



## A Histomorphological Study of Carcinoma Endometrium Conducted in a Tertiary Care Centre

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### Abstract

**Introduction:** Endometrial carcinoma is the second most common malignant tumor of female genital system in India and its incidence is increasing globally. Histological variants include endometrioid carcinoma, serous carcinoma, mucinous adenocarcinoma, clear cell carcinoma, mixed adenocarcinoma and others. Histopathologic prognostic parameters include tumor type, depth of invasion, lymphovascular involvement, FIGO grade and stage.

**Materials and Method:** A cross sectional study was conducted in the department of Pathology, Government medical college, Thrissur, during a period of 18months. Gross examination and morphological assessment of 37 cases of carcinoma endometrium were done. Study was approved by the institutional ethical committee.

**Result:** 83.8% of endometrial carcinomas were endometrioid type, 16.2% were nonendometrioid type. 77.42%, 16.13% and 6.45% of endometrioid carcinomas were grade I, grade II and grade III respectively. 64.86% of endometrial cancers were stage I tumors. Glandular pattern was the predominant pattern (54.1%). 51.4% cases showed invasion less than half of myometrium. Prominent lymphocytic infiltrate was seen in 29.73% cases. Lymphovascular emboli were seen in 10.8% cases. Mitosis was  $\leq 5$  in 86.5% cases.

**Conclusion:** Most cases of endometrial carcinomas were of endometrioid type, with a predominance of grade I tumors. Majority of endometrial carcinomas belonged to FIGO stage Ia.

**Keywords:** Endometrial carcinoma, uterine cancer, endometrioid carcinoma, serous carcinoma

### Introduction

Endometrial carcinoma is the fifth most common cancer in women, affecting 318,000 women per year globally. Incidence rate (ASR) in India is 2.3 per 100,000 population. The dualistic model of endometrial cancer divides it into two types: type I and type II. It was postulated that type I tumors develop in women who have conditions associated with hyperestrogenism, such as obesity, anovulatory

uterine bleeding, polycystic ovary syndrome, infertility, late menopause, and endometrial hyperplasia. This is the most common type of endometrial cancer (85%), and it is characterized by endometrial histology, superficial invasion into the myometrium, high sensitivity to progesterone and has a favorable prognosis. In contrast, type II tumors are not associated with endometrial hyperplasia, develops often in the presence of

atrophy, is of non-endometrioid histology, with a tendency for deep invasion of the myometrium, and has a high frequency of metastatic spread. This type has a rather poor prognosis.

Molecular studies support the dualistic model of endometrial adenocarcinoma. Types I and II endometrial carcinomas are characterized by distinctive types of genetic instability and molecular alterations. Four major genetic changes are responsible for the tumorigenesis in endometrioid (type I) carcinoma: the silencing of the PTEN tumor suppressor gene, loss of PAX-2 nuclear transcription factor, the presence of microsatellite instability, a mutation of the K-ras proto-oncogene, and alteration of the b-catenin gene. In contrast, a p53 mutation, a p16 mutation, loss of E-cadherin, and overexpression of the Her2/neu oncogene are the major genetic alterations in serous and clear cell (type II) carcinomas.

Endometrioid carcinoma, the prototype of type I endometrial carcinoma, is primarily graded based on their architecture into grades 1, 2 and 3. Non-endometrioid endometrial carcinomas are generally high grade neoplasms and are not assigned a separate grade. Serous carcinoma is the prototype of type II endometrial carcinoma. Other histological variants include Mucinous adenocarcinoma, Clear cell adenocarcinoma, Mixed adenocarcinoma, High grade neuroendocrine carcinoma, Undifferentiated and Dedifferentiated carcinomas.

Definite histopathological parameters that define prognostic value include depth of myometrial invasion, lymphovascular involvement, FIGO grade and stage.

## Materials and Methods

### Case Selection

Study material were collected from hysterectomy specimens of carcinoma endometrium received in the department of Pathology during the period February 2014 to July 2015.

### Sample size

A total of 37 specimens were collected and examined.

### Inclusion Criteria

All hysterectomy specimens of carcinoma endometrium received in department of Pathology, Govt. medical college, Thrissur during the study period.

### Exclusion Criteria

- 1) Endometrial curetting samples of endometrial cancer.
- 2) Hysterectomy specimens of other pathologic conditions.

