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Clinicopathological Outcome of Uterine Clear Cell and Pappilary 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 pappilary serous cell carcinoma.
Material methods- A cohort of patients diagnosed and underawent complete surgical staging for upsc and clear cell of the endometrium from 2010- 2018were viewed.The significance of the independent variables were calculated by chi-square.The multivariate regression analysis of the factors influencing the nodal staus.
RESULTS- We could analyse that both clear cell and upsc, was prevalent in 61 yr age . They are associated with co-morbidities. They present with a higher grade(G3) , pre-opimaging , showed more number cases with et of 15 mm. The nodal status was significantly affected by myo-invasion> 50% lvsi in clear cell carcinoma. Where as the lvsi+, adnexa +, omentum+ , peritoneal cytology+, myo-invasion>50% , was significantly found associated with a positive nodal status in uterine pappilary serous cancer.
INDEX TERMS – UPSC – uterine pappilary serous cell carcinoma
ET – endometrial thickness
Mmmt- malignant mixed muellrian tumor
LVSI - lymphovascular space invasion

I. INTRODUCTION –

Clear cell carcinoma of the uterus is the rare subtype accounting for1-6% of uterine cancers, is characterised histologicaly 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 endometroid carcinomas. Clear cell carcinomas are geneticaly distinct from endometroid cancer. Clear cell tumors show similar gene expression profiles regardless of origin.(2)

- Uterine pappilary 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 endometral 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 endometroid and clearcell .UPSC tends to occur in older women .Increase risk is seen africo american women .Upsc is highly aggressive and more likely to be presenting in advanced stage iii and iv.(4). Women , on tamoxifen for breat cancer is at a risk of upsc. Asscociation 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 abdomnal 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. Ther is association of BRCA , ARIDIA with clear cell cancer.There is increase frequency of clear cell , post radiation.(7) Diagnosis and work up endomerial biopsy, by pipelle has sensitivity of 99 %.Ultrasound not reliable for upsc(8)

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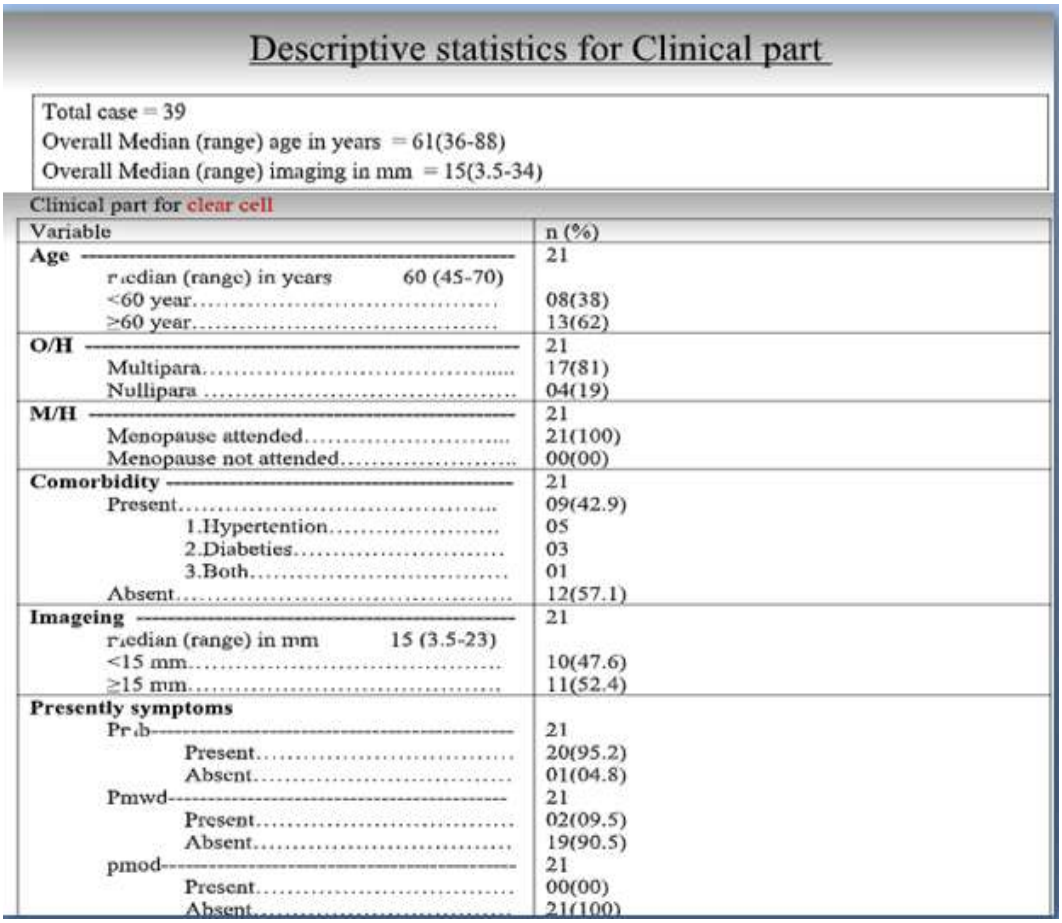
II. MATERIAL- METHODS-

