 year) and BMI (+/− 1) (Table 1). At the time of the study, 10 obese control subjects had T2DM (7 males), 2 of them were treated with insulin, 6 with oral antidiabetic drugs and 2 were on diet only. Thirteen subjects received a multi-drugs therapy for hypertension (10 males). Finally, six individuals (3 males) were taking treatment for lipid abnormalities. Apart from insulin, no control subject was receiving any hormone replacement. Six PWS patients and 5 obese controls were cigarette smokers.

The entire study protocol was approved by the ad hoc Ethical Committee of the Istituto Auxologico Italiano Foundation. All patients and/or their parents gave their written informed consent to participate to the study, when appropriate.

## Anthropometric and blood pressure measurements

Physical examination included determination of height, weight and waist circumference (WC). Standing height was determined by a Harpenden Stadiometer (Holtain Limited, Crymych, Dyfed, UK). Body weight was measured to the nearest 0.1 kg, by using standard equipment. BMI was defined as weight in kilograms divided by the square of height in meters. A BMI cut-off point of >30 was used to define obesity. WC was measured in standing position halfway between the inferior margin of the ribs and the superior border of the crista. Diastolic and systolic blood pressure (BP) were measured to the nearest 2 mmHg in the supine position after 5 min rest, using a standard mercury sphygmomanometer with appropriate sized cuff. The average of three measurements in different days was used.

## Laboratory analyses

The subjects were evaluated after a 12-h overnight fast. Parents of PWS were instructed to strictly supervise all food-related areas in order to avoid food consumption before the blood sampling. Baseline blood samples were drawn by venipuncture for determination of glucose, high density lipoprotein cholesterol (HDL-C) and triglycerides. In addition, insulin levels were measured in 91 PWS patients (72 obese PWS) and in 83 obese control subjects (Table 2), excluding all subjects treated with insulin therapy. Enzymatic methods (Roche Molecular Biochemicals, Mannheim, Germany) were used for measurement of blood glucose, HDL-C and triglycerides. Serum insulin levels were measured by chemiluminescence (Immulite 2000). Insulin resistance was measured by homeostasis model assessment (HOMA-index), calculated as insulin (μU/mL) × [blood glucose (mmoL/L)/22.5] [17].

## Metabolic syndrome

According to the literature [18], we defined subjects with MetS as having three abnormal findings out of the following five parameters: central obesity, high systolic BP and/or diastolic BP, high triglycerides, low HDL-C and raised fasting plasma glucose. Central obesity was defined when WC was ≥94 cm for men and ≥80 cm for women [19]. Hypertension was defined in presence of systolic BP values ≥130 mmHg and/or diastolic BP values ≥85 mmHg, or in case of anti-hypertensive drugs use. Hypertriglyceridemia was defined in presence of triglycerides values ≥150 mg/dl or in case of a specific treatment. Low HDL-C level was defined in

**Table 2** Odds of the metabolic syndrome and its components in non-obese PWS and obese PWS *vs.* obese controls (reference group). The analysis was done both in the entire population (*n* 193) and in the non diabetic subgroup (*n* 160, of which 20 nobPWS, 65 obPWS and 75 obCTRL). Abbreviations: nobPWS = non-obese PWS; obPWS = obese PWS; HDL-C = high density lipoprotein cholesterol; NA = not available. Odds ratio, 95% confidence intervals (L = lower limit, U = upper limit) and *p*-values were obtained using exact logistic regression.

| | All (193) | | | | Non diabetics (160) | | | |
|---|---|---|---|---|---|---|---|---|
| | OR | Exact-*p* | 95% L | 95% U | OR | Exact-*p* | 95% L | 95% U |
| highwc | | | | | | | | |
| nobPWS | 0.02 | 0.000 | 0.00 | 0.14 | 0.02 | 0.000 | 0.00 | 0.15 |
| obPWS | 0.98 | 1.000 | 0.02 | + infinite | 1.10 | 0.951 | 0.03 | + infinite |
| hightg | | | | | | | | |
| treatment | 26.30 | 0.000 | 3.89 | + infinite | 10.42 | 0.029 | 1.25 | + infinite |
| nobPWS | 0.15 | 0.043 | 0.00 | 0.95 | 0.26 | 0.192 | 0.00 | 1.76 |
| obPWS | 2.22 | 0.039 | 1.04 | 4.92 | 3.12 | 0.012 | 1.25 | 8.41 |
| lowhdl | | | | | | | | |
| nobPWS | 0.24 | 0.032 | 0.42 | 0.91 | 0.35 | 0.172 | 0.06 | 1.39 |
| obPWS | 2.01 | 0.033 | 1.06 | 3.89 | 2.20 | 0.037 | 1.07 | 4.59 |
| highbp | | | | | | | | |
| treatment | 89.05 | 0.000 | 15.41 | + infinite | 53.40 | 0.000 | 8.90 | + infinite |
| nobPWS | 0.27 | 0.065 | 0.04 | 1.06 | 0.23 | 0.077 | 0.02 | 1.12 |
| obPWS | 0.79 | 0.640 | 0.37 | 1.70 | 0.99 | 1.000 | 0.44 | 2.25 |
| highg | | | | | | | | |
| treatment | 1.00 | 0.000 | 0.00 | + infinite | N.A. | | | |
| nobPWS | 0.41 | 0.434 | 0.00 | 3.05 | 0.41 | 0.434 | 0.00 | 3.05 |
| obPWS | 0.87 | 1.000 | 0.22 | 3.45 | 0.58 | 0.625 | 0.12 | 2.59 |
| ms | | | | | | | | |
| nobPWS | 0.07 | 0.001 | 0.00 | 0.49 | 0.12 | 0.018 | 0.00 | 0.74 |
| obPWS | 1.20 | 0.660 | 0.63 | 2.30 | 2.10 | 0.058 | 0.98 | 4.64 |

