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Clinico-Pathological Study of Precancerous AndCancerous Conditions of Endometrium

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Abstract:
Introduction: *Endometrial cancer is the most common invasive cancer of female genital tract. In the absence of treatment endometrial hyperplasia may progress to cancer. Endometrial cancer is more common in women with obesity, diabetes, hypertension and infertility.*
Aim&objectives: *To determine the frequency of occurrence and to observe the correlation between clinical features and pathological findings in pre-cancerous and cancerous conditions of the endometrium.*
Methods:*The present study included evaluation of 190 cases of hyperplastic and neoplastic lesions of the endometrium. Elicited clinical details were statistically correlated with histopathological findings.*
Results: *Out of 190 cases, hyperplastic lesions accounted for 95.8% of the cases and carcinomas accounted for 4.2% of cases. Hyperplastic lesions included cystoglandular hyperplasia (72.5%), complex hyperplasia (23.6%) and complex hyperplasia with atypia (3.9%). The mean age of patients with hyperplasia was 50 years and menorrhagia being the commonest mode of presentation. Mean weight and parity of the patients were 50Kg and 2.58 respectively. Diabetes and hypertension were detected in 11% and 10% of these patients with hyperplasia respectively. Carcinoma was seen in patients with the mean age of 61years who presented with postmenopausal bleeding. Mean weight and parity of these patients were 49.8Kgs and 3.5 respectively. Hypertension and diabetes was seen in 25% and 12.5% of patients respectively.*
Conclusion: *The present study assesses the frequency of occurrence of pre-cancerous and cancerous conditions of endometrium with clinical correlation. A strong association was observed between age and endometrial lesions where as insignificant association was observed between patients with endometrial lesions and risk factors like weight, parity, hypertension and diabetes.*
Key words:*Endometrial hyperplasia, endometrial carcinoma, diabetes, hypertension, parity.*

I. Introduction

Endometrial hyperplasia is classified generally as simple (non-neoplastic) or complex (sometimes neoplastic), with or without nuclear atypia (neoplastic), based on nuclear cytology and architectural complexity and also it is a precursor lesion to endometrial carcinoma [(1)]. Among different types of endometrial hyperplasia, endometrial hyperplasia with nuclear atypia is the least common type, but most likely it will progress to type 1 endometrial carcinoma [(1)]and it accounts for 97% of all uterine cancers, but simple hyperplasia rarely progresses to endometrial carcinoma [(1,2)]. Thedegree of architectural or cytological atypia determines the probability of progression of endometrial hyperplasia to adenocarcinoma. There are two different pathogenic types of endometrial carcinoma depending on epidemiology, presentation, and prognosis, these are type I endometrial carcinoma (estrogen related, endometrioid type) and type II endometrial carcinoma (non-estrogen related, non-endometrioid type). But untreated hyperplasia can progress into endometrioid type of adenocarcinoma; so, it is very important to identify the precursor lesions. Till date, there are very limited studies regarding to biology of hyperplastic lesions of the endometrium which are documented from India [(3)].The present study was conducted to find out the frequency of occurrence of pre-cancerous and cancerous conditions of endometrium out of routine endometrial biopsy and to observe the correlation between clinical features and the pathological findings in pre-cancerous and cancerous conditions of endometrium.

II. Materials and Methods

The present study was conducted in the department of Pathology, Government Medical College, Mysore after getting the Institutional Human Ethical Committee clearance and after getting the informed consent from the patients. The biopsy specimens received were that of dilatation and curettage and Hysterectomy. They were examined for gross findings like size, shape, colour and consistency. The specimens were fixed in 10% formalin, routinely processed and embedded in paraffin. 4µm thick sections were taken and stained with hematoxylin and eosin. Appropriate special stains like per-iodic acid Schiff was done as and when required. In case of curettage, the entire tissue was processed whereas, in case of hysterectomy specimens

representative sections were processed. Detailed clinical history was collected from the patients and statistical analysis was done.

