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Surface epithelial ovarian tumors and p53 immunoexpression: an observational study in tertiary teaching hospital in Western Uttar Pradesh

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ABSTRACT

BACKGROUND- Ovarian tumors display a variety of histopathological patterns and varying degree of aggressiveness. The final diagnosis, staging, treatment protocol and prognosis of ovarian tumors are primarily dependent upon histopathological type. Defects in p53 tumor suppressor pathway have association with bad prognosis in ovarian tumors.

MATERIAL AND METHODS-The present study was hospital based observational study in Department of Pathology in Western Uttar Pradesh for duration of 18 months. In this study histomorphological analysis of surface epithelial ovarian tumors with special emphasis to p53 immunoexpression was done.

OBSERVATION AND RESULTS-

Seventy cases of surface epithelial ovarian tumors were studied. 41.43% patients were in 4^{th} decade followed by 32.86% in 5^{th} decade. Serous tumors constituted the majority (62.86%) followed by mucinous tumors (28.60%). p53 immunoexpression was maximum in malignant tumors (80%) followed by 22.22% in borderline ovarian tumors and 04.35% in benign ovarian tumors. The difference was statistically significant (p value <.00001)

CONCLUSION- Ovarian tumors are usually benign. Surface epithelial ovarian tumors are most common category of ovarian tumors. Immunohistochemistry for p53 can be used as an aid in the prognosis and prediction of response to specific therapy in malignant neoplasms.

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KEY WORDS- Cancer, Histopathology, Immunohistochemistry, Neoplasia, Ovary

INTRODUCTION-

The ovaries are paired pelvic organs that lie on either aspect of the uterus close to the lateral pelvic wall. The surface of the ovary is covered up by a mono layer of cuboidal cells, which forms germinal epithelium that is continuous with the mesothelial covering, the mesovarium.[1]
Fundamentally, ovary contains four major types of tissue (Epithelium, Sex Cords, Ovarian stroma and Germ cells), all of which can give rise to a variety of neoplasms. These four categories of neoplasms are Epithelial tumors, sex cords-stromal tumors, germ cells tumors and miscellaneous tumors.[2]
Almost eighty percent are benign ovarian tumors. Ovarian cancer is the most common cause of death due to malignancy of female genital tract. It comprises of 30% of all cancer cases of female genital tract.[3] The final diagnosis, staging, treatment protocol and prognosis of ovarian tumors is primarily dependent upon histopathological type.[4]
Surface epithelial ovarian tumors are subclassified based on cell type as serous, endometrioid, clear cell, mucinous, seromucinous, or transitional (Brenner). Most tumor are subdivided into Benign, Borderline, Malignant category.
p53 (Tp53, tumor protein p53) is the most relevant human oncosuppressor gene that has role in controlling cell cycle and initiating carcinogenesis. Defects in p53 tumor suppressor pathway are present in over eighty percent of human cancers and have association with bad prognosis in ovarian tumors. p53 mutation and p53 protein overexpression are common findings in ovarian carcinomas. p53 tumor protein accumulation is a marker of poor prognosis in a subset of patient with ovarian cancer. A dual oncogenic pathway describes step wise transformation of serous benign and borderline ovarian tumors into low grade and high-grade serous carcinomas, arising de novo from surface epithelia due to p53. [5]

AIMS AND OBJECTIVES-

The present study was intended to study immunohistochemical expression of p53 in ovarian surface epithelial tumors.

MATERIAL AND METHODS-

The study was conducted in Department of Pathology in a tertiary teaching hospital in western Uttar Pradesh for duration of 18 months (12 months for data collection and 6 months for data compilation). It was a hospital based observational descriptive study. Written informed consent and institutional ethical clearance was obtained in all prospective cases. Complete anonymity of the patient was maintained in retrospective cases

Sample size: Eighty-seven cases of neoplastic ovarian lesions were studied, out of which 70 cases were of surface epithelial ovarian tumors.

Inclusion criteria: Cases of ovarian lesions were included in study in which adequate tissue material an1d clinical data were available and falling within specific time period.