presence of HDL-C values <40 mg/dl in males and <50 mg/dl in females. Raised fasting plasma glucose was defined in presence of glucose levels ≥100 mg/dl, or in case of anti-diabetic drugs use.

### Statistical analysis

Continuous variables are reported as 50th, 25th and 75th percentiles because of skewed distributions (Shapiro–Wilk test). Categorical variables are reported as the number and percentage of subjects with the characteristic of interest. Between-group comparisons (obese PWS *vs.* non-obese PWS *vs.* obese controls) of continuous variables were performed with the exact Wilcoxon–Mann–Whitney test with Bonferroni's correction for 3 groups. Exact logistic regression was used to test whether the odds of the metabolic syndrome (1 = yes; 0 = no) and its components (high WC, elevated triglycerides, low HDL-C, elevated fasting glucose and high BP, all codes as 1 = yes and 0 = no) were similar in obese PWS and non-obese PWS *vs.* obese control subjects after correction for specific pharmacological treatment (1 = yes and 0 = no). Exact logistic regression was also used to test whether the odds of the metabolic syndrome (1 = yes; 0 = no) and its components differed in DELETED *vs.* UPD15 and translocated PWS subjects.

In order to remove the influence of T2DM on the risk for MetS and its components, we have repeated the analysis after exclusion of diabetic subjects.

## Results

The measurements of the study subjects are given in Table 1. PWS patients showed lower weight and height than obese controls. According to BMI values, 21 PWS subjects were non-obese and 87 obese. BMI values were similar between obese PWS and obese control subjects. Non-obese PWS showed lower WC, insulin, HOMA-index, triglycerides, diastolic BP, and higher HDL-C than both obese PWS and obese controls. Obese PWS showed higher glucose and systolic BP than both non-obese PWS and obese controls.

Figure 1 shows frequency of the MetS and its components in non-obese PWS, obese PWS and obese controls. The presence of MetS was found in 1/21 (4.8%) non-obese PWS, 36/87 (41.4%) obese PWS and 39/85 (45.9%) obese controls. Non-obese PWS showed lower frequency for each MetS component as compared with obese PWS and obese controls. In the comparison with obese controls as reference, odd ratios were significantly lower in non-obese PWS except for high glucose and high BP (borderline) (Table 2), while obese PWS showed higher odd ratios for high triglycerides and low HDL-C, even if the lowest value of the confidence interval was very close to 1 in both cases. The odd ratio for MetS was significantly lower in non-obese PWS but unchanged in obese PWS respect to obese controls. PWS patients receiving antihypertensive and/or antidiabetic therapy were all obese, with the exception of one female treated with metformin. Specific treatments

