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A study of immuno-histochemical markers estrogen receptor and progesterone receptor in ovarian neoplasms

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Abstract
Introduction: Among genital malignancies, Ovarian Cancer has the most increased mortality rate. ER and PR expression levels depend on tumour histologic grade and stage of disease and are variable between tumours of the same grade.
Aims: To study the clinicopathological parameters in ovarian tumours with reference to age, histologic type and grade and their correlation with ER and PR status.
Methodology: The prospective study of 2 ½ years was conducted on 100 resected ovarian tumour specimens from June 2017 to December 2019 received in the Department of Pathology, JLN Medical College, Ajmer. Sections were stained and examined for presence of ovarian tumour, Histological type, Grade and for ER and PR status, immunohistochemistry was done.
Results: Out of 100 cases, 72 cases were benign, 03 cases were borderline and 25 cases were malignant. 60% were of surface epithelial neoplasm, followed by germ cell tumors. Serous tumors were most common among all epithelial tumors (61%). Malignant cases showed maximum positivity with ER and PR as 61.76% and 68% respectively. ER and PR positivity in serous epithelial tumors was 76.47% and 84% and in mucinous tumors was 20.59% and 12% respectively. ER and PR positivity in endometrioid tumor was 2.94% and 4% respectively. Majority of positive ER and PR receptors was observed in Age groups of >40 years as 64.71% and 64% respectively. ER and PR positivity seen in higher grade and stage tumors as 76.19% and 76.47% in grade 3 and stage 3 tumors respectively.
Conclusion: The higher expression of ER and PR is associated with progression of invasive cancer, higher grade and stage of ovarian tumors, higher age group, and mulitparity.

Keywords: ovarian cancer, immunohistochemistry, genital malignancies

Introduction

Ovarian cancer is one of the most frequent cancers in female patients [1]. Among genital malignancies, Ovarian Cancer has the most increased mortality rate. The low survival is due to the lack of symptoms in early stages. Therefore, the diagnosis is delayed and the prognosis is poor. About 80% are benign, these occur mostly in young women between the ages of 20 and 45 years. Borderline tumours occur at slightly older ages. Malignant tumours are more common in older women between the ages of 45 and 65 years. The most common symptoms include: Bloating, pelvic or abdominal pain, urinary symptoms such as urgency or frequency, and heaviness in abdomen [2]. The initial assessment of patients with suspected ovarian cancer, following the initial history-taking, physical examination, laboratory results, Pelvic ultrasound, preferably using colour Doppler are done. It has been shown that ER and PR expression levels depend on tumour histologic grade and the stage of the disease, and are variable between tumours of the same grade [3]. The ER and PR expression levels correlate with ovarian cancer patients' survival. TheHer-2/Neu gene is amplified and/or over expressed in 25%-30% of human ovarian cancers and is associated with progression of invasive cancer, poor prognosis and resistance to chemotherapy. Immunohistochemistry is helpful in vast number of cases to resolve the diagnostic dilemma [4].

Aims and objectives

To study the clinicopathological parameters in ovarian tumours with special reference to age, histologic type and grade and evaluate the role of immune-histochemical profile of ER and PR in ovarian neoplasms and also correlate the results of immunohistochemistry with clinicopathological parameters.

Methodology

The prospective study of 2 and ½ years was conducted on 100 surgically resected ovarian tumours samples from June 2017 to December 2019 received in the Department of Pathology, Jawahar Lal Nehru Medical College and Associated Groups of Hospital, Ajmer. Non-neoplastic lesions and metastatic lesions of ovary were excluded. On receiving the specimens in 10% neutral buffered formalin, a systematic gross examination was performed. Gross features like size, shape, colour, external appearance on cut section and contents were noted. The

tumors were cut at various levels and adequate tissue slice (<5mm) submitted which were routinely processed 3 to 5micron sections were cut from paraffin embedded blocks. These sections were routinely stained with Harri's H & E stain and was examined for presence of ovarian tumour, Histological type, and grade. For Immuno-histochemistry, the primary antibody used was Estrogen receptor and Progesterone receptor along-with positive and negative controls. The positive control for ER and PR, fibroadenoma tissue section was taken. The IHC staining was studied in correlation to clinicopathologic factors of ovarian tumours which include age, laterality, parity, histological type, tumour grade, tumour stage.

