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Original Article

Pathology Section

Clinicohistopathological Features and Immunohistochemical Expression Patterns of p53 in Epithelial Ovarian Tumours: A Cross-sectional Study

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ABSTRACT

Introduction: Ovarian tumours represent 3% of female malignancies, with epithelial tumours constituting more than 90% of all ovarian cancers. Tumour suppressor gene 53 (TP53) mutations play an important role in the prognosis and treatment of ovarian cancer. The tumour suppressor gene Tumour Protein 53 (p53), located on the short arm of chromosome 17, acts by suppressing abnormal cell growth at the beginning of the Synthesis phase (S-phase) of the cell cycle. Previous studies have shown a correlation between p53 mutation or overexpression and patient prognosis in various types of tumours, including breast cancer, rectal cancer, intestinal cancer, lung cancer, and ovarian cancer.

Aim: To investigate the clinicohistopathological features and immunohistochemical expression of p53 in Epithelial Ovarian Tumours (EOT).

Materials and Methods: A cross-sectional study was conducted in the Department of Pathology at Hind Institute of Medical Sciences, Barabanki, Uttar Pradesh, India. The duration of the study was one year and two months, from September 2021 to November 2022. A total of 80 cases of EOT were included and histopathological diagnosis was performed, and immunohistochemical expression of p53 was evaluated in all cases. The Chi-square test was used to compare categorical data (the number of benign, borderline, and malignant EOT) and determine whether the difference in p53 expression (positive or negative) was statistically significant, using Statistical Package for the Social Sciences (SPSS) version 26.0.

Results: The total of 80 cases of EOT in the present study comprised 56 (70%) benign, 5 (6.25%) borderline, and 19 (23.75%) malignant tumours. The p53 expression was statistically significant. Immunohistochemistry (IHC) for p53 showed diffuse strong positive nuclear staining (>60%) of the tumour cells in 14 cases, all of which were malignant epithelial tumours. Focally weak and patchy positive nuclear staining patterns (5%-60%) were observed in 64 cases, including 56 benign cases, four borderline cases, and four cases of malignant epithelial tumours, respectively. p53 positivity (<5% staining of tumour cells) was seen in two cases, one each of borderline and malignant epithelial tumour, respectively.

Conclusion: The IHC marker p53 serves as a surrogate marker for p53 gene mutation, and its positivity is observed in serous EOT. Understanding p53 staining patterns can be used in conjunction with a panel of other antibodies to correctly classify morphologically confusing EOT. This can aid in assessing prognosis and understanding the biological behaviour of the tumour, which can be helpful in modifying the treatment plan.

Keywords: Immunohistochemistry, Tumor protein 53 expression, Tumour supressor gene

INTRODUCTION

Ovarian tumours represent 3% of female malignancies, of which epithelial tumours constitute over 90% of all ovarian cancers [1-3]. In ovarian cancer, the five-year survival rate of patients is 25%-30%. Most patients with ovarian cancer have distant spread even at the time of diagnosis, often without specific symptoms [4]. Pathological diagnosis of ovarian cancer is essential, as different histological subtypes require different treatment approaches [5]. Type II epithelial tumours are usually High Grade Serous Carcinomas (HGSC), accounting for about 90% of all Epithelial Ovarian Cancers (EOCs). They are highly aggressive, develop rapidly, and are typically diagnosed at an advanced stage. They are genetically unstable and commonly express a mutated TP53 gene. Mutations in TP53 play an important role in the prognosis and treatment of ovarian cancer [6].

Immunohistochemistry staining for p53 is considered an essential biomarker for diagnosing carcinomas in various organs, including ovarian cancers. Strong and diffuse immunostaining of p53 is typically associated with a TP53 gene mutation. However, the significance of completely negative immunostaining is controversial [7]. It is sometimes used as a substitute for TP53 mutational analysis, which is prevalent in High Grade Serous Ovarian Cancer (HGSOC) (over 96% of cases have mutations). Therefore, p53 immunostaining is also used to differentiate between HGSC and Low Grade Serous Carcinomas (LGSC) [8].

