Original Research Article

A case control analysis to find association between PCO and endometrial carcinoma (EC)

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Abstract

Background: Endometrial cancer is one of the commonest cancers in women. Unopposed estrogen stimulation of the uterus is amongst one of the etiologies postulated for this condition. It is generally assumed that women with polycystic ovary syndrome are more likely to develop endometrial carcinoma.

Aim: This study hypothesized comparing the ovarian morphology of women diagnosed with endometrial carcinoma and those with benign gynecological conditions.

Materials and methods: The present study included a total 64 patients who had been diagnosed with endometrial carcinoma and with 42 age matched control. All biopsy samples were undergone routine histological process with Hematoxylin-Eosin stain to check morphological differentiation.

Results: There was found no significant difference in the prevalence of PCOS (using this as a marker of PCOS in the absence of information on biochemistry) in the ovaries of patients diagnosed with endometrial cancer compared to women with benign gynaecology disease.

Conclusion: Although our numbers were small, these results challenge the assumption that PCOS is a risk factor for endometrial cancer. Investigation of patient records revealed there was no significant difference in the demographic profile between subjects with endometrial carcinoma or benign gynecological conditions.

Key words

Endometrial carcinoma, EC, Polycystic ovarian syndrome, PCOS.

Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrine disease. It is affecting 5-10% of women in reproductive age with uncertain etiology [1]. In 2003, an international consensus group proposed that the diagnosis of PCOS will be done based on the symptoms oligomenorrhea or amenorrhea, hyperandrogenemia [2]. Endometrial cancer (EC) is the most common female genital tract malignancy in most countries affecting 2–3% of women, with majority postmenopausal [3, 4].

Women with PCOS have several clinical, metabolic and molecular risk factors that may develop endometrial cancers includes unopposed estrogen stimulation of the endometrium in anovulatory PCOS women, obesity, insulin resistance, insulin like growth factors, diabetes, nulliparity, Cyclin D1, gluthathione S transferase and progesterone resistance [5, 6, 7].

For a number of decades, there has been a general assumption that women with PCOS are at increased risk of developing endometrial carcinoma. This is thought to be due to the fact that these women are subjected to high estrogen and insulin levels [8]. The number of women with PCOS in the UK is around 1 million and affecting 10 % of the reproductive population aged 20-50 [9]. If we arbitrarily assign the risk of EC to be as low as 1% in PCOS women, this would give an incidence of EC of 10,000 each year. This raises doubt as to whether the two conditions are really linked. It could be that only a sub-group of PCOS women only are at risk of developing EC. This study was aimed to investigate the exact strength of the association between PCO and Endometrial Carcinoma.

Materials and methods

This study was held in Department of Obstetrics and Gynecology, in association with Department of Pathology, ESIC Hospital, Nacharam, Hyderabad during July 2012 to July 2015. The present study included a total 64 patients who had been diagnosed with endometrial carcinoma and patient selection was based on the availability of their preserved ovaries and endometrial tissues.

A total 42 age matched control subjects were considered and were derived from a larger group of patients with benign gynaecological conditions operated on in the hospitals above over the same time periods, for whom preserved ovaries and endometrium were available. Controls had also undergone total hysterectomy and bilateral oophorectomy. No other selection criteria were applied and patients with gynaecological cancers other than endometrial carcinoma were excluded.

The prevalence of PCO morphology in subjects operated on for endometrial carcinoma or for benign gynaecological conditions was assessed by examination of archived Haematoxylin-eosin stained 5µm ovary sections from each patient. In clinical histopathological practice, PCO morphology is often diagnosed using a qualitative assessment.

Results

The present study included 64 patients with mean age 59.8 and 42 matched controls with mean age of 54.2 years (**Table - 1**). All subjects preserved ovarian sections were investigated to determine the prevalence of features consistent with PCO morphology.

Table – 1: Demographics of the patients.

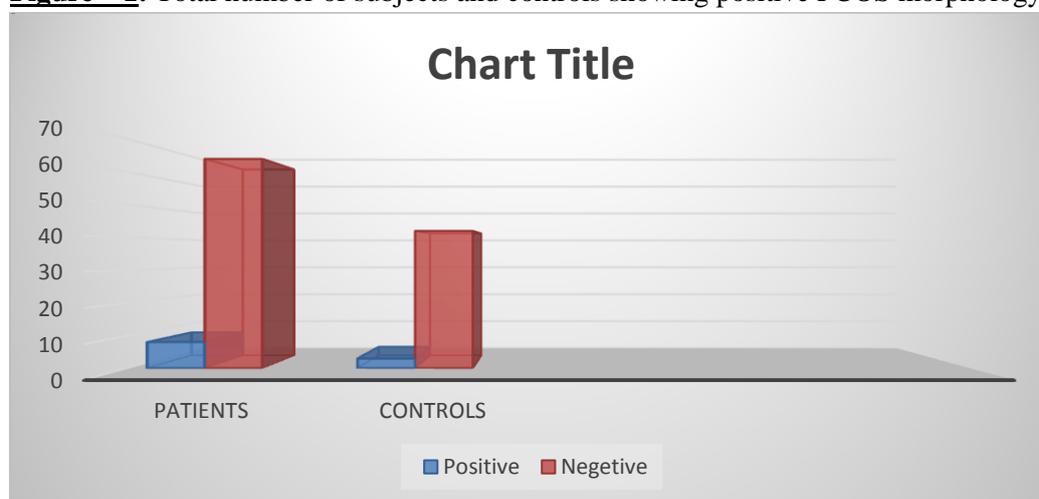|	Subjects	Controls
No. of patients	64	42
Mean age	59.8	54.2
Number of PCO	8	3
Percentage PCO	8	7.14

