Fat-free mass is better related to serum uric acid than metabolic homeostasis in Prader-Willi syndrome.

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Background: Prader-Willi syndrome (PWS) is conventionally regarded as a model of genetic obesity carrying a metabolically healthier profile and fat compartmentalization than subjects with non-syndromic obesity. Serum uric acid (sUA) is a recognized surrogate marker of metabolic derangement. As no information is currently available on sUA levels in adults with PWS, we aimed
to analyze sUA in a large cohort of adult patients with PWS in comparison to a control counterpart; secondly, we aimed to investigate the metabolic and non-metabolic determinants of sUA in PWS.
Methods: A cross-sectional study was conducted on 89 consecutive adult patients with genetically confirmed PWS spanning a wide BMI range (17.2-56.7 kg/m^2). As controls, 180 age-, sex- and BMI-matched healthy controls were included. sUA levels were analyzed in relation to the PWS status, metabolic variables, hormone status, body composition, and resting energy expenditure (REE). Bivariate correlation and multivariable regression studies were used to test for predictors of sUA in PWS.
Results: Despite having similar BMI values, patients with PWS presented with higher FM ($p < 0.0001$), lower FFM ($p < 0.0001$) and REE values than controls ($p < 0.0001$). In PWS, sUA levels were non-significantly different between subjects with and without obesity (5.4 ± 1.3 vs. 4.9 ± 1.1 mg/dL, $p = 0.09$), and did not vary significantly in relation to genotype, sex steroid or GH replacement, as well as psychiatric treatments. Rates of hyperuricaemia (19.1% *vs*. 33.7%, $p < 0.01$) and absolute sUA levels were lower in patients with PWS compared to controls owing to significant differences between subgroups with obesity (5.5 ± 1.4 *vs*. 6.6 ± 1.6 mg/dL, $p < 0.0001$). In merged populations, sUA increased in parallel with age, BMI, FM, FFM, REE, glucolipid homeostasis, and inflammatory markers. In a separate analysis in PWS, however, sUA correlations with BMI, FM, and inflammatory markers were null. Stepwise multivariable regression analysis in the PWS group adjusted for karyotype, age, sex, FM, FFM, obesity, triglycerides, and HDL cholesterol, showed that sUA levels were independently associated with FFM ($\beta = 0.35$, $p < 0.0001$) and, albeit less significantly, with triglycerides ($\beta = 0.23$, $p < 0.05$). The introduction of height-normalized FFM (FFM index) in the regression model, however, abrogated the predictive role of FFM on sUA. Conclusions: FFM mass is a strong predictor of sUA. PWS is associated to lower sUA levels than controls likely due to genetic predisposition to different body composition and healthier metabolic phenotype. Further studies are warranted to assess purine metabolism and the clinical significance of the FFM index in PWS.