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Original Article

Pathology Section

Histomorphological Features of Ovarian Neoplasms and Expression of p53 and WT1 in Surface Epithelial Tumours: A Cross-sectional Study

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ABSTRACT

Introduction: Ovary is the most common site of neoplastic and non neoplastic lesion, can present in childhood to postmenopausal age group and remain the most lethal of all gynaecological malignancies. Tumour Protein (p53) gene mutations or deletions are most common in ovarian carcinoma. However, Wilms' Tumour gene1 (WT1) and p16 expression are also seen in serous ovarian carcinoma. These Immunohistochemistry (IHC) markers are useful in the differential diagnosis of serous ovarian carcinomas.

Aim: To study histomorphology of ovarian neoplasm along with expression of p53 and WT1 in surface epithelial tumours and to assess the prevalence of various ovarian neoplasms in different age groups.

Materials and Methods: This cross-sectional study was conducted in Department of Pathology, Sarojini Naidu Medical College, Agra, Uttar Pradesh, India, over a period of two years (from September 2018-September 2020). A total of 78 ovarian specimen received in histology laboratory was studied for gross and microscopic features. The p53 and WT1 IHC expression pattern was studied in surface epithelial tumours. Statistical significance was calculated in relation to p53 and WT1 expression with histological type and grade of tumour using Chi-square test.

Results: A total of 78 cases were studied, out of which benign tumours were the most common 40 (51.3%) cases, followed by malignant tumours 32 (41.0%) cases and borderline malignancy 6 (7.7%) cases. The most common benign lesions were mucinous cystadenoma 20 (50%) cases. Serous carcinomas were most common malignant tumours 19 (59.3%) cases followed by Germ Cell Tumours (GCT) 5 (15.6%) cases. All benign and borderline epithelial ovarian tumours were found p53 and WT1 negative. Out of 22 cases of malignant surface epithelial tumour, 14 (63.6%) and 12 (54.4%) were positive for p53 and WT1 respectively and all were serous carcinomas.

Conclusion: Ovarian lesions present with wide spectrum of histomorphological features. The p53 and WT1 show different rates of expression and staining pattern in various epithelial ovarian carcinomas. Hence routine gross, proper histological examination and correct IHC interpretation is required for specific diagnosis.

Keywords: Benign, Dysgerminoma, Immunohistochemistry, Malignant, Serous carcinomas

INTRODUCTION

Ovarian tumours represent 3% of female malignancies [1]. The estimated incidence of developing ovarian cancer in a women lifetime is one in 70, which keep increasing with age, and peaks around the eighth decade [2]. They are diverse group of tumours with multiple, poorly understood pathogenesis. Understanding genetic mutations, tumour suppressor/oncogenes, and cell regulators provide insight in their pathogenesis and help developing new technologies for early detection [1]. Mutations or deletions of p53 gene are the most common molecular alteration in ovarian carcinoma [3]. WT1 expression is also associated with variable human cancers and its location in female genital tract which can help in differentiating serous ovarian carcinoma from other tumour. The clinical presentation does not differentiate between benign and malignant tumours. Though the morphology of the ovarian tumours provide a diagnostic clue, but IHC help in differential diagnosis, evaluating molecular changes, which further abet in the characterisation of morphology and clinical behaviour [4]. The aim was, to study histomorphology of ovarian neoplasm along with expression of p53 and WT1 in surface epithelial tumours and to assess the prevalence of various ovarian neoplasms in different age groups.

MATERIALS AND METHODS

This cross-sectional study was hospital-based, conducted in Department of Pathology, Sarojini Naidu Medical College, Agra, Uttar Pradesh, India, over a period of two years (from September 2018-September 2020). The study was carried out on all gross specimens of clinically diagnosed ovarian neoplasms received in histology laboratory. A total of 78 patients showing ovarian neoplasm on histology were studied. Ethical approval from Institutional Ethics Committee (IEC) was obtained for the present study (Ethical Clearance Certificate Number of IEC/2021/13). Written consent was taken from all patients and data was used in unidentified manner.

