Section: Pathology

Original Research Article

CLINICOPATHOLOGICAL ANALYSIS OF OVARIAN TUMORS AND P53 EXPRESSION IN SURFACE EPITHELIAL TUMORS AT A TERTIARY CARE CENTER

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Abstract

Background: Ovarian tumors are a significant health concern, with varied histopathological presentations and molecular characteristics. This study aims to evaluate the clinicopathological features of ovarian tumors and the expression of p53 in surface epithelial tumors at a tertiary care centre. **Material & Methods:** This prospective study included 150 female patients diagnosed with ovarian neoplasms at King George Hospital, Visakhapatnam, between January 2021 and December 2022. We analyzed the clinical presentation, age distribution, WHO classification, histopathological subtypes, gross features, laterality, tumor grading, and p53 expression. **Results:** The most common clinical presentation was abdominal mass (63.3%). The age group 31-40 years had the highest prevalence (26.7%). Surface epithelial tumors were the predominant type (88%), followed by germ cell tumors (10%) and sex cord-stromal tumors (2%). Among surface epithelial tumors, serous tumors were most frequent (62.8%), and predominantly cystic in morphology. The p53 expression analysis showed wild-type expression in all low-grade serous carcinomas, while high-grade serous tumors exhibited mutant p53 patterns. Mature teratomas dominated the germ cell tumor category, mostly presenting as cystic and unilateral. Sex cord stromal tumors were rare, with granulosa cell tumors and fibrothecomas showing solid and unilateral characteristics. **Conclusion:** This study underscores the diversity in the clinicopathological presentation of ovarian tumors. The predominance of surface epithelial tumors, particularly serous tumors, and the distinct p53 expression patterns in high-grade serous carcinomas highlight the importance of histopathological and molecular analyses in the diagnosis and management of ovarian neoplasms. Early detection and tailored treatment strategies can be enhanced by understanding these patterns.

INTRODUCTION

Ovarian tumors represent a diverse group of neoplasms with varying etiologies, histopathological features, and clinical outcomes.[1,2] They pose significant challenges in diagnosis and management due to their often asymptomatic nature and late presentation.[3] This study aims to provide a detailed clinicopathological analysis of ovarian tumors, focusing on surface epithelial tumors and their expression of the p53 protein, a key tumor suppressor involved in cell cycle regulation and apoptosis.

The significance of ovarian tumors lies in their impact on women's health globally.[4] They range from benign lesions to aggressive malignancies, with epithelial tumors being the most common type.[5] The World Health Organization (WHO) classified ovarian neoplasms into three major categories: surface epithelial tumors, germ cell tumors, and sex cord-stromal tumors, each with unique pathological and clinical characteristics.[6]
Surface epithelial tumors, derived from the coelomic epithelium covering the ovary, account for a majority of ovarian cancers.[7] Their classification into serous, mucinous, endometrioid, clear cell, and

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other subtypes and subclassification into benign, borderline and malignant is crucial for determining prognosis and treatment strategies. Among these, serous tumors are the most prevalent and are further categorized based on their malignant potential.[8]

The p53 gene plays a critical role in maintaining genomic stability and preventing tumor development. Mutations in p53 are among the most common genetic alterations in human cancers, including ovarian carcinomas.[9] The expression of p53, whether wild-type or mutant, can provide valuable insights into the tumor's behavior, aggressiveness, and response to therapy.[10]

In this context, our study conducted aims to elucidate the clinicopathological features of ovarian tumors, emphasizing the prevalence and histological subtypes as per WHO classification, and examining the expression of p53 in surface epithelial tumors. This comprehensive approach is anticipated to contribute to a better understanding of ovarian tumor pathology and aid in the advancement of diagnostic and therapeutic modalities in this domain.

MATERIALS AND METHODS

Source of Study

This hospital-based prospective observational study included 150 female patients diagnosed with ovarian neoplasms from January 2021 to December 2022. Ethical approval was obtained from the institutional committee, and informed consent was secured from all participants. The study included specimens from unilateral or bilateral salpingo-oophorectomy, total abdominal hysterectomy, and ovariotomy.

Study Duration

The study was conducted over two years, from January 2021 to December 2022.

Inclusion Criteria

- Patients diagnosed with primary ovarian tumors on histopathology.
- Willingness to undergo immunohistochemistry for tumor marker p53.

