

HISTOMORPHOLOGICAL STUDY OF OVARIAN NEOPLASMS AND TO EVALUATE THE P53 OVEREXPRESSION IN MALIGNANT OVARIAN TUMORS AMONG PATIENTS ATTENDING TERTIARY CARECENTRE: A CROSS SECTION STUDY

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ABSTRACT

Background: Ovarian cancer, the most common gynecological neoplasm, predominantly affects women aged 55-64. Ninety percent of these cancers are epithelial and primarily occur in postmenopausal women, contributing to 2,39,000 new cases and 1,52,000 deaths worldwide annually. The incidence varies from 0.9 to 8.4 per 100,000 women in India, with surface epithelial tumors being the most common. Risk factors include familial genetic syndromes like BRCA mutations and Lynch syndrome, while non-genetic factors involve obesity and hormonal factors. p53 overexpression, linked to cell cycle dysregulation and apoptosis, is a significant prognostic marker, with immunohistochemical studies showing its presence in up to 69% of ovarian carcinomas. This study aims to examine ovarian neoplasms' histomorphological aspects and p53 overexpression in malignant cases. **Objectives:** 1. To study the prevalence of benign and malignant ovarian neoplasms. 2. To study the degree of overexpression of p53 in malignant ovarian neoplasm. **Materials and Methods:** The study included 80 cases of ovarian neoplasms from patients who underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, with specimens examined at Karpagam Faculty of Medical sciences and Research, Coimbatore over two years. Both retrospective and prospective data were collected, including clinical history, external and microscopic features, and final diagnosis. Histopathological categorization followed WHO guidelines, with malignant cases subjected to p53 immunohistochemistry. Data were analyzed using IBM SPSS version 22.0, with Spearman's rho test used to correlate p53 expression with FIGO staging and histological grading, considering a p-value <0.05 as significant. **Result:** This study extensively analyzed ovarian neoplasms' histomorphology and its correlation with clinicopathological parameters, focusing on p53 expression. Out of 80 cases, 63% were benign, 11.25% borderline, and 25% malignant, with most malignant tumors occurring in patients aged 50-60. The most common symptoms were abdominal pain and mass, with serous carcinoma being the predominant malignant tumor. p53 positivity was observed in 50% of malignant cases, correlating with tumor grade and FIGO stage, and was more frequent in high-grade tumors and those over 55 years old. The study confirms p53 as a significant prognostic marker, reflecting aggressive disease and poor differentiation. **Conclusion:** Ovarian neoplasms pose significant challenges in diagnosis and management, with accurate morphological categorization aiding in treatment. This study found benign and borderline tumors predominantly in those under 40, while malignant tumors were more common in those over 50. Serous cystadenoma was the most common benign tumor, and serous cystadenocarcinoma was the most common malignant tumor. p53 positivity, assessed semi-quantitatively, was higher in serous carcinoma and correlated with tumor grade and FIGO stage, indicating aggressive disease. This study highlights that p53 mutations are linked to poor differentiation and aggressive behavior, suggesting p53 as a valuable prognostic marker in ovarian cancer.

INTRODUCTION

Ovarian cancer is the most common gynecological neoplasms. It is diagnosed in those between 55-64 yrs of age.^[1] 90% of the ovarian neoplasms are epithelial ovarian cancers and occurs in the post menopausal women and has a life time risk of only 1.3% in the general population. It accounts for the fifth leading cause of cancer related deaths in women. Ovarian cancer accounts for around 2,39,000 new cases and 1,52,000 deaths world wide.^[2]

The incidence of ovarian tumors are 3% world wide, in India it varies from 0.9 to 8.4 /100,000 women years. Incidence of ovarian neoplasm in surface epithelium is 65%, germ cell 15%, sex cord stromal 10%, metastasis 5% as per WHO.^[3] Ovarian cancer is the most frequent cause of death from gynecological cancers and the fourth most common cause of death in Europe, united states and eastern India.^[2] A lifetime risk of developing OC is 1 in 75 and her chance of dying the disease is 1 in 1004. All benign and malignant ovarian neoplasms originates from one of the three cell types like epithelial cells, stromal cells and germ cells.^[2]

