



A Clinicopathological Study of Malignant Tumors of the Uterine Corpus in a Tertiary Care Center

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aim: To study the clinicopathological spectrum of malignant tumors of the uterine corpus in a tertiary care center and classify it according to the latest WHO classification.

Methods: A 2 year study was conducted on 22 diagnosed cases of malignant tumors of uterine corpus. Retrospectively clinical and histopathological details were collected and analyzed.

Results: In our study majority (40.90%, 9 of 22) cases belong to the age group of 51-60 years. Abnormal uterine bleeding was the most common clinical presentation. A large share (81.81%) of the tumours was of epithelial origin, followed by mixed and mesenchymal tumors. Nearly 94% of the epithelial tumours were Endometrioid Adenocarcinomas. Majority of the cases were at pT1a stage (42.1%) at the time of diagnosis, followed by pT1b stage (31.57%). Very few cases (21%) presented with nodal metastasis. All the cases with nodal metastasis showed Lymphovascular invasion in the tumor proper and were usually high grade tumors.

Conclusion: The prognosis of the patients with malignant tumors of uterine corpus depends on stage, grade, myometrial invasion, tumor size, lymphovascular invasion etc. Clinical findings in these tumors are not specific, so Histopathological examination plays a vital role in diagnosing and assessing the prognosis of these tumors. Classifying these tumors according to the recently proposed molecular classification will aid in patient specific targeted therapy.

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1. INTRODUCTION

Cancer of the uterine corpus is a major gynecological malignancy that is responsible for mortality in women of reproductive and postmenopausal age. It is the 6th most common cancer among women worldwide and 2nd most common cancer of the female genital tract [1]. The uterine corpus includes the endometrium consisting of glands and stroma and myometrium made up of smooth muscle. Almost 90% of the cancers in the uterine corpus occur in the endometrium [2].

The development of uterine tumors is multifactorial (i.e.) Hormonal imbalance due to: early menarche, late menopause, infertility, oral contraceptives pills, estrogen therapy, PCOS, chronic use of tamoxifen, lifestyle, dietary habits, obesity, diabetes mellitus, hypertension, genetic predisposition and old age [2].

Long-term unopposed estrogen therapy or hormone treatment without progesterone causes frequent mutations in DNA replication and hence, increases the risk of uterine cancers [3]. Changing trends in lifestyle and reproductive profile of women is a risk factor responsible for rise in the incidence of uterine cancer in India. All the other causative factors amount to almost 5% of uterine cancer [2].

The main clinical presentations include abnormal uterine bleeding, menorrhagia, dysmenorrhea and irregular menstrual cycle [4]. Biopsy is the definitive method of diagnosis. Management of patients depends upon the stage, grade of the tumor and presence of metastasis. Surgical resection and Chemotherapy are the most preferred methods for management [5]. The aim of this paper is to study the clinicopathological spectrum such as demographic variables, presenting complaints, gross appearance, microscopic findings etc. of malignant tumors of the uterine corpus in a tertiary care center.

2. MATERIALS AND METHODS

This was a retrospective study undertaken at Saveetha medical college, Chennai. Complete enumerative sampling method was used. The records of 22 cases reported as malignant tumors of uterine corpus during the study period of 2 years (2018 – 2020) were analyzed. The

specimens that were used to make unbiased diagnosis were – Total abdominal hysterectomy with bilateral salpingo-oophorectomy, endometrial curetting and endometrial biopsy. The gross and histological study of these specimens was performed by initially fixing them using 10% formalin. The tissue bits were then processed into paraffin-embedded blocks and thin sections measuring 4-micron were stained using H&E stain. This section of tissue was morphologically studied and diagnoses were made.

Retrospectively the reports and the slides were analyzed and the tumors were classified according to the latest WHO classification. Variables such as age of presentation, presenting complaints, gross appearance, microscopic morphology, myometrial invasion, lymph node metastasis, etc. were studied and descriptive statistical analysis was done. Benign tumors of the uterine corpus were excluded from the study. Staging of the tumors were done according to the latest AJCC 8th edition (pTNM staging).