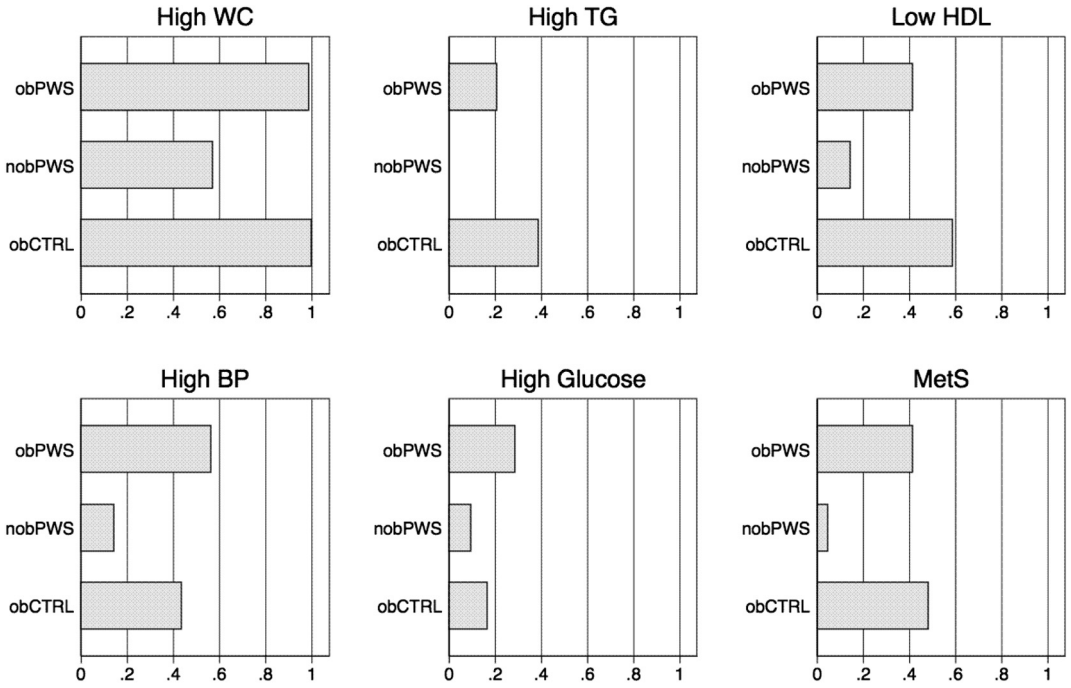


**Figure 1** Frequency of the metabolic syndrome and its components in obese PWS, non-obese PWS and obese controls. Abbreviations: obPWS = obese PWS; nobPWS = non-obese PWS; obCTRL = obese controls; WC = waist circumference; TG = triglycerides; HDL = high density lipoprotein; BP = blood pressure; MetS = metabolic syndrome.

had a significant effect on the risk for high triglycerides, high glucose and high BP in obese PWS: treated subjects showed higher values than untreated ones for all these parameters (Table 2), suggesting that their treatments were probably suboptimal. Looking to the comparison for MetS components between DELETED PWS and non DELETED PWS, independently from the BMI status, DELETED patients showed a lower risk for low HDL-C ($p = 0.01$) and a trend towards a lower MetS risk ($p = 0.06$) (Table 3).

When all diabetics were excluded (Table 2), non-obese PWS maintained a significantly lower risk for high WC and MetS but not for high triglycerides and low HDL. Concerning obese PWS, the odds were similar to those found in the entire population.

**Table 3** Odds of the metabolic syndrome and its components in DELETED ($n = 73$) *vs.* UPD15 ($n = 27$) and translocated PWS ($n = 2$), independently from BMI status. Odds ratio, 95% confidence intervals and *p*-values were obtained using exact logistic regression.

| | OR | 95% CI | Exact-*p* |
|---|---|---|---|
| High waist circumference | 1.34 | 0.20—6.84 | 0.95 |
| High triglycerides | 0.48 | 0.14—1.68 | 0.29 |
| Low HDL-C | 0.29 | 0.10—0.77 | 0.01 |
| High glucose | 0.39 | 0.13—1.18 | 0.10 |
| High blood pressure | 0.71 | 0.27—1.87 | 0.59 |
| Metabolic syndrome | 0.38 | 0.13—1.03 | 0.06 |

## Discussion

Factors that determine the high rate of death seen in PWS are not fully clarified. In the general population, MetS is believed to represent a strong risk factor for the subsequent development of atherosclerotic cardiovascular disease and T2DM [20]. Concerning PWS individuals, previous observation reported that obese children with PWS have a similar prevalence of MetS to obese controls [14]. Thus, it is conceivable that MetS may be involved in the pathogenesis of morbidity and early mortality in adult patients with PWS. However, PWS subjects showed distinct metabolic characteristics related to obesity that are not comparable to what is observed in nonsyndromic obesity. In this respect, most of subjects with MetS have insulin resistance [18], whereas PWS adults seem to have a more favorable insulin profile compared with obese controls [9,21]. In addition, only few cases of coronary artery and atherosclerotic heart diseases have been reported in PWS subjects [2,22,23]. Nevertheless, this circumstance may be simply related to an early mortality of PWS, since ischemic heart disease is generally observed after middle age. In this context, abnormal microcirculatory responses to ischemia have been reported in young PWS adults as well as a trend toward increased mean intima—media thickness [12]. Moreover, inflammatory markers, such as C-reactive protein and interleukin-6, have been found significantly increased in obese adults with PWS [24,25]. Altogether, these findings are potentially associated with coronary artery disease. In this respect, it is noteworthy to document if the pathogenetic relationships between cardiovascular disease and metabolic complications and the mechanisms

responsible for the development of MetS in PWS adults are common to those reported in nonsyndromic obesity.

