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Polycystic Ovary Syndrome, Combined Oral Contraceptives, and the Risk of Dysglycemia: A Population-Based Cohort Study With a Nested Pharmacoepidemiological Case-Control Study

Balachandran Kumarendran ^{1 2}, Michael W O'Reilly ^{3 4}, Anuradhaa Subramanian ¹, Dana Šumilo ¹, Konstantinos Toulis ¹, Krishna M Gokhale ¹, Chandrika N Wijeratne ⁵, Arri Coomarasamy ⁴, Abd A Tahrani ⁴, Laurent Azoulay ⁶, Wiebke Artl ^{7 8}, Krishnarajah Nirantharakumar ^{9 4}

Affiliations

Affiliations

- 1 Institute of Applied Health Research, University of Birmingham, Edgbaston, Birmingham, U.K.
- 2 Department of Community and Family Medicine, Faculty of Medicine, University of Jaffna, Kokkuvil, Sri Lanka.
- 3 Department of Medicine, Royal College of Surgeons in Ireland, University of Medicine and Health Sciences, Dublin, Republic of Ireland.
- 4 Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, U.K.
- 5 Department of Obstetrics and Gynecology, Faculty of Medicine, University of Colombo, Colombo, Sri Lanka.
- 6 Department of Epidemiology, Biostatistics and Occupational Health and Gerald Bronfman Department of Oncology, McGill University, Toronto, Canada.
- 7 Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, U.K. w.artl@bham.ac.uk k.nirantharan@bham.ac.uk.
- 8 NIHR Birmingham Biomedical Research Centre, University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Birmingham, U.K.
- 9 Institute of Applied Health Research, University of Birmingham, Edgbaston, Birmingham, U.K. w.artl@bham.ac.uk k.nirantharan@bham.ac.uk.

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Abstract

Objective: Irregular menstrual cycles are associated with increased cardiovascular mortality. Polycystic ovary syndrome (PCOS) is characterized by androgen excess and irregular menses; androgens are drivers of increased metabolic risk in women with PCOS. Combined oral contraceptive pills (COCPs)

are used in PCOS both for cycle regulation and to reduce the biologically active androgen fraction. We examined COCP use and risk of dysglycemia (prediabetes and type 2 diabetes) in women with PCOS.

Research design and methods: Using a large U.K. primary care database (The Health Improvement Network [THIN]; 3.7 million patients from 787 practices), we carried out a retrospective population-based cohort study to determine dysglycemia risk (64,051 women with PCOS and 123,545 matched control subjects), as well as a nested pharmacoepidemiological case-control study to investigate COCP use in relation to dysglycemia risk (2,407 women with PCOS with [case subjects] and without [control subjects] a diagnosis of dysglycemia during follow-up). Cox models were used to estimate the unadjusted and adjusted hazard ratio, and conditional logistic regression was used to obtain adjusted odds ratios (aORs).

Results: The adjusted hazard ratio for dysglycemia in women with PCOS was 1.87 (95% CI 1.78-1.97, $P < 0.001$; adjustment for age, social deprivation, BMI, ethnicity, and smoking), with increased rates of dysglycemia in all BMI subgroups. Women with PCOS and COCP use had a reduced dysglycemia risk (aOR 0.72, 95% CI 0.59-0.87).

Conclusions: In this study, limited by its retrospective nature and the use of routinely collected electronic general practice record data, which does not allow for exclusion of the impact of prescription-by-indication bias, women with PCOS exposed to COCPs had a reduced risk of dysglycemia across all BMI subgroups. Future prospective studies should be considered for further understanding of these observations and potential causality.

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