The objective of the present study was to evaluate the expression of p53 in various histological types of EOT and to examine their clinicohistopathological features. Hence, the present study aimed to collect data on the types of EOT in terms of age of presentation, parity, clinical symptoms, and histopathological diagnosis. Additionally, it aimed to investigate the role of p53 expression and its relationship with the histopathological diagnosis at a Tertiary Healthcare Centre located in the central Awadh region of Uttar Pradesh, India.

MATERIALS AND METHODS

A cross-sectional study was conducted in the Department of Pathology at Hind Institute of Medical Sciences, Barabanki, Uttar Pradesh, India. The duration of the study was one year and two months, from September 2021 to November 2022. A total of 80 cases of EOT over a period of 14 months. The study received

approval from the Institutional Scientific and Ethical Committee (HIMSB/RD-04/9-21) and was conducted in accordance with the principles of the Helsinki Declaration.

Sample size calculation: Sample size calculation was performed using OpenEpi software version 3.01, with a confidence interval of 95%, determining a minimum sample size of 80.

Inclusion criteria: All cases of EOT diagnosed through histopathology were included in the study.

Exclusion criteria: Non neoplastic lesions, stromal tumours, germ cell tumours, tumours of rete ovarii, and miscellaneous tumours of non epithelial origin were excluded from the study.

Study Procedure

The ovarian specimens were grossed and processed to produce formalin-fixed paraffin-embedded sections. The sections were then stained with Haematoxylin and Eosin (H&E) and subjected to IHC staining using a p53 antibody. The stained sections were examined under a microscope. For p53 IHC staining, 3-4 micrometer thick sections were taken on poly-L-lysine-coated slides. Antigen retrieval was performed by heating the sections in citrate buffer at pH 6.0 using a pressure cooker. A mouse monoclonal antihuman p53 antibody (DO-7, DAKO) was used for IHC at a dilution of 1:200 for 30 minutes at room temperature. The expression of p53 was measured as the percentage of cells showing definite nuclear staining. A p53 immunopositive breast carcinoma was used as a positive control.

The Chi-square test was used to compare categorical data (the number of benign, borderline, and malignant EOT) and determine if the difference in p53 expression (positive or negative) was statistically significant.

Interpretation of staining: Nuclear staining was considered, and the results were expressed as a percentage.

Positive: Two types of positive staining patterns were considered.

a) If >60% of cells were positive, diffuse positivity due to missense mutation of p53 was considered.

b) If <5% of cells were positive, null positive staining was considered due to a nonsense mutation of p53.

c) Cases were considered negative if 5%-60% of cells showed patchy staining due to the wild/normal type of p53 mutation [7,9].

STATISTICAL ANALYSIS

The results were statistically analysed using SPSS version 26.0. The data were expressed as mean and Standard Deviation (SD). The Chi-square test was used to compare nominal variables and identify associations or relationships. A p-value <0.05 was considered statistically significant.

RESULTS

In the present study, a total of 80 cases of EOT were included, consisting of 56 (70%) benign, 5 (6.25%) borderline, and 19 (23.75%) malignant tumours. The peak incidence of epithelial tumours was in the 51-60 years age group (30%). Among these, 16 (28.57%) out of 56 benign tumours were noted between 51-60 years, 1 (20%) out of five borderline tumours were noted between 31-40 years, and 7 (36.84%) out of 19 malignant tumours were noted between 51-60 years. Additionally, it was observed that the proportion of cases increased with higher age [Table/Fig-1]. The most common presenting symptom in the present study, was an abdominal mass (61.25%). Other common complaints included lower abdominal pain in 40/80 patients (50%), bleeding per vagina in 15/80 patients (18.75%), primary infertility in 5/80 patients (6.25%), and urinary retention and anorexia in 6/80 patients (7.5%) [Table/Fig-2]. In the present study, among the 80 cases, only 46.25% had high parity, followed by low parity (36.25%). The remaining cases were unmarried (6.25%) and nulliparous (11.25%). This difference was found to be statistically significant with p=0.0361, in the occurrence of benign, borderline, and malignant tumours with respect to parity [Table/Fig-3].