Inclusion criteria: All the ovarian tumour specimens, clinically diagnosed as ovarian neoplasms with definite histopathological diagnosis were considered.

Exclusion criteria: Non neoplastic lesions were excluded. Ovarian tumours treated with neo-adjuvant chemotherapy or radiotherapy was excluded as it could potentially interfere with IHC staining. Inadequate samples were excluded.

Study Procedure

The histopathological sections from the surgical specimen of ovarian tumours were taken. The samples were fixed in 10% neutral buffered formalin for duration of 12-24 hours. Fixation for long duration greater than 72 hours was avoided. Paraffin wax blocks were made and 3-4 µm sections were taken on poly-L-lysine coated slides. Three sections were taken; one was processed for Haematoxylin and Eosin (H&E) staining while other for p53 and WT1 IHC staining with DAKO FLEX monoclonal mouse antihuman p53 and WT1 antibody. The ovarian tumours were classified according to WHO classification of Tumours of Female Reproductive organ (2014) [5].

Gross and histomorphological features of all ovarian neoplasms were studied. p53 and WT1 expression and staining pattern of all surface epithelial tumours were studied. Clinical and histomorphological parameters like age, stage of presentation, histological differentiation and grade of tumours were studied in relation to p53 and WT1 expression. All the patients of malignant surface epithelial tumours were followed till the end of study.

Interpretation of staining [6]:

1) Nuclear staining for the marker was considered and expressed in percentage.
2) The criteria used to define p53 positive cells are:
a) If >60% of cells are positive, diffuse positive due to missense mutation of p53.
b) If <5% of the cells positive, null positive staining due to nonsense mutation of p53.
3) Cases are considered negative when 5-60% cells show patchy/focal staining due to wild/normal type of p53 mutation.

Nuclear WT1 protein expression was analysed in the cases with >1% positive tumour nuclei was considered positive, and those with zero or <1% was considered negative [4].

STATISTICAL ANALYSIS

The proportion of tumours showing p53 and WT1 positivity is expressed as percentage. Chi-square test was used to find if there is any statistically significant association between p53 and WT1 expression and the parameters studied. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) version 16.0. The p-value of <0.05 was considered statistically significant.

RESULTS

Among the 78 cases of ovarian neoplasms, the histomorphological diagnosis was made according to the WHO classification [Table/Fig-1]. The most common type was surface epithelial tumours in 63 (80.8%) cases, followed by GCT in 07 (8.9%) cases, Sex-Cord Stromal Tumour (SC-ST) in 06 (7.7%) cases and secondary tumours in 02 (2.6%) cases. Metastatic tumours of ovaries were far less common than primary ovarian tumours. Out of 78 cases, 40 (51.3%) cases were benign followed by malignant 32 (41.0%) cases and borderline type 06 (7.7%) cases.

S. No.	Histological types	Number of cases	Total	Percentage of cases (%)
1	**Surface epithelial tumours**			
a)	Benign	35	63	80.8
b)	Borderline	6		
c)	Malignant	22		
2	**Germ cell tumours**			
a)	Benign	2	7	8.9
b)	Malignant	5		
3	**Sex-cord stromal tumours**			
a)	Benign	3	6	7.7
b)	Malignant	3		
4	**Secondary tumours**	2	2	2.6
	Total	78	78	100

[Table/Fig-1]: Distribution of histological types of ovarian tumours.