Histopathological examination plays a crucial role in classifying ovarian tumors for better prognosis. Strongest known risk factors are Familial genetic syndromes and it accounts for about 10-20% of ovarian cancers. BRCA gene mutations are seen in about 10% of ovarian cancers. Lynch syndrome HNPCC is involved in 2-3% of cases. As due to increasing rates of hormonal contraceptives and decreasing post menopausal hormone use. So the incidence and mortality have decreased over the previous decades. Main etiology for all these ovarian tumors is increasing age of reproduction, positive family history, high socio economic status, nulliparity.^[4] Non genetic risk factors includes obesity, weight gain, post menopausal hormone therapy.^[1]

Early age at menarche and late age at menopause increase the risk by increasing the number of ovulatory cycles.^[2] Two theories have been proposed, the "incessant ovulation" suggests that number of ovulatory cycles increases the rate of cell division which leads to repair of surface epithelium and thereby leads to increasing spontaneous mutations. Other hypothesis "gonadotropin hypothesis" suggest the impact to gonadotrophins, such as luteinizing

hormone and follicle stimulating hormone. Ovarian tumors are insidious in onset and are diagnosed at a late age. Presenting symptoms will be abdominal pain, a mass or menstrual irregularities. One of the most significant risk factor is family history of disease, First degree relatives have a 3-7 fold increased risk.^[2]

Borderline ovarian tumors are neoplasms of epithelial origin and it is characteristically upregulated by cellular proliferation and by the

presence of nuclear atypia without any distortion of the underlying stroma.^[5] Previously it was known as "Tumors of low malignant potential", but in the current WHO 2014 Classification of tumors of Female genital tract "Borderline tumor" is interchangeable with "Atypical proliferative tumor". Only 10 to 12% of cases have genetic basis most of them have relevant family history. Role of diet, non steroidal anti-inflammatory drugs, perineal talc exposure and smoking are controversial.^[2] Some of the common genetic syndromes include Hereditary breast and ovarian cancer syndrome. Lynch Syndrome (HNPCC), MUTYH –associated polyposis, Peutz –Jeghers syndrome, PTEN hamartoma tumor syndrome.^[1] These ovarian tumors are complex with variety of histological patterns which ranges from epithelial tissues, connective tissues, hormone secreting germinal and embryonal cells.^[7]

Introduction on p53

P53 is a 393 amino acid phosphoprotein and has five main active domains with specific functions linked to one of these domains. This protein enhances the transcription of its target genes such as p21, a kinase inhibitor which is implicated in cell cycle arrest and apoptosis initiation and MDM2 which is responsible of the repression and degradation of p53. The basic modular structure of p53 family members comprises a N-terminal transcriptional activation domain, a central DNA binding domain and a C-terminus with oligomeric and regulation activities. The transcriptional activity of p53 is mainly regulated at the posttranslational level.^[5] One of the extensively studied prognostic markers in ovarian cancer so far is overexpression of p53. In response to a stress signal the p53 protein is activated in a specific manner by post translational modifications which leads to cell cycle arrest, cellular apoptosis. This leads to a variety of intrinsic and extrinsic stresses that results in loss of fidelity in DNA expression, genome stability, cell cycle progression.^[6] IHC has the advantage of being an easy procedure and it is cost effective. Intracellular accumulation of p53 has been detected in as many as 69% of ovarian carcinoma by immunohistochemical studies.^[8] The purpose of this study is to study in detail about the histomorphological study of ovarian neoplasms and to evaluate the benign and malignant neoplasms and to study the overexpression of P53 in malignant neoplasms.

Aims and Objectives

1. To study the prevalence of benign and malignant ovarian neoplasms.
2. To study the degree of overexpression of p53 in malignant ovarian neoplasm.