3. RESULTS AND DISCUSSION

In our study majority (40.90%, 9 of 22) cases belong to the age group of 51-60 years at the time of diagnosis. Followed by age groups 61 -70 years and 71 to 80 years which each had 4 cases (18%). This was similar to the study conducted by Prathyusha Nakka et al, in which a large percentage of cases (12/35 cases, 34.28%) were between the age group of 51-60 years [6]. In a study conducted by Cameselle-Teijeiro et al the commonest age group was observed to be 61–70 years [7].

Most of the patients presented with abnormal uterine bleeding. Total abdominal hysterectomy with bilateral salpingo-oophorectomy and lymph nodes was the specimen received in most cases. Two cases of endometrial carcinoma were diagnosed with endometrial curetting specimen; pathological staging was not performed in these two cases.

Majority of the tumors were epithelial in origin (18 cases, 81.81%), followed by mixed epithelial and mesenchymal tumors (3 cases, 13.63%). There was only one case of pure mesenchymal tumor in our study. These results were similar to study

conducted by Cameselle-Teijeiro JF et al, which also showed a significant preponderance of epithelial tumours comprising 93.9% of cases [7].

Nearly all epithelial tumours (ie) 17 of 18 cases (94%) were Endometrioid adenocarcinomas, of which 2 cases of endometrioid adenocarcinoma had a component of squamous differentiation. There was a single case of serous carcinoma

which we received within the study period. These findings are similar to study conducted by ImranaTanvir et al, where 80% of the cases were of Endometrioid type (42/52) and 6/52, 11% of cases are serous carcinoma. There were three cases of carcinosarcoma (Malignant mixed mullerian tumor) and a case of High grade Endometrial stromal sarcoma included in the study.