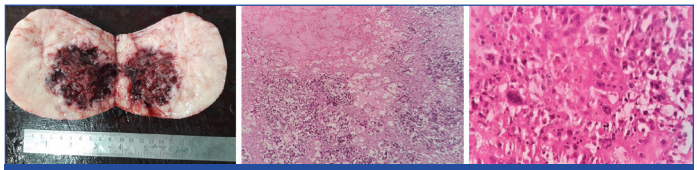
The maximum numbers of cases were found in 31-40 years of age group. The most common age group for benign lesion was 31-40 years with 15 out of 40 (37.5%, cases) and for malignant lesions was 51-60 years with 12 out of 32 (37.5% cases), while borderline type tumours were found in 21-50 years age group. The mean age for benign lesion was 37 years, borderline lesion was 35.5 years and for malignant lesions it was 50.18 years. The lowest age in which the tumour found was 17-year-old girl who presented with pain in abdomen and was diagnosed as mucinous cystadenoma. The oldest lady aged 72 years, presented with abdominal pain and distention and diagnosed as high-grade serous cystadenocarcinoma [Table/Fig-2].

Histomorphological type	Age groups (years)								
	11-20	21-30	31-40	41-50	51-60	61-70	71-80	Total cases	Percentage (%)
Serous cystadenoma	-	6	2	3	-	-	-	11	14.1
Serous cystadenofibroma	-	-	4	-	-	-	-	4	5.1
Serous cystadenoma, (Borderline)	-	-	1	-	-	-	-	1	1.2
Serous cystadeno-carcinoma (low-grade)	-	-	-	1	2	1	-	4	5.1
Serous cystadeno-carcinoma, (high-grade)	-	-	-	1	6	7	1	15	19.3
Mucinous cystadenoma	1	3	9	6	-	1	-	20	25.6
Mucinous cystadenoma, (Borderline)	-	2	1	2	-	-	-	5	6.4
Clear cell carcinoma	-	-	-	-	2	-	-	2	2.5
Endometrioid carcinoma	-	-	-	-	-	1	-	1	1.2
Dysgerminoma	1	2	-	-	-	-	-	3	3.8
Mature cystic teratoma	1	1	-	-	-	-	-	2	2.5
Immature cystic teratoma	-	1	-	-	-	-	-	1	1.2
Choriocarcinoma	-	1	-	-	-	-	-	1	1.2
Ovarian fibroma	-	-	-	1	2	-	-	3	3.8
Granulosa cell tumour, adult type	-	1	2	-	-	-	-	3	3.8
Secondary tumour	-	-	-	-	2	-	-	2	2.5
Total	3	17	19	14	14	10	1	78	100

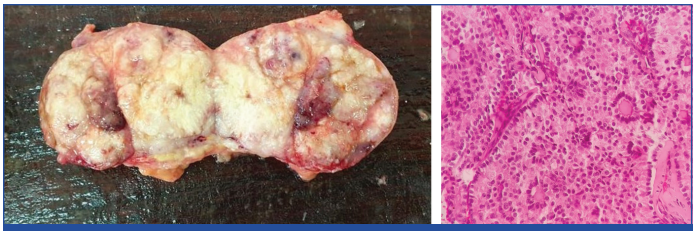
[Table/Fig-2]: Age wise distribution of all histomorphological types of ovarian neoplasms.

Out of total 78 cases, the most common benign tumour was mucinous cystadenoma 20 (25.6%) cases, most common malignant tumour was high-grade serous cystadenocarcinoma 15 (19.3%) cases and most common borderline was mucinous cystadenoma borderline type 5 (6.4%) cases. Benign serous tumours were found between 21-50 years of age group. All serous carcinomas cases were found above 40 years of age.

Out of total 78 cases, 7 (8.9%) cases were GCT seen below 30 years of age [Table/Fig-3-5] followed by SC-STs 6 (7.7%) cases of all ovarian tumours seen above 20 years of age [Table/Fig-6,7]. Metastatic tumours of ovaries were far less common than primary tumours and found in only 2 (2.6%) cases.



