IJPSR (2016), Vol. 7, Issue 2 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 11 November, 2013; received in revised form, 03 November, 2015; accepted, 23 January, 2015; published 01 February, 2016

THE CLINICOPATHOLOGICAL PROFILE IN PATIENTS WITH EPITHELIAL OVARIAN CARCINOMA

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Keywords:

Ovarian tumor, Surface Epithelial tumor, Radiotherapy, Chemotherapy.

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ABSTRACT: The malignant tumors of ovary are a group of disease with varying clinical and biological behavior. It is fifth leading cause of death from cancer in women and the leading cause of death from gynecological cancer. This retrospective study has been undertaken to analyze patients of epithelial ovarian cancers. These cases were analyzed for various features like age, stage at presentation, histological type, and treatment pattern. Eighty seven patients with ovarian cancer registered at department of Radiotherapy -II, Pt. BDS PGIMS, Rohtak, Haryana from January 2010 to December 2011 have been evaluated in this retrospective study. Histopathological analysis showed 71(82%) cases of epithelial tumors, 5 cases (6%) of sex cord stromal tumor and 11 (13 %) of germ cell tumors. Among the individual tumors serous tumors were the commonest 51%, followed by 18% mucinous carcinoma and 20% undifferentiated carcinoma. The peak incidence was in 5th – 6th decades. Most of the patients were referred after surgery. Surgery performed was TAH & BSO in almost all patients. All patients were staged according to FIGO staging. Sixty five percent patients had stage III at presentation, 17% patients had Stage IV, 13% and 6% had stage II and I respectively.

INTRODUCTION: The malignant tumors of ovary are heterogeneous disease with varying clinical and biological behavior. Epithelial ovarian malignancies are one of the common gynecological malignancies, and the fifth frequent cause of cancer death in woman and leading cause of death from gynecological malignancies. [1, 2]

The overall annual incidence of ovarian cancers is 17 cases per 10,000 women.[3] Epithelial ovarian cancer accounts for 25% of all malignancies affecting the female genital tract.[4]

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.7(2).868-72

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.7 (2).868-72

During the period 2004 -2005, in various urban and rural population based registries operating under the network of the National Cancer Registry Program of Indian Medical Council Research, proportion of ovarian cancer varied from 1.7 % to 8.7% of all female in India. [5]

The standard of care for patients with these malignancies includes surgery for diagnosis, staging and initial treatment followed by chemotherapy. Chemotherapy with taxens and platinum has become a corner stone of treatment for ovarian malignancies. Overall response rate was observed in the 60%-80% with first line chemotherapy regimens. [7] This retrospective study has been undertaken to analyze patients of epithelial ovarian cancers. These cases were analyzed for various features like age, stage at

presentation, histological type, and treatment pattern.

METHODS:

Eighty seven patients with ovarian cancer registered at department of Radiotherapy -II, Pt. BDS PGIMS, Rohtak, Haryana from January 2010 to December 2011 have been evaluated in this retrospective study. These cases were analyzed for various features like age, clinical presentation, stage at presentation, histological type. Histologically they were classified according to WHO Classification and staging was done by FIGO staging system. All patients evaluated for treatment pattern including surgery, adjuvant or neoadjuvant chemotherapy, single agent or combination chemotherapy, chemotherapy regimes. All patients followed up for 8 -10 months.

RESULT:

Total number of registered cases were 87. Histopathological analysis showed 71(82%) cases of epithelial tumors, 5 cases (6%) of sex cord stromal tumor and 11 (13 %) of germ cell tumors. Among the individual tumors serous tumors were the commonest 51%, followed by 18% mucinous carcinoma and 20% undifferentiated carcinoma. The peak incidence was in 5^{th} – 6^{th} decades. (**Table 1**)

TABLE 1: PATIENT CHARACTERISTICS

Age Distribution	n=87	%
30-40	09	10
41-50	09	10
51-60	17	20
61-70	40	46
71-80	12	14
Histopathological Distribution		
Epithelial Histology	71	81.6
Germ cell tumors	11	12.6
Sex chord stromal tumor	5	5.74
Classification of Epithelial ovarian cancers	n=71	
Serous carcinoma	36	51
Mucinous carcinoma	13	18.3
Undiff carcinoma	14	20
Others	08	11.2

All patients were staged according to FIGO staging. Sixty five percent patients had stage III at presentation, 17% patients had Stage IV, 13% and 6% had stage II and I respectively.(**Fig. 1**)

