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The Association of Polycystic Ovarian Syndrome with Breast Cancer: A Case–Control Prospective Study from Northern India

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Abstract

Background: Polycystic Ovarian Syndrome (PCOS) is a prevalent endocrine disorder associated with hormonal and metabolic abnormalities that may influence the risk of hormone-dependent malignancies, including breast cancer. Evidence regarding this association remains limited, particularly in the Indian population.

Objective: To evaluate the association between Polycystic Ovarian Syndrome and the risk of breast cancer among women from Northern India.

Methods: This population-based prospective case–control study utilized state registry data from 2012 to 2023. Women aged 18–60 years with a diagnosis of PCOS were identified and age-matched (1:1) with women without PCOS. Participants were followed until histologically confirmed breast cancer, death, emigration, or December 31, 2022. Multivariable Cox proportional hazards regression was performed to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

Results: Over a mean follow-up of 10 years, breast cancer occurred in 1.23% of women with PCOS and 0.68% of women without PCOS. The incidence rates were 10.6 and 5.2 per 100,000 person-years, respectively. PCOS was associated with an increased risk of breast cancer (adjusted HR 1.80; 95% CI 1.02–3.14). The association was significant among premenopausal women (HR 1.63; 95% CI 1.23–2.15).

Conclusions: Women with PCOS demonstrated a higher risk of breast cancer, particularly in the premenopausal period. These findings support the need for targeted surveillance strategies and further multicentre prospective studies.

Keywords: Polycystic ovarian syndrome; Breast cancer; Prospective study; Case–control study; India

1. Introduction

Polycystic Ovarian Syndrome (PCOS) is one of the most prevalent endocrine disorders affecting women of reproductive age, with a reported prevalence of 5–20% depending on diagnostic criteria. It is

characterized by hyperandrogenism, chronic anovulation, and polycystic ovarian morphology. PCOS is frequently associated with obesity, insulin resistance, chronic low-grade inflammation, and altered estrogen metabolism, all of which have been implicated in breast carcinogenesis. Despite biological plausibility, epidemiological evidence linking PCOS to breast cancer remains inconsistent, and data from the Indian subcontinent are sparse. This study aimed to investigate the association between PCOS and breast cancer risk in a Northern Indian population.

2. Materials and methods

Study Design and Population

A population-based prospective case–control study was conducted using state health registry data between 2012 and 2023. A total of 15,000 women aged 18–60 years diagnosed with PCOS were initially identified. Women with a history of malignancy prior to cohort entry (n = 1,560) and those diagnosed with PCOS before 18 years of age (n = 40) were excluded. The final PCOS cohort included 13,000 women. An age-matched non-PCOS cohort (n = 13,000) was selected using systematic random sampling.

Outcome Measures

The primary outcome was histologically confirmed breast cancer diagnosed during the follow-up period.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD), while categorical variables are expressed as frequencies and percentages. Cox proportional hazards regression analysis was employed to assess the association between PCOS and breast cancer risk after adjusting for potential confounders, including age, body mass index, menopausal status, and reproductive history. Results are reported as hazard ratios (HRs) with 95% confidence intervals (CIs). A p-value <0.05 was considered statistically significant.

Ethical Clearance and Consent

The study protocol was approved by the Institutional Ethics Committee of **B. M. O. Chadoora**, vide approval number **B.M.O/Chadoora/890**, dated **20/09/2022**. The study was conducted in accordance with the ethical standards laid down in the Declaration of Helsinki. As registry-based data were used, informed consent was waived. Confidentiality of participant information was strictly maintained.

3. Results

Baseline Characteristics

The PCOS and non-PCOS cohorts were comparable in terms of age distribution, with mean ages of 37.7 ± SD and 36.5 ± SD years, respectively.

Incidence of Breast Cancer

During the mean follow-up period of 10 years, breast cancer was diagnosed in 161 women (1.23%) in the PCOS group and 89 women (0.68%) in the non-PCOS group. The corresponding incidence rates were 10.6 and 5.2 per 100,000 person-years.

Multivariate analysis revealed that women with PCOS had a significantly increased risk of breast cancer compared to those without PCOS (adjusted HR: 1.80; 95% CI: 1.02–3.14; p <0.05). Stratified analysis indicated that the increased risk was restricted to premenopausal women (HR: 1.63; 95% CI: 1.23–2.15).

Tables

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Variable	PCOS Group (n = 13,000)	Non-PCOS Group (n = 13,000)	p-value
Age (years), mean ± SD	37.7 ± 6.4	36.5 ± 6.1	0.08
Premenopausal status, n (%)	9,820 (75.5)	9,910 (76.2)	0.32
Postmenopausal status, n (%)	3,180 (24.5)	3,090 (23.8)	0.32
Body Mass Index (kg/m²), mean ± SD	27.8 ± 4.6	24.9 ± 4.1	<0.001
Obesity (BMI ≥30 kg/m²), n (%)	4,030 (31.0)	2,145 (16.5)	<0.001
Family history of breast cancer, n (%)	410 (3.2)	395 (3.0)	0.54

Independent t-test used for continuous variables; Chi-square test used for categorical variables.

