Original Article

Frequency of P53 Overexpression in Epithelial Ovarian Cancer

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Abstract

Objective: To determine the frequency of P53 overexpression in epithelial ovarian cancer.
Methodology: The cross-sectional study was conducted at the Department of Pathology, KRL Hospital Islamabad, from April 2018 to October 2019. Ninty four biopsy specimens using Non-probability consecutive sampling technique from the gynaecology department patients aged between 25-65 years, Biopsies and resected specimens of all adult females diagnosed by histopathologist as epithelial ovarian cancer was chosen. Immunohistochemical processing was performed using a Dako M7007 Kits were used applying FISH method. Results were interpreted by the consultant pathologist for overexpression (positive/negative) of p53. All this data was recorded on a predesigned proforma.
Results: An average of 47.00 years and a standard deviation of 10.80 years were found among the participants in this study. On average, the illness persisted for 5.79 2.00 months, with a mean. age of 46. Ovarian cancer was found in 12.77% of the patients (n = 12). In 34 (36.17%) of the cases of epithelial ovarian cancer, p53 overexpression was found.
Conclusion: Epithelial ovarian cancer has had a high prevalence of P53 overexpression. Immunostaining of p53 in epithelial ovarian cancer may improve overall health and reduce mortality and morbidity for the general population.
Keywords: Epithelial Ovarian Tumors, p53, overexpression.

Cite this articleas Sharif S, Zaib L, farwa UE, Afshan S, Faridi J, Akbar A. Frequency of P53 Overexpression in Epithelial Ovarian Cancer. J Soc Obstet Gynaecol Pak. 2022; 12(2):100-104.

Introduction

Cervical cancer appears to frequently include the inactivation of p53 gene products, either through mutation or through complex formation with the E6 oncoprotein expressed by high-risk HPV. Over 20,000 new cases and 15,000 fatalities from ovarian cancer are expected in 2006, making it the second most frequent gynecological tumor. While death rates for breast and cervical cancers have decreased significantly over the last 30 years, mortality rates for ovarian cancer have stayed almost unchanged.[1] For advanced ovarian cancer, the 5-year survival rate is 29%. This has prevented the creation of treatment regimens and screening programs.[2]

Ovarian cancer is the fifth most prevalent cause of cancer-related mortality in women and the fatal gynecologic malignancy. 239,000 people are expected to be diagnosed with this illness per year, and 152,000 people are expected to die from it in 2012.[3] The cause of EOC is not well-known. Risk factors are many, but their direct participation remains largely neglected. In contrast, the molecular pathways that contribute to the development of ovarian cancer have not been discovered.[4] Many oncogenes have been linked to ovarian cancer's development. When it comes to hereditary ovarian cancer, BRCA1 and BRCA2 germline mutations are the most prevalent, although p53 and

Authorship Contribution: [1]Concept and Idea, Data collection, Methodology, final approval and authored the study, [2-4]Data collection, Data analysis literature review, [5]assisted in drafting the work, critically revising the important intellectual contents and reviewed the study, [6]Active participation in active methodology

Funding Source: none
Conflict of Interest: none

Received: Dec 12, 2021
Accepted: April 28, 2022

pathway mutations are significantly more common in sporadic EOC.[5]

Recent research employing serial transvaginal ultrasonography showed that about half of the ovarian carcinomas developed from pre-existing benign cysts or endometriotic lesions, while the remaining cases had no pre-existing lesions 12 months before diagnosis, no pre-existing lesions were seen to develop.[6]

Several recent studies have revealed that alterations to genes on chromosome 17 may commonly be of importance in the course of ovarian cancer. The most prevalent single genetic change in sporadic human EOC is the p53 gene mutation.[7]

According to Vincent Hospital and Health Care Center, Indiana, quantifiable assessments of p53 staining can be obtained using image analysis. Staining of p53 is substantially more pronounced in advanced stage, high-grade tumors, which are inoperable and cannot be cytoreduced. In individuals with epithelial ovarian carcinomas, p53 expression is an independent predictive indication of survival.[8]

The p53 overexpression in epithelial ovarian cancer is associated with poor prognosis and requires more attention and intensive treatment, so our study will encourage clinicians/ oncologists to advise the p53 expression in these particular patients for early recognition and management.

Methodology

The cross-sectional study was conducted at the Department of Pathology, KRL Hospital Islamabad, from April 2018 to October 2019. The sample size is determined by the formula n= Z^2 (1 P) /d, Where z=1.96, p=41.66%,[17] Where z=1.96, p=41.66%[17]and d=10%. Thus, sample size n = 94 patients. Non-probability Consecutive sampling technique was used.