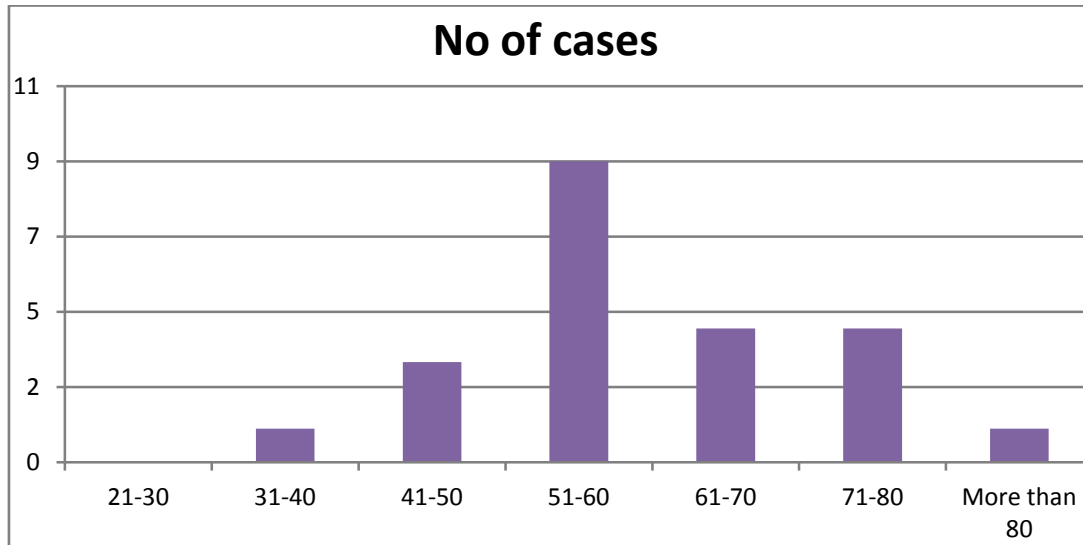


Fig. 1. Age wise distribution of malignant tumors of uterine corpus

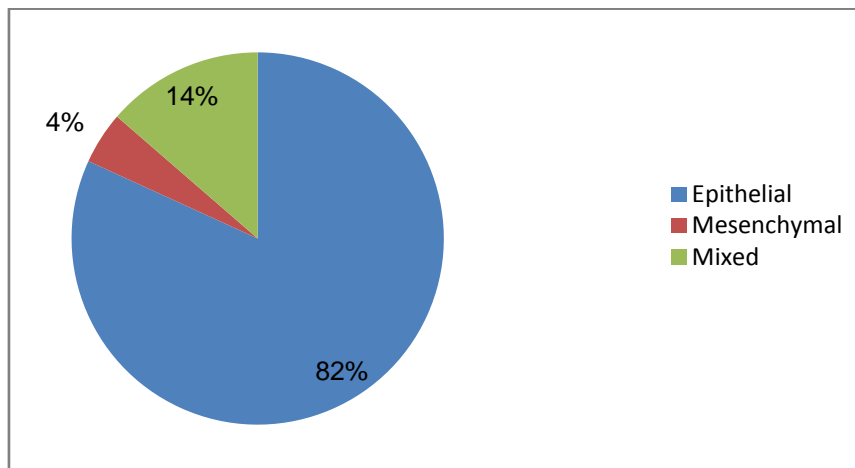


Fig. 2. Distribution of malignant tumors of uterine corpus

Table 1. Epithelial tumors- histological type

Type of epithelial tumor	Number of cases	Percentage
Endometrioid adenocarcinoma NOS	15	83.33
Endometrioid adenocarcinoma, with squamous differentiation	2	11.1
Serous carcinoma	1	5.55
Total	18	100

FIGO grading was done on all endometrioid adenocarcinomas, in which the tumors were graded based on the percentage of solid growth pattern. Majority of the endometrioid adenocarcinoma were in G1 and G2 with 8 cases (47%) each. One case showed extensive solid growth pattern and only focal areas of glandular formation, which was reported as grade 3. This is similar to results of the study by P S Rathod, where 66% (81/123 cases) belonged to Grade 1 and grade 2. Tumors other than endometrioid and mucinous carcinomas in which FIGO grading is not applicable were regarded as high grade [8].

The tumors were staged according to the latest AJCC 8th edition (pTNM staging). Most of the cases belong to pT1a stage (8 of 19 cases, 42.1%) where the tumour invades the endometrium and less than one-half of the myometrium. 6 of 19 cases (31.57%) belong to pT1b stage where, tumour invades greater than or equal to one-half of the myometrium but, does not extend beyond uterus. 15.78% (3/19 cases) fall under pT2 stage where, tumor invades the stromal connective tissue of the cervix but doesn't extend beyond the uterus. Stages pT3a and pT3b in which the tumor involves the serosa, adnexa, vagina, or parametrium make up 5.26% each (1/19 cases). This showed a variation from

the study conducted by P S Rathod et al, in which 16.12 % (15/93) cases belong to stage pT1a, 51.61% (48/93) cases belong to pT1b. Whereas there was the similarity in the statistics of stage pT2 (16.2%, 21/131 cases) and stage 3 (12.9%, 17/131 cases) [9].

Majority of the cases (14 of 19, 74%) did not have any nodal metastasis at the time of presentation and 4 of 19 cases (21%) had regional lymph node metastasis to pelvic lymph nodes (pN1 stage). No nodes were found or submitted in the remaining two cases. Lymph node metastasis was seen mostly in grade 3 (high grade) tumors (4/5, 80%). This was similar to the study conducted by P S Rathod et al, the number of lymph node metastasis in Grade 3 and undifferentiated carcinomas (10/129, 7.75%) was higher than Grade 1 and Grade 2 tumors (4/129, 3.1%) [9]. All the cases with nodal metastasis had lymphovascular invasion (LVI) at the periphery of the tumor. This indicates LVI is reliable marker for metastasis and prognosis.

Other additional pathological findings in our study were chronic cervicitis which was seen in majority of cases, other findings include adenomyosis, Cervical nabothian cyst, leiomyoma, Squamous metaplasia cervix, para tubal cyst, benign endometrial polyp etc.