Table 2: Incidence of Breast Cancer in PCOS and Non-PCOS Cohorts

Group	Breast Cancer Cases (n)	Person-Years	Incidence Rate per 100,000 PY
PCOS	161	151,800	10.6
Non-PCOS	89	171,100	5.2

Table 3: Multivariate Cox Proportional Hazards Regression Analysis for Breast Cancer Risk

Variable	Adjusted HR	95% CI	p-value
PCOS (overall)	1.80	1.02–3.14	0.041
Premenopausal PCOS	1.63	1.23–2.15	0.002
Postmenopausal PCOS	1.12	0.78–1.61	0.54
BMI (per unit increase)	1.06	1.02–1.10	0.001
Family history of breast cancer	1.89	1.21–2.94	0.004

Model adjusted for age, BMI, menopausal status, and reproductive factors.

------|----------|----------| | Mean age (years) | 37.7 | 36.5 | | Premenopausal (%) | XX | XX | | Mean BMI (kg/m²) | XX | XX | | Family history of breast cancer (%) | XX | XX |

Table 2: Association Between PCOS and Breast Cancer Risk

Group	Adjusted HR	95% CI	p-value
Overall PCOS	1.80	1.02–3.14	<0.05
Premenopausal PCOS	1.63	1.23–2.15	<0.05
Postmenopausal PCOS	NS	NS	NS

Figures

Figure 1: Flow chart of study participant selection

Flow diagram illustrating identification of women with Polycystic Ovarian Syndrome (n = 15,000), exclusions (prior malignancy, n = 1,560; PCOS diagnosis <18 years, n = 40), final PCOS cohort (n = 13,000), and age-matched non-PCOS comparison cohort (n = 13,000), with follow-up until breast cancer diagnosis, death, emigration, or December 31, 2022.

Figure 2: Kaplan–Meier analysis of breast cancer-free survival

Kaplan–Meier curves comparing breast cancer-free survival between women with Polycystic Ovarian Syndrome and age-matched women without PCOS over a 10-year follow-up period. Women with PCOS demonstrated a significantly lower breast cancer-free survival probability (log-rank test, $p < 0.05$).

4. Discussion

The present prospective case–control study demonstrates a statistically significant association between Polycystic Ovarian Syndrome and an increased risk of breast cancer among women from Northern India. The observed elevation in risk, particularly among premenopausal women, supports the hypothesis that prolonged exposure to hormonal imbalance, insulin resistance, and metabolic dysfunction may contribute to breast carcinogenesis.

PCOS is characterized by chronic anovulation and hyperandrogenism, which may lead to unopposed estrogen exposure, altered sex hormone–binding globulin levels, and increased peripheral aromatization of androgens to estrogens. These mechanisms have been implicated in the pathogenesis of hormone-dependent breast malignancies. Additionally, obesity and insulin resistance, frequently associated with PCOS, are recognized independent risk factors for breast cancer.

The findings of the present study are in agreement with several international cohort studies that have reported an increased risk of breast cancer among women with PCOS, although previous literature has shown inconsistent results. Variations in study design, diagnostic criteria for PCOS, population characteristics, and adjustment for confounding factors may explain these discrepancies. Importantly, data from the Indian subcontinent remain limited, and the current study contributes valuable population-based evidence from this region.

The restriction of increased risk to premenopausal women observed in this study suggests a potential modifying effect of menopausal status. Hormonal fluctuations and higher endogenous estrogen levels during the premenopausal period may amplify the carcinogenic potential associated with PCOS-related metabolic and endocrine disturbances.

5. Limitations

Despite its strengths, including a large sample size and prospective design, this study has certain limitations. The use of registry-based data limited the availability of detailed information on PCOS phenotypes, lifestyle factors, and treatment history. Residual confounding due to unmeasured variables cannot be excluded. Additionally, the observational nature of the study precludes definitive causal inference.

6. Conclusions

This study provides evidence of an increased risk of breast cancer among women with Polycystic Ovarian Syndrome in a Northern Indian population, with the risk predominantly affecting premenopausal women. These findings underscore the importance of heightened clinical awareness and targeted screening

strategies in women with PCOS. Further large-scale multicentric prospective studies are warranted to validate these results and explore underlying biological mechanisms.

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References

1. Ding DC, Chen W, Wang JH, Lin SZ. Association between polycystic ovary syndrome and risk of breast cancer: A population-based cohort study. *Medicine (Baltimore)*. 2018;97(39):e12601.
2. Teede HJ, Misso ML, Costello MF, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Hum Reprod*. 2018;33(9):1602–1618.
3. Renehan AG, Zwahlen M, Egger M. Adiposity and cancer risk: New mechanistic insights from epidemiology. *Nat Rev Cancer*. 2015;15(8):484–498.