MATERIALS AND METHODS

All those patients with ovarian neoplasm underwent TAH with BSO specimens sent for histopathological

examination to the Department of Pathology, Karpagam Faculty of Medical sciences and Research, Coimbatore were included in the study which includes 80 cases. This was both retrospective and prospective study done for the period of 2 years. Institutional ethical approval committee approval was obtained.

Data's were also obtained from patients inpatients and outpatients records and by the request forms accompanying the specimens to the department.

All details of the case consisting of clinical history, external examination, gross features and microscopy features, final diagnosis were filled in the request form.

Representative sections and paraffin blocks were taken and stained by haematoxylin and eosin staining as per standard guidelines and examined under light microscopy. Histopathological categorization was done as per WHO classification as benign, borderline and malignant after examining the slides under light microscopy. Patients who were diagnosed as malignant ovarian neoplasms, representative blocks were taken and subjected to p53 immunohistochemistry as per standard guidelines.

Expression of p 53 was deduced by nuclear staining either as coarse or fine granular dots was considered positive. The intensity of staining and the number or percentage of positive cells was assessed.

Data Analysis: The collected was entered in excel sheet and descriptive analysis and correlation was done using IBM Corp. Released 2013. IBM SPSS statistics for windows, version 22.0. Armonk, NY: IBM corp. Correlation between p53 intensity, FIGO staging and histological grading was performed using Spearman's rho bivariate correlation test. The p value of < 0.05 was considered statistically significant.

RESULTS

Table number 1 shows the frequency of distribution histopathological diagnosis in this study. Majority of the cases diagnosed were Serous cystadenoma (33.8%). It was followed by mucinous cystadenoma (20%) and mucinous borderline tumour (10%). Serous carcinoma was found in 8.8% of cases followed by benign teratoma in 7.5% of cases. Mucinous carcinoma was seen in 6.3% of cases followed by endometrioid carcinoma in 5% of cases.

Germ cell tumour, Malignant and benign Brenner tumour constituted 2.5% cases each. Least number of case was seen in serous borderline with 1.3%.

Table number 2 shows the frequency distribution of histopathology examination in patients. Majority of the cases were benign (63.8%) followed by Malignant (25%). Borderline cases (11.3%) were the least.

Among the 20 malignant cases, 40% of the cases (8) belonged to the age group 51 - 60 years, 25% of the cases (5) belonged to 61 - 70 years, 15% of the cases

(3) belonged to 41 - 50 years. Least number of cases (2 each) 10% each were seen in the age groups 21 - 30 and 31 - 40 years.

Table 3 shows, among 80 cases 60 cases were falls under the category of benign and borderline whereas 20 cases are found to be malignant.

Among the 20 malignant cases, 50% (10) of cases showed positive p53 expression and 50% showed negative p53 expression.

Among the 20 malignant cases, 50% (10) of cases showed no staining. Weak staining (10-25% tumour cells) and moderate staining (26 - 50% tumour cells) was seen in 15% (3,3) of cases each. Strong staining ($>50\%$ of tumour cells) was seen in 20% (4) of cases.

Among the 20 malignant cases, 75% (15) of the cases were low grade and 25% (5) were high grade.

Among the 20 malignant cases, mixed consistency was most common with 60% (12). It was followed by cystic consistency 35% (7) and last it solid consistency 5% (1).

Table 4 shows, Among the 20 malignant cases, 35% (7) of the cases were of serous carcinoma type. It was followed by mucinous carcinoma - 25% (5) and endometrioid tumour 20% (4). Least number of cases were of germ cell tumour and malignant Brenner tumour 10% (2,2) each.

Totally 20 malignant cases were present in the study of which 10 cases (50%) were tumours limited to ovaries. Four cases (20%) were tumours which extended outside the pelvis with peritoneal implants. Distant metastasis and tumours which extended to uterus, fallopian tubes and pelvic extension had three cases each (15% each).