Exclusion Criteria

- Patients already receiving treatment for ovarian neoplasms.
- Non-neoplastic ovarian lesions (e.g., infarction, hemorrhagic cysts, torsion, infection).
- Metastatic ovarian lesions.
- Refusal to undergo p53 tumor marker testing.

Collection of Data

Specimens were fixed in 10% neutral buffered formalin. Systematic gross examination was followed by representative tissue sectioning for routine histopathological processing. Sampling varied based on tumor type and size, with 4-5 bits taken from cystic neoplasms and 3-4 bits (or more, based on size) from solid tumors. Tissue sections of 4-5 micrometers were stained with Hematoxylin and Eosin. Clinical history and histopathological parameters, including age, clinical presentation, and tumor features (laterality, consistency, size), were recorded. Histological typing and subtyping followed the WHO Classification of Tumors of the Ovary, 5th Edition. Serous carcinomas were graded as low-grade or high-grade, endometrioid carcinomas per WHO criteria, and other tumors using a three-tier Universal grading system. Staging was based on the FIGO Classification.

Immunostaining for p53

Immunostaining was performed on surface epithelial carcinoma cases using p53-BP-53-12 Mouse Monoclonal Antibody and PolyExcel HRP/DAB Detection system (Path insitu, Livermore, CA, USA). Sections were deparaffinized, and antigen retrieval was conducted using a Decloaking chamber set to 120 degrees Celsius with Tris-EDTA Buffer. Between each step, sections were thoroughly washed with Tris-buffered saline.

p53 immunostaining was evaluated based on the percentage of positively stained tumor nuclei. The scoring for p53 immunoreactivity was adapted from various studies and classified as follows:

Diffuse positive: When >60% of cells are positive, indicating a missense mutation of p53.

Null positive: If <5% of the cells are positive, suggesting a nonsense mutation of p53.

Wild type: Cases showing 5-60% patchy staining, indicative of wild/normal type p53 mutation.

RESULTS

Clinical Presentation of Ovarian Neoplasms

Our study included 150 female patients diagnosed with ovarian neoplasms. The most common clinical presentation was a mass in the abdomen (63.3%), followed by abdominal pain (16.6%), menstrual irregularities (6.6%), ascites (2%), and gastrointestinal issues (11.3%). [Table 1]

Age Incidence of Ovarian Tumors

The age distribution showed the highest prevalence in the 31-40 age group (26.7%), followed by the 21-30 (20%) and 41-50 (21.3%) age groups. The least affected were those aged 71-80 years (3.3%). [Table 2]

WHO Classification of Ovarian Tumors

According to the World Health Organization classification, surface epithelial tumors were predominant (88%), followed by germ cell tumors (10%) and sex cord-stromal tumors (2%). [Table 3]

Histopathological Categories

In surface epithelial tumors, serous tumors were the most common (62.8%), followed by mucinous (22.7%), seromucinous (9.8%), and endometrioid tumors (4.5%). Neither Brenner nor clear cell tumors were observed in our cohort. [Table 4]

Gross Features and Laterality

Predominantly cystic morphology was observed in serous (53 cases) and mucinous tumors (23 cases). Serous tumors were more often right-sided (50 cases), while mucinous tumors showed a more balanced distribution between right (14 cases) and left (11 cases) sides. [Table 5]

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Sub classification of Surface Epithelial Tumors

Among the serous tumors, 35.3% were benign, 1.3% borderline, and 18.6% malignant. Mucinous tumors were predominantly benign (15.3%), with a smaller proportion of borderline (2.7%) and malignant cases (2.7%). [Table 6]

Grading of Serous Carcinomas

Of the serous carcinomas, 45.5% were classified as low grade, and 54.5% as high grade. [Table 7]

Universal Grading of Non-Serous Carcinomas

All mucinous and endometrioid carcinomas were graded as Grade 1. No cases were classified as Grade 2 or Grade 3 in this group. [Table 8]

p53 Expression in Ovarian Neoplasms

p53 expression analysis revealed that all low-grade serous carcinomas (7 cases) exhibited wild-type p53, while high-grade serous tumors (9 cases) showed mutant p53 expression. A single case of endometrioid carcinoma also demonstrated mutant p53 expression. One borderline mucinous tumor showed wild-type p53 expression. [Table 9]

Characteristics and Laterality of Germ Cell Tumors

Among germ cell tumors, mature teratomas were the most prevalent (14 cases), primarily exhibiting cystic morphology and unilateral distribution. One case of dysgerminoma presented as a solid tumor and was also unilateral. [Table 10]

