

FREQUENCY OF P53 EXPRESSION IN EPITHELIAL OVARIAN CANCER

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Background: In females, ovarian cancer is among the most common causes of cancer deaths. The most common and lethal gynecological malignancy is malignant epithelial tumor. p53 may be used as a marker to predict aggressive behavior and poor response to standard chemotherapy.

Objective: To observe the frequency of positive immunohistochemical expression of p53 in surface epithelial carcinoma.

Methods: The immunohistochemical expression of p53 on 100 diagnosed cases of surface epithelial carcinoma was conducted in this cross-sectional study in the department of Histopathology, Chughtai Institute Pathology, Lahore during a period of 6 months. Nuclear staining for p53 was considered as positive. Cases with more than 10% positivity in tumor cells were considered as positive.

Results: The mean age of patients and size of tumor were 48.70 ± 10.5 years and 9.83 ± 5.33 cm respectively. 25% (n=25) patients had low histologic grades while 75% (n=75) patients had high histological grades. 47% (n=47) patients were p53 positive and 53% (n=53) patients were negative for immunohistochemical expression of p53.

Conclusion: The present study states p53 positivity in 47% cases of epithelial ovarian cancer and the data fits to the proposed dualistic pathway of ovarian carcinogenesis as expression of p53 positive cases in high grade cancers is statistically significant (<0.05).

Keywords: Ovary, p 53, Cancer, Immunochemistry

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INTRODUCTION

Ovarian malignancies are one of the deadliest cancers among women. They have been responsible for over 13,000 deaths in the US population¹. These are the fourth most common tumor in Pakistani women². Almost 90% of these cases are due to malignant tumors of epithelial origin. These are categorized in five categories on histopathological and molecular genetic alterations basis, into high grade serous (70%), mucinous (3%), clear cell (10%), endometrioid (10%), and low-grade serous carcinoma ($<5\%$)³.

Based on various studies, epithelial ovarian carcinomas comprising of varied groups can be categorized on the basis of their distinct morphology and genetic makeup. According to a study by Kurman and Shih⁴, one group of tumors designated type I comprises of low grade serous, low-grade endometrioid, clear cell, mucinous and transitional (Brenner carcinomas). This group has a benign presentation. These tumors present within the ovary and have genetic stability. Group designated type II are highly aggressive tumors. They have a rapid turnover and mostly present at an advanced stage. This group includes conventional high grade serous carcinoma, undifferentiated carcinoma and malignant mixed mesodermal tumors (carcinosarcoma). p53 mutations are seen in more than 80% of cases.⁵ Steps taken for early detection and newer therapeutic approaches have shown no clear advantage⁶. It is the need of hour to understand the exact pathogenesis of these

diverse groups of tumors so that more effective treatment options and more early diagnostic tools can be discovered. immunohistochemical stains p53 has been applied in several studies to understand the pathogenesis and to diagnose early lesions. According to a study by Sundov et al⁶, all low grade ovarian serous carcinoma cells were negative for p53 immunostaining while in the high grade group 85.7 percent cases showed strong positive nuclear expression of p53. Another study by Choudhury et al⁷, states no significant correlation of p53 immunoreactivity with serous versus non serous histology of tumors. According to study by Giurgea et al⁸, p53 was positive in 42.3 % in ovarian malignancies. The purpose of our study is to observe the immunohistochemical expression of p53 in epithelial ovarian cancers in the local population. No such study has been published in Pakistan.

METHODS

This cross-sectional study was carried out in the department of histopathology, Chughtai Institute of Pathology, Lahore for a period of 6 months to find out the expression of p53 in diagnosed cases of surface epithelial carcinoma. Sample size of 100 was included using non-probability, consecutive sampling technique at expected frequency of 42.3 % for p53 positivity in epithelial carcinomas at 95% CI and 10% margin of error⁸.

Specimens fulfilling the selection criteria, after overnight fixation, were grossed using College of American Pathologists (CAP) protocols and were paraffin-embedded. p53 immunohistochemistry was performed after routine histological examination. Nuclear staining for p53 was considered as positive. Cases with more than 10% positivity in tumor cells were considered as positive. Data was entered and analyzed using SPSS 18.0. For quantitative variables i.e., age, tumor size, mean and standard deviation was calculated. Frequencies and percentages were given for qualitative variables like histological grades and immunohistochemical expression of p53. Data was stratified for size of tumor, age and histological grades. Chi- square test was applied and p value less than 0.05 was considered as significant.

