

Women with Polycystic Ovary Syndrome is Associated with Longer Anogenital Distance: a Meta-analysis Based on Case-control Studies

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 March 2024 and was last updated on 15 March 2024.

INTRODUCTION

Review question / Objective This meta-analysis was conducted to evaluate the clinical association between PCOS and AGD.

Condition being studied Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age and lacks sensitive clinical biomarkers. Fetal androgen exposure is a critical risk factor for PCOS in adulthood and could lead to increased Anogenital distance (AGD), which is measurable. The measurement of AGD contains two parts: AGD-ac (measured from the anterior clitoral surface to the anus) and AGD-af (measured from the posterior fourchette to the anus).

METHODS

Participant or population A total of 4 studies with 837 participants were included. Countries included

in the studies were China, Spain, Turkey, and the Netherlands.

Intervention None.

Comparator PCOS group and control group.

Study designs to be included Meta-analysis.

Eligibility criteria Studies comparing AGD in women with vs. without PCOS were identified. Cohort, case-control, and cross-sectional observational studies reporting on AGD in women with versus without PCOS were included, regardless of the setting. Trials where the PCOS patients of reproductive-aged women with a diagnosis of polycystic ovary syndrome (PCOS) based on the National Institute of Health (NIH) diagnostic criteria (1990), the Rotterdam.

Information sources A search of the literature was conducted in the PubMed, MEDLINE, EMBASE, Cochrane Library, CBM, CNKI, WANFANG, and VIP for articles to assess AGD of PCOS and non-

PCOS adults irrespective of language published before Dec 2023.

Main outcome(s) All studies got AGD-ac measurements from the anterior clitoral surface to the anus and AGD-af measurements from the posterior fourchette to the anus. The main outcome showed an increase of the AGD-ac in PCOS patient compared with control groups.

Quality assessment / Risk of bias analysis According to the Newcastle-Ottawa Scale (NOS), the scores ranged from 7 to 9 stars, so 4 studies were rated as high. These 4 studies all provided quite comparability of cases and controls about the design and analysis.

Strategy of data synthesis Outcomes across each trial were presented as continuous data. Mean differences (MDs) with 95% confidence intervals (CIs) were adopted to calculate the overall estimates and were presented in forest plots. The heterogeneity variance using the Q-statistic and inconsistency index (I²) was calculated. I² values of 0%, 25%, 50% and 75% representing no, low, moderate and high heterogeneity, respectively. According to the Cochrane review guidelines, if severe heterogeneity was present at I² >50%, the random effect models were chosen, otherwise the fixed effect models were used and the random-effects method for meta-analysis was utilized to combine data, given the potential heterogeneity related to study populations, number of included study and assessment methods. Subgroup analyses was conducted based on geographical region, measure method and history of vaginal delivery. Moreover, sensitivity analyses were conducted where appropriate to determine the robustness of the results. Two-sided P < 0.05 was considered of statistically significance. All analyses were carried out in Review Manager software (Version 5.3; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) and STATA software (Version 13.0; Stata Corporation, College Station, TX).

Subgroup analysis In order to figure out the possible sources of heterogeneity, the subgroup analyses were conducted based on geographical region and history of vaginal delivery by Review Managersoftware.

Sensitivity analysis We finished sensitivity analyses by STATA software (Version 13.0; Stata Corporation, College Station, TX). As for AGD-ac, the significance of the effect size remained robust when leave-one-out models were used for the sensitivity test. No study has an extreme influence

on the pooled MD of AGD-ac between PCOS and control women.

Country(ies) involved China.

Keywords Anogenital distance, Polycystic ovary syndrome, Androgens, Prenatal exposures.

Contributions of each author

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