Age group (in years)	Number of cases n (%)			Total n (%)
	Benign n (%)	Borderline n (%)	Malignant n (%)	
20-30	11 (13.75)	1 (1.25)	0	12 (15)
31-40	11 (13.75)	1 (1.25)	1 (1.25)	13 (16.25)
41-50	11 (13.75)	1 (1.25)	5 (6.25)	17 (21.25)
51-60	16 (20)	1 (1.25)	7 (8.75)	24 (30)
61-70	6 (7.5)	1 (1.25)	4 (5)	11 (13.75)
71-80	1 (1.25)	0	2 (2.5)	3 (3.75)
Total	56 (70)	5 (6.25)	19 (23.75)	80 (100)
Mean±SD	46.26±13.70	45.60±16.24	54.10±9.25	

[Table/Fig-1]: Age distribution of cases of Epithelial Ovarian Tumours (EOT).

Symptoms	Number (n)	Percentage (%)
Abdominal mass	49	61.25
Pain abdomen	40	50
Bleeding per vagina	15	18.75
Primary infertility	5	6.25
Urinary retention, anorexia	6	7.5

[Table/Fig-2]: Distribution of cases according to symptoms (N=80).

Parity	Number of cases n (%)			Total n (%)
	Benign n (%)	Borderline n (%)	Malignant n (%)	
Unmarried/Nulliparous	2/3	1/1	2/5	14 (17.5)
Low parity (<2)	24	1	4	29 (36.25)
High parity (≤2)	27	2	8	37 (46.25)

[Table/Fig-3]: Parity status of the cases.

The EOT were mostly right-sided in 35 (43.75%) cases, left-sided in 29 (36.25%) cases, and bilateral in 16 (20%) out of 80 cases. Benign epithelial tumours were mostly right-sided in 26 (46.42%) out of 56 cases. Borderline EOT were right-sided in 2 (40%) out of 5 cases. Malignant EOT were mostly bilateral in (42.10%) out of 19 cases. This difference was found to be statistically significant with p=0.0311, in the occurrence of benign, borderline, and malignant tumours with respect to laterality [Table/Fig-4].

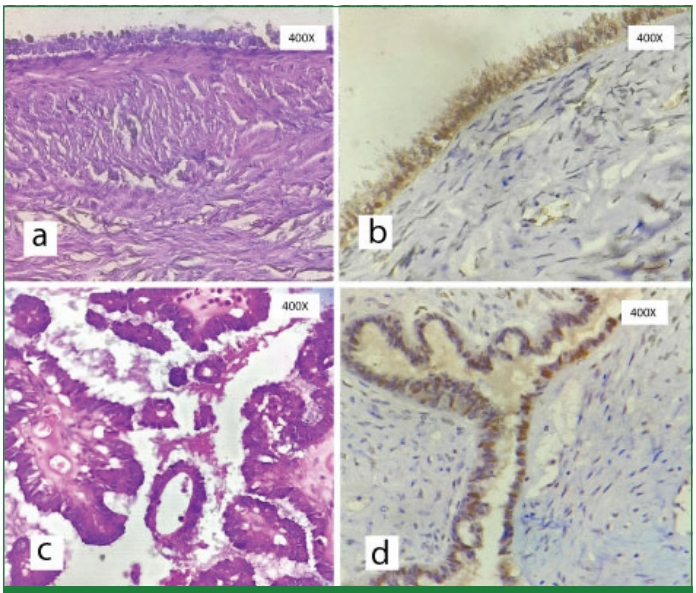
Laterality	Number of cases n (%)			Total n (%)
	Benign n (%)	Borderline n (%)	Malignant n (%)	
Right	26 (46.42)	2 (40)	7 (36.84)	35 (43.75)
Left	24 (42.85)	1 (20)	4 (21.05)	29 (36.25)
Bilateral	6 (10.71)	2 (40)	8 (42.10)	16 (20)

[Table/Fig-4]: Laterality of Epithelial Ovarian Tumour (EOT).