Inclusion Criteria: Patients Aged between 25-65 years, Biopsies and resected specimens of all adult females diagnosed by histopathology as epithelial ovarian cancer. Both married and unmarried females were included in our study.

Exclusion Criteria: Patients with malignancy in other organ systems & Metastatic tumors to the ovary (assessed on medical record) were excluded from our study.

Data was collected after the approval from ethics committee. Each patient was given a copy of their informed written permission. 94 biopsy specimens from the Gynecology department that met the inclusion criteria were chosen. Immunohistochemical processing was done using Dako M7007 Kits were used applying FISH method. Results were interpreted by the consultant pathologist (at least 5 years of post-fellowship experience) for overexpression (positive/negative) of p53. All this data was recorded on a predesigned proforma.

Overexpression of P53:

Sections cut of ovarian tissue containing representative area were stained Immuno histo chemically. Nuclear staining (brown colored staining of nuclei of tumor cells) was scored according to the following scoring system:

- 0 = <5%, absolutely no staining.
- 1+ ≤50% of the staining of nuclei of tumor cells.
- 2+ >50%, strong staining of nuclei of tumor cells.
- P53 overexpression was considered positive if
- immunohistochemistry score was 2+ and 1+, otherwise taken as
- negative.

SPSS 22.0 was used for statistical analysis. The mean and standard deviation were shown for the age and duration of the illness. Marital status (married/unmarried), menopausal status (pre-menopause/post-menopause), type of ovarian carcinoma (serous/mucinous/endometroid/clear cell) and overexpression of p53 (Positive / negative) were presented as frequency and percentage. A post-segregation analysis of factors such as age, illness duration and menopause status (pre-menopause/post-menopause) was carried out using the Chi-square test to determine their impact on the result. The significance of a P-value 0.05 was determined.

Results

Age range in this study was from 25 to 65 years with mean age of 47.00 ± 10.80 years, as shown in Table I.

The sickness lasted for a mean of 5.79 ± 2.00 months on average having a mean. The course of illness & Distribution of patients according to menopausal status is offered, as shown in Table II.

Table I: Age Distribution of Patients

Age (in years)	No. of Patients	% age
25-45	47	50.0
46-65	47	50.0
Total	**94**	**100.0**

Our study included 35(37.23%) patients with serous ovarian cancer, 27(28.72%) with mucinous ovarian cancer, and 20(21.28%) individuals with Endometroid. A clear cell form of ovarian cancer was detected in 12 of the individuals (12.77 percent), as shown in Figure I.

Table II: Distribution of Patients According to Duration of Disease

Duration (months)	No. of Patients	% Age
≤6 months	54	57.45
>6 months	40	42.55
According to Menopausal Status		
Menopausal status	No. of Patients	% Age
Pre-menopause	42	44.68
Post-menopause	52	55.32

Frequency of p53 Overexpression in epithelial ovarian cancer was seen in 34 (36.17%) cases, as shown in Figure II.

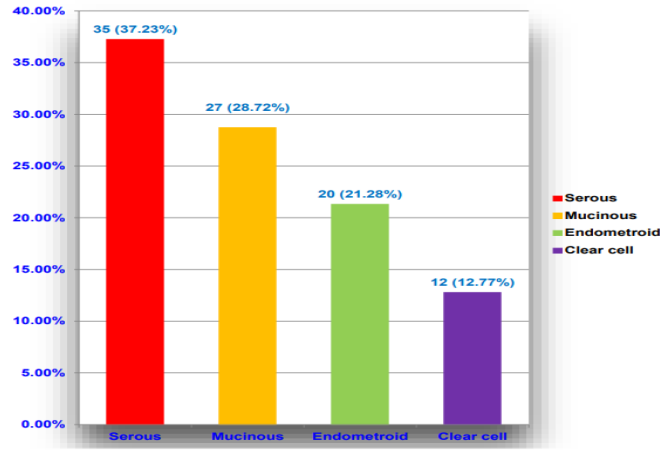

Figure I: Distribution of Patients According to Type of Ovarian Cancer

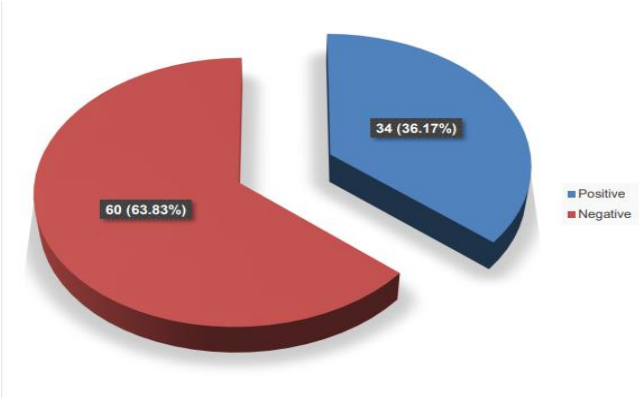

Figure II: Frequency of p53 Overexpression in Ovarian Cancer

Fourteen patients (30.98%) in the 25-45-year-old age range had overexpressed p53. A p value of 0.198 was found in 20 of the 46-65-year-old patients with positive Overexpression of p53. 24 patients (44.44 percent) with positive Overexpression of p53 had an illness duration of less than 6 months. A p value of 0.198 indicates that 10 (33.3 percent) patients with positive Overexpression of p53 had an illness duration of less than 6 months, is shown in Table III, respectively