Sex Cord Stromal Tumors

Sex cord stromal tumors were least common, with only 3 cases. These included two granulosa cell tumors and one fibrothecoma, all presenting with solid morphology and unilateral distribution. [Table 11]

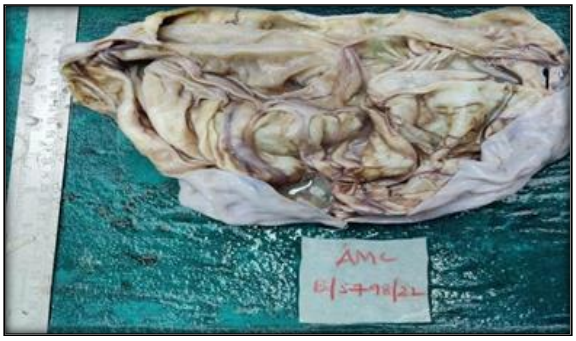

Figure 1: Cut section of Benign Serous Cystadenoma -Unilocular Cyst

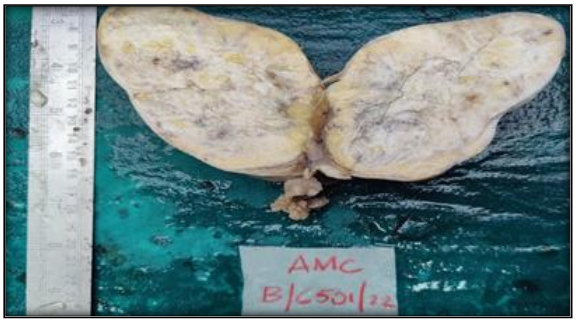

Figure 2: Cut section of a Ovarian Fibrothecoma- solid gray white and yellow areas

Figure 3: Cut section of Granulosa Cell Tumour with solid and necrotic areas

Figure 4: Cut section of Dysgerminoma with solid fleshy and lobulated appearance

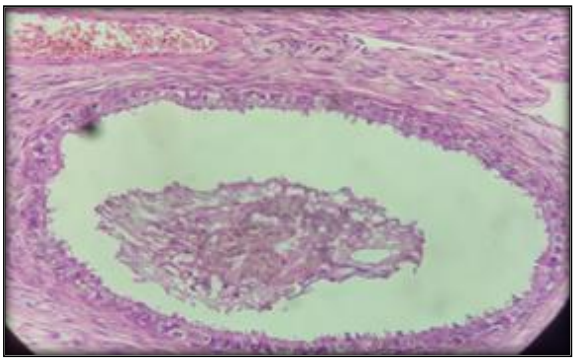

Figure 5: Mucinous Cystadenoma of Ovary Stain H and E, 20 X

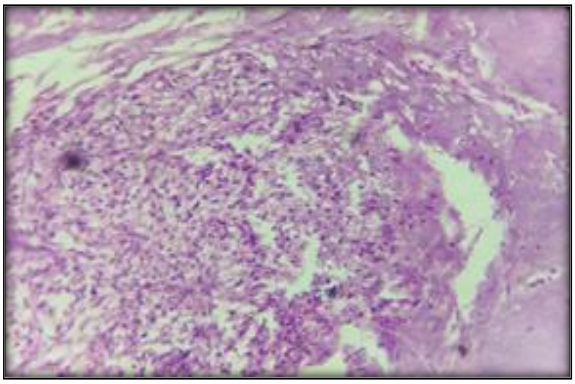

Figure 6: Fibrothecoma of Ovary. stain H and E, 20 X

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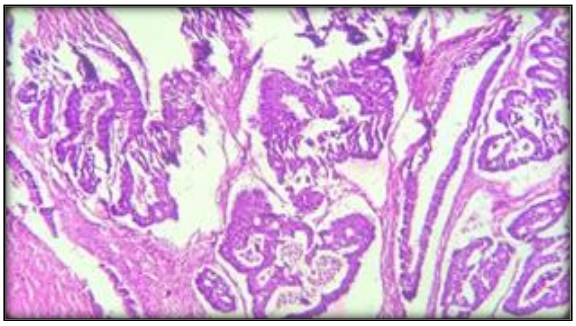