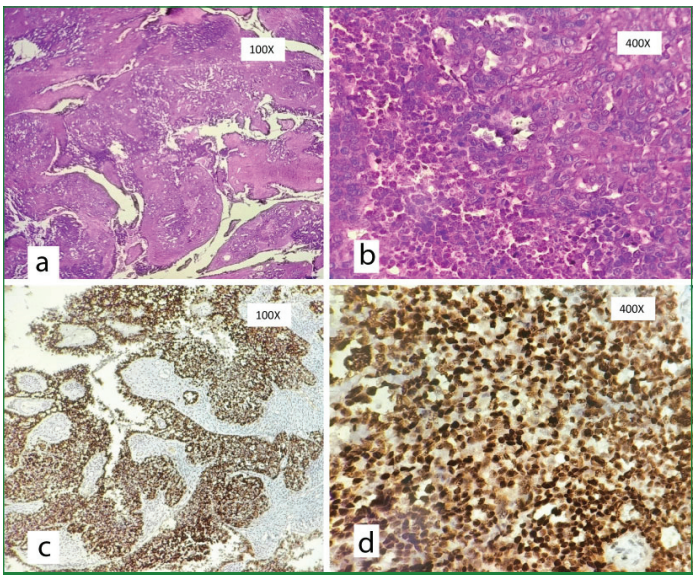
In the present study, all benign tumours were predominantly cystic in nature, with 51/56 (91.07%) cases exhibiting this pattern. Malignant EOT were mostly solid-cystic in 13 (68.42%) out of 19 cases. Overall, EOT were mostly cystic in 55/80 (68.75%) out of 80 cases, followed by cysts with serous fluid in 35 (43.75%) cases, cysts with mucinous fluid in 29 (36.25%) cases, solid-cystic in 20/80 (25%) cases, cysts with papillary excrescences in 10/80 (12.5%) cases, solid with variegated appearance in 6 (7.5%) cases, and solid in 5 (6.25%) cases. This difference was found to be statistically non significant with p=2.16, in the occurrence of benign, borderline, and malignant tumours with respect to the consistency of EOT.

Out of 34 cases of benign serous cystadenoma, most showed unilocular or multilocular cysts lined by a single layer of tall, columnar, ciliated lining with dense fibrous stroma forming papillary projections. All four cases of borderline serous cystadenoma showed a hierarchical branching pattern with focal areas showing epithelial stratification and a thin fibrous cyst wall with focal papillary projections.

The papillary fronds progressively branch into the stromal core, and mild nuclear atypia is also observed [Table/Fig-5a-d]. Out of 22 cases of benign mucinous cystadenoma, most showed multiple cysts and glands lined by a single layer of columnar lining exhibiting small nuclei located basally and cytoplasm containing mucin. Fifteen cases of high-grade serous cystadenocarcinomas showed solid masses of columnar to cuboidal cells with eosinophilic cytoplasm, severe nuclear atypia with prominent nucleoli and nuclear pleomorphism, including large, bizarre multinucleated forms, and a high mitotic index. Necrosis is frequent [Table/Fig-6a-d]. All three cases of mucinous cystadenocarcinomas showed stromal tissue infiltrated with malignant epithelial cells in solid sheets, tubular or cystic papillary disposition, and were lined by tall columnar, mucin-secreting epithelial cells. The epithelial cells lining the cystic spaces are in single or stratified layers showing mild to moderate atypia with increased mitosis in many areas. In the present study, among the 19 malignant tumours, 15 (78.94%) were p53 positive. All benign EOT were p53 negative. Among the five cases of borderline serous cystadenoma, one case was p53 positive, while the remaining four cases were negative. This association of p53 overexpression with biological tumour behaviour was found to be statistically significant (p<0.002) [Table/Fig-7].



[Table/Fig-5]: Photomicrograph shows cyst wall lined by a single layer of tall, columnar, ciliated epithelium in serous cystadenoma (a). Papillary architecture and cell crowding and mild nuclear atypia in borderline serous tumour (H&E x400); (b) Serous cystadenoma (38%) (x400); (c) Expression of p53 in epithelial and stromal cells (H&E, x400); (d) Borderline serous cystadenoma (44%), respectively (x400).