**Study Design:** Cross sectional study

### Methodology

- Gross examination of hysterectomy specimens of endometrial carcinomas was done and tumour size, appearance of the cut surface, depth of myometrial invasion, involvement of cervix, adnexal structures and omentum were documented.
- Tissue sampling was done.
- All samples were routinely fixed, processed and paraffin – embedded.
- 4 micron thick sections were stained with Hematoxylin and eosin.
- Assessment of histological grading, staging, myometrial and lymphovascular invasion were done.

### Histologic Grading of Endometrial carcinoma

Endometrioid carcinomas are primarily graded based on their architecture.

Grade 1 - 5% or less of a nonsquamous or nonmorular solid growth pattern

Grade 2 - 6%-50% of a nonsquamous or nonmorular solid growth pattern

Grade 3 - >50% of a nonsquamous or nonmorular solid growth pattern

Marked nuclear atypia upgrades the tumor grade by 1.

FIGO 2009 staging system of endometrial carcinoma was used.

### Observations and Results

In the present study, 37 hysterectomy specimens with a diagnosis of Carcinoma endometrium were studied.

**Table.1**

Age group	Frequency	Percent
31-40	3	8.1
41-50	5	13.5
51-60	14	37.8
61-70	14	37.8
71-80	0	0
81-90	1	2.7
Total	37	100.0

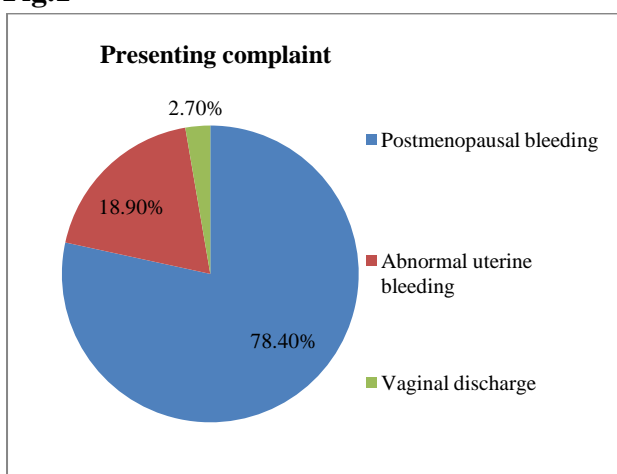
**Fig.2-** Gross specimen of endometrioid carcinoma showing a friable grey white growth in endometrial cavity, invading into myometrium.



**Table.2**

Parity	Frequency	Percent
Nulliparous	3	8.1
Parous	34	91.9
Total	37	100.0

**Fig.1**



**Table.5**

Tumor size	Frequency	Percent
≤ 2cm	8	21.6
> 2cm	29	78.4
Total	37	100.0

**Table.6**

Tumor type	Frequency	Percent
Endometrioid	31	83.8
Serous	4	10.8
Clear cell	1	2.7
Mucinous	1	2.7
Total	37	100.0

**Table.3**

Clinical diagnosis	Frequency	Percent
Ca Endometrium	33	89.2
Atypical endometrial hyperplasia	2	5.4
Ca cervix	1	2.7
Endometrial polyp	1	2.7
Total	37	100.0

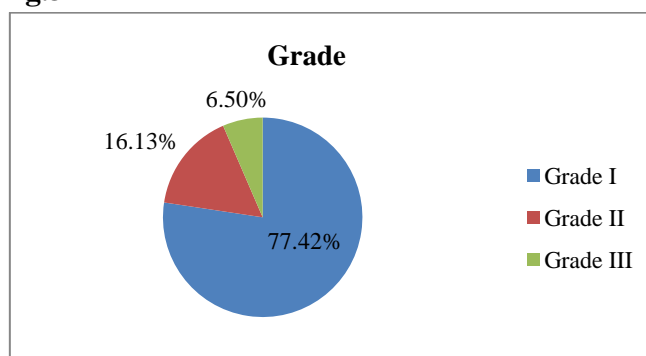
**Table.7**

Pattern	Frequency	Percent
Glandular	20	54.1
Villoglandular	1	2.7
Glandular and villoglandular	3	8.1
Papillary	3	8.1
Glandular and papillary	3	8.1
Sheets	2	5.4
Sheets and glands	4	10.8
Tubulocystic and papillary	1	2.7
Total	37	100.0

