

Oestrogen Receptor, Progesterone Receptor Expression on Epithelial Tumours of Ovary and Correlation with Their Clinicopathological Features

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ABSTRACT

BACKGROUND

Ovarian carcinoma is one of the most lethal malignancies. Their histogenesis and complex pathogenesis remain largely unknown in spite of the many studies and research carried out in the field. The receptors for female sex hormones are implicated in the pathogenesis of ovarian tumours in many studies. This concept points out the necessity of developing a highly affected targeted therapy, which requires a proper understanding of the pathogenesis of the tumours. This study was done to evaluate the expression of these receptors on the primary epithelial tumours of the ovary and explore the possible correlation with clinical and pathological features.

METHODS

A hundred cases of primary epithelial tumours of the ovary were selected; tissue samples were taken from appropriate areas and processed. Tissues were cut into sections of three to five-micron thickness. Sections from the tissues were stained and examined. Once the histological type was clear, the receptor expression was assessed with immunohistochemistry markers.

RESULTS

Among the hundred tumours studied, serous tumours were the commonest, accounting for 65 % followed by mucinous tumours which constituted 34 %. Clear cell tumours accounted for 1 %. Endometrioid and transitional cell tumours were still rarer. Among these, oestrogen receptor (ER) was expressed in 78.5 % of serous tumours and progesterone receptor (PR) was expressed in 64.6 % of serous tumours.

CONCLUSIONS

Serous tumours were seen to show maximum expression of the hormone receptors among the surface tumours of ovaries. Furthermore, the expression of the receptors was more consistently seen in high-grade tumours. This finding may be of help in designing personalized hormone therapy in epithelial tumours.

KEY WORDS

Surface Epithelial Tumours, Receptors, ER, PR.

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BACKGROUND

Carcinoma of the ovary is a leading cause of death due to gynaecological malignancies. 60 % of all ovarian tumours and 90 % of malignant ovarian tumours are surface epithelial tumours. The knowledge about the risk factors and molecular alterations associated with these tumours is relatively poor. Besides, most cases of ovarian carcinoma are detected at late stages. These factors, along with the low response to chemotherapy make the treatment of ovarian surface epithelial tumours, difficult. This warrants a highly effective targeted therapy for these tumours. For this, a better understanding of the pathogenesis is necessary. This in turn means a better understanding of the mutations, overexpression of oncogenes, and the role of cell cycle regulators like cyclins and cyclin dependent kinases.

The female hormones, oestrogen and progesterone are implicated in the pathogenesis of epithelial tumours, for a long time.¹ As these hormones are secreted by the ovary, it is natural for their receptors to be present on the ovary. It is logical to think that hormone receptor determination and the correlation with clinicopathological findings can be helpful in targeted therapy of these tumours. Even in this era of advanced molecular diagnostic technologies, queries regarding the exact molecular basis and pathogenesis of ovarian epithelial tumours remain unsolved. The literature says that research work has been going on in this field for some time. The importance of female hormones, oestrogen and progesterone and their receptors has been widely studied with various levels of results.

It has been noticed that the expression of ER, PR is different in tumours with different grades. Hence, the tumours were graded according to WHO classification. The tumours accordingly were divided into benign, borderline and malignant tumours. This classification was done based on features of the tumours like stratification of nuclei, invasion of the stroma and the degree of atypia.

Though several advancements have been achieved regarding ovarian tumour pathogenesis the prognosis of the patients with ovarian malignancies did not show much improvement for the past few decades. This warrants highly motivated and perseverant efforts to be laid in this field. Results of targeted therapy in breast cancer² and endometrial cancers³ have been quite encouraging. Hence it is speculated that the same would be applied with ovarian malignancies too shortly. For this purpose, the study of the presence of the receptors for these hormones is of utmost importance.

METHODS

This descriptive study was conducted in the Department of Pathology, Government Medical College, Trivandrum, for one year.

Sample Collection

A hundred consecutive specimens with primary surface epithelial tumours of the ovary were collected. These included oophorectomy as well as pan hysterectomy specimens.

