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Original Article

Expression of Estrogen Receptor and Progesterone Receptor Status In Patients of Carcinoma of Ovary and Carcinoma of Endometrium

Razia Irshad, Ghulam Haider, Anusha Hassan, Madiha Hashmi

Department of Medical Oncology, Jinnah Postgraduate Medical Centre, Karachi Pakistan

ABSTRACT

Objective: To evaluate the expression of estrogen and progesterone receptor status in patients of carcinoma of ovary and carcinoma of endometrium.

Study Design: Cross-sectional study.2

Place and Duration of Study: Department of Medical Oncology of Jinnah Postgraduate Medical Centre, Karachi Pakistan, from Feb 2019 to Feb 2020.

Methodology: Seventy females of age 18-70 years with histologically proven diagnosis of ovarian carcinoma or endometrial carcinoma were included in the study. Each patient was interviewed for obtaining demographic details, medical history and presenting symptoms with help of validated questionnaire. Immunohistochemical analysis was performed for confirming estrogen and progesterone receptor expressions.

Results: Out of 72 evaluated patients, ovarian carcinoma was present in 45(62.5%) patients and endometrial carcinoma in 27(37.5%) patients having mean age of 52.6±10.1 (30-69) years. Mean body mass index was 30.4 ± 5.7(18-39) Kg/m2 with obesity in 42(58.3%) patients. Immunohistochemistry showed estrogen receptor positive in 32(71.1%) and 18(66.7%) patients, estrogen receptor negative in 13(28.9%) and 9(33.3%) patients, progesterone receptor positive in 31(68.9%) and 19(70.4%) and progesterone receptor negative in 14(31.1%) and 8(29.6%) patients of ovarian and endometrial carcinoma respectively. Overall it showed higher expression of ER and PR in patients of ovarian and endometrial carcinoma.

Conclusion: The study concludes that approximately two third of patients showed estrogen and progesterone receptor expression in ovarian and endometrial carcinoma. These ER and PR expressions have capability to be utilized as prognostic indicator for ovarian and endometrial carcinoma.

Keywords: Carcinoma, endometrium, estrogen, ovary, progesterone.

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INTRODUCTION

Gynecologic carcinoma is defined as "presence of any carcinoma in genital tract of females". There are five types of carcinomas commonly reported in genital tract including cervical, ovarian, uterine, vaginal and vulvar.[1]

Ovarian carcinoma is ranked 9th among all types of carcinomas in women and 3rd among gynecologic carcinomas with increased rate of morbidity and mortality. According to International Agency for Research on Cancer (IARC) age-standardized rates (ASR) of ovarian carcinoma is 6.6% throughout the world in 2020.[2-3] Prevalence of ovarian carcinoma is 9.2 per 0.1 million in women of Asian region.[4-5] In Pakistan, reported prevalence of new cases of ovarian carcinoma is 4.9%.[6]

Correspondence: Dr Razia Irshad, Department of Medical Oncology of Jinnah Postgraduate Medical Centre, Karachi Pakistan
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Endometrial carcinoma is ranked 4th among all types of carcinomas in women and 2nd among gynecologic carcinomas. According to IARC, ASR of endometrial carcinoma is 8.7% throughout the world in 2020.[2-3] In Pakistan, reported prevalence of new cases of endometrial carcinoma is 3.1%.[6] Increasing prevalence with poor survival is mainly because of delayed diagnosis and progression of gynecologic carcinoma that enforce the researchers to identify new biomarkers for early diagnosis and predicting prognosis of carcinoma. The estrogen receptor (ER) and progesterone receptor (PR) play active role in the development of these carcinomas. Ovaries are considered as a main source as well as targets of sex hormones including estrogen and progesterone. Estrogen is mainly responsible for ovarian cancer, approximately 70% cases shows estrogen receptors (ER). In contrast progesterone play protective role in ovarian cancer.[7-8] Endometrial cancer shows both expression of ER and PR, uterus lining is extremely sensitive to hormonal activity, through binding to

their receptors, estrogen drives epithelial proliferation, and progesterone inhibits growth and causes cell differentiation.[9] Different researchers reported the ER and PR positivity in ovarian and endometrial carcinoma and their association with prognosis and treatment.[10]

ER and PR expression are also used to identify patients that could benefit from hormonal therapy. Studies of ER and PR expression in ovarian and endometrial carcinoma are limited throughout the world and in local population of Pakistan. Therefore, current study was designed to evaluate the expression of ER and PR status in patients of carcinoma of ovary and endometrium.