**Table.4**

Co-morbidity	Frequency	Percent
Diabetes mellitus	9	24.3
Hypertension	10	27
Ca Breast	2	5.4
Renal cell cancer	1	2.7

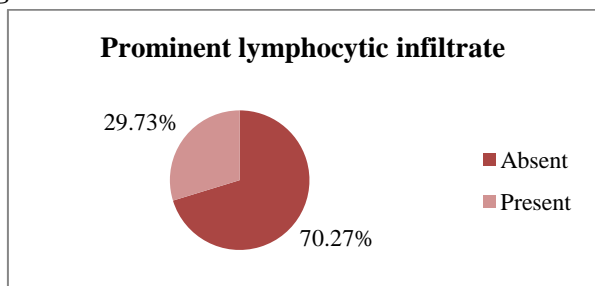
**Fig.3**



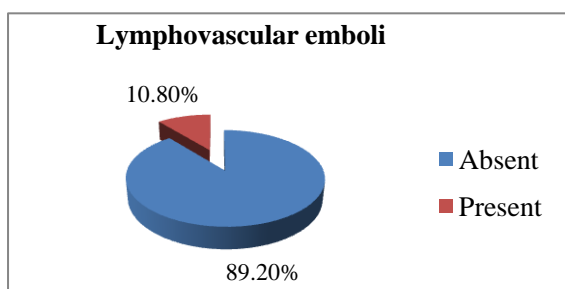
**Table.8**

Mitosis	Frequency	Percent
≤ 5	32	86.5
6-10	2	5.4
11-15	1	2.7
≥ 16	2	5.4
Total	37	100.0

**Fig.4**



**Fig.5**



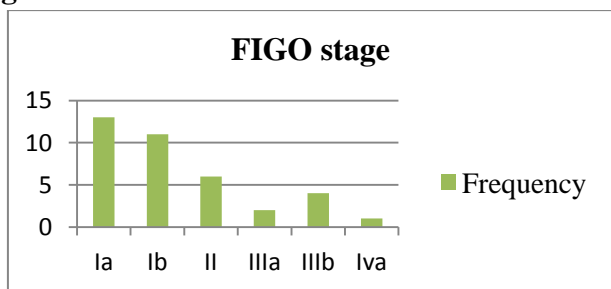
**Table.9**

Myometrial invasion	Frequency	Percent
< half of myometrium	19	51.4
> half of myometrium	18	48.6
Total	37	100.0

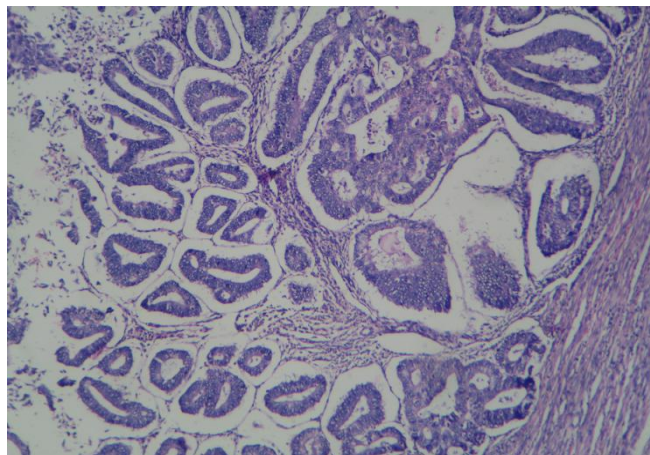
**Table.10**

Co-existing lesions	Frequency
None	7
Leiomyoma	6
Chronic cervicitis	27
Adenomyosis	3