Table III: Stratification of p53 Overexpression concerning Age Groups & Duration of Disease

Age (years)	p53 Overexpression		p-value
	Positive	Negative	
25-45	14	33	0.198
46-65	20	27	
Duration of Disease			
≤6 months	24	30	0.052
>6 months	10	30	

Table IV shows the stratification of p53 Overexpression concerning menopausal status and type of tumor, respectively

Table IV: Stratification of P53 Overexpression concerning Menopausal Status & Type of Tumor

Menopausal Status	p53 Overexpression		p-value
	Positive	Negative	
Pre-menopause	13	29	0.344
Post-menopause	21	31	
Types of Tumors			
Endometroid	14	21	
Mucinous	08	19	
Serous	08	12	0.827
Clear cell	04	08	

Discussion

Cervical cancer is the most common, followed by ovarian. Gynecological malignancies kill more women than all other gynaecological tumours combined. Despite much research, progress in figuring out the pathophysiology has been slow. Various EOC subtypes have been identified. By now, it's safe to conclude that these distinctions between the various histological subtypes are well-known in terms of their presentation, treatment response, IHC reactivity, and molecular profiling.[9]

EOC is more likely to be discovered when distant metastases have occurred. This could be because there aren't enough screening methods in place to catch the disease in its early stages. The 5-year survival rate for this malignancy is now less than 20% due to the ineffectiveness of conventional chemotherapy

(paclitaxel/carboplatin). EOCs have also been associated with protein 53 mutations (p53).[10]

Thirty four (36.17%) of the ovarian cancer cases in the current study had p53 overexpression. According to a study by Aslani FS, almost all patients with epithelial ovarian cancer had p53 overexpression. [11] In another study, 41.66%tof participants had positive P53 immunoreactions.[12]

Although 60 % of EOC expressed p53, only 29 % showed widespread p53 expression in a meta-analysis conductee by Kmet et al.[13] Diffuse p53 positivity has been reported by other authors to be as high as 25% in Sweden[14] and as low as 40% in Iran (40.7%). [15]

p53 expression has been linked to tumor progression in both serous[16] and mucinous [17] tumors, however our analysis found that p53 expression was present in 29.62% of mucinous and 40% of serous tumors.

The most common genetic modification in cancer is the p53 mutation. Zhang Y et al[18] observed that 51% of the 6839 ovarian cancer patients they examined had overexpressed p53. A monoclonal antibody used in immunohistochemical methods can alter the results. The most often used p53 antibodies are DO-7 and PAb-1801. P53 "mutant" and "wild" versions can be detected using these antibodies. However, we discovered that p53 overexpression occurred in both p53 mutation-positive and p53 mutation-negative scenarios when we used the p53 DO- 7 monoclonal antibodies (e.g., DNA repair process). P53 mutations can only be confirmed by the use of single-strand conformation polymorphism (SSCP) and polymerase chain reaction (PCR). These methods result in a mutation rate of 51% in serous carcinomas.[18]

Silwal et al [19] estimate that 59% of serous carcinomas have elevated levels of p53 overexpression and 58% have p53 mutations. There is a statistically significant link between overexpression and mutation, even if immunohistochemistry data does not completely match data from particular mutation testing.[20] There is a 68% correlation between the results of immunohistochemistry and p53 mutation analyses.

An immunohistochemistry investigation of normal ovary tissue, benign epithelial tumors, borderline tumors, and carcinomas identified p53 expression in 43% of normal tissue, 18% of epithelial tumors, 19% of borderline tumors, and 53% of carcinomas. In both cases, the mutation rate for p53 was 55%. Whereas we had 35 patients with serous ovarian cancer (37.23%), 27 (28.17%) with mucinous ovarian cancer, and 20 with Endometroid cancer in our study, as opposed to their (21.28 percent).[21]

Conclusion

P53 overexpression was shown to be quite common in epithelial ovarian cancer. A better quality of life and lower mortality and morbidity rates for the general population may be achieved by regularly using immunostaining of p53 in epithelial ovarian cancer.

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