Association of Polycystic Ovarian Syndrome with Endometrial Carcinoma among Premenopausal Females

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ABSTRACT

Objective: To determine the association of polycystic ovarian syndrome (PCOS) with endometrial carcinoma in premenopausal females.

Study Design: Cohort study.

Place and Duration of the Study: Department of Obstetrics and Gynaecology, Unit II, Sir Ganga Ram Hospital, Lahore, Pakistan, from July 2020 to January 2021.

Methodology: Females aged between 20-45 years, presenting with irregular uterine bleeding were included. Females with PCOS were considered as the exposed group and females without PCOS were considered as the unexposed group. Dilation and curettage was performed, and histopathology reports were assessed.

Results: There were total 70 patients (35 in each group). The mean age was 34.93±8.64 years in the exposed and 30.92±5.98 years in the unexposed group. Frequency percentage of endometrial carcinoma was 34.3% (n=24) in the exposed and 15.7% (n=11) in the unexposed group (OR=10.54).

Conclusion: PCOS was found to be one of the risk factors for endometrial carcinoma.

Key Words: *Polycystic ovarian syndrome (PCOS), Endometrial carcinoma, Premenopausal pre-menopause*.

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INTRODUCTION

Among the gynaecological disorders, polycystic ovary syndrome (PCOS) is a common condition. It affects 8% of women of any age.[1] It is more prevalent in reproductive age group affecting about 4-21% in reproductive-aged women.[2] The presentation of PCOS may vary from irregular menstrual cycle to manifestations of high androgen levels and morphological change of ovaries as polycystic on pelvic ultrasound.[3] Due to endocrine changes, the prevalence of insulin resistance and insulin secretory defects, menstrual dysfunction and androgen excess is high in patients with PCOS.

The prevalence of PCOS was found to be as high as 26% among some populations. The exact cause of PCOS is still unknown.

Irregular hormonal levels and metabolic changes in women with PCOS may increase their risk of some cancer types.[4,5] An important association was found between PCOS and endometrial cancer over fifty years ago that was reported as case series reports.[6,7]

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Endometrial carcinoma is among the most common cancer in women all over the world, found in about 320,000 women all over the world yearly; about 76,000 women die because of the endometrial cancer.[8] Endometrial cancer is more common in developed countries where the lifetime risk of endometrial cancer is 1.6%, compared to 0.6% in developing countries.[9] Endometrial carcinoma was found in 12.9 out of 100,000 women in the developed world annually.[10] Another studies also reported the higher association of endometrial carcinoma with polycystic ovarian syndrome *i.e*. 56.25% in patients with PCOS versus 26.11% without PCOS ($p < 0.05$). There is a four-fold increased risk of endometrial carcinoma in patients with polycystic ovarian syndrome as compared to patients without PCOS (OR 4.0, 95% CI 1.7-9.3).[11] But another study reported that there is non-significant association of PCOS with endometrial carcinoma *i.e*. 36.76% in patients with PCOS and 33.18% without PCOS ($p > 0.05$).[12,13]

In this prospectus, this study was conducted to get local evidence and to implement the results of this study in local settings. By screening, early diagnosis of endometrial carcinoma can be made. It can further prevent morbidity and mortality, and quality of life can be improved. By the data emerged by the study, local practices will be improved, to determine the association of PCOS with endometrial carcinoma in premenopausal females. The objective of this study was to determine the association of PCOS with endometrial carcinoma in premenopausal females.

Table I: Association of PCOS with endometrial carcinoma (n=70).

		Exposed Group	Unexposed Group	Total	p-value
Endometrial Carcinoma	Positive	24	11	35	0.001
	% of Total	34.3%	15.7%	50.0%	
	Negative	6	29	35	
	% of Total	8.6%	41.4%	50.0%	
	Total	30	40	70	
	% of Total	42.9%	57.1%	100%	

Risk ratio = 10.54. 95% confidence interval = 0.399-32.719.

Table II: Stratification of both groups or endometrial carcinoma with respect to age using chi-square test (risk ratio, n=70).