These specimens were sampled, and gross morphology was studied. Appropriate tissue bits were taken. Then the tissues were processed, cut into sections, stained with H & E and studied under a microscope. Once identified as a surface epithelial tumour, appropriate immunohistochemistry markers were used to demonstrate the receptors.

ER, PR activity was assessed using the Allred score.⁴ This score is calculated from the proportion of positive cells and intensity of staining. Tumours that had scored less than or equal to two were considered negative and those with a score of more than two were considered positive.

Positive Cell Proportion	Proportion Score
0	0
0-1%	1
1% -10%	2
10% -33%	3
33% -66%	4
67% -100%	5
Marking intensity	Intensity score
Lack of Marking	0
Low intensity	1
Moderate Intensity	2
High Intensity	3

Table I. Allred Scoring

Statistical Analysis

The data were entered in Microsoft Excel and statistical analysis was done using SPSS software.

RESULTS

Age

Of the hundred cases, the maximum incidence of ovarian tumours was seen in the age group, between 30 years and 40 years. This was similar to some previous studies.⁵ Youngest patient was 22 years and the eldest was 75 years old.

Age	Frequency	Percentage
20 -30 yrs.	19	19
30 -40 yrs.	29	29
40 -50 yrs.	22	22
50- 60 yrs.	15	15
60 -70 yrs.	13	13
70 -80 yrs.	2	2
Total	100	100

Table 2. Age-Wise Distribution of Tumours

The behaviour of the tumour: Regarding the behaviour of the tumours, 79 % were benign, 8 % were borderline and 13 % were malignant.

Type of Tumour	Percentage	Number
Serous	65%	65
Mucinous	34%	34
Clear cell	1%	1

Table 3. Distribution of Cases According to Histological Subtypes

Among the variants, serous tumours accounted for the majority, which was 65 % similar to the previous studies in ovarian tumours.⁶ This was followed by mucinous tumours accounting for 34 %. Clear cell carcinoma accounted for 1 % of endometrioid and transitional cell tumours that were still rare.

ER and PR Expression

Among the hundred cases, 59 cases were positive for ER. 49 were positive for PR. The maximum frequency of PR expression was seen in the group 50 to 60 years.

Histological Subtypes	Frequency	Percentage
Benign serous tumour	52	52
Borderline serous tumour	4	4
Serous cystadenocarcinoma	9	9
Benign mucinous tumour	27	27
Borderline mucinous	4	4
Mucinous cystadenocarcinoma	3	3
Clear cell carcinoma	1	1

Table 4. Distribution of Histological Subtypes

ER	Frequency	Percentage
Negative	41	41
Positive	59	59
Total	100	100

Table 5. Frequency of ER Expression

PR	Frequency	Percentage
Negative	59	59
Positive	41	41
Total	100	

Table 6. Frequency of PR Expression

Frequency of ER PR expression according to the behaviour of the tumour: In the present study, among the malignant tumours 69.2 % showed ER expression whereas among the benign tumours only 58.2 % and among the borderline, only 50 percent showed ER expression. On the other hand, PR expression was seen in only 15.4 % of the malignant tumours and 50 percent of the borderline tumours whereas the percentage of benign tumours with PR expression was 54.4 %

ER	Benign	Borderline	Malignant	Total
Negative	33	4	4	41
Positive	46	4	9	59
Total	79	8	13	100

Table 7. ER Expression According to Tumour Behaviour

PR	Benign	Borderline	Malignant	Total
Negative	36	4	11	51
Positive	43	4	2	49
Total	79	8	13	100

Table 8. PR Expression According to Tumour Behaviour

Regarding the correlation of histological type with ER PR expression, 78.5 % of the serous tumours were ER-positive, 21.9 % of the mucinous tumours were ER positive.

To summarise, serous tumours expressed ER more frequently than other tumours. Regarding PR expression, 64.6 percent of serous tumours were positive, only 18 % of mucinous tumours showed PR expression. Borderline serous tumours and serous carcinoma showed maximum ER and clear cell tumours did not show expression.