III. Results

The present study included evaluation of 190 cases of hyperplastic and neoplastic lesions over a period of 18 months. Distribution of various hyperplastic and neoplastic endometrial lesions are as mentioned in table no 1, 2 & 3.

Table 1: Distribution of Hyperplastic and Neoplastic lesions of Endometrium

S.No	Type	Number of cases	Percentage(%)
1	CGH	132	69.5
2	CH	43	22.6
3	CHA	7	3.7
4	Ca	8	4.2
		190	100

CGH: Cystoglandular hyperplasia, CH: Complex hyperplasia, CHA: Complex hyperplasia with atypia, Ca: Carcinoma.

Table 2: Distribution pattern of Hyperplastic lesions

S No	Type	Number of cases	Percentage
1	CGH	132	72.5
2	CH	43	23.6
3	CHA	7	3.9
		182	100

CGH: Cystoglandular hyperplasia, CH: Complex hyperplasia, CHA: Complex hyperplasia with atypia.

Table 3: Distribution pattern of Neoplastic lesions

S No	Type	Number of cases	Percentage
1	Endometrial adenocarcinoma	6	75
2	Clear cell carcinoma	1	12.5
3	Carcinosarcoma	1	12.5
		8	100

As seen from table 1, out of 190 cases, hyperplastic lesions accounted for 182 cases (95.8%) whereas carcinomas accounted for 8 cases (4.2%). Out of 182 cases of hyperplastic lesions encountered in this study, CGH (Fig 1A) was the most common pathology detected which accounted for 72.5% of the cases (table 2). It was followed by complex hyperplasia without atypia (Fig 1B), which accounted for 23.6% of the cases and complex hyperplasia with atypia (Fig 1C) accounting for 3.9% of the cases. Among 8 cases of endometrial carcinoma (Table 3), adenocarcinoma seen in 6 cases (Fig 1D) and one case of each of clear cell carcinoma (Fig 1E) and carcinosarcoma(Fig 1F).

Various demographic, clinical and pathological characters are as mentioned below in tables.

Table 4: Age distribution of endometrial lesions

Age (yrs.)	CGH	CH	CHA	Ca	Total
<20	1	1	0	0	2
21-30	19	3	0	0	22
31-40	50	18	3	0	71
41-50	58	17	4	2	81
51-60	3	2	0	2	7
61-70	1	1	0	4	6
71-80	0	1	0	0	1
Total	**132**	**43**	**7**	**8**	**190**
CC= 0.546, 0<0.000(HS)					

CGH: Cystoglandular hyperplasia, CH: Complex hyperplasia, CHA: Complex hyperplasia with atypia, Ca: Carcinoma.

A highly significant association was found between age groups and endometrial lesions. From the table 4, it is clear that endometrial lesions occurred in women over a wide range of age group (20-80 yrs.). Cystoglandular hyperplasia was found to be highest in the age group of 41-50yrs. Complex hyperplasia was commonly observed between 31-40 yrs. Complex hyperplasia with atypia was encountered most commonly in

the age group of 41-50 yrs. Endometrial adenocarcinoma was observed most commonly in the age group of 61-70 yrs.

Table 5: Association of endometrial lesions with parity

Parity	CGH	CH	CHA	Ca	Total
0	11	3	1	0	15
1	9	4	0	0	13
2	44	15	2	2	63
3	39	13	0	2	54
4	22	4	3	2	31
5	4	2	1	2	9
6	3	2	0	0	5
	132	**43**	**7**	**8**	**190**

CGH: Cystoglandular hyperplasia, CH: Complex hyperplasia, CHA: Complex hyperplasia with atypia, Ca: Carcinoma.

As seen from table no 5, no significant association was observed between parity and endometrial lesions. Eleven patients with CGH, three patients with CH and one patient with CHA were nulliparous. Cystoglandular hyperplasia: The parity of patients with CGH ranged from nulliparous to para six. In this study 11 patients were nulliparous and maximum number of patients were para two, mean parity was 2.5.Complex hyperplasia: There were 43 patients with CH. The parity of the patients with CH ranged from nulliparous to para six. Three patients with CH were nulliparous and maximum number of patients were para two. Mean parity was 2.58.Complex hyperplasia with atypia: There were seven patients of CHA. Only one patient was nulliparous whereas maximum number of patients were para three. Mean parity was 3.Carcinoma: There were eight patients with endometrial carcinoma. The parity of patients ranged from para two to para five. Mean parity was 3.5.