Age group		Exposed	Unexposed	Total	p-value
20-30 years	Positive	8	8	16	0.013
Endometrial	% of Total	23.5%	23.5%	47.1%	RR=8.00
carcinoma	Negative	2	16	18	CI=1.367-
	% of Total	5.9%	47.1%	52.9%	46.812
	Total	10	24	34	
	% of Total	29.4%	70.6%	100%	
31-45 years	Positive	16	3	19	0.001
Endometrial	% of Total	44.4%	8.3%	52.8%	RR=17.3
carcinoma	Negative	4	13	17	CI=3.275-91.23
	% of Total	11.1%	36.1%	47.2%	
	Total	20	16	36	
	% of Total	55.6%	44.4%	100%	

Table III: Stratification of both groups or endometrial carcinoma with respect to BMI using chi-square test (risk ratio, n=70).

BMI				Group		Total	p-value
				Exposed	Unexposed		
17-25 Kg/m^2	Endometrial carcinoma	Positive	Count	17	10	27	0.001
			% of Total	28.3%	16.7%	45.0%	RR=8.00
							CI=1.367-46.812
		Negative	Count	4	29	33	
			% of Total	6.7%	48.3%	55.0%	
	Total		Count	21	39	60	
			% of Total	35.0%	65.0%	100.0%	
>25 Kg/m^2	Endometrial carcinoma	Positive	Count	7	1	8	0.598
			% of Total	70.0%	10.0%	80.0%	RR=0.875
							CI=0.673-1.137
		Negative	Count	2	0	2	
			% of Total	20.0%	.0%	20.0%	
	Total		Count	9	1	10	
			% of Total	90.0%	10.0%	100.0%	

METHODOLOGY

This cohort study was carried in Gynaecology Unit II, Sir Gangaram Hospital, Lahore, Pakistan, from July 2020 to January 2021. Females aged 20-45years, any parity, presenting with uterine bleeding out of menstrual cycle were included in this study. Females with PCOS were considered the exposed group and the females without PCOS (normal ovaries) were considered the unexposed group. Females already diagnosed with ovarian, endometrial, cervical or breast carcinoma or metastasis were excluded.

After taking approval from the Hospital Ethical Committee, 70 females (35 in each group) who fulfilled the selection criteria were enrolled from the Outpatient Department of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, Lahore. Informed consent was taken. Patients were registered with their demographic details including name, age, marital, and social status. Patients' medical, obstetrical, and gynaecological history was noted. General physical examination including weight and height was noted for calculation of body mass index (BMI). Distribution of hair and hirsutism was noted. Details of presenting complaints including abnormality of menstrual bleeding were taken. Then they were divided in two groups *i.e*. exposed (PCOS females) and unexposed (non-PCOS females). After evaluation in indicated cases, patients had dilation and curettage by a single surgical team. Sample was taken and sent to the Pathology Department of the hospital for histopathology assessment of the endometrial sample. Reports were assessed and findings of histopathology were recorded. Presence of endometrial carcinoma presence was

noted according to the operational definition and females with endometrial carcinoma were managed as per standard protocol. All this information was recorded on proforma.

Data were entered and analysed through SPSS v. 22.0. Mean and standard deviation was computed for age, duration of symptoms and BMI. Frequency was computed for marital status and parity. Relative risk (RR) was calculated to measure the association of PCOS with endometrial carcinoma. RR>1 was taken as significant. Data were stratified for age, marital status, parity, duration of symptoms, BMI and use of contraceptives. Post-stratification, RR was calculated to measure the association of PCOS with endometrial carcinoma in each stratum. RR>1 was taken as significant.

RESULTS

Age distribution showed that out of 70 patients, 14.3% (n=10) were between 20-30 years of age; and 28.6% (n=20) were in 31-45 years of age in the exposed group. In contrast, 34.3% (n=24) were between 20-30 years of age; and 22.9% (n=16) were in 31-45 years of age in the unexposed group. Mean age was calculated as 34.93±8.64 years in the exposed group and 30.92±5.98 years in the unexposed group.

