Endorsed by AME

Italian Association of Clinical Endocrinologists

ITALIAN CHAPTER
www.aaceitalianchapter.com

PCOS and risk factors for gestational diabetes

Gestational Diabetes Mellitus (GDM) and Polycystic Ovarian Syndrome (PCOS) are the most common endocrine disorders in women of child-bearing age. Their prevalence ranges between 9%-25% for GDM and 5%-15% for PCOS. Both of the disorders are associated with insulin resistance, overweight-obesity and increased risk of type 2 diabetes mellitus (T2DM), dyslipidemia, metabolic syndrome and cardiovascular diseases.

While some studies suggest that PCOS increases the risk of GDM, when the data are stratified for body mass index (BMI) the results become non-conclusive (1, 2). In Finland, all pregnant women with PCOS undergo an early oral glucose tolerance test (OGTT) regardless of their BMI. Finnish researchers recently performed a case-control study (3) to verify the value of this practice and establish the role of PCOS as a risk factor for GDM.

The primary end-point was evaluation of PCOS as independent risk factor for GDM. Secondary end-points evaluated other risk factors shared by both PCOS and GDM (e.g. overweight or obesity and family history).

Cases were 1146 women with GDM in the final phase of pregnancy, recruited between 2009 and 2012 from the *Finnish Gestational Diabetes Study*. Controls were 1066 women without GDM who delivered a child in the same hospital during the same period. All participants received a questionnaire on personal and family medical history, lifestyle, previous oligo-amenorrhea, hirsutism, or diagnosis of PCOS. The questionnaire was completed by 1030 cases (89.9%) and 935 controls (87.7%). Clinical information from the questionnaire was integrated with data from the *Finnish Medical Birth Register*. Based on the report of oligomenorrhea and hirsutism and/or previous diagnosis of PCOS, 174 participants were considered having PCOS. Participants were stratified in 4 subgroups:

- GDM+/PCOS+ : N = 105;
- GDM+/PCOS- : N = 909;
- GDM-/PCOS+ : N = 69
- GDM-/PCOS- : N = 858

Women with GDM, PCOS or both were then compared with controls.

Primary End-Point

The prevalence of oligomenorrhea and hirsutism and/or previous diagnosis of PCOS was 10.4% among women with GDM, and 7.4% among non-diabetic women (OR 1.44; 95% CI 1.05-1.97). The difference remained significant after adjustment for parity, smoking in pregnancy, educational level and hospital of delivery (OR 1.47; 95% CI 1.07-2.02). After adjustment for age and BMI before pregnancy, however, the result was no longer significant (OR 1.07; 95% CI 0.74-1.54), suggesting that PCOS is not an independent risk factor for GDM.

Weight at birth

Women with lower birthweight or pre-term birth had an increased risk of GDM, independent from the presence of PCOS.

Educational level and clinical manifestations

Compared to controls, women with GDM, regardless of the presence of PCOS, had lower educational level (p = 0.012). The educational level also correlated with increasing pre-pregnancy BMI (p < 0.001). Women with a lower educational level were significantly older (p < 0.001) and often had had more pregnancies (≥ 3) (p = 0.001) and labors (p = 0.014).

Pre-gestational BMI was also significantly higher in the GDM+/PCOS+ group compared to the other groups, and these women were more frequently obese.

Cecilia Motta (dott.cecilia.motta@gmail.com)
UOC Endocrinologia, Dipartimento Medicina Clinica e Molecolare, Sapienza Università di Roma, AO Sant'Andrea

Family History

The risk of GDM doubled in the presence of maternal history of GDM or T2DM, and it was 40% higher if the father had T2DM. A family history of diabetes or other cardiovascular diseases was not associated with PCOS.

Risk factors for GDM

In the multivariate regression analysis, the variables with a significant independent association to GDM were: overweight/obesity, age ≥ 35, pre-term birth, GDM in the mother or at least one parent with T2DM. Overall, 27 (26%) women in the GDM+/PCOS+ and 149 (16.8%) women in the GDM+/PCOS- group received insulin in pregnancy (p = 0.022). The between group difference correlated with BMI (p = 0.056).

Conclusions

This study suggests that oligomenorrhea, hirsutism or PCOS are not independent risk factors for GDM. Prevalence of GDM was higher in women with PCOS in comparison to controls, but weight and increased age acted as confounders. A family history of GDM and T2DM was predictive of GDM. Obesity appears to be the most important risk factor for GDM in women with PCOS. These results are in agreement with the results of another Finnish study (4), but not with other studies (1), which report PCOS as an independent risk factor for GDM. The discordance may be due to difference in diagnostic criteria and populations assessed. In the current study, for instance, patients with PCOS but not GDM were significantly thinner than women with GDM, and their average BMI was similar to controls. A significant association with GDM was also found for age and family history. In particular, the risk of GDM was 2-3 times higher if the patient's mother had GDM or T2DM. In these women, the risk remained elevated after adjustment for BMI, which suggests an important role for inheritance in the origin of the disorder.

An important limit of the study is the definition of PCOS, based on response to a questionnaire. Importantly, in the study all the women with PCOS had a pregnancy at term, which raises the possibility that their PCOS and metabolic derangement was less severe.

References

1. Rees DA, Jenkins-Jones S, Morgan CL. Contemporary reproductive outcomes for patients with polycystic ovary syndrome: a retrospective observational study. J Clin Endocrinol Metab 2016, 101: 1664-72.
2. Haakova L, Cibula D, Rezabek K, et al. Pregnancy outcome in women with PCOS and in controls matched by age and weight. Hum Reprod 2003, 18: 1438-41.
3. Mustaniemi S, Vääräsmäki M, Eriksson JG, et al. Polycystic ovary syndrome and risk factors for gestational diabetes. Endocr Connect 2018, 7: 859–69.
4. Olilla ME, West S, Keinanen-Kiukaaniemi S, et al. Overweight and obese but not normal weight women with PCOS are at increased risk of type 2 diabetes mellitus-a prospective, population-based cohort study. Hum Reprod 2017, 32: 423-31.