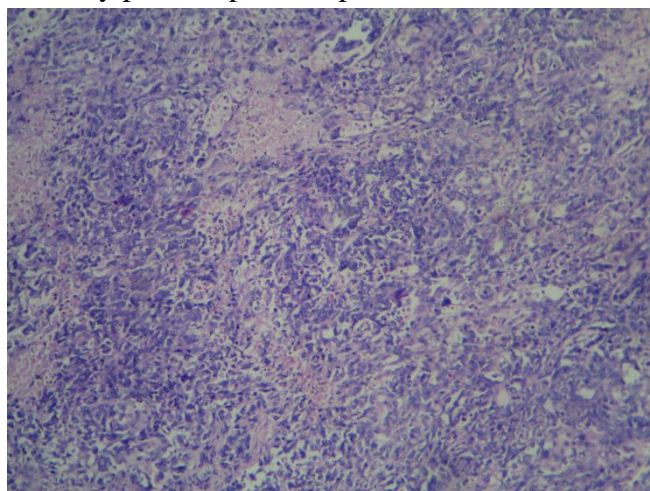
**Fig.6**



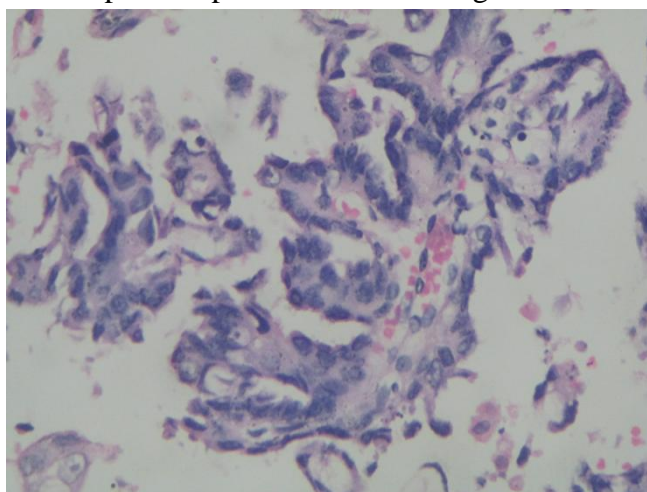
**Fig.7-** Endometrioid carcinoma, grade 1 showing neoplastic cells arranged in glands.



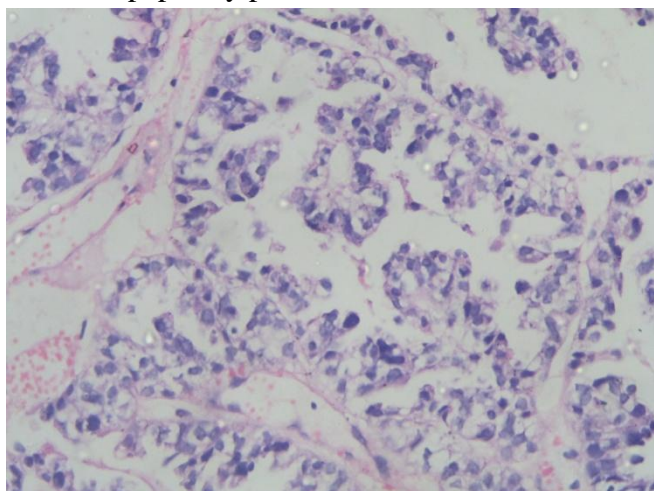
**Fig.8-** Endometrioid carcinoma, grade 3 showing markedly pleomorphic neoplastic cells in sheets



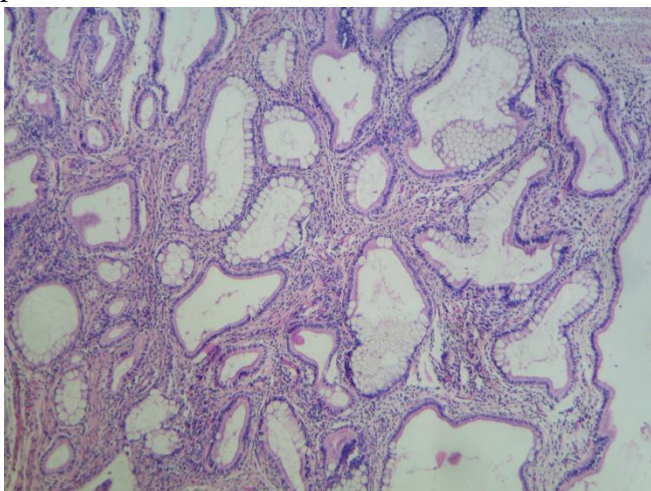
**Fig.9-** Serous carcinoma showing papillary pattern, nuclear pleomorphism and hobnailing.