Table 5 shows, Low grade malignant tumours: Serous carcinoma had total of 3 cases in which 2 cases (66.7%) had no staining and one case (33.3%) had moderate staining. Mucinous carcinoma had total of 4 cases of which 2 cases (50%) had no staining, 1 case (25%) had weak staining and one case (25%) had strong staining. Endometrioid tumour had total of 4 cases of which three cases (75%) had no staining and one case (25%) had weak staining. Germ cell tumour had total of 2 cases and both the cases had no staining. Malignant Brenner tumour had 2 cases of which one case (50%) had no staining and one case (50%) had moderate staining. High grade malignant tumours: Serous carcinoma had a total of 4 cases of which weak and moderate staining had one case (25% each) each. Strong staining was seen in 2 cases (50%). Mucinous carcinoma had 1 case which had strong staining.

Table 6 shows, Correlations were performed using bivariate correlation Spearman's rho test. p53 intensity and FIGO staging had a correlation coefficient (r) value of 0.99 at p value ≤ 0.01 This indicates a strong, positive high correlation and a marked relationship between the variables at a statistically significant level. P53 intensity and grade had a r value of 0.65 at p value ≤ 0.0 . This indicates a moderate positive correlation and a substantial relationship between the variables at a statistically

significant level. p53 intensity and histological grade had a r value of 0.68 at p value ≤ 0.01 . This indicates a moderate positive correlation and a substantial relationship between the variables at a statistically significant level. FIGO staging and grade of the tumour had a r value of 0.62 at a p value ≤ 0.01 . This indicates a moderate positive correlation and a substantial relationship at a statistically significant level. FIGO staging and histological grade had a r value of 0.68 at p value ≤ 0.01 . This indicates a moderate positive correlation and substantial

relationship between the variables at statistically significant level.

Table 7 shows in FIGO stage I, there were 10 cases and all of them had no p53 intensity staining. In FIGO stage II, there were 3 cases and all had weak p53 intensity staining. In FIGO stage III, there were totally 4 cases of which 3 cases (75%) had moderate p53 intensity staining and one case (25%) had strong p53 intensity staining. In FIGO stage IV, there were 3 cases and all had strong p53 intensity staining.

Table 1: Frequency distribution of histopathological diagnosis

Diagnosis	Frequency	Percent
Serous carcinoma	7	8.8
Mucinous carcinoma	5	6.3
Endometrioid carcinoma	4	5.0
Germ cell tumour	2	2.5
Malignant Brenner tumour	2	2.5
Serous cystadenoma	27	33.8
Mucinous cystadenoma	16	20.0
Benign teratoma	6	7.5
Mucinous borderline tumour	8	10.0
Benign Brenner tumour	2	2.5
Serous borderline	1	1.3
Total	80	100.0

Table 2: Frequency distribution of Histopathology examination

Histopathology T2	Frequency	Percent
Benign	51	63.8
Borderline	9	11.3
Malignant	20	25
Total	80	100

Table 3: Frequency distribution of p53 expression

p53 expression	Frequency	Percent
Positive	10	50.0
Negative	10	50.0
Total	20	100.0

Table 4: Frequency distribution of diagnosis of tumour

Diagnosis T8	Frequency	Percent
Serous carcinoma	7	35.0
Mucinous carcinoma	5	25.0
Endometrioid carcinoma	4	20.0
Germ cell tumour	2	10.0
Malignant Brenner tumour	2	10.0
Total	20	100.0

Table 5: Frequency distribution of diagnosis and p53 intensity in high and low grade tumours