DISCUSSION

Ovarian malignancies are the most lethal malignancies of the female genital tract. Their intricate origin and histopathogenesis are always challenging to the researchers. The present study is an attempt to explore the various clinicopathological parameters involved in the pathogenesis of primary surface epithelial tumours of the ovary with special emphasis on the expression of ER and PR. The objectives are to study the expression of ER and PR and

correlate the same with the age of the patient, histological type and grade of the tumours and behaviour of the tumours.

The age of the patients showed wide variation ranging from 23\2 to 75 years, maximum incidence noted in the age group of 30 to 40 years. Malignant tumours were seen more in the higher age group. These observations agree with some of the previous studies.⁶ However, age cannot be considered as an independent prognostic factor, although it is an important prognostic factor since there is a complex interplay of various factors affecting tumour genesis.

Among the tumours, the serous type was the commonest followed by mucinous and then clear cell type. Regarding the role of ER and PR receptors in the pathogenesis of ovarian tumours, an unequivocal association could not be established. The immune reactivity of each case was assessed by the Allred scoring system. It was found that 59 % of cases were positive for ER and 48 % for PR expression.

It was seen that the ER expression was the highest in malignant neoplasms. This is in agreement with the previous studies conducted on the topic. The highest PR expression was noted among benign tumours which were different from previous studies, some of which showed borderline tumours and some showed malignant tumours having the strongest expression of ER and PR.

In General, the Findings in the Study can Be Summarised as-

1. Maximum incidence of surface epithelial tumours was seen in the age group 30 to 40 yrs.
2. The incidence of malignancy increases with the age.
3. Majority of the tumours studied were benign, the predominant histological subtype was serous, followed by mucinous and clear cell tumours.
4. ER PR receptors were more frequently expressed by serous tumours.
5. ER expression was mainly seen in malignant tumours and PR expression was more in benign tumours.

Thus, the expression of ER and PR is associated with histological subtypes and behaviour of the tumour. Further studies in this field may reveal more concrete associations.

CONCLUSIONS

In the present study, the maximum incidence of ovarian tumours was noted in the age group 30 to 40 years. Malignant tumours occur at a higher age group. A hundred tumours studied were classified according to the WHO classification. Serous tumours formed the majority among malignant and benign tumours. The second commonest was mucinous tumours and the third was clear cell carcinoma.

Over the past two decades, there has been so much effort to find out the relation of ER, PR expression and pathogenesis of carcinoma ovary. In our study, 59 % of tumours showed ER and 49 % showed PR expression. The ER expression was found to be the highest in malignant tumours (69.2 %) rather than borderline tumours (50 %) and benign (58.2 %). This finding was supported by previous studies.

On the contrary, PR expression was more in benign tumours according to this study. This was in contrast to some other studies.

To summarise, ER and PR expressions in ovarian carcinomas are associated with the histological subtypes and the behaviour of the tumours. This point out the fact that extensive studies in this field can help in targeted therapy for these tumours.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

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REFERENCES

- [1] Syed V, Ulinski G, Mok SC, et al. Expression of gonadotrophin receptors and growth responses to key reproductive hormones in normal and malignant human ovarian surface epithelial cells. *Cancer Res* 2001;61(18):6768 -76.
- [2] Brekelmans CTM. Risk factors and risk reduction of breast and ovarian cancer. *Curr Opin Obstet Gynecol* 2003;15(1):63-8.
- [3] Gambacciani M, Monteleone P, Sacco A, et al. Hormonal replacement therapy and endometrial, ovarian and colorectal cancer. *Best Pract Res Clin Endocrinol Metab* 2003;17(1):130-47.
- [4] Qureshi A, Pervez S. Allred score for ER reporting and its impact in clearly distinguishing ER negative from ER positive breast cancers. *J Pak Med Assoc* 2010;60(5):350-3.
- [5] Garg S, Marwah N, Chauhan G, 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.
- [6] Ghartimagar D, Ghosh A, Ranabhat S, et al. Surface epithelial tumours of ovary - an analysis in a tertiary referral hospital. *Journal of Pathology of Nepal* 2013;3(5):397-402.