AEPCOS QUARTERLY PUBLICATION LIST

JANUARY—MARCH 2015

Highlighted articles

Alpañés M, Luque-Ramírez M, Martínez-García MA, Fernández-Durán E, Alvarez-Blasco F, Escobar-Morreale HF. Influence of adrenal hyperandrogenism on the clinical and metabolic phenotype of women with polycystic ovary syndrome. Fertil Steril. 2015 Mar;103(3):795-801.e2. doi: 10.1016/j.fertnstert.2014.12.105. Epub 2015 Jan 10. PMID: 25585504.

Commentary (CM):
The predominant source of androgen overproduction in PCOS patients is from ovaries more than from adrenals. However, high levels of DHEAS have been reported in 20-65% of PCOS patients, depending on the definition used, age, body mass index (BMI) and race. The authors question that conflicting results have been reported about the effect of adrenal hyperandrogenism (AH) on insulin resistance and hypercholesterolemia. They studied the possible impact of AH on cardiometabolic risk factors of PCOS patients by a cross-sectional study, including 298 patients with clinical and/or biochemical hyperandrogenism together with anovulatory dysfunction; ovarian morphology was not taken into account. Patients with related disorders and chronic diseases such as hypertension, diabetes or cardiovascular events before the enrolment were excluded from the study. AH was defined by the presence of high levels of DHEAS, using a cut-off value of the 95th percentile (9.1 µmol/L) of 147 healthy control women. Main outcome measures included anthropometry, blood pressure, 75 g oral glucose tolerance test, hormonal levels, lipid profile and C-reactive protein. The participants were classified in AH PCOS patients (n=55, nonobese 32 and obese 23) and non-AH PCOS patients (n=243, nonobese 146 and obese 97). There were no differences in BMI between AH PCOS and non-AH PCOS patients. AH PCOS patients presented higher total and free testosterone levels than non-AH PCOS patients. AH PCOS patients had higher insulin circulating levels and lower insulin sensitivity than non-AH PCOS patients. An inverse correlation between DHEAS levels and LDL cholesterol (ρ=0.16, P<0.04) was found. AH and obesity increased the prevalence of prehypertension and hypertension. In conclusion, the authors found that the presence of AH in PCOS patients is associated with reduced insulin sensitivity and increased blood pressure, but may have beneficial effect on the lipid profile. The frequency of AH (18%) found in this study is similar to that of other studies (22-25%); however, contrary to the same BMI between AH and non-AH PCOS patients observed in this study it was found that AH PCOS patients had lower BMI than non-AH PCOS patients (Fertil Steril 1999; 71: 671-4). This study does not agree with other studies that have found AH is inversely related to insulin

resistance (J Endocrinol Invest 2007; 30: 111-6; Fertil Steril 2009; 91: 1848-52), or without any relationship with insulin resistance (J Clin Endocrinol Metab 2015; 100: 942-50). So, the discussion on metabolic impact of AH in PCOS patients follows; maybe the great variability of the results in clinical and metabolic expression of AH PCOS patients has to do with other variables such as the race of patients.

Moran LJ, March WA, Whitrow MJ, Giles LC, Davies MJ, Moore VM. Sleep disturbances in a community-based sample of women with polycystic ovary syndrome.Hum Reprod. 2015 Feb;30(2):466-72. doi: 10.1093/humrep/deu318. Epub 2014 Nov 28. PubMed PMID: 25432918.

Commentary (KMH):

Women with PCOS have a number of known metabolic risks and there is some concern that sleep disorders may exacerbate insulin resistance in PCOS and contribute to the metabolic dysfunction, particularly type 2 diabetes risk. Women attending PCOS based clinics whohave been studied, more frequently report sleep distubances but it is not clear if these represent a more severe phenotype of PCOS. This study attempted to investigate a community-based sample of women with PCOS with respect to sleep disturbance and to assess whether there is a contribution from obesity, depression or other factors. The study assessed a cohort of women born between 1973-1975 in a large hospital in Adelaide, South Australia. They were able to trace 93% of the cohort or 2046 women. 974 agreed to participate (49%) and this included providing health information and an interview with a research nurse. 756 were able to be examined in person. After exclusions, the final sample included 724 women. Using the Rotterdam criteria 87 (12%) met the criteria for PCOS. In the PCOS cohort, depression was noted in one half (49.4%) of the respondents compared to 30.1% of nonPCOS women. BMI was significantly greater in the PCOS women (30.1 versus 25.4). They were also less likely to be living with a partner (54% versus 65.8%). With respect to the sleep profiles, women with PCOS reported worse sleep patterns; 35% reported difficulty falling asleep compared with 20% of non PCOS and a higher proportion had nighttime wakening with difficulty falling back asleep. Women with PCOS were 70% more likely to self-percieve as a poor sleeper but when adjusted for depression and BMI, this was no longer significant. However women with PCOS had twice the odds of reporting difficulty falling asleep even when controlling for BMI and depressive symptoms. This study, while it is questionnaire based, has important implications for understanding the possible role of PCOS in sleep disorders. While research has focussed on the presence of obstructive sleep apnea in women with PCOS, the majority of research has focussed on women presenting with a more severe phenotype. This is the first community based assessment of sleep disturbance in PCOS and demonstrates that sleep disturbances overall are increased in women with PCOS across the severity spectrum. While BMI had a minor role in sleep disturbance, depressive symptoms demonstrated a stronger mediating role. As noted, the investigators relied on questionnaires and could not provide polysomnography assessments. This limits the ability to assess the specifics of the sleep disorder but in this community based sample,

women with PCOS had twice the likelihood of reporting a sleep disturbance. Given the relationship with depressive symptoms and the possible impact on quality of life, these data raise important questions about the overall impact of a PCOS diagnosis. Based on these findings, assessing sleep quality is another important component in the care of women with PCOS.

**Publications were searched in pubmed with primary search criteria congenital adrenal hyperplasia, premature adrenarche or PCOS with secondary subcategory, inclusive of the quarter dates. Every attempt was made to include all papers in English in these categories but may not be an exhaustive list. If a related paper was published in this quarter and was inadvertently not included, please notify the publications committee so that we may include in the following quarterly review.*

List of publications

Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis

Abbo O, Ferdynus C, Kalfa N, Huiart L, Sauvat F, Harper LH. Male infants with hypospadias and/or cryptorchidism show a lower 2D/4D digit ratio than normal boys. Arch Dis Child. 2015 Feb 16. pii: archdischild-2014-306454. doi: 10.1136/archdischild-2014-306454. [Epub ahead of print] PubMed PMID: 25688099.

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Auchus RJ. Management considerations for the adult with congenital adrenal hyperplasia. Mol Cell Endocrinol. 2015 Jun 15;408:190-197. doi: 10.1016/j.mce.2015.01.039. Epub 2015 Jan 30. Review. PubMed PMID: 25643980.

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congenital adrenal hyperplasia. Clin Endocrinol (Oxf). 2015 Jan;82(1):37-44. doi:10.1111/cen.12526. Epub 2014 Jul 7. PubMed PMID: 24953648.

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PCOS-Adolescence

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