RESULTS

One hundred cases of epithelial carcinomas of patients between 18 and 60 years with mean ± standard deviation of 48.70 ± 10.51 years were included. Sizes of tumors were between 1cm and 25 cm with mean ± standard deviation 9.83 ± 5.33cm. Tumors were classified as either high histological grade or low histological grade. There were 25 patients (25%) having low histologic grades and 75 patients (75%) having high histologic grades (Table I). Immunohistochemical expression of p53 was found to be positive in 47% cases(n=47) while 53% cases (n=53) were negative.

Table 1: Comparison of age, size and histologic grades of ovarian epithelial cancer(n=100)

Parameter	Positive (n=47)	Negative (n=53)	N=100	Chi-square	DF	p-value
Age (Years)						
• 18-30	00 (0.000%)	05 (100%)	05	10.89	2	0.004
• 31-45	11 (32.35%)	23 (67.65%)	34			
• 46-60	36 (59.02%)	25 (0.98%)	61			
Size of Tumors (cm)						
• 01.0-08.0	20 (40.82%)	29 (59.18%)	49	2.281	2	0.3196
• 08.1-15.0	19 (57.58%)	14 (42.42%)	33			
• 15.1-25.0	08 (44.45%)	10 (55.55%)	18			
Histologic grades						
• Low	02 (8%)	23 (92%)	25	20.35	1	0.000
• High	45 (33.33%)	30 (66.67%)	75			

Data was stratified on immunohistochemical expression of p53 according to age of the patient, size of tumor and histological grades. Stratification of immunohistochemical expression of p53 according to age of the patients revealed that 32.35% (n=11) patients between 31 to 45 years and 59.02% (n=36) patients between 46 to 60 years were noted as positive cases while no patient with age between 18 to 30 years was found positive. Statistically the association between p53

immunohistochemical expression and age was significant (p value <0.05). Stratification of immunohistochemical expression of p53 according to size of tumors shows that 40.82% (n=20) patients between 1-8cm, 57.58% (n=19) patents between 8.1-15cm and 44.45% (n=8) patients between 15.1-25cm were positive cases. Statistically the association between p53 IHC expression and size of tumor was not significant (p>0.05). Stratification of immunohistochemical expression of p53 according to

histologic grades shows that only 8% (n=2) patients with low histologic grades and 33.33%(n=45) patients with high histologic grades were positive, respectively. Statistically the association between p53 IHC expression and grade was significant (p<0.05).

DISCUSSION

Currently epithelial ovarian cancer is divided into two main groups which are designated type I and type II tumors⁹. Type II tumors are highly aggressive tumors. They tend to progress rapidly. Metastatic potential of these tumors is high. They usually have already extended beyond the ovaries at the time of initial diagnosis which makes their management quite problematic. Furthermore, they constitute the most common type (> 70%) of epithelial ovarian cancer. Histologically, type II tumors are mainly high-grade serous (HGS) carcinomas and the remainders are high grade endometrioid, undifferentiated carcinomas or a subset of clear cell carcinoma. High grade serous carcinoma accounts for ~85% of all ovarian cancer deaths. In various previous studies p53 expression is tested by immunohistochemical analysis by p53 antibody on ovarian epithelial cancer^{7,8}. In our study overall frequency of p53 positivity is 47% in epithelial ovarian cancers which is comparable to the study by Giurgea et al⁸ where p53 was positive in 42.3 % in ovarian epithelial cancer. However, my data results do not support study of Choudhury et al⁷ which states no correlation of p53 immunoreactivity with ovarian tumors. High grade cancer cases in our study show p53 positivity in 45 out of 75 cases and only two p53 positive cases are observed in low grade cancers. The results of the present study also support dualistic model of approach to epithelial ovarian cancer which suggests more frequency of p53 mutation in high-grade ovarian cancers⁴. The results can be compared with study of Sundov et al⁶ study in which they stated a significantly higher immunoexpression of p53 in high-grade group of ovarian serous carcinomas. These results are also in accordance with studies by O'Neill et al¹⁰ and Mishra et al.¹¹

CONCLUSION

The present study states p53 positivity in 47% cases of epithelial ovarian cancer. The data fits to the proposed dualistic pathway of ovarian carcinogenesis as value of p53 positive cases in high grade cancers is statistically significant (<0.05).

ETHICAL REVIEW BOARD APPROVAL

The study was approved from Institutional Review Board of Chughtai Institute of Pathology, Lahore via reference No. CIP/IRB/1037 dated August 5,2020.

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