Table 2. Grade (FIGO grading) distribution of endometrioid adenocarcinoma

Grade	Number of cases	Percentage
G1	8	47%
G2	8	47%
G3	1	6%
Total	17	100%

Table 3. Pathological stage classification – Tumor staging

Primary tumor	Number of cases	Percentage
pT1a	8	42.10
pT1b	6	31.57
pT2	3	15.78
pT3a	1	5.26
pT3b	1	5.26
Total	19	100%

Table 4. Pathological stage classification – Nodal staging

Nodal stage	Number of cases	Percentage
pNx	1	5
pN0	14	74
pN1	4	21
Total	19	100

Table 5. Lymphovascular invasion

Lymphovascular invasion	No of cases	%
Identified	5	26%
Not identified	14	74%
Total	19	100%

Table 6. Additional pathological findings

Additional pathological findings	No of cases
Chronic cervicitis	14
Benign endometrial polyp	1
Benign endocervical polyp	1
Leiomyoma	4
Adenomyosis	5
Squamous metaplasia - cervix	3
Paratubal cyst	2
Nabothian cyst - cervix	5
Hydrosalphinx	1

According to 2014 WHO Classification of tumors of female reproductive organs the tumors of uterine corpus are divided broadly into epithelial tumours and precursors, Mesenchymal tumours, Mixed epithelial and mesenchymal tumours, Lymphoid/ myeloid tumours, and Secondary tumours.

Bokhman classified endometrial tumors into type 1 and type 2 tumors [10]. Carcinomas of endometrium occurring in women aged less than 40 years of age are usually of endometrioid type, which usually occurs in a background of endometrial hyperplasia associated with unopposed estrogen exposure (Type 1). Conversely, tumors occurring in elderly patients

are more likely to be High grade tumors, not associated with oestrogen exposure and they occur *de novo* (Type 2) [11].

Serous carcinoma is the prototype of type 2 carcinomas. The prognosis of type 2 carcinomas are worse compared to type 1 carcinomas [11]. The Cancer Genome Atlas (TCGA) study proposed a molecular classification of endometrial carcinomas, which includes CN low, CN high, hypermutated and ultramutated [12]. Copy number low corresponds to type 1 carcinomas with wild type p53. Similarly, copy number high corresponds to type 2 carcinomas with mutant p53. Hypermutated carcinomas are characterized by micro satellite instability [12].

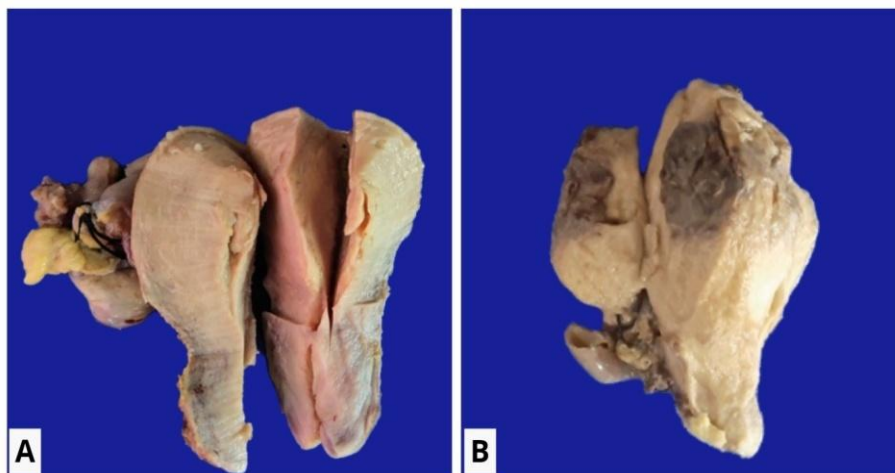


Fig. 3. Gross picture of– (A) Endometrioid adenocarcinoma presenting as a polypoid lesion in the endometrial cavity, (B) Endometrial stromal sarcoma presenting as a grey brown mass in the myometrium