Our study is the first to document the frequency of MetS in a large cohort of adult patients with PWS. The lack of data about the components of MetS in PWS patients might be related to their lower life expectancy in comparison to the general population and to the rarity of these patients. On the whole, the number of PWS subjects diagnosed to suffer from the MetS was 34.2%. However, our PWS population included both obese PWS and non-obese PWS individuals. Because the presence of obesity is strongly associated with an increased risk of MetS [26], we compared the metabolic profile of obese PWS with both non-obese PWS and obese control subjects. For this purpose, we have adopted the conventional BMI cut-off point of $>30$ to define obesity, bearing in mind however the limitation that BMI is an inadequate measure of adiposity in PWS since it underestimates the severity of obesity [27]. In spite of this, we have found that non-obese PWS showed a more favorable metabolic status (lower glucose, insulin, HOMA-index, triglycerides and diastolic BP, and higher HDL-C), and a lower frequency for each MetS component. In this context, low HDL-C, high BP and DMT2 were present in only three, two and one non-obese PWS, respectively. Consequently, MetS was observed in only one patient of the group of 21 non-obese PWS (4.7%), similarly to what was observed in normal-weight general population of the same age range [28]. On the contrary, obese PWS showed a metabolic pattern very similar to that of obese controls, with the exception of higher glucose levels in the PWS group. When all diabetics were excluded, the same results were observed in obese PWS, while non-obese PWS maintained a significantly lower risk for high WC and MetS but not for the other variables. This was probably due to the smaller number of subjects respect to the previous analysis and the consequent lack of statistical power.

In general, obesity status clusters with other MetS components. However, since non-obese PWS showed an unexpected increase of WC in approximately 50% of subjects (52.3%), this finding could probably suggest the need to use of different WC cut-off values in such patients. It has to be underlined that very similar insulin levels and HOMA-index values were seen in obese PWS and obese control subjects. These findings are in contrast with the bulk of evidence, i.e. with low insulin levels and reduced insulin resistance both in children [29,30] and in adults [31,32] with PWS. The identification of a selective reduction of visceral fat in adult PWS females after adjustment for total adiposity has been advocated to explain a higher insulin sensitivity, in comparison to matched obese population [10,27,33]. In this respect, a limitation of this study is the lack of body composition measurement of our patients. Dual-energy X-ray photon absorptiometry and computed tomography seem to be the best available technique to evaluate body composition, but their use is impracticable for epidemiological studies because of the high costs. The discrepancies among results on this matter, however, may be related to the smaller number of subjects taken into consideration by other reports respect to our, as well as to the high BMI of our patients. In this regard, we have previously showed a similar proportions of abdominal subcutaneous and visceral fat in PWS and controls with severe obesity in respect to previous studies [11]. Other authors, however, have recently reported that PWS adults and obese controls were similarly insulin resistant and had similar insulin levels [34]. On the other hand, a subgroup of PWS individuals does develop insulin resistance and the absolute prevalence of T2DM in PWS subjects over the age of 20 years is high [35]. In this context, we have previously found that a clear relationship between obesity status and insulin levels was still detectable in PWS children, as obese subjects showed higher insulin levels and HOMA-index than non-obese patients [14]. It is interesting to note that in the present study the risk for high glucose levels was not different between obese PWS and non-obese PWS, suggesting that other factors beyond obesity are involved in the risk. Furthermore, a familial component in insulin resistance, as in non-PWS subjects, might also contribute in PWS subjects [35].

In the present report we searched for a correlation between MetS and molecular characteristics of the studied PWS cohort, in a view of defining risk categories. The existence of a specific genotype—phenotype correlation is known in PWS [7]. We have found that DELETED subjects showed a trend towards a lower MetS risk, with a lower risk for low HDL-C in comparison to non DELETED patients. These results seem to suggest that DELETED may constitute a subgroup of patients with a healthier metabolic profile among PWS adults.

In conclusion, we reported MetS frequency evaluated in the largest cohort of PWS adults, with and without obesity. Overall, our findings suggest the main role that obesity status plays on the individual metabolic risk clustering in PWS population. The risk for MetS and its components seems to be unaffected by the presence of T2DM. Insulin resistance seems to have the same metabolic impact in both PWS and non-PWS obesity. Moreover, we were able to provide some additional insight into the assessment of MetS in PWS, by identifying UPD15 patients as those with more risk. Altogether, our study confirms that improvement in weight control remains the main goal of any PWS treatment program. In addition, screening for associated MetS should be a routine element of care and treatment for all obese adults with PWS. Early identification and treatment of MetS could be helpful to improve morbidity and prevent mortality in these patients. Additional research, however, is needed to better understand the role of body composition and other possible confounders, like diet and physical activity, that may affect the prevalence of MetS and its components in adult patients with PWS. Similarly, a larger sample of patients is needed in order to analyze the potential influence of neuroleptics, sex steroids and cigarette smoking on our findings.

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