METHODOLOGY

A cross-sectional study on female patients suffering either from carcinoma of ovary or endometrium was carried out at oncology department of Jinnah postgraduate medical centre Karachi. The ethical review committee approval was taken before conduct of the study (NO.F.2-81-IRB/2019-GENL/10415/JPMC) and informed consent from all the eligible patients were obtained before collection of data. Socio-demographic data along with clinicopathological features and medical history were noted on predesigned proforma validated by research committee of Jinnah postgraduate medical centre. Data of diagnosed patients of carcinoma of ovary or endometrium was collected for one year from February 2019 to January 2020.

World Health Organization (WHO) Global Cancer Observatory report on Pakistan reports the 4.8% incidence of new cases of ovary carcinoma in Pakistani females, 6 with confidence interval of 95% and absolute precision 5%; calculated sample size was 72.

Inclusion Criteria: Consecutive female patients with age 18-70 years and diagnosed cases of ovarian or endometrial carcinoma, willing to take part were enrolled in study.

Exclusion Criteria: whereas female patients with age lower than eighteen years, diagnosed with other gynecological carcinomas or refused to take part were excluded from study.

Each patient's specimen was analyzed for histological classification on the basis of World Health Organization (WHO) 2014 criteria, surgical staging on the basis of Federation of Gynecology and Obstetrics (FIGO) 2018 criteria and Immunohistochemical (IHC) analysis was performed for confirming ER and PR expressions. ER and PR expression status was analyzed using Allred scoring system in each case by taking into consideration the proportion of positive cells and staining intensity.

Total estrogen and progesterone receptor score used the combination of proportion (0-2 negative and 3-5 positive) and intensity score (0 negative, 1 weak, 2 intermediate, 3 strong). Total score 0-2 was considered as negative and ≥3 as positive for estrogen and progesterone receptor.[11] BMI of each patient was calculated by using BMI formula (BMI=weight/height^2). Statistical analysis was performed with version 25 of statistical package for social sciences. Quantitative variables were presented as means and standard deviation, whereas qualitative data in frequency and percentages in both groups. Chi-square test was applied by taking ≤ 0.05 as significant *p*-value.

RESULTS

A total of 72 patients of ovary or endometrium carcinoma were evaluated. Out of which ovarian carcinoma was reported in 45(62.5%) patients and endometrial carcinoma in 27(37.5%) patients.

The mean age of the study participants was 52.6±10.1 (30-69) years. The mean age of patients with ovarian carcinoma was lower (50.2±10.2) compared with patients of endometrial carcinoma (56.7±8.7).

The mean BMI of evaluated patients was 30.4±5.7 (19-39) Kg/m^2, with obesity (BMI >30 Kg/m^2) in 42(58.3%) patients. Ovarian carcinomas were diagnosed in 16(36.1%) pre-menopausal and 29(64.4%) postmenopausal patients, whereas endometrial carcinomas were diagnosed in 29(64.4%) pre-menopausal and 17(63.0%) postmenopausal patients. ER expression was positive in 32(71.1%) and 18(66.7%) patients and negative in 13(28.9%) and 9(33.3%) patients in ovarian and endometrial carcinoma respectively. PR expression was positive in 31(68.9%) and 19(70.4%) and negative in 14(31.1%) and 8(29.6%) patients in ovarian and endometrial carcinoma respectively (Table-I).

Association of ER PR status with stage, grade and histology in ovarian and endometrial carcinoma is described in Table II and III that shows high expression of ER and PR in early stage and low grade tumors.

Table-I: Characteristics of study variables among study participants

Variables	Carcinoma	
	Ovarian (%) (n=45)	Endometrial (%) (n=27)
Age (Years)		
Range	30-69	37-67
Mean±SD	50.2±10.2	56.7±8.7
<50	20(44.4)	6(22.2)
≥50	25(55.6)	21(77.8)
BMI (Kg/m2)		
Range	18-39	20-38
Mean ± SD	30.6±5.9	30.1±5.4
Obesity (>30)	26(57.8)	16(59.3)
Menopausal status		
Pre-menopausal	16(35.6)	10(37.0)
Postmenopausal	29(64.4)	17(63.0)
Comorbid Conditions		
Hypertension	13(28.9)	11(40.7)
Diabetes Mellitus	8(17.8)	10(37.0)
Ischemic heart disease	2(4.4)	0(0.0)
Hepatitis C	2(4.4)	1(3.7)
Family History of Cancer	12(26.7)	11(40.7)
Transfusion History	19(42.2)	10(37.0)
Modality of Treatment Received		
Surgery	30(66.7)	18(66.7)
Surgery+ Chemotherapy	13(28.9)	7(25.9)
Surgery+ Radiotherapy	2(4.4)	2(7.4)
ER PR Expression		
ER+	32(71.1)	18(66.7)
ER-	13(28.9)	9(33.3)
PR+	31(68.9)	19(70.4)
PR-	14(31.1)	8(29.6)

DISCUSSION

In Pakistan, ovarian carcinoma and endometrial carcinomas are ranked 2nd and 3rd among gynecologic carcinomas with reported incidence of 4.9% and 3.1% respectively.[6]

This study evaluates the expression of ER and PR status in patients of carcinoma of ovary and endometrium. Identification of ER PR will be helpful in using them as prognostic indicator for ovarian and endometrial carcinoma and developing appropriate treatment for morbidity and mortality associated with ovarian and endometrial carcinoma.