Frequency percentage of endometrial carcinoma was 34.3% (n=24) in exposed group and 15.7% (n=11) in the unexposed group (OR=10.54, Table I).

The data were stratified for age, marital status, parity, duration of symptoms, BMI, and use of contraceptives in Tables I-III, respectively.

DISCUSSION

PCOS is a hormonal disorder that can affect women of different age groups. The most common presentation is with the menstrual irregularity presents especially oligomenorrhea *i.e*, infrequent periods. The other common presentation is due to high levels of male hormones. For diagnosing polycystic ovarian syndrom, hirsutism severity was found as best measure.[14] Among the endocrine dysfunction, many women with PCOS have insulin resistance. This may be associated with irregular steroid synthesis. It may lead to clinical picture of PCOS. Insulin levels build up in the body and may cause higher androgen levels. Evidence also suggests that disturbance in steroid synthesis, ovarian dysfunction, and abnormal follicle development are correlated.[15] Obesity can also increase insulin levels and make PCOS symptoms worse.

In the current study, the pattern of age distribution showed that out of 70 patients, 28.6% (n=20) subjects were of older age (31-45 years) in the exposed group whereas 34.3% (n=24) subjects were of younger aged between 20-30 years in the unexposed group. The allover frequency percentage of endometrial carcinoma was 34.3% in the exposed group and 15.7% were in the unexposed group. There was a significant association of PCOS with endometrial carcinoma ($p<0.05$, OR=10.54). This is the same as already published studies.[16] Among the endocrine dysfunction, many women with PCOS have insulin resistance. This may be associated with irregular steroid synthesis which may lead to clinical picture of polycystic ovarian syndrome. Insulin levels build up in the body and may cause higher androgen levels. Evidence also suggests that disturbance in steroid synthesis, ovarian dysfunction, and abnormal follicle development are correlated.[17] Obesity can also increase insulin levels and make PCOS symptoms worse. It is a well-known fact that the most important treatment method for cancer is early diagnosis. When the literature is examined, we have seen lots of studies about endometrial cancer, but no results could be reached for its aetiology and early diagnosis.[18]

The limitation of the study is that all patients were from urban areas. Further multi-centric studies may be conducted in future to address this issue and included the rural population as well. This study can be further used for research at different levels so preventive protocols can be planned for early diagnosis of endometrial carcinoma in patients with polycystic ovaries.

CONCLUSION

PCOS is a risk factor for endometrial cancer increasing the risk of endometrial cancer by 10-fold in females with PCOS.

ETHICAL APPROVAL:
Ethical approval was taken from the ethical committee of Sir Ganga Ram Hospital.

PATIENTS' CONSENT:
Informed consent were taken from all patients to publish the data.

COMPETING INTEREST:
There is no competing interest in the study.

AUTHORS' CONTRIBUTION:
KI: Conceptualisation, data collection, and manuscript writing.
ZK, AP: Supervisor and collaborator.
All the authors have approved the final version of the manuscript to be published.

REFERENCES

1. Barry JA, Azizia MM, Hardiman PJ. Risk of endometrial, ovarian and breast cancer in women with polycystic ovary syndrome: A systematic review and meta-analysis.

Hum Reprod Update 2014; **20(5)**:748-58. doi: 10.1093/humupd/dmu012.