Results

A total of 100 ovarian tumors were studied, out of which 72% are benign, 3% borderline and 25 % malignant. Out of 100 studied ovarian tumors, 60% are epithelial tumors, 33% are germ cell tumors, and 7% are sex cord tumors. Out of epithelial tumors, 55% tumors are benign, 5% are borderline and 40% are malignant. Out of germ cell tumors, 96% are benign and 4% are malignant. Out of sex cord tumors, 100% are benign tumors. Serous tumors are most common among all epithelial tumors (61%). Out of total 37 serous tumors, 49% are benign. Serous adenocarcinomas are the most common malignant tumor accounting for 32% of all epithelial tumors and 51% of serous tumors. Out of total 21 mucinous tumors, 72% are benign, 14% are borderline and 14% are malignant. One case of endometrioid tumor and poorly differentiated tumor is present. Majority (96%) of germ cell tumors are mature cystic teratoma, 4% are dysgerminoma but yolk sac tumors and malignant mixed germ cell tumors are not found.

Among sex cord stromal tumors, most common tumor is fibroma (72%) followed by granulosa cell tumor (14%) and stromal Leydig cell tumor (14%). None of the case of granulosa theca cell tumor is found. Out of total positive Estrogen receptors (34), 61.76% was positive in malignant cases followed by 32.35% in benign cases and rest 5.88% in Borderline cases. While out of total positive Progestrone receptors (25), 68% was positive in malignant cases followed by 32% in benign cases. ER positivity in serous epithelial tumors (Figure 1 & 3) is 76.47%, in mucinous tumors is 20.59% and in endometrioid tumor is 2.94%. PR positivity seen in serous tumors (Figure 2 & 4) is 84%, in mucinous tumors is 12% and in endometrioid tumor is 4%. Rest brenner, sex cord stromal tumors and mature cystic teratomas do not show any ER and PR positivity. No significant difference was observed of Status of ER and PR and classification of ovarian tumors (Table 1).

Table 1: Status of ER and PR in ovarian tumors

	ER		PR		P value LS
	No.	%	No.	%	
Serous (37)	26	76.47	21	84	
Mucinous (21)	7	20.59	3	12	
Endometrioid (1)	1	2.94	1	4	0.697NS
Brenner (0)	0	0.00	0	0.00	
SCST (7)	0	0.00	0	0.00	
MCT (32)	0	0.00	0	0.00	
Total	34	100	25	100	

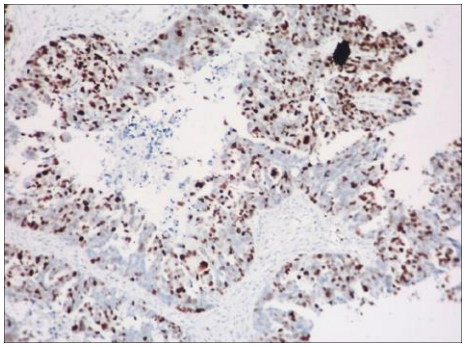

Fig 1: Photomicrograph of malignant papillary serous tumour showing ER positivity with IHC score 6 (400x)

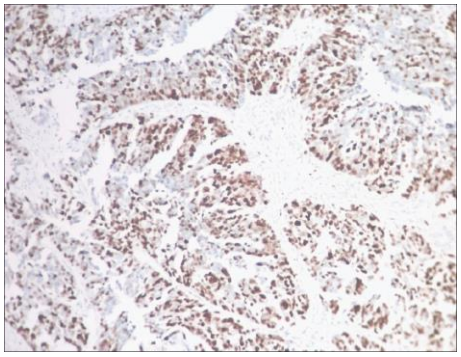

Fig 2: Photomicrograph of malignant papillary serous tumour showing PR positivity with IHC score 6 (400x)

Epithelial tumors and Sex cord tumors were significantly more in >40 years of age groups (70% and 57.14% respectively) as compared to Germ cell tumors which was significantly more (87.88%) in <40 years of age groups.

