

Clinicopathological Outcome of Uterine Clear Cell and Pappillary Carcinoma at AHRCC Ongoing Study

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Abstract- OBJECTIVE –The objectives of this study were to analyse clinico-pathological determinants of the clear cell and uterine papillary serous cell carcinoma.

Material methods- A cohort of patients diagnosed and underwent complete surgical staging for upsc and clear cell of the endometrium from 2010- 2018 were viewed. The significance of the independent variables were calculated by chi-square. The multivariate regression analysis of the factors influencing the nodal status.

RESULTS- We could analyse that both clear cell and upsc, was prevalent in 61 yr age . They are associated with comorbidities. They present with a higher grade(G3) , pre-op imaging , showed more number cases with et of 15 mm. The nodal status was significantly affected by myo-invasion > 50% lvs in clear cell carcinoma. Where as the lvs+, adnexa +, omentum+, peritoneal cytology+, myo-invasion > 50% , was significantly found associated with a positive nodal status in uterine papillary serous cancer.

Index Terms- UPSC – uterine papillary serous cell carcinoma, ET – endometrial thickness, Mmmt- malignant mixed muellerian tumor, LVSI - lymphovascular space invasion

I. INTRODUCTION

Clear cell carcinoma of the uterus is the rare subtype accounting for 1-6% of uterine cancers, is characterised histologically by clearing of cytoplasm(1). They present in higher stage .comprehensive surgical staging is recommended in all clear cell carcinoma. Aggressive , multimodality of treatment (Including surgery, chemotherapy, and /or radiation therapy), is recommended as compared to endometrioid carcinomas. Clear cell carcinomas are genetically distinct from endometrioid cancer. Clear cell tumors show similar gene expression profiles regardless of origin.(2)

- Uterine papillary serous cancer is the most common prototype of type II endometrial cancer, which accounts for only 10% of all endometrial cancer but is responsible for 40% death in endometrial cancer(3). The most common symptom diagnosed in UPSC, as is for women with endometrial cancer , is post menopausal bleeding .This is usually mixed with grade 3 endometrioid and

clear cell .UPSC tends to occur in older women .Increase risk is seen african american women .Upsc is highly aggressive and more likely to be presenting in advanced stage iii and iv.(4). Women , on tamoxifen for breast cancer is at a risk of upsc. Association between BRCA and upsc , is evident in the emerging data. There is a precursor lesion for, but it may present late, at advanced stage There are some similarities in serous ovarian cancer and UPSC such as tendency for peritoneal carcinomatosis, presenting with ascites, upper abdominal involvement and early lymph node involvement (5). The 5 yr survival for patients with upsc has been reported from 18% to 27%, which is probably due to extra uterine spread in 60 - 70% of the patients at diagnosis(6) .

- Although clear cell serous cancer constitutes less than 10 % of the endometrial cancers, they account 50% of recurrences and disease related deaths. The most common presentation in clear cell carcinoma is post menopausal bleeding. There is association of BRCA , ARID1A with clear cell cancer. There is increase frequency of clear cell , post radiation.(7) Diagnosis and work up endometrial biopsy, by pipelle has sensitivity of 99 % .Ultrasound not reliable for upsc(8)

II. MATERIAL- METHODS-

Inclusion criteria- 1. all cases of clear cell and upsc of the endometrium

- Exclusion - 1.all endometrioid
2.mmmt
3. sarcomas
4. cervical cancers

the clinical and pathological data were reviewed at ahrcc. all the specimen were evaluated by pathologists. The patients underwent the surgical staging, histopathology was analysed. Their comorbidities, preop imaging with respect to endometrial thickness were taken into consideration. The age , parity, menopausal status and presenting symptoms. the chi –square and the multivariate regression analysis done using the SPSS

Descriptive statistics for Clinical part	
Total case = 39	
Overall Median (range) age in years = 61(36-88)	
Overall Median (range) imaging in mm = 15(3.5-34)	
Clinical part for clear cell	
Variable	n (%)
Age	21
Median (range) in years 60 (45-70)	
<60 year.....	08(38)
≥60 year.....	13(62)
O/H	21
Multipara.....	17(81)
Nullipara.....	04(19)
M/H	21
Menopause attended.....	21(100)
Menopause not attended.....	00(00)
Comorbidity	21
Present.....	09(42.9)
1.Hypertention.....	05
2.Diabeties.....	03
3.Both.....	01
Absent.....	12(57.1)
Imaging	21
Median (range) in mm 15 (3.5-23)	
<15 mm.....	10(47.6)
≥15 mm.....	11(52.4)
Presently symptoms	
Pr. b.....	21
Present.....	20(95.2)
Absent.....	01(04.8)
Pmwd.....	21
Present.....	02(09.5)
Absent.....	19(90.5)
pmod.....	21
Present.....	00(00)
Absent.....	21(100)