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

- Exclusion - 1.all endometroid

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 co-morbidities, preop imaging with respect to endomerial thickness were taken into consideration. The age , parity, menopausal staus 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)
Imageing	21
Median (range) in mm 15 (3.5-23)	
<15 mm	10(47.6)
≥15 mm	11(52.4)
Presently symptoms	
Prob	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

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Clinical part for papillary serous

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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	(47.6)
≥15 mm	(52.4)

Page 1 / 2

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

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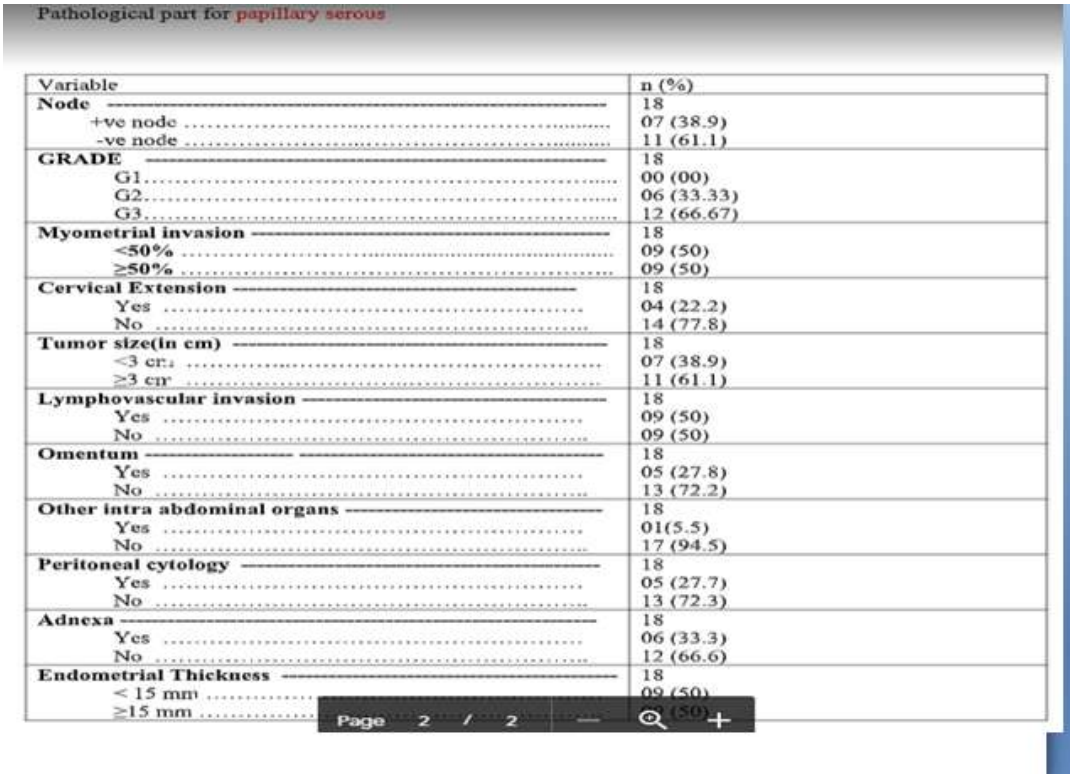
Volume 3, Issue 2,Mar-Apr 2021 pp 202-208 www.ijdmsrjournal.com ISSN: 2582-6018