2. Harris HR, Terry KL. Polycystic ovary syndrome and risk of endometrial, ovarian, and breast cancer: A systematic review. *Ferti Res Prac* 2016; **2**:14. doi: 10.1186/s40738-016-0029-2.
3. Kok VC, Tsai HJ, Su CF, Lee CK. The risks for ovarian, endometrial, breast, colorectal, and other cancers in women with newly diagnosed endometriosis or adenomyosis: A population-based study. *Int J Gynecol Cancer* 2015; **25(6)**: 968-76. doi: 10.1097/IGC.0000000000000454.
4. Ding DC, Chen W, Wang JH, Lin SZ. Association between polycystic ovarian syndrome and endometrial, ovarian, and breast cancer: A population-based cohort study in Taiwan. *Medicine Baltimore* 2018; **97(39)**:e12608. doi: 10.1097/ MD.0000000000012608.
5. Shen CC, Yang AC, Hung JH, Hu LY, Tsai SJ. A nationwide population-based retrospective cohort study of the risk of uterine, ovarian and breast cancer in women with polycystic ovary syndrome. *Oncologist* 2015; **20(1)**:45-9. doi: 10. 1634/theoncologist.2014-0311.
6. International agency for research on cancer. World cancer report 2014. World Health Organization; 2014. p. 12.
7. Galaal K, Al Moundhri M, Bryant A, Lopes AD, Lawrie TA. Adjuvant chemotherapy for advanced endometrial cancer. *Cochrane Database Syst Revi* 2014; **15(5)**: Cd010681. doi: 10.1002/14651858.CD010681.pub2.
8. Ahmmad E, Abdulkarim AS, Dirweesh A. Peri-ampullary metastasis from endometrial adenocarcinoma: A rare etiology of obstructive jaundice. *Gastroenterol Res* 2019; **12(1)**:37-9. doi: 10.14740/gr1129.
9. Fearnley EJ, Marquart L, Spurdle AB, Weinstein P, Webb PM. Polycystic ovary syndrome increases the risk of endometrial cancer in women aged less than 50 years: An Australian casecontrol study. *Cancer Causes Control* 2010; **21(12)**: 2303-8. doi: 10.1007/s10552-010-9658-7.
10. Umland EM, Weinstein LC, Buchanan EM. Menstruation-related disorders. In: DiPiro JT, Talbert RL, Yee GC, *et al*. editors. Pharmacotherapy: A Pathophysiologic Approach. 8th ed. New York: McGraw-Hill; 2011. p. 1393.
11. Lin LH, Baracat MC, Gustavo AR, Soares JM, Baracat EC. Androgen receptor gene polymorphism and polycystic ovary syndrome. *Int J Gynaecol Obstet* 2013; **120(2)**: 115-8. doi: 10.1016/j.ijgo.2012.08.016.
12. Escobar-Morreale HF. Polycystic ovary syndrome: Definition, aetiology, diagnosis and treatment. *Nat Rev Endocrinol* 2018; **14(5)**:270. doi: 10.1038/nrendo.2018.24.
13. Xita N, Georgiou I, Tsatsoulis A. The genetic basis of polycystic ovary syndrome. *Eur J Endocrinol* 2002; **147(6)**: 717-25. doi: 10.1530/eje.0.1470717.
14. Khan SH, Rizvi SA, Shahid R, Manzoor R. Dehydro-epiandrosterone sulfate (DHEAS) levels in polycystic ovarian syndrome (PCOS). *J Coll Physicians Surg Pak* 2021; **31(3)**: 253-7. doi: 10.29271/jcpsp.2021.03.253.
15. Azhar A, Abid F, Rehman R. Polycystic ovary syndrome, subfertility and vitamin D deficiency. *J Coll Physicians Surg Pak* 2020; **30(5)**:545-6. doi: 10.29271/jcpsp.2020.05.545.
16. Zucchetto A, Serraino D, Polesel J, Negri E, De Paoli A, Dal Maso L, *et al*. Hormonerelated factors and gynecological conditions in relation to endometrial cancer risk. *Eur J Cancer Prev* 2009; **18(4)**:316-21. doi: 10.1097/cej.0b013-e328329d830.
17. Costas L, Frias-Gomez J, Guardiola M, Benavente Y, Pineda M, Pavon MA, *et al*. New perspectives on screening and early detection of endometrial cancer. *Int J Cancer* 2019; **145(12)**:3194-206. doi: 10.1002/ijc.32514.
18. Strauss JF. Some new thoughts on the pathophysiology and genetics of polycystic ovary syndrome. *Ann NY Acad Sci* 2003; **997**:42-8. doi: 10.1196/annals.1290.005.