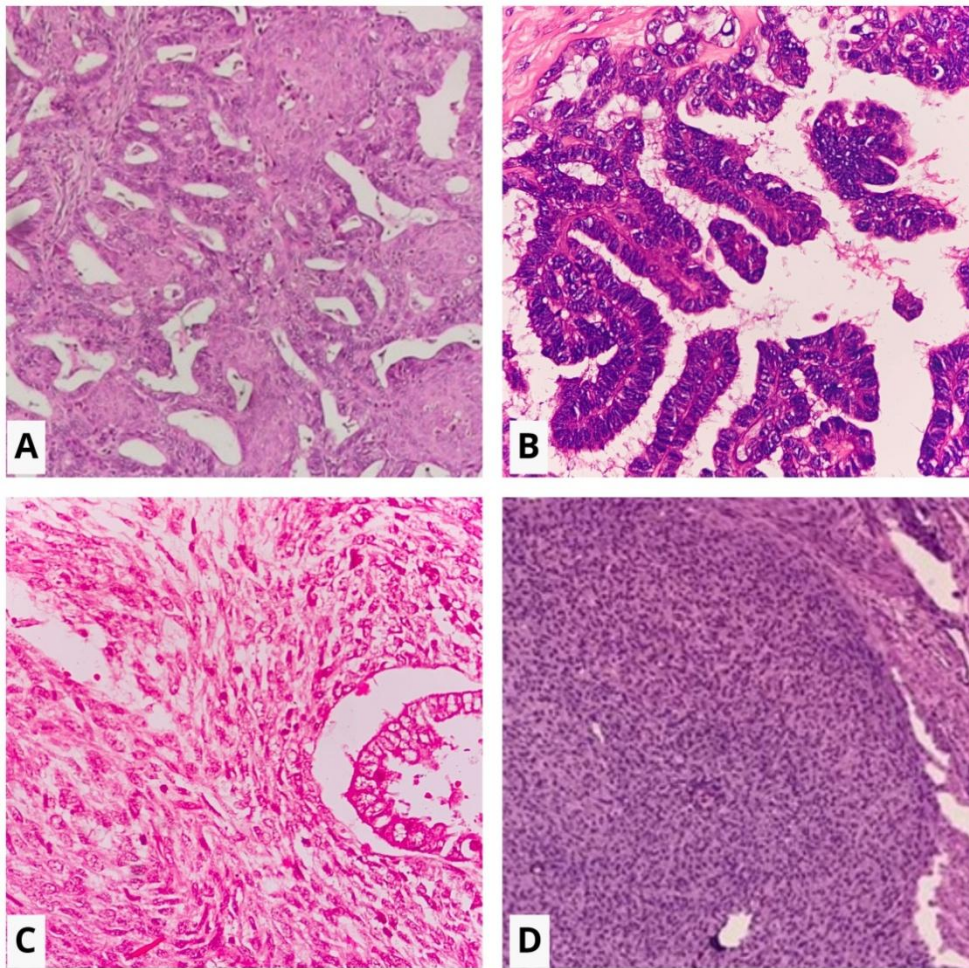


Fig. 4. Microscopy, 40X, H&E stain – Endometrioid adenocarcinoma (A), Serous carcinoma (B), Carcinosarcoma (C), Endometrial stromal sarcoma (D)

Carcinosarcoma, also known as malignant mixed müllerian tumor is a biphasic tumour composed of high grade carcinomatous and sarcomatous elements. They account for less than 5% of all uterine tumors [13]. Carcinosarcoma occurs mostly in post-menopausal women [13]. The 3 cases of carcinosarcoma included in this study showed, malignant epithelial component was of endometrioid type and the sarcomatous component was of a high grade nonspecific sarcoma with no heterologous elements.

Endometrial stromal tumors usually occur in middle-aged women with an average age of 45 years [14]. Endometrial stromal tumors classified into endometrial stromal nodule, low grade endometrial stromal sarcoma and high grade endometrial stromal sarcoma [14]. Endometrial stromal nodule is differentiated from endometrial stromal sarcomas based on the presence of myometrial invasion [14]. We received a single

case of high grade endometrial stromal sarcoma within the study period [15-21].

4. CONCLUSION

From the study conducted it was evident that a vast majority of malignancies of the uterine corpus occur in the 5th decade of life. Epithelial tumors were most frequently encountered than other tumors. Among the epithelial tumors endometrioid adenocarcinoma was the most common type. The prognosis of the patients with malignant tumors of uterine corpus depends on stage, grade, myometrial invasion, tumor size and lymphovascular invasion etc. Clinical findings in these tumors are not specific, so Histopathological examination plays a vital role in diagnosing and assessing the prognosis of these tumors. Classifying these tumors according to the recently proposed molecular classification will aid in patient specific targeted therapy.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical clearance- institutional ethics committee approval was obtained.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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