[Table/Fig-6]: Photomicrograph shows solid diffuse pattern of tumour cells with focal papillary architecture in a case of high-grade serous cystadenocarcinoma (a) Photomicrograph of the same case showing hyperchromasia, nuclear pleomorphism, vesicular chromatin and nuclear atypia with prominent nucleoli in tumour cells (H&E x100) (b) Malignant cells shows strong and diffuse nuclear staining >60% with p53 (x100 and x400) in high-grade serous cystadenocarcinoma (c,d respectively).

Histopathological diagnosis	Total no. of cases (80)	No. of cases showing p53 expression	Type of expression
Benign serous cystadenoma	34	-	Negative
Borderline serous cystadenoma	4	1	Positive
Serous cystadenocarcinoma	15	15	Positive
Benign mucinous cystadenoma	22	-	Negative
Borderline mucinous cystadenoma	1	-	Negative
Mucinous cystadenocarcinoma	3	-	Negative
Endometroid adenocarcinoma	1	-	Negative

[Table/Fig-7]: p53 expression in Epithelial Ovarian Tumours (EOT).

Immunohistochemistry for p53 showed diffuse strong positive nuclear staining (>60%) of tumour cells in 14 cases, all of which were malignant serous epithelial tumours. Focally weak and patchy positive nuclear staining pattern (5%-60%) was seen in 64 cases, comprising 56 cases of benign tumours, four cases of borderline tumours, and four cases of malignant epithelial tumours. p53 positive (<5%) staining of tumour cells was seen in two cases, consisting of one case each of borderline and malignant epithelial tumour, respectively [Table/Fig-8].

Histopathological diagnosis	p53 positive (<5% staining of tumour cells)	p53 negative (5%-60% focally present weak and patchy nuclear positivity of tumour cells)	p53 positive (>60% diffuse strong nuclear positivity of tumour cells)
Benign serous cystadenoma (34)	0	34	0
Borderline serous cystadenoma (4)	1	3	0
Serous cysadenocarcinoma (15)	1	0	14
Benign mucinous cystadenoma (22)	0	22	0
Borderline mucinous cystadenoma (1)	0	1	0
Mucinous cystadenocarcinoma (3)	0	3	0
Endometroid adenocarcinoma (1)	0	1	0
Total	2	64	14

[Table/Fig-8]: Staining pattern of p53 expression of EOT (N=80).

DISCUSSION

The present study included 80 cases of EOT, consisting of 56 benign tumours (70%), 19 malignant tumours (23.75%), and 5 borderline tumours (5%). The peak incidence of epithelial tumours in the present study was observed in the 51-60 years age group (30%), which was much higher than the age group of

40-49 years (35.3%) reported in a previous study [10]. Among the benign tumours, 16 (28.57%) cases were noted between 51-60 years of age, 2 (40%) borderline tumours were noted between 31-40 years of age, and 7 (36.84%) malignant tumours were noted between 51-60 years of age. Moreover, in the present study, it was observed that the proportion of cases increased with increasing age [11]. However, this difference between benign, borderline, and malignant EOT (p=0.05851) was not found to be statistically significant on analysis. A significant difference in age was found between benign and malignant epithelial tumours (p=0.01142), while it was not statistically significant between borderline and malignant EOT (p=0.1126). In current study, among the 80 cases, only 41.25% had high parity, followed by 40% with low parity (40%). The remaining cases were unmarried (10%) and nulliparous (6.25%). This difference was found to be statistically significant with p=0.0361, in the occurrence of benign, borderline, and malignant tumours with respect to parity in the present study. Studies have shown that increasing parity decreases the risk of this disease, especially that of epithelial cancer [12]. It has also been observed that infertility is associated with an increased risk of ovarian cancers [13].

In the current study, out of 80 patients, 49 (61.25%) cases presented with an abdominal mass. The other common complaints in 40 (50%) patients were lower abdominal pain, bleeding per vagina in 15 (18.75%) patients, primary infertility in 5 (6.25%) patients, urinary retention in 4 (5%) patients, and anorexia in 2 (2.5%) patients. Similar findings were observed in another study where out of 100 patients, patients with early-stage disease presented with atleast one symptom. Among these, three symptoms are relevant, such as abdominal swelling, abdominal bloating, and pelvic pain. To diagnose ovarian cancer, importance should also be given to non specific symptoms like abdominal, gastrointestinal, and constitutional symptoms [14]. A previous study reported that symptoms of abdominal distension, urinary frequency, and abdominal pain are associated with a diagnosis of ovarian cancer [15].