[Table/Fig-3]: Gross specimen of dysgerminoma showing solid tumour with fleshy, homogenous, and tan to white. Focal area of haemorrhage and necrosis also seen. **[Table/Fig-4]:** Showing lobules of tumour cells with abundant clear cytoplasm are separated by fibrous septa that contain numerous lymphocytes with adjacent normal ovarian stroma; Dysgerminoma (40X, H&E). **[Table/Fig-5]:** Showing the cytotrophoblastic cells have pale cytoplasm and vesicular nuclei with prominent chromatin clumps. The syncytiotrophoblastic cells have multiple smaller nuclei with syncytium; Choriocarcinoma (400X, H&E). (Images from left to right)

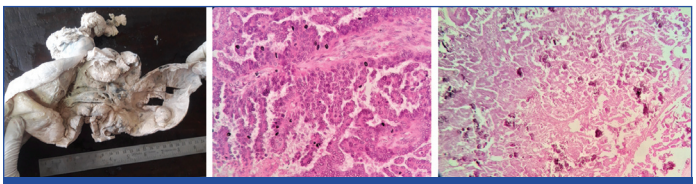


[Table/Fig-6]: Gross specimen of granulosa cell tumour showing entirely solid, with few cystic areas. Solid portions are light yellow to pink colour with soft to firm in consistency. **[Table/Fig-7]:** The cells are monotonous with Call-Exner bodies. These are microcystic spaces that contain eosinophilic secretions or cellular debris. They are lined by palisaded granulosa cells; Adult granulosa cell tumour (400X, H&E). (Images from left to right)

Abdominal pain was the most common presenting complaint in all patients. Few patients who complained of abdominal distention along with abdominal pain were diagnosed as having malignant neoplasms subsequently. Only one patient diagnosed with choriocarcinoma presented with abnormal bleeding per vaginum.

Bilateral ovarian tumours were seen in 30 patients. Mostly benign tumours were unilateral; only 9 (22.5%) cases out of 40 benign tumours were bilateral. Maximum numbers of malignant tumour were bilateral in 18 (56.2%) cases out of 32 cases, in which 15 (46.8%) were serous carcinomas. Equal numbers of borderline type cases were unilateral and bilateral respectively. No single case of mucinous cystadenomas was seen bilaterally while all cases were unilateral.

Out of 63 cases of surface epithelial tumours, maximum was benign 35 (55.5%) cases followed by malignant 22 (34.9%) cases. Papillary was the most common growth pattern seen in 40.9% cases. Micropapillary fronds were seen in 03 (75%) cases out of four cases of low-grade serous cystadenocarcinoma; however, tubulo-cystic pattern was seen in 02 (100%) cases of clear cell carcinoma. Majority of cases of high-grade serous cystadenocarcinomas showed characteristic histopathological features, represented by destructive infiltration of tumour cells forming branching papillae, slit-like fenestrations and complex glandular architecture. The tumour cells showed mild to moderate to severe nuclear atypia, and frequent mitosis [Table/Fig-8-10].



[Table/Fig-8]: Gross specimen of high-grade serous carcinoma showing a mixture of papillary and solid growth pattern with foci of necrosis. **[Table/Fig-9]:** The tumour cells cover papilla. They have large vesicular Fig-nuclei with coarse chromatin, and some have prominent nucleoli and mitosis; High-grade serous carcinoma (400X, H&E). **[Table/Fig-10]:** Micropapillary fronds, many surrounded by the clear spaces, infiltrate the ovarian stroma; Low-grade serous carcinoma (400X, H&E). (Images from left to right)

p53 and WT1 expression in relation to histological type of tumours: Among the total 63 cases of surface epithelial tumours, 22 cases were malignant. Out of 22 epithelial malignant cases 14 (63.6%) and 12 (54.4%) were positive for p53 and WT1, respectively and all were serous carcinomas. All cases of clear cell carcinoma and endometrioid carcinomas were found p53 and WT1 negative. In malignant surface epithelial tumours, statistical association of p53 and WT1 expression with histological type of tumours was found to be insignificant (p-value >0.05). All benign and borderline epithelial tumours were found p53 and WT1 negative [Table/Fig-11,12].