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Exclusion criteria: Autolyzed or poorly preserved tissue [prospective]; Non availability of representative tissue in the slide and paraffin blocks in archives of Department of pathology [retrospective]

Procedure- The sample of ovarian lesions was fixed in 10% formalin overnight, later was grossed and processed. Tissue sections taken were kept in cassettes and labeled accordingly. These were processed in semi automated tissue processor. Tissue was finally transferred from last wax bath to plastic embedding ring filled with molten paraffin wax. Sections were stained with hematoxylin and eosin. Diagnosis was made. Surface epithelial tumors were selected for immunohistochemistry. On 3-5 µm cut sections mounted on PLL (Poly-l-lysine) coated slides, immunohistochemistry for p53 was applied. Results were recorded by counting number of positive cells and intensity. **(Table 1)** Aggregate score was evaluated by combining results for both staining, intensity and number of cells. This >3 out of 6 aggregate score was considered positive.0,2 scores were considered negative while 3,4 were considered low positive and 5,6 were considered high positive.[6]

Statistical analysis: The appropriate statistical test was applied using SPSS (ver 20) Software; p value < 0.05 will be considered as statistically significant.

RESULTS

A hospital based observational study was conducted in the Department of Pathology at a tertiary teaching hospital in western Uttar Pradesh. After getting proper approval from Institutional Ethical Committee and strictly following inclusion and exclusion criteria, eighty-seven specimens of ovarian tumors were included in the study. Out of 87 neoplastic ovarian lesions, 70 cases were of surface epithelial ovarian tumors. Forty-six cases (46/70; 65.71%) were of benign, 09 cases (9/70; 12.86%) were of borderline and 15 cases (15/70; 21.43%) were of malignant surface epithelial ovarian tumors.

Most surface epithelial ovarian tumors were seen in mostly 4th decade (29 cases, 41.43%) followed by 23 cases (32.86%) in 5th decade.

Majority of cases of surface epithelial ovarian tumors were unilateral. 58 (82.86%) while bilateral cases were 12 (17.14%). Benign cases were mostly unilateral.

On gross appearance, most cystic surface epithelial ovarian tumors were benign (44; 62.86%) and majority of the mixed tumors (cystic plus solid) were borderline and malignant (24; 34.28%). There were two solid tumors on gross appearance; both came out to be malignant on histopathology.

Histomorphological categorization of ovarian tumors showed that surface epithelial tumors were maximum (80.46%; 70 cases) followed by germ cell tumors (16.09%; 14 cases) and sex cord stromal tumors (3.45%; 03 cases).

Serous tumors constituted the majority i.e., 62.86% followed by 28.60% in mucinous tumors on histomorphological categorization of surface epithelial tumors. **(Table 2)**

Equal number of cases 2.86% was seen in Endometroid tumor, Seromucinous and Brenner tumor. Serous tumors were mostly benign; 48.57%, followed by malignant (10%) in 07

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cases and 4.28% in borderline cases. Mucinous tumors were mostly benign (14.285%) in 10 cases followed by equal proportion 7.14% in borderline and malignant tumor. Endometroid tumors were all malignant 2.857%. Seromucinous tumor had equal proportion 1.42% in benign and malignant ovarian tumors. Brenner tumor constitutes 1.42% which was benign and malignant both. (**Photomicrograph 1)**

The overall immunohistochemical expression of p53 in various ovarian tumors included in this study was 22.86%. The expression of p53 was maximum in malignant tumors (80%) followed by 22.22% in borderline ovarian tumors and 04.35% in benign ovarian tumors. (**Photomicrograph 2)**

The difference in IHC expression of p53 in various histopathological categories of ovarian tumors was statistically significant (p value < .00001).

DISCUSSION

Ovary is an important organ as it is concerned with the production of progeny. The ovary consists of sex cells and mesenchymal cells which are totipotent and multipotent respectively. So, when it becomes neoplastic, almost any types of tumors can result. [1]

Ovarian non neoplastic and neoplastic lesions often have similar clinical presentations like abdominal pain, abdominal mass etc. depending on size of lesion making preoperative distinction between them difficult. Hence, it is often diagnosed as mass or cyst on ultrasonography and is removed for histopathological examination. Hence, their proper diagnosis by histopathological examination is essential for further management.[7]

We observed that majority cases of surface epithelial ovarian tumor were from 31 to 50 years of age. Similar results were reported in a study conducted by Hamdi et al [8] on ovarian tumors and Mohapatra et al [9] on surface ovarian tumors where maximum cases were seen from 31-60 years of age.