The EOT were right-sided in 35/80 (43.75%) cases, left-sided in 29/80 (36.25%) cases, and bilateral in 16/80 (20%) cases. In the present study, benign epithelial tumours were mostly right-sided in 26/56 (46.42%) cases, borderline EOT were right-sided in 2/5 (40%) cases, and malignant EOT were bilateral in 8/19 (42.10%) cases. In the current study, this difference was found to be statistically significant with p=0.0311, in the occurrence of benign, borderline, and malignant tumours with respect to laterality. Similarly, a study identified most benign tumours to be unilateral, while malignant and metastatic tumours were bilateral [16]. There was an increased bilaterality in serous malignant ovarian tumours, the tumour size was considerably large in serous malignant ovarian tumours, and the grade of the tumour was higher in serous malignant ovarian tumours [17].

All the benign tumours were predominantly cystic (51/56, 91.07%), and malignant EOT were mostly solid-cystic (13/19, 68.42%). Similarly, in a pilot study, benign tumours were found to be cystic, while malignant and metastatic tumours were solid or solid-cystic [16]. All EOT were mostly cystic (55/80, 68.75%), followed by cysts with serous fluid (35/80, 43.75%), cysts with mucinous fluid 29/80 (36.25%), solid-cystic 20/80 (25%), cystic with papillary excreescences (10/80, 12.5%), solid with variegated appearance 6 (7.5%) and solid 5 (6.25%) in the present study.

Benign serous tumours have a smooth external surface, with the majority of them being unilocular, while mucinous tumours show a nodular external surface due to their multilocular nature [18]. Malignant tumours exhibit breach of the capsule and have a variegated appearance on the cut surface, with predominant solid areas and areas of haemorrhage and necrosis, while benign tumours do not show these features. Similar findings were observed in the present study as well. On the cut section, papillary projections can be seen in benign, borderline, or malignant tumours, as seen in previous studies [18,19].

The prsent study shows, out of 19 malignant tumours, 15 (78.94%) were p53 positive. All benign EOT were p53 negative. Among the five borderline serous cystadenomas, one case was p53 positive, and the remaining four cases were negative [Table/Fig-3]. The p53 expression was statistically significant (p<0.002). Immunohistochemistry for p53 showed diffuse strong positive nuclear staining (>60%) of the tumour cells in 14 cases, all of which were malignant serous epithelial tumours. Focally weak and patchy positive nuclear staining pattern (5%-60%) was seen in 64 cases, of which 56 cases were benign, four cases were borderline, and four cases were malignant epithelial tumours, respectively. The p53 positive (<5%) staining of tumour cells was seen in two cases, comprising one case each of borderline and malignant epithelial tumour, respectively [Table/Fig-4]. This similar interpretation of p53 staining was also done by Yemelyanova A et al., and Amanullah NAR et al., in their studies [7,9].

In a prior study, the most common histological type observed was serous epithelial tumours (50%), followed by mucinous tumours (30.8%). Benign ovarian tumours accounted for 40% of cases, followed by malignant tumours (36%) and borderline tumours (23%). The highest p53 immunoreactivity was observed in malignant tumours (89.5%), followed by borderline tumours (75%) and benign tumours (14.3%). This association of p53 overexpression with biological tumour behaviour was found to be statistically significant (p<0.05) [20]. The high incidence of p53 positivity was also reported in serous cystadenocarcinomas [10,21]. In a prior study, no significant relationship between the histopathological type of epithelial tumours and p53 overexpression could be found (p-value >0.05) [20]. Conversely, p53 positivity was seen in 94% of serous carcinomas only. Two of the serous tumours (HGSC and LGSC) were p53 negative. The results were comparable to pilot studies [22-26]. Previous studies indicate p53 positivity in 80% of serous ovarian carcinomas, with protein expression differences depending on the degree of differentiation, high-grade tumours being diffusely p53 positive [26,27].