In current study, mean age was 52.6±10.1 years higher than 50 years in both type of carcinomas. Average mean age was higher in endometrial carcinoma 56.7±8.7 years as compared to ovarian carcinoma 50.2±10.2 years. Most of the carcinoma patients 46(63.9%) were in age group of >50 years followed by 26(36.1%) patients in age group of <50 years. A Pakistani study by Chaudhry S, *et al.,*. was conducted on gynaecological malignancy in Ziauddin Hospital reported the approximately 90% of patients with age of >50 years.[12] Another study by Chaudry S, *et al.,*. also reported the mean age of 50 years and 66.7% patients with age of >50 years.[13] Mohyuddin S, *et al.,*. reported the mean age of 53.09±11.82 years and approximately 60.0% of patients with age of >50 years.[14] All studies are showing the mean age of diagnosis of gynecologic carcinoma is greater than 50 years because gynecologic carcinomas are more common in postmenopausal females.

Table-II: Association of ER PR with Stage, Grade and Histology in Ovarian Carcinoma (n=45)

Variables	Estrogen Receptor (ER)		*P* -value
	Positive (%)	Negative (%)	
Stage			
IA	11(34.3)	6(46.2)	0.691
IB	7(21.9)	4(30.7)	
IC	8(25.0)	1(7.7)	
IIIA	4(12.5)	1(7.7)	
IV	2(6.3)	1(7.7)	
Grade			
I	18(56.3)	5(38.5)	0.555
II	5(15.6)	3(23.1)	
III	9(28.1)	5(38.5)	
Histology			
Serous	19(59.4)	8(61.5)	0.348
Clear cell	3(9.4)	3(23.1)	
Endometroid	3(9.4)	0(0.0)	
Mucinous	3(9.4)	2(15.4)	
NOS	4(12.5)	0(0.0)	
Progesterone Receptor (PR)			
Stage			
IA	12(38.7)	5(35.7)	0.769
IB	9(29.0)	2(14.3)	
IC	5(16.1)	4(28.6)	
IIIA	3(9.7)	2(14.3)	
IV	2(6.5)	1(7.1)	
Grade			
I	18(58.1)	5(35.7)	0.182
II	6(19.4)	2(14.3)	
III	7(22.6)	7(50.0)	
Histology			
Serous	19(61.3)	8(57.1)	0.491
Clear cell	4(12.9)	2(14.3)	
Endometroid	3(9.7)	0(0.0)	
Mucinous	2(6.5)	3(21.4)	
NOS	3(9.7)	1(7.1)	

Table-III: Association of ER PR with Stage, Grade and Histology in Endometrial Carcinoma (n = 27).

Variables	Estrogen Receptor (ER)		*P*-value
	Positive (%)	Negative (%)	
Stage			
IA	8(44.4)	4(44.4)	0.945
IB	6(33.3)	3(33.3)	
II	3(16.7)	1(11.1)	
IIIB	1(5.6)	1(11.1)	
Grade			
I	10(55.6)	3(33.3)	0.490
II	5(27.8)	3(33.3)	
III	3(16.7)	3(33.3)	
Histology			
Endometroid	14(77.8)	7(77.8)	0.829
Serous	3(16.7)	1(11.1)	
Clear cell	1(5.6)	1(11.1)	
Progesterone Receptor (PR)			
Stage			
IA	6(31.6%)	6(75.0%)	0.161
IB	7(36.8%)	2(25.0%)	
II	4(21.1%)	0(0.0%)	
IIIB	2(10.5%)	0(0.0%)	
Grade			
I	10(52.6%)	3(37.5%)	0.762
II	5(26.3%)	3(37.5%)	
III	4(21.1%)	2(25.0%)	
Histology			
Endometroid	15(78.9%)	6(75.0%)	0.798
Serous	3(15.8%)	1(12.5%)	
Clear cell	1(5.3%)	1(12.5%)	