FIG-1

DESCRIPTIVE STATISTICS OF THE CLINICAL DETERMINANTS OF CLEAR CELL CARCINOMA UTERUS

Clinical part for papillary serous
 Click to add text

variable	n (%)
Age	17
median (range) in years	61.5 (36-88)
<61.5 year	06(35.3)
≥61.5 year	11(64.7)
O/H	17
Multipara	13(76.5)
Nullipara	04(23.5)
M/H	17
Menopause attended	16(94.1)
Menopause not attended	01(5.9)
Comorbidity	17
Present	08(47)
1.Hypertention	02
2.Diabeties	04
3.Both	02
Absent	09(53)
Imageing	17
median (range) in mm	14.5 (3.5-34)
<14.5 mm	09(53)
≥14.5 mm	08(47)
Presently symptoms	
Pmb	17
Present	17(100)

Fig-2 DESCRIPTIVE STATISTICS OF CLINICAL PART OF PAPPILARY SEROUS CANCER OF UTERUS

Descriptive statistics for Pathological part

Total case = 39	
Overall Median (range) Tumor size in cm = 03 (0.3-10)	
Overall median (range) Endometrial Thickness in mm = 15 (3.5-34)	
Pathological part for clear cell	
Variable	n (%)
Node	21
+ve node	12 (57)
-ve node	09 (43)
GRADE	21
G1	00 (00)
G2	07 (33)
G3	14 (67)
Myometrial invasion	21
<50%	09(42.8)
≥50%	12 (57.2)
Cervical Extension	21
Yes	02 (9.5)
No	19 (90.5)
Tumor size(in cm)	21
<3 cm	12 (57.2)
≥3 cm	09 (42.8)
Lymphovascular invasion	21
Yes	02 (9.5)
No	19 (90.5)
Omentum	21
Yes	02 (9.5)
No	19 (90.5)
Other intra abdominal organs	21
Yes	00 (00)
No	21 (100)
Peritoneal cytology	21
Yes	06 (28.6)
No	15 (71.4)
Adnexa	21
Yes	04 (19)
No	17 (81)
Endometrial Thickness	21
< 15 mm	04 (19)
≥15 mm	17 (81)

FIG 3 – DESCRIPTIVE STATISTICS OF THE PATHOLOGICAL PART OF CLEAR CELL CARCINOMA OF UTERUS.

Pathological part for papillary serous

Variable	n (%)
Node	18
+ve node	07 (38.9)
-ve node	11 (61.1)
GRADE	18
G1	00 (00)
G2	06 (33.33)
G3	12 (66.67)
Myometrial invasion	18
<50%	09 (50)
≥50%	09 (50)
Cervical Extension	18
Yes	04 (22.2)
No	14 (77.8)
Tumor size(in cm)	18
<3 cm	07 (38.9)
≥3 cm	11 (61.1)
Lymphovascular invasion	18
Yes	09 (50)
No	09 (50)
Omentum	18
Yes	05 (27.8)
No	13 (72.2)
Other intra abdominal organs	18
Yes	01(5.5)
No	17 (94.5)
Peritoneal cytology	18
Yes	05 (27.7)
No	13 (72.3)
Adnexa	18
Yes	06 (33.3)
No	12 (66.6)
Endometrial Thickness	18
< 15 mm	09 (50)
≥15 mm	09 (50)

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FIG4 DESCRIPTIVE STATISTICS OF THE PATHOLOGICAL PART OF UPSC

Univariate analysis for Pathological part

For **clear cell**

Variable	χ^2 -value	p-value
Age	2.036	0.154
Grade	0.000	1.000
Myometrial invasion	3.646	0.056
Cervical Extension	1.658	0.198
Tumor size (in cm)	0.016	0.899
Lymphovascular invasion	3.646	0.056
Omentum	1.658	0.198
Peritoneal cytology	2.353	0.125
Adnexa	0.643	0.422
Endometrial Thickness (in mm)	1.289	0.256

N.B.: Statistical significance ($p < 0.05$) i.e, 5% level of significance, χ^2 : chi-square, Total no of cases = 21.

FIG-5 UNIVARIATE ANALYSIS OF THE FACTORS AFFECTING THE NODAL STATUS UTERINE CLEAR CELL CARCINOMA

For **papillary serous**

Variable	χ^2 -value	p-value
Age	0.234	0.629
Grade	5.727	0.017
Myometrial invasion	5.844	0.016
Cervical Extension	0.417	0.518
Tumor size (in cm)	0.177	0.732
Lymphovascular invasion	5.844	0.016
Omentum	4.923	0.026
Peritoneal cytology	4.923	0.026
Adnexa	7.481	0.006
Endometrial Thickness (in mm)	2.104	0.147

N.B.: Statistical significance ($p < 0.05$) i.e, 5% level of significance, χ^2 : chi-square, Total no of cases = 18.