Our histopathological results were in concordance with results of Naik et al, Singh et al. [10,11] They observed that benign tumors were most common histopathological category followed by borderline and malignant tumors respectively.

In present study, most surface epithelial tumors were cystic (44/70; 62.86%), while most cystic lesions were benign (44/46; 95.65%). Surface epithelial tumors with mixed gross appearance were mostly borderline (9/9) and malignant (13/15). However, all solid tumors were malignant on histopathology, although 2/15; 13.33% of malignant tumors were solid in gross appearance. In study by Choudhury et al studied various ovarian tumors and concluded that 68% of benign tumors were predominantly cystic, while 35% of malignant tumors were predominantly solid and all the solid cystic tumors were malignant. [12]

In study by Laishram et al observed in his study on surface epithelial ovarian tumors that on cut section, the most common morphological feature found was mixed solid and cystic in 45.95% cases while the least common morphological feature was solid which was found

In a study by Mahadevappa et al, 70% of surface epithelial ovarian carcinomas were solid in consistency, 27.5% were solid-cystic and only 2.5% were purely cystic.[14]

The present study showed surface epithelial tumors 70(80.45%), Sex cord stromal tumor

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03(3.44%) and Germ cell tumors 14(16.09%). In study by Panchonia A et al showed surface epithelial tumors 68.0%, Sex cord stromal tumor 6.1% and germ cell tumors 24.7%. [15] In study by Singh M et al [11] showed surface epithelial tumors 32.64%, sex cord stromal tumor 2.08% and germ cell tumors 64.76%. %. In study by Sawant A et al and Mahajan S et al showed surface epithelial tumors 25(84.8%),Sex cord stromal tumor 02(6.1%) and Germ cell tumors 3(9.1%). [16] Our study is comparable with Sawant and Mahajan et al. In study by Suleiman AY [17] showed surface epithelial tumors 60.2%, sexcord stromal tumor 2.9% and germ cell tumors 35.95%. **(Table 4)**

We also observed in our study that immunohistochemical expression of p53 in various surface epithelial ovarian tumors was 18.18%, the expression being absent in benign and borderline surface epithelial ovarian tumors (SEOT's). However, it was 71.4% in malignant SEOT's included in the study. Our results were in concordance with Amanullah et al [21] which showed that overall immunohistochemical expression of p53 in various SEOT's was 25%. The expression was absent in benign and borderline tumors while it was positive in 65.2% of malignant SEOT's included in the study. Kmet et al [22] the p53 expression to be 45%, 5%, and 1%, for invasive, borderline and benign tumors respectively. Similar pattern of increasing p53 expression from benign to malignant ovarian tumors was reported by Havrilesky et al, Chiesa et al and Bilyk et al. [23,24,25]

CONCLUSIONS-

There occur numerous types of 'Neoplastic ovarian lesions.' About 80% were benign ovarian tumors. Ovarian cancer constituted 30% of all cancer cases of female genital tract. Among them, surface epithelial ovarian tumors constituted more than 90% of malignant neoplasms arising in ovary. The correlation in IHC expression of p53 in various histopathological categories of surface epithelial ovarian tumors was statistically significant (p value < .00001). Similar studies should be carried out in larger sample size. The present study highlights the importance of p53 expression in ovarian neoplastic patients and can be potential target for future therapy.

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Table 1-Determination of p53 Expression in malignant cells (Nuclear staining)

Intensity of staining	Percentage of tumor cell showing staining	Score
Negative	< 10 %	0
Weak Positive	10-30 %	1+
Moderate Positive	31-50 %	2+
Intense Positive	> 50 %	3+

Table 2 : Histomorphological Categorization of Surface Epithelial Tumors (n=70)

HISTOMORPHOLOGICAL TYPE	Number	Percentage
SEROUS TUMORS (n=44)		
Serous cyst adenoma	32	45.71
Serous cystadenofibroma	02	2.85
Serous borderline	03	4.28
Low grade	04	5.71
High grade	03	4.28