Majority of positive ER and PR receptors was observed in Age groups of >40 years as 64.71% and 64% respectively (Table 2).

Table 2: Status of ER and PR According to Age

	ER		PR		P value LS
Age group	No.	%	No.	%	
<40 yrs	12	35.29	9	36	0.233NS
>40 yrs	22	64.71	16	64	
Total	34	100	25		

Chi-square = 2.998 with 2 degrees of freedom; P = 0.223

Although the unilateral tumors were more in epithelial tumors (60%) and Germ cell tumors (72.73%) as compared to Sex cord tumors (42.86%).

Epithelial tumors (81.67%) and sex cord tumor (71.43%) was statistically more significant in multipara as compared to Germ cell tumors (24.24%), whereas Germ cell tumors are common in nullipara women. Bilateral Positivity of the receptors was observed in majority of cases.ER positive were 64.71% bilateral, while PR receptors were 64%. Positivity of the receptors was observed in majority of multipara cases. ER positive were 85.29% of Multipara, while PR positive were 88% of Multipara. Out of total malignant surface epithelial tumors, serous tumors were 36.84% as grade 2, while 63.16 % as grade 3.

Malignant mucinous and endometrioid tumor were 100% as

grade 3. ER and PR positivity seen in higher grade tumors as 76.19% and 76.47% in grade 3 tumors respectively (Table 3). Out of total malignant surface epithelial tumors, serous tumors were 36.84% as stage 2, while 63.16 % as stage 3. Malignant mucinous and endometrioid tumor were 100% as stage 3. ER and PR positivity seen in higher stage tumors as 76.19% and 76.47% in stage 3 tumors respectively.

Table 3: Distribution of Malignant Epithelial Tumors According to Grade of Tumor

Malignant Epithelial Tumors (n= 24)		Grade of Tumor								
		I		II		I	II	Total	P value LS	
		No	%	No	%	No	%	No	%	
1	Serous tumors	0	0	7	36.84	12	63.1 6	19	100	0.289NS
		0		0		5				
2	Mucinous tumors	0	0	0	0	3	100	3	100	0.611NS
		0		7		14				
3	Endometrioid tumors	0	0	0	0	1	100	1	100	0.640NS
		0		7		16				
	Total	0	0	7	29.17	17	70.8 3	24	100	

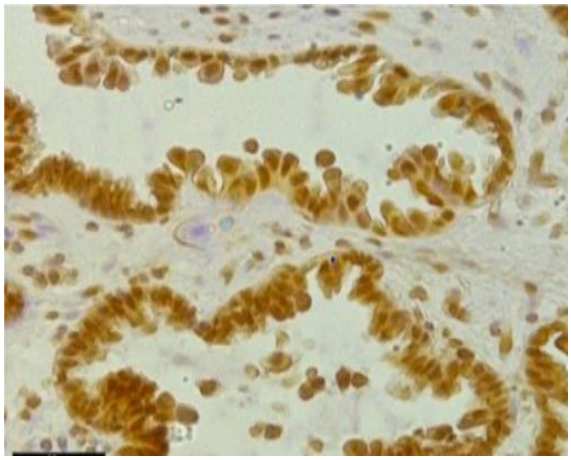

Fig 3: Photomicrograph of high grade serous tumour showing ER positivity with IHC score 8, (400x)