Grade	Diagnosis	p53 intensity	Frequency	Percent
Low	Serous carcinoma	No staining	2	66.7
		Moderate staining	1	33.3
		Total	3	100
	Mucinous carcinoma	No staining	2	50
		Weak staining	1	25
		Strong staining	1	25
		Total	4	100
	Endometrioid carcinoma	No staining	3	75
		Weak staining	1	25
		Total	4	100
High	Germ cell tumour	No staining	2	100
		Moderate staining	1	50
		Total	2	100
	Malignant Brenner tumour	No staining	1	50
		Moderate staining	1	50
		Total	2	100
	Serous carcinoma	Weak staining	1	25
		Moderate staining	1	25
		Strong staining	2	50
		Total	4	100
	Mucinous carcinoma	Strong staining	1	100

Table 6: Correlation between variables

Parameter	Parameter	p53	FIGO		Hist
		intensity	staging	Grade	Grade
p53 intensity	Correlation Coefficient	1	1.000	.99	.65
	Sig. (2-tailed)		0	.000	.002
FIGO staging	Correlation Coefficient	—	1.000	0.62	0.68
	Sig. (2-tailed)			.004	.001
Grade	Correlation Coefficient	—	—	1.000	0.37
	Sig. (2-tailed)				.105

Table 7: Frequency distribution of p53 intensity according to FIGO staging

FIGO STAGE	p53 intensity	Frequency	Percent
Stage I	No staining	10	100
Stage II	Weak staining	3	100
Stage III	Moderate staining	3	75
	Strong staining	1	25
	Total	4	100
Stage IV	Strong staining	3	100

DISCUSSION

In the present study histomorphology of ovarian neoplasms was extensively studied and correlated with various Clinicopathological parameters. P53 expression of malignant ovarian neoplasms were studied and correlated with the grade of tumors. There were totally 80 cases of which benign was 51, borderline was 9 and malignant cases were 20 which constitutes 63%, 11.25% and 25% respectively.

In the present study majority of the patients with malignant ovarian tumors were in 5th and 6th decade of life. These results were similar to studies done by et al and Vijay kumar Bodal et al.^[9]

Knowledge of morphology and age specific characteristics can help in refining the diagnosis. In the present study most common symptoms were Pain abdomen and Mass abdomen were which was 41.3% each and menstrual irregularities around 17.5%. Most of the literature on ovarian cancers states that there are no early warning symptoms and ovarian cancer is referred to as silent killer because women are unaware of it and not accurately diagnosed until the disease is in advanced stage. Early diagnosis of ovarian cancer is a challenge to the gynecologists, due to nonspecific nature of symptoms in early disease.

In the present study of the 20 malignant cases, most common were the surface epithelial tumors in which serous carcinoma was seen in 8.8% cases followed by mucinous carcinoma in 6.3% cases and then endometrioid carcinoma in 5% cases.

In a study done by Mitchell M Fetal,^[10] serous carcinoma was seen in 11.3% cases followed by mucinous carcinoma of 3.3% cases and then endometrioid carcinoma in 1.2% cases.

In a study done in eastern India, endometrioid tumors were found to be around 5% of the cases. In a study done by Tortolero –Luna G et al,^[11] endometrioid tumors constituted 4.2% cases of

all malignant tumors which is similar to our present study. This may be a reflection of geographical variation of diseases.

In the present study borderline mucinous tumors were seen in 10% of cases and borderline serous tumors in 1.3% of cases. In the study done by Tortolero –Luna G et al,^[11] borderline mucinous tumors were seen in 15.7% of cases and borderline serous tumors in 27.4% of cases.

Considering the malignant cases alone, the mean age of the patient was 51.±11.3 yrs. This was found to be similar to the other studies done by Oo-kyung Lee et al,^[12] & Hui-rong Shi et al.^[13]

Considering the 20 malignant cases, on gross examination 60% of cases were mixed in consistency which is found to be 63% and 55% in the studies done by Phukan J Petal et al,^[14] and Kanithkar S. netal,^[15] respectively. Whereas in our study 35% of cases was found to be cystic in nature which is found to be 70% in the study conducted by Rjhaetal,^[16] Finally 5% of cases was solid in consistency which is concordance with the study of Rjhaetal.

