

# A Study on Endometrial Carcinoma Cases in a Tertiary Care Centre

Saravanan B<sup>1</sup>, Gomathi S<sup>2\*</sup>, Rajavelu Indira<sup>3</sup>

<sup>1,2</sup>Associate Professor of Pathology, Department of Pathology, Government Medical College Hospital, Chennai-2, Tamilnadu, India

<sup>3</sup>Professor of Pathology, Department of Pathology, ISO& Kasturibai Gandhi Govt Hospital, Chennai-2, Tamilnadu, India

\*Corresponding Author: Gomathi S

**Abstract:** Endometrial cancer is the most common malignancy of female genital tract in US. Common in postmenopausal women with mean age of 65 years. Aim: To study histological type, grade, surgical stage of endometrial cancer. Correlate pre and postoperative grades with nodal metastasis. **Methodology:** Retrospective and Prospective study of 106 cases of endometrial carcinoma was done. Required data was collected from medical records department for retrospective cases. Specimen were received, processed and studied in prospective cases using routine H&E stain. Histological grades were grouped into two groups. Well differentiated and moderately endometrial carcinoma as Group I. Poorly differentiated and undifferentiated as group II. Chi square test was used to correlate groups (pre and postoperative) and nodal metastasis. **Observation and results:** Most common histological type is Endometrioid carcinoma (grade 1) with mean age of 55 years. Presented as postmenopausal bleeding with or without vaginal discharge. 76.42%, 9.43%, 6.60%, 2.83% and 4.72% of cases presented in FIGO Stage IA, IB, Stage II, Stage III C1 and IIIc2 respectively. Significant correlation between grade 3 and UDC (group II) and nodal metastasis with p value of 0.000016 and 0.000002 (pre and postoperative) respectively. **Conclusion:** High grade tumours show significant correlation with nodal metastasis when compared to low grade. In high grade tumours, staging surgery with wide nodal excision improves survival.

**Keywords:** Endometrial Carcinoma, UDC-Undifferentiated Carcinoma, H&E; Haematoxylin and Eosin, FIGO-international federation of Gynaecology and Obstetrics, G-grade of Tumor

## 1. Introduction

Endometrial cancer is the most common malignancy of female genital tract in US [14]-[12]. While it holds second place in developing countries [14]. It is reported to be the fourth most common cancer of female in Chennai as per population based cancer register [17].

Endometrial cancer is common in postmenopausal women with 65 as mean age [1]. The various factors associated with development of endometrial cancer are excess estrogen exposure, obesity, diabetes, nulliparity, late menopause, oral contraceptive pills and Tamoxifen therapy [9]. The common presentation is postmenopausal bleeding. Conditions like atrophic vaginitis, cervicitis, endometritis, senile atrophic vaginitis, myoma uterus, hyperplasia, polyp etc can also present with postmenopausal bleeding [13]. The other features like intermenstrual bleeding in premenopausal women can also occur in hyperplasia, anovulatory cycle, myoma, polyp, cervix cancer, adenomyosis, So it must be thoroughly investigated to rule out endometrial cancer [15]. Rarely Endometrial cancer can present as vaginal discharge and lower abdominal pain.

Diagnosis of endometrial cancer is made with histopathological assessment of endometrial specimen after dilation and curettage. Clinical staging done by clinical examination with radiological imaging like CT and contrast enhanced MRI to detect myometrial invasion, cervix extension and nodal metastasis. The surgical management is planned based on clinical staging, histological type and grading. The surgical staging comprises of Total hysterectomy with bilateral salpingo-oophorectomy and removal of pelvic & Para aortic lymph node followed by peritoneal fluid cytology. It is recommended in Stage I with high risk, stage II, III and IV cases [3]. The surgical staging

may be considered in Intermediate risk cases also [13]. Complete staging surgery with pelvic and Para aortic lymph node removal may not be necessary for low grade tumor without deep myometrial invasion due to associated morbidity [8]-[4]. Preoperative assessment of myometrium invasion in MRI with diffusion weighted imaging is highly accurate [11]. The PET/CT and DWI are not found to be accurate enough to assess nodal metastasis compare to surgical lymphadenectomy [14]. PET/CT is highly sensitive and specific to detect nodal and distant metastasis in selected high risk cases only. In the absence of above radiological imaging technology for assessing myometrial invasion and nodal metastasis. Proper preoperative selection of cases remains problematic. Our study by analysis pre and postoperatively histopathology data may lend a helping hand for surgeon to decide in management, in addition to the radiological imaging studies.

## 2. Objective

To study histological type, grade, surgical stage of endometrial cancer in our institution. To correlate between preoperative and postoperative tumor grade with lymph node metastasis.