The prevalence of PCO was comparable in women with endometrial carcinoma i.e. in patients 8 of 64 (8%), in controls 3 of 42 (7.14%) respectively (**Figure – 1**). Effect of ethnicity have less impact on prevalence of PCOS as in the endometrial carcinoma set, 5 women with PCO

were belongs to urban area and 2 were related to rural area and 1 of unknown ethnicity. While in the benign controls with PCO, 2 were urban, one belongs to rural and no reports in unknown subjects (**Table - 2**).

Table – 2: Data of the patients with endometrial cancer and controls by ethnicity.

Ethnicity	Endometrial cancer cases			Matched controls		
	N	% of total	% of reported	N	% of total	% of reported
Urban	31	48.4	16.1	18	42.8	88.9
Rural	25	40.0	0.8	10	23.8	5.6
Un-reported	08	12.5	12.5	14	33.3	-
Total	64	-	-	42		

Figure – 1: Total number of subjects and controls showing positive PCOS morphology.

When subjects were subdivided by age, there were again no differences in the prevalence of PCO between the Endometrial Carcinoma patients and benign controls, non-significant effects were noted in women aged 20 – 39 years and 40 – 49 years.

For the second subjects were again divided into two groups aged < 50 years and >50 years because 50 years is being the average age of menopause. The prevalence of PCO in patients aged <50 years was greater in those with EC than in controls i.e. in patients 7 of 12, in controls 5 of 14 respectively. No difference was noted in PCO prevalence in patients aged >50 years.

However, we did find that there was a significant difference in the prevalence of PCO in the younger patients with endometrial cancer when compared to controls of a similar age-group.

Discussion

The present study was conducted to determine the association between PCO and Endometrial cancers. PCO as a marker of PCOS as it is a known fact that a great percentage of people diagnosed with PCOS will also exhibit PCO morphology.

Hyperandrogenemia has been associated with EC in post-menopausal women on the basis that those with testosterone levels in the upper quartile, have an approximate threefold increased risk of EC [10]. The lack of association between PCO and EC in postmenopausal women in the present study may reflect the hypo-estrogenic environment in post-menopausal women.

Alternatively, the absence of an increased prevalence of PCO morphology in women aged ≥50 years with EC, may be because it is difficult to identify such morphology in this age-group. One of the mechanisms by which patients with PCOS are thought to develop cancer is via unopposed estrogenic stimulation of the endometrium resulting from chronic anovulation [11].

The association between PCO and endometrial carcinoma has been reported for many years. One report of 16 cases indicated such factors as age ranging from 27 to 48 years, a high rate of prolonged amenorrhoea, obesity and hypertension and nulliparity in 13 of the 15 married women [12].

The true risk of endometrial carcinoma in women with PCOS however is difficult to ascertain. studies to date have been limited by the relatively small numbers of cases of endometrial carcinoma identified specifically in women with PCOS and thus the confidence limits for relative risks are very wide [13, 14].

This study revealed that on stratifying patients according age, PCO morphology was significantly more prevalent in women aged less than 50 years, because 50 years old being the average age of menopause. A criticism of the study is that PCO was used as a marker of PCOS. It is known that 70- 85% of women with PCOS will exhibit PCO morphology [15]. However women with PCO only are also known to exhibit metabolic and endocrine disorders similar to those exhibited in women with PCOS, but to a lesser degree.
Pillay, et al. looked at the prevalence of polycystic ovaries (PCOs), as a marker of PCOS and was investigated in ovarian sections from 128 women with EC and 83 women in the control group with benign gynaecological conditions [16]. Iatrakis, et al. included a group of women with a mean age of 46.3 years diagnosed with histologically EC. The control group was randomly selected from women between the ages of 43 and 48 years attending the gynaecology clinic without any EC diagnoses [17]. In the study by Fearnley, et al. data came from a national population based case–control study in Australia in which 156 cases with histologically confirmed newly diagnosed EC were identified and 398 controls were randomly selected from the national electoral roll [18].

Conclusion

This study was performed to compare the prevalence of polycystic ovaries in women with endometrial cancer with women without endometrial cancer. We did not find the prevalence of PCO to be raised overall in women with endometrial cancer. However, when we stratified women into different age groups, we found that younger women with endometrial cancer seem to exhibit polycystic ovaries. We also found that there are no set criteria to assess polycystic ovaries in women and the condition in post-menopausal women is even less described.

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