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MUCINOUS TUMORS (n=20)		
Mucinous cyst adenoma	10	14.28
Mucinous borderline	05	7.14
Mucinous adenocarcinoma	05	7.14
SEROMUCINOUS TUMORS (n=02)		
Seromucinous cystadenoma	01	1.42
Seromucinous borderline tumor	01	1.42
BRENNER TUMOR (n=02)		
Brenner Tumor benign	01	1.42
Brenner tumor malignant	01	1.42
ENDOMETROID CARCINOMA (n=02)		
Endometroid adenocarcinoma NOS	02	2.85
Total	70	

Table 3: Distribution Of Immunohistochemical Expression Of p-53 On Surface Epithelial Tumors (n=70)

Histological Category	Positivity for p-53		Negativity for p-53		p- value
	(n)	%	(n)	%	
BENIGN (n=46)	02	04.35	44	95.65	
BORDERLINE(n=9)	02	22.22	07	77.78	
MALIGNANT(n=15)	12	80.00	03	20	
TOTAL (n=70)	16	22.86	54	77.14	<.00001

Table 4- Comparative analysis of immunohistochemical expression of p53 in various histopathological categories of surface epithelial ovarian tumors with previous studies.

Title of Study	Year	No of Cases	p53 positive cases (%)		
			Benign	Borderline	Malignant
Present Study	2022	70	4.35%	22.22%	80.00%

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Mohapatra et al [9]	2021	52	14.3	75	89.5
Zahir et al [18]	2018	86	11.1	40	80
Qasim et al [19]	2017	60	35	20	90
Naik et al [10]	2015	110	6.1	75	81.25
Sylvia et al [20]	2012	60	0	20	57.6