## 3. Material and Methods

Retrospective and prospective study of 106 cases of endometrial cancer was carried out in the department of pathology at our institution. Required data were collected from Medical record, gynecological and pathology department for retrospective cases. Wax blocks of both pre and post operative cases from pathology lab were collected. Fresh slides were prepared from paraffin wax block and stained by routine hematoxylin and eosin staining. The Slides were reviewed.

In prospective cases, initial diagnosis was done by Dilation and endometrial curetting. Subsequently total abdominal hysterectomy and bilateral salphingo-opherectomy with removal of pelvic and paraaortic node for surgical staging done with peritoneal fluid wash for cytology based on clinical assessment. Adequate bits were taken from received specimen and processed. The slides were prepared using routine hematoxylin and eosin stain. Peritoneal fluid was centrifuged and cytological slides were prepared and studied.

After diagnosis, endometrial carcinoma is classified based on WHO histological classification 2014 into Endometrioid carcinoma, mucinous carcinoma, serous carcinoma, undifferentiated carcinoma etc. Mixed epithelial and mesenchymal tumors, secondary deposit, endocervical adenocarcinoma extending into uterus were all excluded from the study. Cases with inadequate data and incomplete surgery were also excluded. Tumors were graded and staged based on FIGO grading and staging system 2009. Entire data is computed in excel sheet. Histological grades were grouped into Group I (well differentiated and moderately differentiated) and Group II (poorly differentiated and undifferentiated carcinoma). Chi Square test was done using socscistatistic software for significant correlation between pre and post operative grades and lymph node metastasis.

#### 4. Results

**Table 1:** Clinical features

No of patients	106 cases
Mean age	55 (28-72)
Parity	
Multiparous	88 (83.02%)
Nulliparous	18 (16.98%)
Clinical presentation	
Post menopausal bleeding with or without vaginal discharge	85(80.19%)
Intermenstrual bleeding	15(14.15%)
Intermenstrual bleeding with lower abdominal pain	6(5.66%)

Mean age of endometrial carcinoma in our study is 55 year. The youngest age of presentation is 28 years with Villoglandular type of Endometrioid carcinoma (grade I).The oldest age in our study is 72 years with 2 cases of Villoglandular (grade 1) and moderately different type (grade 2) respectively. Out of 106 cases, 85 (80.19%) occurred in postmenopausal, 13(12.26 %) in premenopausal and remaining 8(7.55 %) under 40 years.

88 (83.02 %) out of 106 cases occurred in Multiparous women, remaining 18 cases (16.98%) occurred in Nulliparous women. Majority of cases 85 (80.19 %) presented as Postmenopausal bleeding with or without vaginal discharge. 21(19.81%) cases presented as intermenstrual heavy flow, out of this 6 cases presented with associated lower abdominal pain [Table 1].

Postoperatively out of 97 cases of Endometrioid carcinoma, 75 cases were well differentiated type (G1) [Fig:4] and 22 cases were moderately differentiated type (G2). Mucinous carcinoma (G1) was found in one case only. In the

remaining 8 cases, 6 belong to serous carcinoma [Fig:3] and 2 cases are undifferentiated type.

Preoperatively 82 cases were Endometrioid type with 60 G1cases and 22 G2cases. Mucinous carcinoma (G 1) was found in one case. Remaining cases belong to serous carcinoma (6cases) and undifferentiated carcinoma (2cases) [Table 4].

Grade 1 carcinoma was found in 61(57.55%) cases preoperatively and in 76(71.70%) cases postoperatively. The number of G2, G3 and undifferentiated carcinoma remained the same in both pre and postoperative data. The number of G2, G3 and undifferentiated carcinoma were 22(20.75%), 6(5.66%) and 2(1.89%) respectively.

15 cases (14.15%) reported as complex hyperplasia with atypia/suspicious for malignancy in preoperative assessment later turn out to be well differentiated Endometrioid carcinoma (G1) [Table 4].

**Table 4:** Histopathological features

Histopathological diagnosis	Preoperative	Postoperative
Complex hyperplasia with atypia	15	0
Endometrioid carcinoma	82	97
Mucinous carcinoma	1	1
Serous carcinoma	6	6
Undifferentiated carcinoma	2	2
Grade		
Grade I	61(57.55%)	76(71.70 %)
GradeII	22(20.75%)	22(20.75%)
GradeIII	6(5.66%)	6(5.66%)
Undifferentiated	2(1.89 %)	2(1.89 %)

Myometrial invasion (>1/2 thickness) was found in 11 cases (10.38%), out of which 8 cases (7.55%) show nodal metastasis [Fig: 5]. In the node positive cases, 3 cases (2.83%) were of well differentiated type (G1) with metastasis to pelvic nodes only. The remaining five cases (4.72%) consisting of 1 moderately differentiated (G2), 3 serous (G3) and 1 undifferentiated carcinoma had both pelvic and Para aortic nodal metastasis.