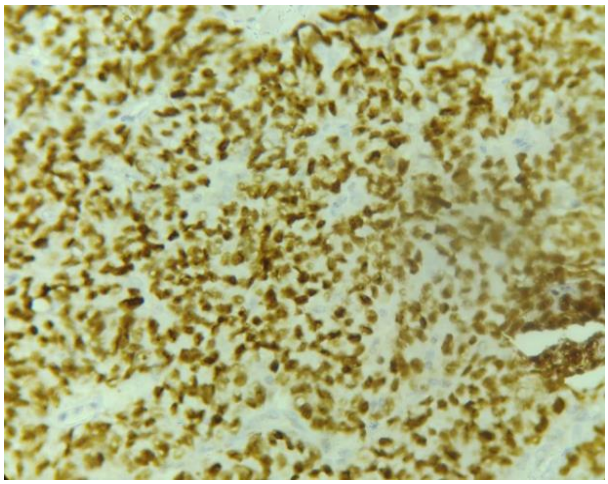

Fig 4: Photomicrograph of malignant serous tumour showing PR positivity with IHC score 8 (400x)

Discussion

In our study, 72 cases are benign, 03 cases are borderline and 25 cases are malignant. Among the various neoplasms studied, 60% are of surface epithelial neoplasms, followed by germ cell tumors accounting for 33% of all tumors, sex cord stromal tumors accounting 7% of all tumors. Our results are comparable with results of study done by Bhagya Lakshmi *et al* (2016) [5] on 42 ovarian tumors, where surface epithelial tumors constituted around 59.5% of all tumors. Similarly, Lubna khan *et al* (2014) [6] studied 80 operated cases of ovarian tumors and found that benign lesions were more common (75%) the malignant lesions (25%). In our study serous cyst adenocarcinoma was the most common malignant tumor among all epithelial tumors accounting for 37.5% of all epithelial tumors and 54.5% of all serous tumors. Bhagya Lakshmi Atla (2016) [5] and Krigman *et al* (1994) [7] gave similar results with incidence of 59% and 36% among all epithelial tumors respectively. Serous cystadenoma was the commonest benign tumor (45%). Overall surface epithelial carcinomas were responsible for 52 % and 70 % of all malignant lesions among which serous cyst adenocarcinoma was the most common (45%).[5] In our study, out of total positive Estrogen receptors (34), 61.76% was positive in malignant cases followed by 32.35% in benign cases and rest 5.88% in Borderline cases. While out of total positive Progestrone receptors (25), 68% was positive in malignant cases followed by 32% in benign cases. According to Pooja S Naik *et al* (2015) [8], the expression of ER was more in malignant tumors (81.25%) than borderline (75%) and benign (24.39%). This is parallel to study done by Sylvia *et al* [9]. In our study, ER positivity in serous epithelial tumors is 76.47%, in mucinous tumors is 20.59% and in endometrioid tumor is 2.94%. PR positivity seen in serous tumors is 84%, in mucinous tumors is 12% and in endometrioid tumor is 4%. Rest brenner, sex cord stromal tumors and mature cystic teratomas do not show any ER, PR and Her2/neu positivity. MT Sylvia *et al* (63.6%) [10] Reported higher expression for PR while Shilpa *et al* (27.5%) [11] reported lower PR expression in their study, but still both the studies had higher PR positivity than our study. In our study, Majority of positive receptors was observed in Age groups of >40 years as ER 64.71% and PR 64% respectively. According to Bhayga Lakhsmi Atla *et al* (2016) [5], ER and PR showed higher expression in age group above 40 years. Bilateral Positively of the receptors was observed in majority of cases. ER positive were 64.71% bilateral, while PR receptors were 64%. Positivity of the receptors was observed in multipara cases. ER positive were 85.29% of Multipara, while PR receptors were 88% of Multipara. Our study is comparable with Bhayga Lakhsmi Atla *et al* (2016) [5] and MT Sylvia *et al* (2012). [10] in our study, we observed that ER and PR positivity seen in higher grade tumors as 76.19% and 76.47% in grade 3 respectively. Majority of ER and PR positivity seen in higher stage tumors as 76.19% and 76.47% in stage 3 respectively. Our study is comparable with Bhayga Lakhsmi Atla *et al* (2016) [5] and MT Sylvia *et al* (2012) [10] showing similar results. As per Bhayga Lakhsmi Atla *et al* (2016) [5] majority of the ovarian carcinomas were of grade 2 and stage 3. Most of these high grade tumors had higher association with ascites suggesting an aggressive tumor type and advanced stages