In the present study, the most common malignant tumor was serous carcinoma in 35% of cases followed by mucinous carcinoma in 25% of cases and endometrioid tumors in 20% of cases and then germ cell tumors and malignant Brenner tumor in 10% of cases each. In studies performed by Pradhan A et al (%),^[17] Rjhaetal (%),^[16] and Krishna M et al (%),^[18] shows 8% of cases were serous carcinoma, 4% cases were mucinous carcinoma and 3% cases found to be endometrioid carcinoma respectively.

Amongst the malignant cases in the present study, serous carcinoma was seen in 7 cases of which 57.14% were high grade and 42.85% cases were low grade which is found to be 67% and 33% in the study conducted by Deniz ARIK et al,^[19] respectively.

In the present study, mucinous carcinoma was seen in 5 cases out of which 4 were low grade and 1 was high grade. This is near similar to the study done by Martin Kobel et al,^[20] where all the 100% cases were

low grade. As discussed by Kurman R J et al,^[21] and Lora Hedrick Ellenson et al p53 expression is not associated with mucinous carcinoma, but in our study 40% of mucinous carcinoma were p53 positive, similar to study done by Hui-Rong Shi et al,^[22] (45%).

In the present study, all the 4 cases of endometrial carcinoma were low grade. Of the 20 malignant cases, 50% cases were positive for p53 expression and the rest 50% of the cases were negative for p53 expression. This result was within the range observed by other studies. The p53 expression in various studies ranged from 44% to 66% and the most possible sources for this variation may be attributed to properties of different antibodies, scoring methods applied for p53 immunoreactivity, enzyme and micro wave treatments of the tissue during the staining process and tissue fixation procedure.

While comparing the incidence of expression of P53 in malignant tumor of ovaries in various studies, our study was found to be 50 % which is similar to study conducted by Marks J et al,^[23] and Leanne M. Kmet et al.^[24]

In the present study of the 20 malignant cases, 12 cases were under the age less than 55 yrs of which 5 cases were positive (41.6%) and 7 cases were negative for p53. Of the 8 cases with age more than 55 yrs, 5 were positive (62.5%) and 3 were negative for p53. Our findings were in concordance with the study of B. Berker et al^[8] who found P53 expression 48% in less than 55 years and 62 % in more than 55 years.

It shows that p53 expression is more common among greater than 55 yrs of age than in patient aged less than 55 yrs. This may be related to the accumulation of somatic mutations. It is known that loss of heterozygosity on chromosome 17 increases with age.

In the present study, of the 7 cases of serous carcinoma, p53 expression was positive in 6 cases (85.7%) and negative in 1 case (14.28%) and in mucinous carcinoma of 5 cases, p53 expression was positive in 2 cases (40%) and negative in 3 cases (60%) and in 4 cases of endometrial carcinoma 2 were positive and 2 were negative 50% each. p53 expression was negative in malignant germ cell tumors and Brenner tumors. In the present study p53 expression was positive in serous histological type around 60% than in non serous histological type 40% cases which includes mucinous, Brenner and endometrial tumors. This findings seen in our study was found to be similar in the study done by Elaf Abdul-Wahab Hamdi et al,^[25] who found 62 % were serous type and 45 % was non serous type. Same way Mucinous carcinoma was found to be positive for P53 expression in 45 % in the study done by Hui-Rong Shi et al^[5] which is similar to that of our present study.

Of the seven cases of serous carcinoma, 4 were high grade and all the 4 cases showed p53 positivity (100%) and 3 were low grade of which 2 showed

positivity (66.6%) and 1 negative (33.3%), p53 expression was positive in high grade when compared to the low grade.

This finding was similar to study done by Luminita Nicoleta Giurgea et al,^[26] where they reported positive p53 expression in 56.25% cases in high grade and 12.5% cases in low grade. These results are close to dualistic model of carcinogenesis by Robert J et al,^[27] where they have reported p53 expression positive in most of the high grade tumors.