p53 and WT1 expression in relation to grade of tumour: Out of 19 serous carcinomas 14 (73.6%) and 12 (63.1%) were positive for p53 and WT1 respectively and all were serous malignancies. Fourteen (93.3%) of high-grade serous carcinoma showed diffuse positive staining while 1 (6.7%) showed aberrant null staining. All low-grade serous ovarian carcinomas were negative for p53. Out of

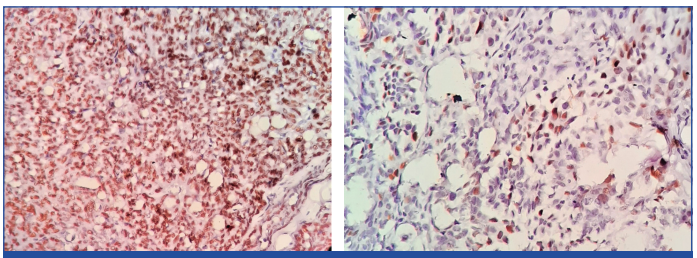
Surface epithelial tumours	Total no. of cases	No. of cases showing p53 expression	Type of expression	Percentage (%)
Benign	35	-	Negative	0
Borderline	6	-	Negative	0
Serous cystadenocarcinoma, (Low grade)	4	0	Negative	0
Serous cystadenocarcinoma, (High grade)	15	14	Positive	93.3
Clear cell carcinoma	2	-	Negative	0
Endometrioid carcinoma	1	-	Negative	0
Total	63	14		22.2

[Table/Fig-11]: p53 immunohistostaining in surface epithelial tumours. (p >0.05 Non significant)

Surface epithelial tumours	Total no. of cases	No. of cases showing WT1 expression	Type of expression	Percentage (%)
Benign	35	-	Negative	0.00
Borderline	6	-	Negative	0.00
Serous cystadenocarcinoma, (Low-grade)	4	2	Positive	50.0
Serous cystadenocarcinoma, (High-grade)	15	10	Positive	66.7
Clear cell carcinoma	2	-	Negative	0.00
Endometrioid carcinoma	1	-	Negative	0.00
Total	63	12		19.04

[Table/Fig-12]: WT1 Immunohistostaining in surface epithelial tumours. (p >0.05 Non significant)

19, 12 serous malignancies were positive for WT1 among which 10 were high-grade serous carcinomas and two were low-grade serous carcinoma. A 66.7% of high-grade serous carcinoma showed positivity for WT1 while 33.3% were negative for WT1, statistical significance of p53 and WT1 expression with grade of tumour was found insignificant (p-value >0.05) [Table/Fig-13-18].

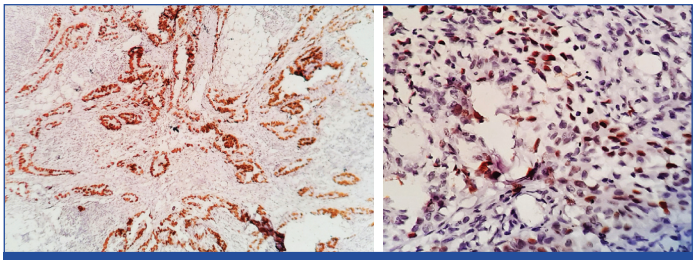


[Table/Fig-13]: High-grade serous carcinoma showing diffuse/strong positive staining for p53 immunostaining (IHC, 400X). **[Table/Fig-14]:** Low-grade serous carcinoma (showing focal/weak positivity) negative staining for p53 immunostaining (IHC, 400X). (Images from left to right)

Type of serous carcinomas	Total no. of cases	p53 positivity <5%	p53 positivity >60%	p53 negative cases (5-60%)
Low-grade	4	0	0	4
		0	0	100
High-grade	15	1	14	0.00
		6.7	93.3	0
Total	19	1	14	4