which is similar to the study by Hellstrom *et al*. [12]. Malignant tumors, serous group, and grade 3 tumors had significant higher proliferation index similar to previous results.

Conclusion

Prognosis and management of ovarian cancer are influenced by classic variables such as histologic type and grade, parity, status of hormone receptors- ER and PR. In conclusion, ER and PR status correlates well with histopathological grading and other clinic-pathological parameters. Hence, immunohistochemical assessment of ER and PR status along with histopathological grading and staging will guide the clinicians to make correct choice of treatment protocols.

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References

1. Merino MJ, Jaffe G. Age contrast in ovarian pathology. Cancer, (supplement), 1993; 71:537-44.
2. Powell CB, Kenley E, Chen, *et al*. Risk reducing salpingo-oophorectomy in BRCA mutation carriers: role of serial sectioning in the detection of occult malignancy. J Clin-Oncol. 2005; 23:127-132.
3. Nadji M, Gomez-Fernadez C, Ganju-Azar P, Morales RA. Immunohistochemistry of estrogen and progesterone receptors reconsidered. Am J Clin Pathol. 2005; 123(1):21-27.
4. The Ovary. In Rosai J, editor. Rosai and Ackerman's surgical pathology, 9th edition, 2004, 2.
5. Bhagyalakshami atla, Rema nair Sarkar, manasa rasaputra. Clinicopathological and IHC study (estrogen receptors, progesterone receptor, Her2/neu) in malignant ovarian tumors. Atla B *et al*. Int J Res Med Sci. 2016; 4(4):1068-1073.
6. Role of immunohistochemistry in ovarian tumors. Lubna Khan, Amita Arora, Asha Agarwal, Chayanika Pantola, Sanjay Kala, Rahul K Rathi. Journal of Evolution of Medical and Dental Sciences. 2014; 3(11):2814+.
7. Krigman H, Bentley R, Robboy SJ. Patholgy of epithelial ovarian tumors. Clinical obstet gynecol. 1994; 37(2):475-491.
8. Epithelial ovarian tumors: Clinicopathological correlation and immunohistochemical study. Pooja S Naik, Sanjay Deshmukh, Siddhi Gaurish Sinai Khandeparkar, Avinash Joshi, Shridhar Babanagare[1], Jyostna Potdar, Neelesh Sharad Risbud. 2015; 6(4):178-183.
9. Sylvia MT, Kumar S, Dasari P. The expression of immune-histochemical markers estrogen receptor, progesterone receptor, Her-2-neu, p53 and Ki-67 in epithelial ovarian tumours and its correlation with clinicopathologic variables. Indian J Pathol Microbiol. 2012; 55:33-7.
10. Mary T Sylvia, Surendra Kumar, Papa Dasari. the expression of immunohistochemical markers estrogen receptor, progesterone receptor, Her-2-neu, p53 and Ki-67 in epithelial ovarian tumors and its correlation with clinicopathologic variables. 2012; 55(1):33-37.
11. Shilpa G, Marwah N, Chauhan G, Gupta S, Goyal R, Dahiya P, *et al*. Estrogen and Progesterone Receptor Expression and its Correlation with Various Clinicopathological Parameters in Ovarian Tumours. Middle East Journal of Cancer. 2014; 5(2):97-103.
12. Hellstrom I, Goodman G, Pullman J, Yang Y, Hellstrom KE. Overexpression of Her2 in ovarian carcinomas. Cancer Res. 2001; 61:2420-3.