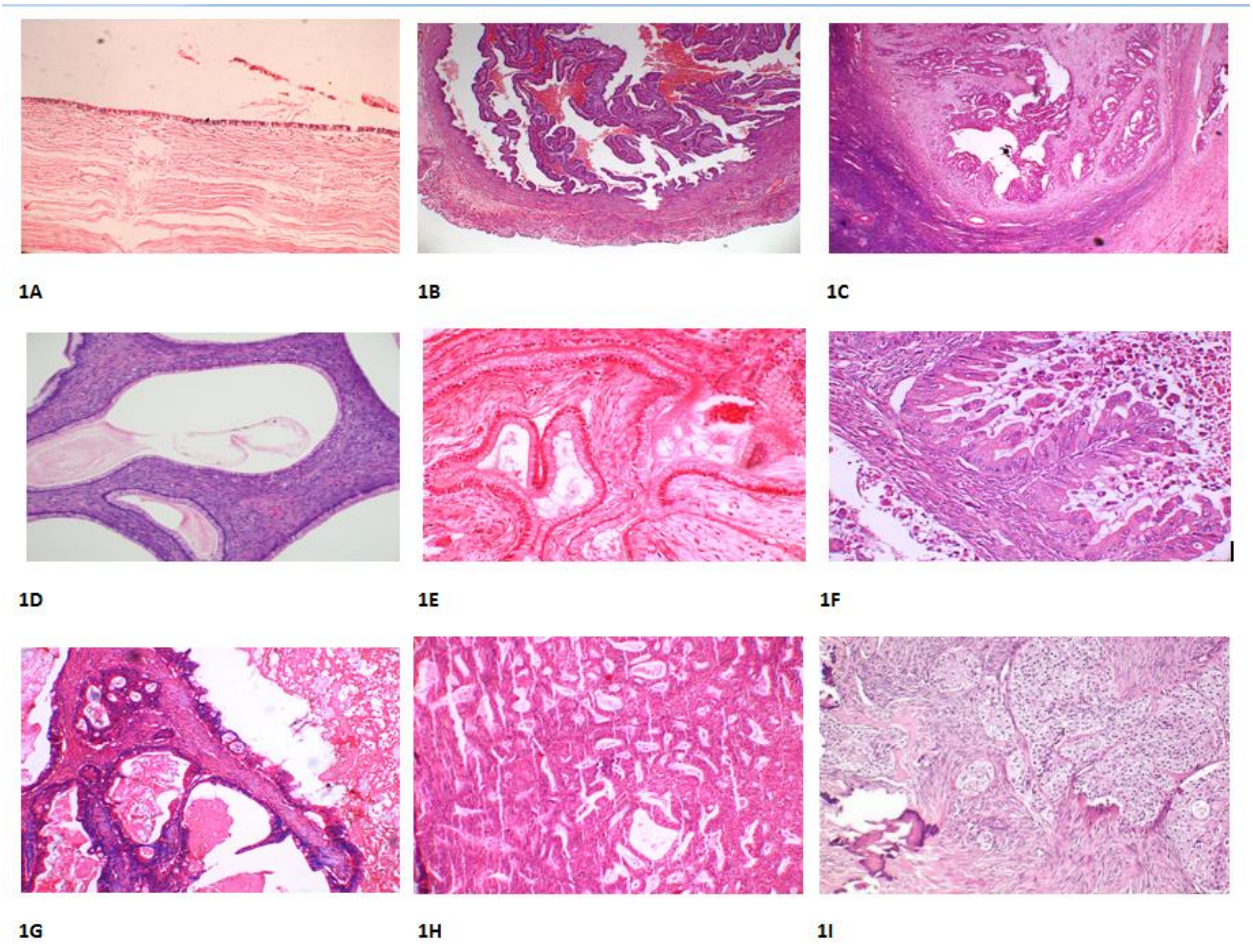

IMAGE 1- Photomicrograph showing H&E-stained sections of: 1A- Serous cystadenoma (100x); 1B- Serous borderline tumor showing papillae (40x); 1C-Serous cystadenocarcinoma. (40x); 1D- - Mucinous Cystadenoma (100x); 1E-Borderline mucinous adenoma. (40x); 1F- Mucinous adenocarcinoma. (100x); 1G- Borderline seromucinous tumor (40x); 1H- Endometroid adenocarcinoma(100x); 1I- Brenner tumor (100x)

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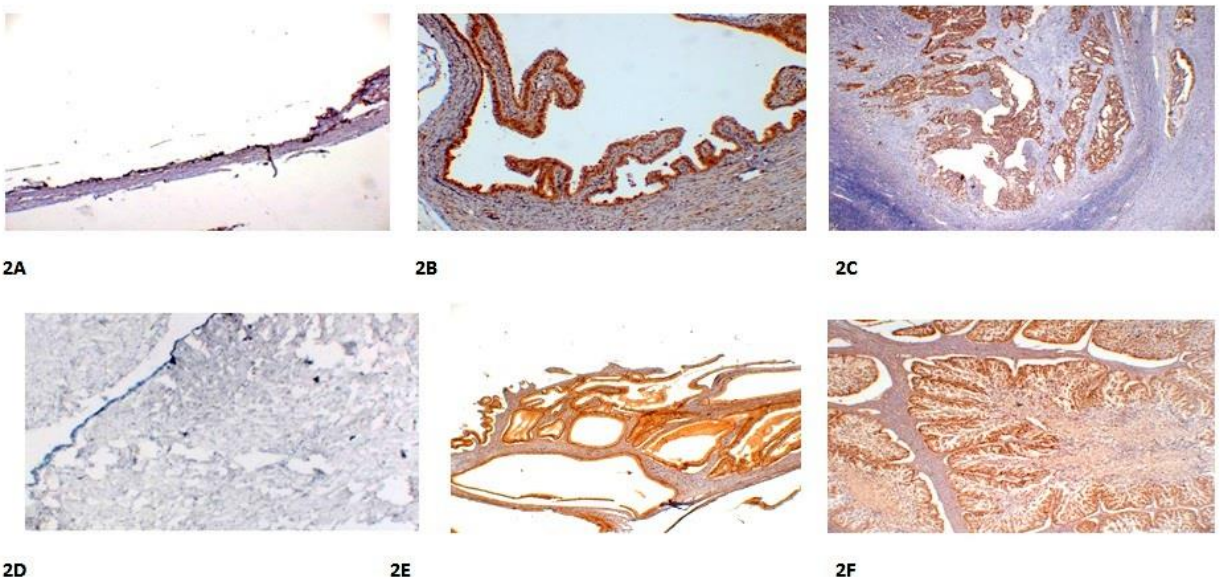

IMAGE 2- Photomicrograph showing p53 immunochemical expression of: 2A- Serous cystadenoma (-); 2B- Serous borderline tumor (+); 2C- High grade Serous cystadenocarcinoma. (+); 2D-Mucinous Cystadenoma (-); 2E-Borderline mucinous adenoma. (+); 2F- Mucinous adenocarcinoma. (+)