FIG -6 UNIVARIATE ANALYSIS OF FACTOR DETERMINING THE NODAL STATUS OF PAPPILARY SEROUS CANCER

Multivariate Analysis of Pathological part

For clear cell

Variables	OR	95% CI		p-value
		Lower	Upper	
Age (in years)				
<60	1			
>60	3.869	.589	25.435	.159
Grade				
Grade-2	1			
Grade-3	1.234	.175	8.710	.833
Myometrial invasion				
<50%	1			
≥50%	11.043	.980	124.383	.052
Tumor size (in cm)				
<2	1			
≥2	7.513	.125	450.375	.334
Lymphovascular invasion				
no	1			
yes	6.000	.893	40.306	.065
Peritoneal cytology				
no	1			
yes	5.714	.532	61.410	.150
Adnexa				
no	1			
yes	5.519	.125	244.172	.377
Endometrial Thickness (in mm.)				
<15	1			
≥15	.357	.059	2.159	.262

N.B.: Statistical significance (p<0.05) i.e, 5% level of significance,
 Statistical significance (p<0.1) i.e, 10% level of significance, Total no of cases = 21

N.B.: None of the above significant at 5% level but Myometrial invasion and Lymphovascular invasion are significant at 10% level.

FIG-7MUTIVARIATE ANALYSIS OF FACTORS INVOLVING THE NODAL STATUS OF CLEAR CELL CARCINOMA

For papillary serous

Variables	OR	95% CI		p-value
		Lower	Upper	
Age (in years)				
<60	1			
≥60	.625	.093	4.222	.630
Myometrial invasion				
<50%	1			
≥50%	16.000	1.315	194.623	.030
Cervical Extension				
no	1			
yes	.440	.036	5.435	.522
Tumor size (in cm)				
<2	1			
≥2	3.373	.161	70.557	.433
Lymphovascular invasion				
no	1			
yes	16.000	1.315	194.623	.030
Omentum				
no	1			
yes	13.333	1.048	169.557	.046
Peritoneal cytology				
no	1			
yes	13.333	1.048	169.557	.046
Adnexa				
no	1			
yes	30.080	1.616	559.773	.022
Endometrial Thickness (in mm)				
<15	1			
≥15	.256	.015	4.331	.345

N.B.: Statistical significance ($p < 0.05$) i.e. 5% level of significance. Total no of cases = 18.

FIG -8multivariate analysis of the factors influencing the nodal status in papillary carcinoma

III. RESULTS

Our study analysis revealed that maximum cases of clear cell in the median age range of 61 yrs, 13 (62%) more than 60yrs. Most of the clear cell associated with co-morbidities 21 cases(100%). 17(81%) were multiparous. They usually present with post-menopausal bleeding 20(95.2%), few presented with watery discharge 2(9.5%) Pre-op imaging revealed, endometrial thickness of 15 mm was detected in 47.5%, range of minimum of 3mm to a maximum of 34 mm recorded. 14(57%) showed a grade 3. The nodal positive status 12(57%). On multi-variate analysis, lymphovascular space invasion and myo-invasion was found to statistically significant, with a p-value. **.052 and .065** respectively that affected the nodal status in clear cell carcinoma. UPSC was, more prevalent in age group of 61 yrs, multiparous 13(76%), median of 61.5 yrs. Most of them was associated with co-morbidities 8(47%), 94% attained menopause and presented with postmenopausal bleeding(100%). The pre-op imaging showed a median of endometrial thickness of 14.5 mm, 9 (53%) the minimum of 3.5 mm to a maximum of 34mm were recorded. (66%) 12 cases presented with grade 3 **11(61.7%)** were nodal status positive in UPSC. The myo-invasion >50%, LVSI+omentum+ peritoneal cytology+, adnexa+, was significantly associated with nodal positivity in UPSC in multivariate regression analysis with a p value of **.03, .03, .046, .046, .022.**

Conclusion – Most of the cases of upsc and clear cell in our study group present in postmenopausal age group, with post-

menopausal bleeding. All cases of clear cell were associated with comorbidities. Although the spectrum of presentation varied from watery discharge to bleeding in clear cell. The range of endometrial thickness varies from 3mm to 34 mm. In our study 57% case clear cell presented in stage III. The nodal status was significantly influenced by lvsi and myo invasion.

All cases of upsc presented with postmenopausal bleeding. maximum number cases had the co-morbidities. 61.7% presented in stage III. The factors such as myoinvasion, lvsi, omentum+ adnexa+, positive peritoneal washings significantly influenced the nodal positivity of upsc.

- **Purpose** – Was to present the clinicopathological features and analyses of the factors influencing the lymphnode, Due to the rarity of the UPSC, the clinicopathological of the patients with upsc is poorly understood. Further more randomized clinical trials aiming at exploring standards of treatment for clear cell and papillary serous cancer

REFERENCES

[1] Creaseman WT, Odicino F, Maisonneuve P et al. carcinoma of the corpus uteri FIGO 26 TH a annual report on the results of treatment in gynaecological cancer.
[2] A, b Olaiwaiye and D.M Boruta (management of women with clear cell endometrial cancer

- [3] Benito V . LUBRANO a ETAL, INTERNATIONAL journal of gynaec – oncology
- [4] solmaz u, mat e ekin , Etal , inter journal surgery
- [5] DEL , CARMAN MG, birrier M a review literature
- [6] huang cy, tang yh (tgog) agroup
- [7] CREASMAN WT, KOHLER mf. Odicino F, ETAL J.GYNAECOLOGY ONCOLY
- [8] martinellif, ditto a, j ., of clinical pathology in uterine malignancies guide clinical practice

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