In an earlier study, it was noted that when both patterns of immunolabeling commonly associated with TP53 mutation (showing 60%-100% of tumour cells to be positive) and tumours with <5% of the tumour cells showing nuclear staining for p53 were combined, IHC analysis would give 95% correlation with nucleotide sequencing of the mutations. It was reported that p53 IHC scoring systems should not interpret the complete absence of expression as consistent with wild-type TP53 [7]. p53 positivity was found in 8 (89%) out of the nine tumours with bilateral ovarian masses. This association was statistically significant and was comparable to another study [28]. All the p53-positive cases had ascites, with 33% of the cases showing intense staining and 17% showing null staining [29].

High-grade serous tumours tend to be p53 positive, and p53 positivity is related to the survival rate [30]. In another study, higher p53 staining was seen in borderline and malignant tumours compared to benign tumours. However, they found a comparable level of p53 staining between borderline and malignant tumours [31]. In a previous study, among 60 EOT cases, 30 (50%) were benign, 7 (11.7%) were borderline, and 23 (38.3%) were malignant. Serous tumours comprised the majority with 29 cases (48.3%). All benign and borderline EOT were p53 negative. Among the 23

malignant tumours, 15 (65.2%) were p53 positive, and all of them constituted serous malignancies. All mucinous carcinomas and clear cell carcinomas were p53 negative. A total of 2 (9%) out of the 17 serous carcinomas were also found to be p53 negative. A total of 63% HGSC showed diffuse p53 staining, while 31% showed aberrant null staining. One HGSC case and the only LGSC were p53 negative [9].

In a prior study, out of 19 serous carcinomas, 14 (73.6%) and 12 (63.1%) were positive for p53 and Wilms' Tumour gene 1 (WT1), respectively, and all were serous malignancies. A total of 14 (93.3%) of HGSC showed diffuse positive staining, while 1 (6.7%) showed aberrant null staining. All low-grade serous ovarian carcinomas were negative for p53. Out of 19 serous malignancies, 12 were positive for WT1, among which 10 were HGSC and two were LGSC. HGSC showed 66.7% positivity for WT1, while 33.3% were negative for WT1. The statistical significance of p53 and WT1 expression with the grade of the tumour was found to be insignificant (p-value >0.05) [32].

Name of the author and year of study	Place	Total cases of EOT	Cases with p53 positivity
Tan L et al., [6] 2019	China	103	59
Amanullah NAR et al., [9] 2020	Saudi Arabia	60	15
Mohapatra I et al., [20] 2021	India	52	29
Kaushik N et al., [32] 2022	India	78	14

[Table/Fig-9]: Comparative studies by other authors [6,9,20,32].

Also, p53 positivity pointed towards the biological behaviour of the EOT (bilaterally, capsule rupture, ascites, poor prognosis). p53-positive cases had more prognostic value than Cancer Antigen 125 (CA-125). The p53 positivity also hinted towards minimal residual disease.

Limitation(s)

The limitations of the present study are the small sample size and the use of a single IHC marker, which is used as a surrogate marker for the type of p53 expression (mutant or wild type). However, p53 mutational studies could not be performed.

CONCLUSION(S)

The present study demonstrates that benign tumours were more common than malignant tumours. In particular, serous epithelial tumours were the most common neoplasms, followed by mucinous tumours. Morphological study by histopathological techniques is the keystone for the diagnosis of EOT. The IHC marker p53 is a surrogate marker for p53 gene mutation, and its positivity is seen in serous EOT, with higher expression in HGSC and advanced stage tumours. It can be applied to differentiate between borderline and malignant tumours, HGSC from LGSC, and endometrioid carcinoma from the serous types. Thus, it plays an important role in the oncogenesis of EOT and a pertinent role in the progression to the invasive phenotype. IHC, being ancillary to the histopathological diagnosis, aids in prognostication and comprehension of the biological tumour behaviour, which further helps in modifying the treatment plan. Understanding of p53 staining patterns is important so that it can be used along with a panel of other antibodies for the correct classification of EOT.

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