Table 6: Clinical presentation of various endometrial lesions

Clinical features	CGH	CH	CHA	Ca	Total
Menorrhagia(M)	92	32	5	2	131
Irregular cycles (I/C)	7	1	0	0	8
Post-menopausal bleeding (PMB)	6	4	1	5	16
M and I/C	27	6	1	1	35
	132	**43**	**7**	**8**	**190**
CC=0.396, p<0.000(HS)					

Between clinical features and endometrial lesions, a highly significant association was observed.

Table 7: Association between endometrial lesion and weight

Weight	CGH	CH	CHA	Ca	Total
<40	6	1	0	0	7
41-45	37	16	1	2	56
46-50	61	20	3	4	88
51-55	12	2	2	1	17
56-60	12	2	0	1	15
61-65	2	2	1	0	5
66-70	2	0	0	0	2
	132	**43**	**7**	**8**	**190**

As shown in the above table7, no significant association was observed between weight and endometrial lesions indicating that weight and endometrial lesions are independent of each other.

Table 8: Association of endometrial lesions with risk factors

	CGH	CH	CHA	Ca	Total
Hypertension	12	3	1	2	18
Diabetes mellitus	5	1	1	1	8
Hypertension and Diabetes mellitus	6	2	1	1	10
	23	**6**	**3**	**4**	**36**
CC=0.229, p<0.76					

As shown in table 8, no significant association was observed between risk factors like hypertension, diabetes mellitus and endometrial lesions.

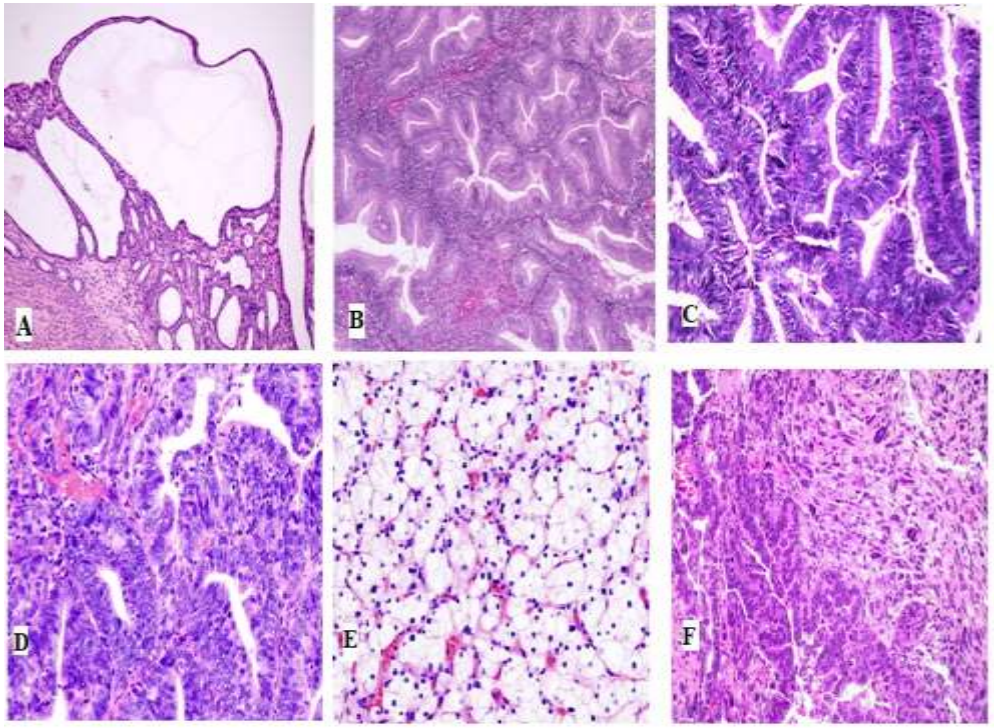

Figure 1: Various endometrial lesions

A: Cystoglandular hyperplasia
B: Complex hyperplasia without atypia
C: Complex hyperplasia with atypia
D: Endometrial adenocarcinoma
E: Clear cell carcinoma: Endometrium
F: Carcinosarcoma-Endometrium