[Table/Fig-15]: Distribution of p53 positivity among the low-grade and high-grade serous malignancies. (p>0.05 Non significant)

Association of p53 and WT1 staining with tumour stage and patient survival: Among 22 cases of malignant serous carcinoma, one case of low-grade serous cystadenocarcinoma belongs to stage I. One case of high-grade serous cystadenocarcinoma belongs to stage II. Twelve cases of serous cystadenocarcinoma (three cases of low-grade and nine cases of high-grade) and one case each of clear cell carcinoma and endometrioid carcinoma



[Table/Fig-16]: High-grade serous carcinoma showing diffuse/strong positive staining for WT1 (IHC, 100X). **[Table/Fig-17]:** Low-grade serous carcinoma showing weak/focal positive staining for WT1 (IHC, 400X). (Images from left to right)

Type of serous carcinomas	Total no. of cases	WT1 positivity >1%	WT1 negative cases 0 or <1%
Low-grade	4	2	2
		50.0	50.0
High-grade	15	10	5
		66.7	33.3
Total	19	12	7

[Table/Fig-18]: Distribution of WT1 positivity among the low-grade and high-grade serous malignancies.
(p>0.05 Non significant)

belong to stage III. Five cases of serous cystadenocarcinoma high-grade type and one case of clear cell carcinoma belong to stage IV. p53 was negative in stage I tumours, all cases of stage II, 57.1% of stage III cases and 83.3% of stage IV cases were positive for p53. This result was statistically significant by Chi-square test with p-value <0.05. Hence, p53 positivity increased with higher stage. WT1 was positive in all stage I and II tumours, 50% of the stage III and 66.7% of stage IV cases. This result was statistically significant by chi-square test with p-value of <0.05 but positivity rate of WT1 is low as compared to p53.

All cases of malignant epithelial tumours were followed till the end of study. Among p53 positive tumours, 9 (64.3%) cases were alive till the end of study, while 5 (35.7%) died. Among WT1 positive tumours, 7 (58.3%) cases were alive till the end of the study, while 5 (41.7%) died. The result was statistically insignificant by Chi-square test with p-value >0.05.

DISCUSSION

Among all gynaecological cancers, ovarian cancer is the second leading cause of mortality [7]. Ovarian lesions are difficult to diagnosis, due to absence of symptoms or similar clinical presentation among benign and malignant lesions [8]. Histomorphological study of tumour is still today a gold standard method, providing information regarding the frequency and pattern of ovarian tumours [9].

Epithelial ovarian cancers are classified into type I and type II based on molecular and clinico-pathological studies. Type I tumours are characterised by mutations in Kirsten Rat Sarcoma viral oncogene homolog (KRAS), v-raf murine sarcoma viral oncogene homolog B1 (BRAF), phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA), Phosphatase and Tensin Homolog deleted on chromosome 10 (PTEN) and Erb-B2 Receptor Tyrosine Kinase (ERBB2), but not TP53, they are genetically stable and typically present at a low stage comprising of low-grade serous, endometrioid, clear-cell, and mucinous ovarian carcinoma. Type II tumours are highly-aggressive, genetically unstable, present in an advanced stage and express a mutated TP53 [10]. The IHC results are known to change according to the monoclonal antibody used. The most common antibodies used for p53 are DO-7 and PAb-1801 monoclonal antibodies. These antibodies detect both "wild" type and mutant p53 proteins [11].

The p53 results are influenced by many factors like: a) type of tissue used (p53 antigen is reported to be better expressed in fresh frozen sections); b) different enzymes used for staining; c) Antigen retrieval technique; d) different reported results in the different "cut-off" values; and e) Interobserver variability [12].