In current study incidence of ovarian carcinoma was high reported in 45(62.5%) patients as compared to endometrial carcinoma reported in 27(37.5%) patients. Chaudhry S, *et al.,*. reported the ovarian carcinoma in 47.3% and endometrial carcinoma in 43.6% patients.[12] Mohyuddin S, *et al.,*. also reported the highest prevalence 62.95 of ovarian carcinoma.[14] Ovarian carcinoma is one of the leading carcinoma in Pakistan followed by endometrial carcinoma. Ovarian cancer is high in Pakistani females because of different hormonal, genetical and environmental factors including age, early menarche, late menopause, nulliparity, family history of breast or ovarian carcinoma, personal history of breast or uterine cancer, talc or asbestos exposure or high fat.[15-17]

Obesity is commonly associated with ovarian and endometrial carcinoma as a risk factor. In current study, mean BMI was 30.4±5.7 Kg/m2, with obesity (BMI >30 Kg/m2) in 42(58.3%) patients. Mean BMI and obesity were similar in ovarian and endometrial carcinoma respectively. Chaudry S, *et al.,*. reported the similar mean BMI 29(20-38) Kg/m2, with obesity (BMI >28) in 67.0% patients.[12]

In current study, stage IA was seen in 17(37.8%) patients followed by stage IB in 11(24.4%) patients, stage IC in 9(20.0%) patients, stage IIIA in 5(11.1%) patients and stage IV in 3(6.7%) patients in ovarian carcinoma, whereas stage IA was seen in 12(44.5%) patients followed by stage IB in 9(33.3%) patients, stage II in 4(14.8%) patients and stage IIIB in 2(7.4%) patients in endometrial carcinoma. Different other studies also report the similar pattern of stages of ovarian and endometrial carcinoma.[13 -14]

In current study, grade I was seen in 23(51.1%) patients followed by grade III in 14(31.1%) patients and grade II in 8(17.8%) patients in ovarian carcinoma whereas grade I was seen in 13(48.2%) patients followed by grade II in 8(29.6%) patients and grade III in 6(22.2%) patients in endometrial carcinoma. Different other studies also report the similar pattern of grades of ovarian and endometrial carcinoma.[13-14]

In current study, commonly reported histology was serous with 27(60.0%) patients followed by clear cell with 6(13.3%) patients in ovarian carcinoma whereas endometroid with 21(77.8%) patients followed by serous with 4(14.8%) patients in endometrial carcinoma. Chaudhry S, *et al.,*. also reported the highest proportion of endometrial carcinoma in 27.2% patients and serous in 16.3% patients.[12] Chaudry S, *et al.,*. reported the similar histological pattern endometrial carcinoma with endometroid 86.0% and serous 14.0%. 13 Similar pattern of histopathology was observed in other studies.[12-13]

In this study, in ovarian carcinoma, ER was positive in 32(71.1%) patients and PR was positive in 31(68.9%) patients, whereas in endometrial carcinoma, ER was positive in 18(66.7%) patients and PR was positive in 19(70.4%) patients. In histology of ovarian carcinoma, serous was most commonly reported in 27(60.0%) patients followed by clear cell in 6(13.3%) patients whereas in endometrial carcinoma endometroid was most commonly reported in 21(77.8%) patients followed by serous with 4(14.8%) patients. Different studies reports the similar pattern of ER and PR expression such as; Wang C, *et al.,*. study reports the similar higher prevalence of ER+ and PR+ expression i.e., 59.8% and 75.0% respectively in endometrial carcinoma, 18 Tomica D, *et al.,*. reports the ER+ in 65.2% and PR+ in 59.4% patients of endometrial carcinoma,[19] Waqar S, *et al.,*. reports the

ER+ in 44.6% and PR+ in 66.1% patients of endometrial carcinoma.[20] and Shen F, *et al.*,. study reports the similar higher expression of ER+ and PR+ expression i.e., 69.0% and 48.0% in ovarian carcinoma.[21] Different studies show relation between ER and PR expression with better survival rate and favorable outcomes in ovarian and endometrial carcinoma.[18-21]

Our study also shows that higher ER and PR expression is seen in early stage and low grade tumors. Similar pattern are seen in similar other studies. This will help in improving treatment strategies and survival rate.[18-21]

CONCLUSION

The study concludes that approximately two third of patients showed estrogen and progesterone receptor expression in ovarian and endometrial carcinoma.These statuses of ER and PR have capability to be utilized as prognostic indicator for ovarian and endometrial carcinoma. This high expression of ER and PR provides rationale for the use of hormonal therapy in these cancers. The present study had its time constraints, more in depth studies should be carried out.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

RI & GH: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

AH & MH: Data acquisition, data analysis, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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