Of the 5 cases of mucinous carcinoma, 4 were low grade and 2 cases showed p53 positive (50%) and two were negative (50%) cases. One was high grade which was negative for p53 expression (100%)

Malignant tumors were correlated with histological grade and figo stage. Fifty percent of the tumors were in stage I and 15% in stage II and stage IV and 20% in stage III.

In the present study stage I and II had weak staining were as in stage III it was 75% strong staining and in stage IV it was 100% strong staining. It had a correlation coefficient with a value of 0.99 at a p value < 0.001. It has been observed that intensity of p53 staining increases as the figo stage is increased. This was similar to the study done by John P geisler et al,^[28] monishachaudary et al,^[29] and marks J et al.^[23]

In the present study 35% of the cases were well differentiated (grade I), 25% of cases in moderately differentiated (grade II) and 40% of cases were in poorly differentiated (grade III).

In the study there was a moderate positive correlation between p53 intensity and histological grade with a value of 0.65 at a p value of 0.01 and was statistically significant which was similar to the studies done by John P geisler et al,^[28] . However in studies done by monishachaudary et al,^[30] , kohler et al,^[31] mark et al,^[32] there was no correlation and was not statistically significant. Prognosis is strongly associated with stage of the disease because the five year survival depends on the stage of the disease. Tumors in stage I and stage II have a better survival rate compared to the stage III and stage IV.

Histological grade also plays a prognostic role in predicting the recurrence grade I and II have lesser recurrence compared to the grade III.

CONCLUSION

Ovarian neoplasms is a silent menace that presents as a tremendous clinical challenge to gynaecologists, medical oncologists and radiotherapists categorization in to exact morphological type will help the gynaecologists for proper management.

Present study has concluded that benign and borderline occurs in the age group less than 40 yrs and malignant tumors in age more than 50 yrs.

Emergence of borderline tumors with prognostic difference from the benign and malignant counterparts, has added a wing to research in the field of ovarian tumors.

It has been concluded from this study the tumors originating from surface epithelium are the commonest variant, so of the benign tumors serous cystadenoma (33.8%) is the most commonest and of the malignant tumors serous cystadenocarcinoma (8.8%) is the most commonest. The p53 positivity was assessed by a semi quantitative method where the number of tumor cells showing positivity (score) and the staining intensity was assessed to determine p53 positivity.

Among 20 malignant cases of all the histological types, p53 expression was more positive in serous carcinoma (60%) than non serous carcinoma and correlated with other studies.

The intensity of p53 positivity was more in high grade (almost 100%) than in low grade ovarian carcinoma and was similar to other studies. P53 positivity increased with age around 62.5% of cases were in 5th and 6th decade of life and was found to be correlating with various studies. Prognosis depends on FIGO staging and histological grade both of these helps in determining the survival rate and rate of recurrence.

To conclude there is strong direct correlation between increase in intensity of p53 staining (>50% of tumor cells) and FIGO stage (IV). There is also a strong direct correlation between increase in intensity of p53 staining in histological grade (III) this concludes that cancer with p53 mutations are in advanced stage of the disease than without p53 mutations.

This study has also proved that tumors with p53 mutations are more aggressive than tumors without p53 mutations. So this may be used to as a marker to predict aggressive behaviour and poor differentiation in malignant tumors of the ovary. Ovarian tumors manifest a wide range of clinical, morphological and histological features. Patients in stage IV are poorly differentiated and had strong positive p53 staining. Increase in intensity of p53 staining is directly related to decreased length of survival.

To conclude Histomorphological study remains the gold standard for the proper classification and the management of ovarian neoplasms and p53 is a better independent indicator of prognosis and 5yr survival rate in patients with ovarian carcinoma. In conclusion, in future only prospective, larger studies will permit a better understanding of the prognostic role of p53 immunoreactivity in ovarian carcinoma patients. So p53 can be used as independent marker to predict aggressive behaviour and poor differentiation in malignant tumors of ovary.

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