In the present study, gross and microscopic features of all 78 ovarian neoplasms were studied. Expression of p53 and WT1 was studied in surface epithelial tumours. In the present study, out of total 78 ovarian neoplasms cases, most common lesions were benign 40 (51.4%) cases followed by malignant 32 (41.0%) cases and borderline malignancy 6 (7.7%) cases. The incidence of malignant tumours was higher in present study as compared to Sawant A and Mahajan S; Gupta N et al., Pilli G et al., who found that malignant ovarian tumours constituted 18.2%, 22.9% and 21.6% and of all ovarian tumours, respectively [9,13,14].

In the present study, out of 78 cases, 63 (80.8%) cases of surface epithelial tumours, 7 (8.9%) cases of GCT and 6 (7.7%) cases of SC-ST which was in concordance with different studies and they also found most common surface epithelial tumours followed by GCT and SC-ST [9,13-16]. In this study, 63 cases of surface epithelial tumours were studied. Out of which, 35 (55.5%) were benign tumours, 6 (9.9%) were borderline tumours and 22 (34.6%) were malignant tumours, which was found in accordance with other studies [15-19].

Similar to the present study, other studies have also shown that most ovarian tumours occur in reproductive age group. Peak incidence of ovarian tumour was between 21-40 years. Benign ovarian tumours are common in all age groups whereas malignant ovarian tumours are more common in elderly like in present study most common group was 51-60 years. Malignant GCT are most common ovarian cancers among children and adolescent females. In patients under age of 21, approximately 60% ovarian tumours were GCT, accounting for two-third of ovarian cancer in first two decades of life [16]. In this study, three cases of ovarian tumours were found under the age of 21, out of which 02 (66.7%) were GCT.

According to the literature reports positive results of 48.5% to 69% in studies using the p53 DO-7 antibody [20]. In this study, a p53 over-expression was found in 63.6% (14/22) cases, which was found in concordance to Amanullah NAR et al., Gayathiri G and Umasamundeeswari R, Choudhary P et al., Psyrri A et al., Kuprjanczyk J et al., Ayadi L et al., Reles A et al., they found p53 expression in 62-83.3% [1,15,17,20-23]. Present study result was non concordance with Mohamed AO et al., Sreeja TT et al., de Graeff P et al., Marks JR et al., they found p53 expression in 35.1-54% cases [10,19,24,25]. This may be attributed to heterogeneity of lesions, properties of antibodies used, variability in interpretation of slides, different scoring method applied for p53 immunoreactivity and antigen retrieval technique [17,19].

According to molecular alterations involved in serous carcinogenesis, the new WHO classification categorises serous carcinoma into low-grade and high-grade carcinomas. Histopathologically, nuclear pleomorphism, necrosis and mitotic activity help in differentiating between low-grade and high-grade serous carcinoma. Necrosis is not found in low-grade serous carcinoma and the mitotic activity is also low [26]. In this study, p53 expression was seen in epithelial ovarian cancer cases, strong positive expression was found in high-grade serous cystadenocarcinoma 93.3% (14/15) cases as compared to low-grade, all low-grade serous carcinomas were negative for p53, which was found in concordance to Amanullah NAR et al., {93.7% (15/16) of high-grade serous cystadenocarcinomas}, Gayathiri G and Umasamundeeswari R {85% (12/14) of high-grade and 75% (3/4) of low-grade}, Matsuo K et al., {71.4% cases of high-grade serous carcinoma}, Nofech-Mozes S et al., {83.6% cases of high-grade serous carcinomas} and Koebel M et al., {69% (118/171) cases of high-grade serous carcinomas} [1,15,27-29]; however, Mohamed AO et al., found p53 expression in 53.7% (29/54) cases of high-grade serous carcinomas but none of low-grade carcinomas similar to present study [10].