**Fig.10**-Clear cell carcinoma showing clear cells with distinct cell borders arranged in tubulocystic and tubulopapillary patterns



**Fig.11**-Mucinous carcinoma showing cells with intracytoplasmic mucin, arranged in glandular pattern.



## Discussion

Endometrial carcinoma is one of the most common malignant tumors of female genital system. In this study 37 hysterectomy specimens with a diagnosis of Carcinoma Endometrium were included. The age of the patients ranged from 38-85 years with a mean age of 57.05 years, which is comparable with a study done by Indu Maniketh et al in which the patients' age ranged from 32-77 years with a mean age of 58.13 years.

Majority of the patients were parous women (91.9%) and only 8.1% of cases were nulliparous in our study. This differed from the study by Henderson et al in which 30.9% of patients were

nulliparous. The most common presenting complaint was post menopausal bleeding (78.4%) which is similar to the study by Indu Maniketh et al, in which postmenopausal bleeding was the commonest presenting complaint (75.56%).

In this study the most common clinical diagnosis was endometrial carcinoma (89.2%) and 43.2% cases had co-morbidities like Diabetes mellitus (24.3%), Hypertension (27%), Carcinoma Breast (5.4%) and RCC (2.7%). According to the study by Indu Maniketh et al, 87.9% cases had co-morbidities like Diabetes mellitus (44.2%), Hypertension (32.6%) and other malignancies (11.1%).

In the present study 78.4% of cases had tumor size (greatest dimension) > 2cm and 21.6% had tumor size  $\leq$  2cm. As per the study by AlHilli MM et al, 68% had tumor size > 2cm and 32% had tumor size  $\leq$  2cm.

In the current study majority of cases were of the Endometrioid type (83.8%) and Non endometrioid carcinomas accounted for 16.2% of cases and the predominant pattern was glandular (54.1%). This was similar to the study by Perez Medina et al, which had 78.69% cases of Endometrioid carcinoma and 21.31% cases of Non endometrioid carcinoma.

Out of the 31 cases of endometrioid carcinomas, 24 (77.42%) were grade I tumors, 5 (16.13%) were grade II tumors and 2 (6.45%) were grade III tumors. In the study by Sidonia Catalina Stoian et al 11/22 cases (50%) were grade I tumors, 7/22 cases (31.8%) were grade II tumors and 4/22 cases (18.2%) were grade III tumors.

In this study 32 out of 37 cases (86.5%) had mitosis  $\leq$  5/10 hpf and it was found that mitosis and grade, as well as mitosis and stage, have a statistically significant positive correlation, with higher mitotic rates occurring in high grade, high stage tumors. These findings are similar to the study by Pirog EC et al, in which they found higher mitotic index (>5) were associated with high grade, high stage endometrial carcinomas.

Prominent lymphocytic infiltrates were seen in 29.73% cases. In the study by Svetlana Kondratiev et al 18.66% cases had prominent lymphocytic

infiltrate.

In this study lymphovascular emboli were seen in only 10.8% cases. Study by Yamazawa et al found lymphovascular emboli in more number of cases (25.98%).

Out of 37 cases, 19 showed invasion < half of myometrium (51.4%). InduManiketh et al in their study found 70.5% cases had invasion less than half of myometrium.

In this study 64.86% were stage I tumors, 16.22% were stage II tumors, 16.22% were stage III tumors and 2.70% were stage IV tumors. Similar findings were seen in the study by Svetlana Kondratiev et al which had 58.89% stage I tumors, 24.44% stage II tumors, 15.56% stage III tumors and 1.11% stage IV tumors.

### Conclusion

- In this study, it was observed that 83.8% of endometrial carcinoma were of Endometrioid type (n=31) and 16.2% were of Non endometrioid type (n=6).
- Among the nonendometrioid carcinomas, there were 4 serous carcinomas, 1 clear cell carcinoma and 1 mucinous adenocarcinoma.
- Majority of the endometrioid carcinomas were grade I tumors (77.42%). 16.13% were grade II tumors and 6.45% were grade III tumors.
- In this study most of the endometrial cancers were stage I, with a good prognosis.
- 86.5% cases had mitosis  $\leq$  5/10 hpf and mitosis was found to have a statistically significant association with both histologic grade and FIGO stage with mitotic rates increasing with the grade and stage of tumor.

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