Myometrial invasion (<1/2 thickness) was found in 71 cases (66.98%) and none of the cases had any nodal metastasis. The remaining 24 cases (22.64%) had no myometrial invasion at all [Table 5]. Based on FIGO staging system, 81(76.42%) cases were in stage IA, 10 (9.43%) cases in Stage IB, 7(6.60%) in stage II, 3(2.83%) stage IIIC1 and 5 (4.72%) cases in stage III C2. Peritoneal wash cytology was positive for malignancy in14 (13.21 %) out of which 8, 2, 4 are in G1, G2 and G3 respectively [Table 2]-[Table 3].

**Table 2:** Postoperative Surgical stage

Stage	No of cases
IA	81(76.42%)
IB	10(9.43%)
IC	0
II	7(6.60%)
IIIA	0
IIIB	0
IIIC1	3(2.83%)
IIIC2	5(4.72%)

**Table 3:** Fluid cytology positive cases within Postoperative grade

Peritoneal fluid cytology	14(13.21%)
Grade 1	8(7.55 %)
Grade 2	2(1.89 %)
Grade 3	4(3.77 %)

Study of correlation between grades with lymph node metastasis was done using Chi square test after separating grades and undifferentiated carcinoma into 2 groups with G1 and G2 in Group I, G3 and undifferentiated carcinoma as group II.

No significant correlation between the grades G1 and G2 (pre & postoperatively) in group I with lymph node metastasis was found. Similarly, in group II there was no significant correlation between G3 and undifferentiated carcinoma with nodal metastasis.

The correlation between two groups (Group I & Group II) both pre and post operatively with lymph node metastasis was found to be significant with p value 0.000016 and 0.000002(pre and postoperative) [Table 6]-[Table7].

**Table 6:** Correlation between Preoperative grade and LN involvement

Group	LN positive	LN negative
Group I(Gr1&2)	4	79
Group II (Gr3& undifferentiated)	4	4
Chi square statistic is 18.5758, P valve is 0.000016		

**Table 7:** Correlation between Postoperative grade and LN involvement

Group	LN positive	LN negative
Group I(Gr1&2)	4	94
Group II (Gr3& undifferentiated)	4	4
Chi square statistic is 22.3501, P valve is 0.000002		

**Table 5:** Correlation with Grade, Myometrial invasion and LN metastasis.

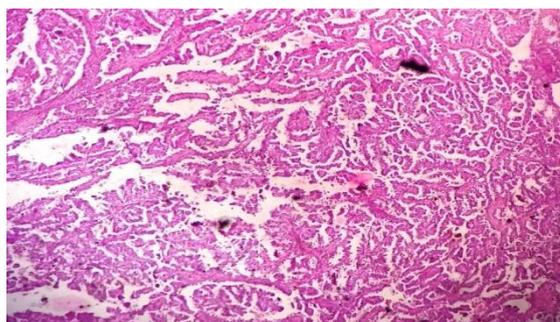
Grade	No MM invasion	< 1/2 MM invasion	> 1/2 MM invasion	>1/2 MM invasion with LN metastasis(8/11)
I	21	52	3	3
II	2	18	2	1
III	0	1	5	3
UDC	1	0	1	1
Total cases	24	71	11	8



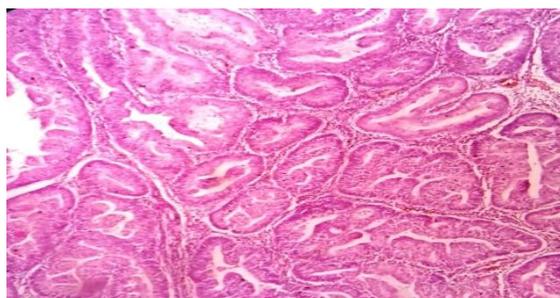
**Figure 1:** Total hysterectomy specimen showing endometrial carcinoma



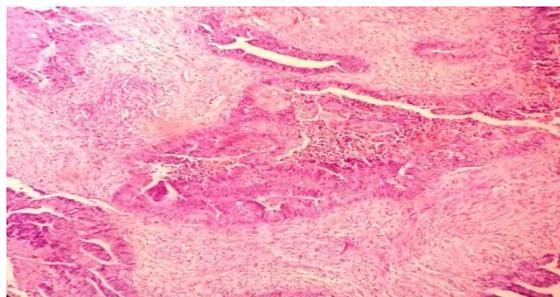
**Figure 2:** Uterus specimen showing myometrial invasion > 1/2 thickness



**Figure 3:** Serous carcinoma of endometrium (grade 3), Under 400x (H&E)



**Figure 4:** Endometrioid carcinoma -Grade I Under 400x (H&E stain)



**Figure 5:** Endometrioid carcinoma infiltration into myometrium Under 400 x(H&E stain)

## 5. Discussion

Among gynecological cancer endometrial carcinoma is the most common malignancy and fourth among the cancer of women in US. In developing countries it is second most common.