Figure 7: High Grade Serous carcinoma of Ovary, stain H and E , 20 X

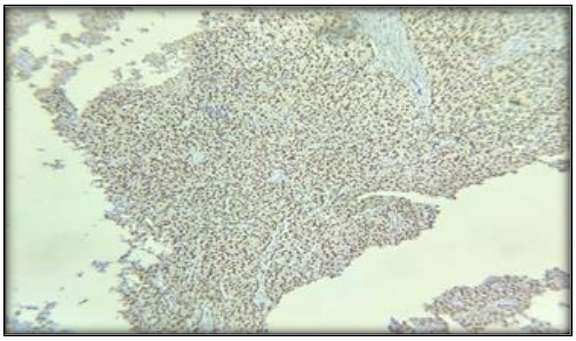

Figure 8: High Grade Serous carcinoma of Ovary, IHC, Diffuse positivity of Mutant Expression of P53, 20X

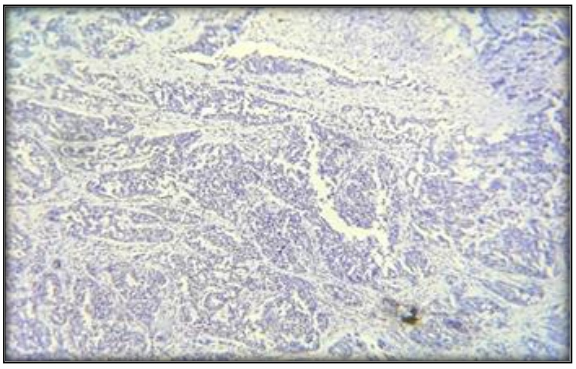

Figure 9: Low Grade Serous carcinoma of Ovary, IHC Showing Null Pattern of P53 Expression, 20X

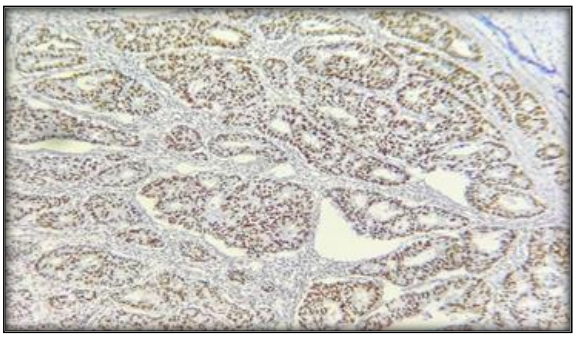

Figure 10: Mucinous Carcinoma of Ovary, IHC Showing Mutant Type of p53 Expression.20X

Table 1: Clinical Presentation of Ovarian Neoplasms

Chief Complaint	Number of Cases	Percentage (%)
Mass in Abdomen	95	63.3
Abdominal Pain	25	16.6
Menstrual Irregularities	10	6.6
Ascites	3	2.0
Gastrointestinal Issues	17	11.3
Total	150	100

Table 2: Age Incidence of Ovarian Tumors

Age Group (Years)	Total Number of Cases	Percentage (%)
11-20	14	9.3
21-30	30	20.0
31-40	40	26.7
41-50	32	21.3
51-60	19	12.7
61-70	10	6.7
71-80	5	3.3
Total	150	100

Table 3: Classification of Ovarian Tumors (According to WHO)

Type of Ovarian Neoplasm	Number of Cases	Percentage (%)
Surface Epithelial Tumors	132	88
Germ Cell Tumors	15	10
Sex Cord-Stromal Tumors	3	2
Total	150	100

Table 4: Histopathological Categories of Surface Epithelial Tumors

Epithelial Neoplasms	Number of Cases	Percentage (%)
Serous Tumors	83	62.8
Mucinous Tumors	30	22.7
Seromucinous Tumors	13	9.8
Endometrioid Tumors	6	4.5
Brenner Tumors	0	0
Clear Cell Tumors	0	0
Total	132	100

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Table 5: Laterality and Gross Features of Surface Epithelial Tumors

Tumor Type	Pure Cystic	Pure Solid	Mixed	Right	Left	Bilateral
Serous Tumors	53	0	28	50	31	2
Mucinous Tumors	23	0	7	14	11	5
Seromucinous	13	0	0	8	3	2
Endometrioid	6	0	0	4	1	0
Total	95	0	35	76	46	9

Table 6: Subclassification of Surface Epithelial Tumors

Type of Tumor	Benign Cases	Borderline Cases	Malignant Cases
Serous Tumors	53 (35.3%)	2 (1.3%)	28 (18.6%)
Mucinous Tumors	23 (15.3%)	4 (2.7%)	4 (2.7%)
Seromucinous Tumors	13 (8.6%)	0	0
Endometrioid Tumors	5 (3.3%)	0	1 (0.7%)
Total	94	6	33