IV. Discussion

The present study is undertaken to determine the frequency of occurrence of pre-cancerous and cancerous conditions of endometrium and to observe the correlation between clinical factors and pathological findings. This present study revealed that 95.8 % of casesshowed endometrial hyperplasia which was similar to the study done by Muzaffar et al [(4)] who all found that women who were suffering from abnormal uterine bleeding, the leading pathology was endometrial hyperplasia. They also found that in endometrial hyperplasia, menorrhagia was the most common presenting complaint which is followed by polymenorrhoea. Similarly, in our study also, maximum patients presented with menorrhagia. Similar study was done by Takreem et al [(5)] who found out that the commonest complaint in endometrial hyperplasia was menorrhagia (53.3 %). So between clinical features and endometrial lesions, a highly significant association was observed.

They found out that simple hyperplasia was the commonest (66.6 %) and it compares favorably with our present study. Our study revealed that the commonest age group was 41–50 years which was previously indicated by Kurman et al. [(1)] in their study. So highly significant association was found between age groups and endometrial lesions in our present study.

Relationship between hyperplasia and carcinoma had become an actively debated subject. Already several studies have demonstrated a very close relationship between endometrial hyperplasia and endometrial carcinoma. Laceyet al. [(6)] studied that the women with endometrial hyperplasiathe absolute risk factors for endometrial carcinoma during 20-year follow-up and cumulative 20-year progression risk of less than 5 % among women who remained at risk for at least 1 year for non-atypical endometrial hyperplasia but it was 28 % for atypical hyperplasia.

As our present study was of a short duration, out of 190 cases,50 patients had complex hyperplasia (without atypia 43 cases and with atypia 7 cases), follow-up was beyond our scope. Chamlian and Taylor [(7)] found out that 14 % adenomatous and atypical hyperplasias subsequently developed into carcinoma. Other studies also have reported that atypical hyperplasia as the highest risk for progression to carcinoma, and also the highest risk of persistence of the lesion despite hormonal therapy [(8)].

The WHO[(2)] describes the microscopic findings like nuclear rounding, loss of polarity, irregular nuclear membranes, prominent nucleoli and dense chromatin as features of cytologic atypia but acknowledges that by comparing with the adjacent normal glands, nuclear atypia may be best observed. The endometrial intraepithelial neoplasia (EIN) scheme used by Mutter [(9)] is more specific.

Endometrial hyperplasia regardless of its different types must be considered as a warning sign that endometrium is non-cycling and so susceptible to neoplastic events. But mere presence of endometrial hyperplasia is not a basis for hysterectomy. But, in general, more severe the hyperplasia, more likely it is followed by invasive endometrial carcinoma. But in our present study, we did not find any significant association between risk factors like hypertension, diabetes mellitus and endometrial lesions and also did not find association between weight and endometrial lesions indicating that weight and endometrial lesions are independent of each other. And also we did not find any significant association between parity and endometrial lesions. But western studies with endometrial lesions, pointing towards the probability of involvement of other risk factors in the etiopathogenesis.

V. Conclusion

The present study was undertaken to assess the frequency of occurrence of precancerous and cancerous lesions of endometrium amongst women presenting with menorrhagia. In concurrence with other studies a strong association was observed between increased age at presentation and endometrial hyperplasia and carcinoma. Similarly, menorrhagia was seen to be the main presenting complaint of patients with hyperplasia whereas patients with carcinoma presented with post-menopausal bleeding. On the contrary, this study indicated striking difference in the role of predisposing factors including weight, hypertension, diabetes mellitus and gravidity as compared to the western studies with endometrial lesions pointing towards the probability of involvement of other risk factors in the etiopathogenesis.

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