Study of Yemelyanova A et al., reported that p53 immunohistochemical scoring systems should not interpret the complete absence of expression as consistent with wild-type TP53. It is implicated that only when both patterns of immunostaining commonly associated with TP53 mutation (60-100% of tumour cells positive and tumours completely negative for p53) were combined, immunohistochemical analysis would give 95% correlation with nucleotide sequencing of the mutations [30].

p53 expression in relation to histological type of tumours: Present study showed expression of p53 in carcinomas mainly, this was reported by others who found that malignant surface epithelial tumours, especially serous cystadenocarcinomas of ovary showed high expression of p53 as compared to the benign and borderline tumour.

Statistically, there was no significant association between p53 expression and histological type of tumours. Review of literature showed conflicting results; some with no significant relation and others with significant relationship. Gursan N et al., found most significant with serous carcinoma [31]. In the study of Choudhary P et al., and Ayadi L et al., there was no significant difference in expression of p53 between serous and non serous tumours [17,22].

In this study, p53 expression was mainly found in high-grade serous cystadenocarcinoma. All low-grade serous carcinomas were negative for p53. However, the expression of p53 with grade of tumour was statistically non significant which was in concordance with studies conducted by Abubaker J et al., and Herod JJ et al., [32,33].

High proliferation rate is associated with TP53 alteration, but the association between p53 expression and patient prognosis is controversial [4]. Michael A et al., found a significant correlation between the presence of p53 overexpression with stage (p-value <0.01) and poor outcome (p-value=0.05) in patients of ovarian cancer [34]; however, Marks JR et al., found no statistical significance between p53 over expression with stage and poor outcome, while they observed that patient with p53 expression had worse median survival [25]. Shahin MS et al., found that the p53 wild- type tumours provide the best overall survival when compared with p53 having missense mutation and null mutation [35]. In this study, a significant association was found between p53 expression and stage of tumour indicating that increase stage of tumour has high propensity of p53 expression (p-value<0.05), however no statistically significant association was found between patient survival and p53 expression with a p-value of >0.05. Failure of p53 to prognosticate adverse impact on ovarian carcinoma can be explained by the fact that there have been several reports about p53 null mutation which are nearly uniformly non immunoexpressive and sequencing is the gold standard for detection of mutation over immunohistochemistry [35].

WT1 expression in relation to histological type of tumours: WT1 expression is generally used to differentiate serous ovarian carcinomas from other ovarian types in female genital tract [4]. Koebel M et al., stated that WT1 expression suggested serous ovarian cancers and approximately 10% of high-grade carcinomas can be WT1 negative [36]. Sallum LF et al., found 71.4% of low-grade serous cystadenocarcinoma and 57.1% of high-grade serous cystadenocarcinomas showing WT1 expression [4]. In present study, 50% (2/4) of low-grade serous cystadenocarcinoma and 66.7% (10/15) of high-grade serous cystadenocarcinoma showed positive WT1 expression. A significant association was found between WT1 expression and stage of tumour indicating that increase stage of tumour has high propensity of WT1 expression (p-value <0.05). However, the positivity rate of WT1 was low as compared to p53. WT1 expression was low as compared to reports in recent literature, might be due to irregular staining of tissue for WT1. No statistically significant association was found between patient survival and WT1 expression with a p-value >0.05.

The two types of serous ovarian carcinomas harbour different molecular abnormalities. This data from the literature was confirmed from present study by observing the different pattern of expression.

Limitation(s)

The limitation of study was restricted number of samples and use of limited markers.

CONCLUSION(S)

Benign tumours were more common than primary malignant tumours. Surface epithelial tumours were the most common histological types. Mucinous cystadenoma was the most common primary benign tumour. Serous carcinomas were the most common primary malignant tumour followed by dysgerminoma (GCT). p53 over-expression was seen in high-grade serous carcinomas. WT1 can also be used to distinguish serous ovarian carcinomas from another carcinoma. Hence, the use of p53 and WT1 IHC staining is beneficial in the pathologic work-up of ovarian carcinomas.

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