Table 7: Grading of Serous Carcinomas

Grade	Number of Cases	Percentage (%)
Low Grade	15	45.5
High Grade	18	54.5
Total	33	100

Table 8: Universal Grading of Non-Serous Carcinomas

Carcinoma Type	Grade 1	Grade 2	Grade 3	Total
Mucinous	3	0	0	3
Endometrioid	1	0	0	1
Total	4	0	0	4

Table 9: p53 Expression in Ovarian Neoplasms

Tumor Type	Wild Type p53	Mutant p53
Low-Grade Serous	7	0
High-Grade Serous	0	9
Endometrioid	0	1
Borderline Mucinous	1	0
Total	8	10

Table 10: Characteristics and Laterality of Germ Cell Tumors

Germ Cell Tumor Type	Number	Pure Cystic	Pure Solid	Mixed	Right	Left	Bilateral
Mature Teratoma	14	10	0	4	6	5	3
Dysgerminoma	1	0	1	0	1	0	0
Total	15	10	1	4	7	5	3

Table 11: Sex Cord Stromal Tumors - Characteristics and Laterality

Sex Cord Stromal Tumor Type	Number	Pure Cystic	Pure Solid	Mixed	Right	Left	Bilateral
Granulosa Cell Tumor	2	0	2	0	2	0	0
Fibrothecoma	1	0	1	0	1	0	0
Total	3	0	3	0	3	0	0

DISCUSSION

This study provides significant insights into the clinicopathological aspects of ovarian tumors, particularly focusing on surface epithelial tumors and their p53 expression patterns. Our findings are consistent with other research in the field, highlighting the complexity and diversity of ovarian neoplasms.

The predominance of surface epithelial tumors (88%) in our study aligns with global oncology data, underscoring their prevalence in ovarian neoplasms11. Among these, serous tumors were the most common subtype, which is in agreement with literature indicating serous carcinoma as the most frequent and lethal ovarian cancer. The high incidence of these tumors in the 31-40 age group in our study contrasts with some reports that suggest a higher prevalence in postmenopausal women, indicating potential geographic or demographic variations.

Our study's focus on p53 expression revealed distinct patterns that correspond to tumor aggressiveness and potential prognosis. The high-grade serous carcinomas predominantly exhibited mutant p53 expression, in line with existing research that associates p53 mutations with high-grade tumors and poor prognosis. The use of p53 as a biomarker, therefore, can be instrumental in guiding therapeutic decisions,[12] especially in high-grade serous carcinomas. Notably, the finding of wild-type p53 expression in all low-grade serous carcinomas underscores the molecular distinction between low-grade and high-grade serous ovarian cancers, which aligns with current understanding of these as distinct entities with different paths of carcinogenesis.[13]

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The clinicopathological correlation in our study, especially the laterality and gross morphology of the tumors, offers valuable insights for surgical planning and management.[14] The prevalence of cystic morphology in serous and mucinous tumors suggests a potential pathway for early detection and surgical intervention, which is critical given the often asymptomatic nature of early-stage ovarian tumors.[15]

Our methodology, involving systematic histopathological examination and detailed immunohistochemistry, enables a comprehensive evaluation of ovarian tumors. However, the study acknowledges certain limitations, such as its retrospective nature and the single-center design, which may not fully represent the broader population. Additionally, while our study provides valuable information on p53 expression in ovarian neoplasms, the complexity of p53 mutations and their functional consequences warrants further investigation, possibly incorporating molecular techniques like sequencing for a more detailed analysis.

Future studies could expand on these findings by including a larger, more diverse population and exploring the relationship between p53 mutations and other molecular markers in ovarian cancer. Such research could provide deeper insights into the pathogenesis of these tumors and aid in the development of targeted therapies.

CONCLUSION

In this study of 150 ovarian tumors, benign serous cystadenomas were most common. p53 expression in surface epithelial tumors served both diagnostic and prognostic roles, with positive expression indicating poorer prognosis. This marker effectively distinguished between low and high-grade serous tumors and aided in differentiating high-grade endometrioid tumors from mucinous carcinomas. Our findings highlight the need for further evaluation with specific markers for accurate subtyping of non-serous epithelial tumors. Overall, the study underscores the significance of p53 as a prognostic indicator in ovarian cancer, informing clinical practice and promoting personalized treatment strategies.

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