In our study the mean age of presentation is 55 years. Greenlee et al showed 60 years and Arora V et al showed 65 years.

The age group distribution of endometrial carcinoma in our study is 80.19% postmenopausal, 12.26% premenopausal and 7.55% under 40 years. Greenlee et al reported endometrial carcinoma 70% in postmenopausal, 25% in premenopausal age group and 5% in under 40 years.

Our study shows 16.98% in Nulliparous and 83.02% in Multiparous women. P S Rathod et al 2014 reported 13.7% cases in Nulliparous and 86.2% in Multiparous women

On Histological type, our study shows 91.51% Endometrioid carcinoma, 5.66% serous carcinoma, 0.94% mucinous carcinoma and 1.89% undifferentiated carcinoma. Sik B A et al 2016 study showed 87.9% Endometrioid carcinoma, 6.7% serous carcinoma, 1.7% adenosquamous carcinoma and 1.3% clear cell carcinoma.

Our study shows good correlation between grades in G2, G3 and undifferentiated carcinoma both pre and postoperatively. But the correlation becomes poor in grade 1 showing 57.55% preoperatively and 71.70% postoperatively. Rathod P S et al 2014 showed poor correlation in all grades. It showed G1, G2, G3 and undifferentiated carcinoma in 39%, 26%, 21.9%, 12.2% preoperative and 24%, 38%, 32.5%, 4.6% postoperative respectively.

Surgical staging in our study shows 85.85 %, 6.60%, 7.55% and 0 in stage I, II, III and IV respectively. Rathod P S et al: 2014 showed 70.9%, 16.2%, 12.9% and 0 in stage I, II, III and IV respectively.

All cases with Node involvement show myometrial invasion more than fifty percent of uterine thickness. In cases without nodal involvement, the myometrial invasion less than fifty percent of uterine thickness is seen in 66.98% and no invasion in 22.64% cases.

Our study shows statistically significant correlation between pre and postoperative grading with lymph node involvement in group II (G3 and undifferentiated carcinoma) with P value of 0.000016 and 0.000002 respectively. Rathod P S et al: 2014 study also showed significant correlation between grading and lymph node involvement in group II (G3 and undifferentiated) with p value <0.005024.

Our study shows good correlation between pre and postoperative histological grading in cases of undifferentiated, G2 and G3 carcinoma. And there is good correlation between lymph node positivity and histological grades in G3 and undifferentiated carcinoma, but the correlation is found to be insignificant in G2 cases. Thus the correlation is seemed to be increasing with the histological grading. All cases with deeper myometrial invasion showed lymph node involvement irrespective of the grading.

Earlier studies showed better survival rate with wide lymph node dissection in stage I G3 and more advanced cases. A study with 27063 cases showed no additional benefit due to lymph node dissection in stage I G1 and G2. So the lymph node dissection is not considered as a routine procedure [7]. Wider lymph node dissection is required in all cases with deep myometrial invasion [16], but the exact depth of invasion can be accurately assessed only after surgery.

Surgical staging can detect depth of invasion, but carries a risk of morbidity and may negatively affect optimal radiotherapy [6].

The myometrial invasion depth can also be assessed accurately by using MRI with diffusion weighted imaging method but the availability of this advanced imaging technology is limited.

In higher grade of tumor (preoperatively), the likely hood of lymph node involvement is more .So Staging surgery including wider lymph node resection is recommended routinely. In lower grade cases, preoperative assessment with radiological imaging technique and frozen section may be helpful instead of a wider lymph node dissection.

## 6. Conclusion

Statistically significant correlation is found between pre and post operative higher grade of endometrial carcinoma with lymph node metastasis. Staging surgery with wider nodal dissection done in higher grade tumour to improve survival rate. Deeper Myometrial invasion shows significant correlation with nodal metastasis which is an independent risk factor. In lower and intermediate cases, radiological imaging studies and frozen sections are required due to the insignificant correlation with nodal metastasis.

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## Author Profile



**Saravanan B**, Associate Professor of Pathology, Government Medical College.Chennai:2. Done post graduation at Institute of Pathology & Electron microscopy, Madras Medical College. Has sixteen years of teaching experience in various institutions and three years in senior Cytopathologist, Government Arignar Anna Cancer Hospital and Regional Cancer Centre.