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	(50)

Page 2 / 2

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

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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

Multivari[illegible] analysis for 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% [illegible]

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

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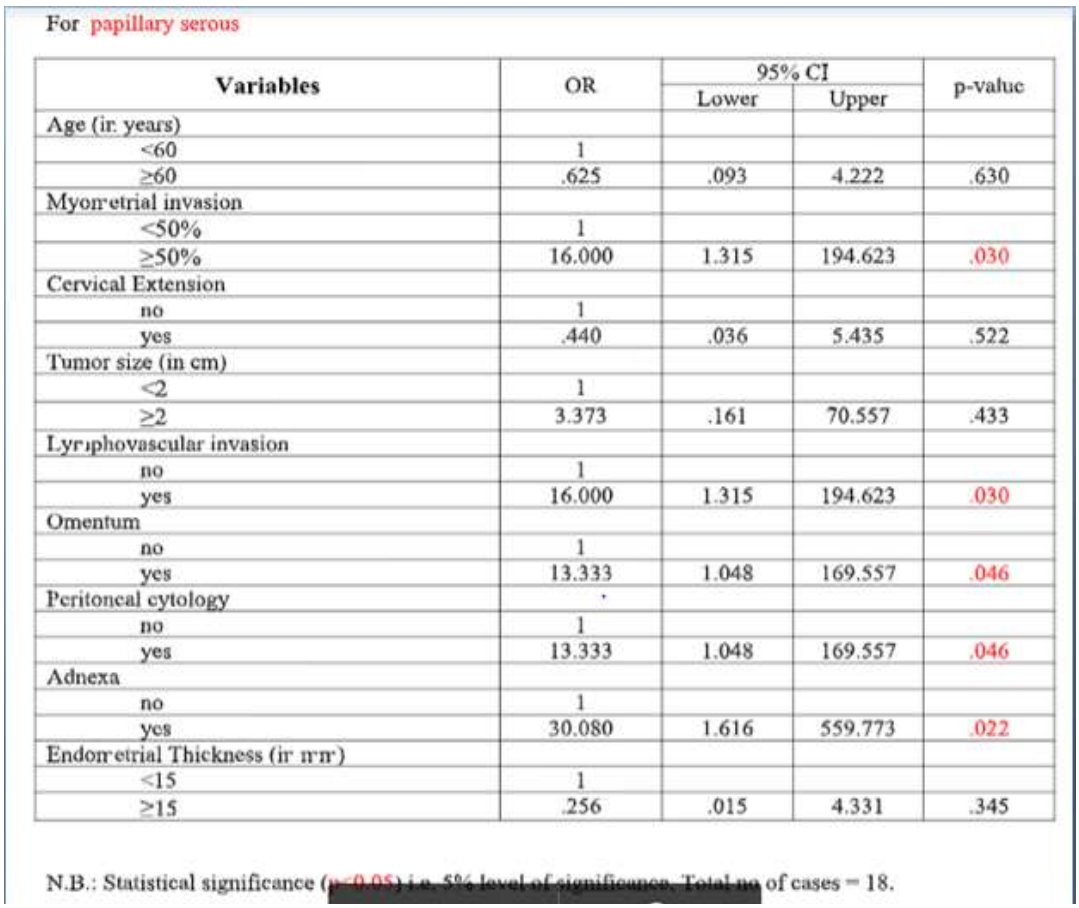

For papillary serous

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 pappilary 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(09.5%) Pre –op imaging revealed ,endometrial thickness of 15 mm was detected in 47.5% , range of minimimum 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, multiparous13(76%), median of 61.5 yrs. Most of them was associated with co-morbidities8(47%),94% attained menopause and presented with post menopausal 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 grade3**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 multi-variate regression analysis with a p value 0f**.03,03,.046,.046, .022.**

IV. CONCLUSION

Most of the cass of upsc and clear cell in our study group present in postmenopausal age group, with post- menopausal bleeding. All cases of clear cell were asscociated with comorbidities. Although the spectrum of presentation varied from watery discharge to bleeding in clear cell.The range of endometrial thickess varies from 3mm to 34 mm. In our study 57% case clear cell presented in stage III. The nodal staus 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+ adnexal+, 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 pappilary serous cancer

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