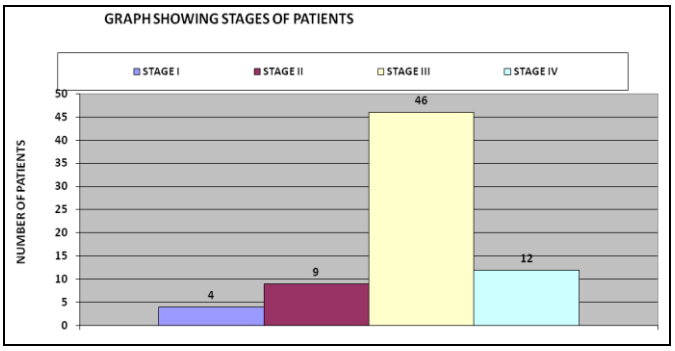

FIG.1: SHOWING STAGES OF PATIENTS

Most of the patients were undergone exploratory laparotomy for staging and primary removal of tumour. Eighty seven percent patients in this series underwent surgical procedure includes exploratory laparotomy for staging and primary removal of tumor. Fourteen percent of patients have unresectable disease. These patients were given neoadjuvant chemotherapy. (**Fig. 2**)

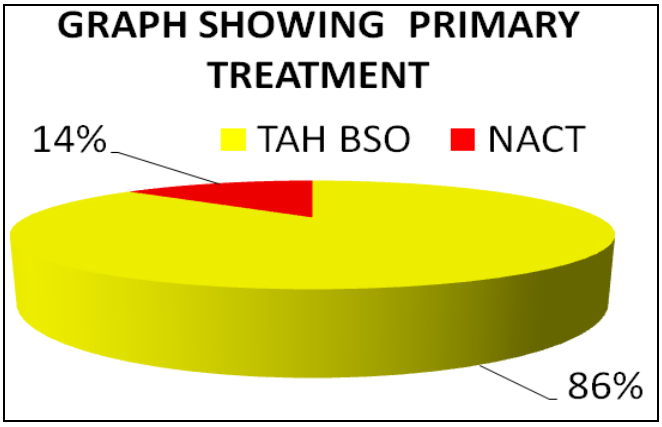

FIG.2: GRAPH SHOWING PRIMARY TREATMENT

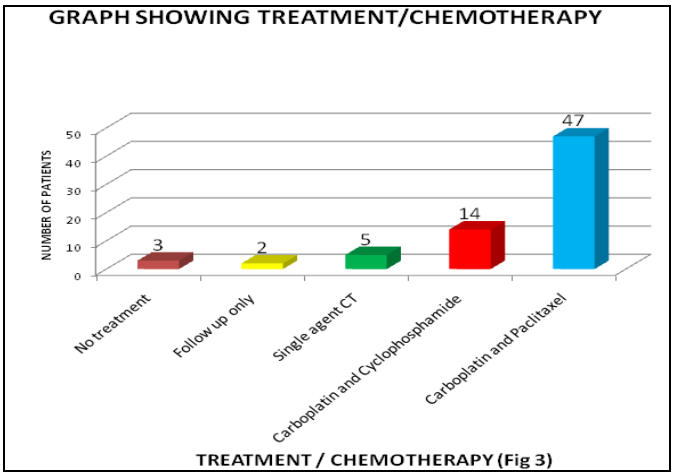

FIG. 3: GRAPH SHOWING TREATMENT/ CHEMOTHERAPY

Three patients did not receive treatment; two patients (3%) kept on follow up only. Five patients (7%) receive only single agent chemotherapy. Majority of patients (86%) received combination chemotherapy with paclitaxel and carboplatin and carboplatin and cylophosphamide. (**Fig. 3**)

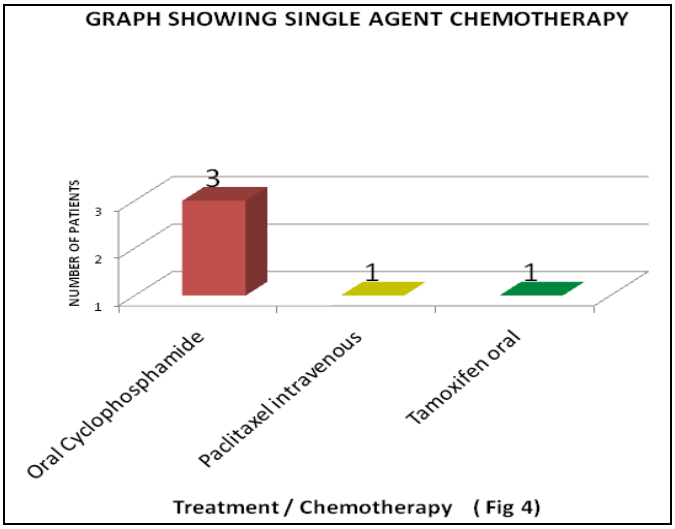

FIG.4: SINGLE AGENT CHEMOTHERAPY

Three patients received oral Cyclophosphamide, one patient received oral tamoxifen and one patient received single agent weekly low dose paclitaxel intravenously. (**Fig. 4**)

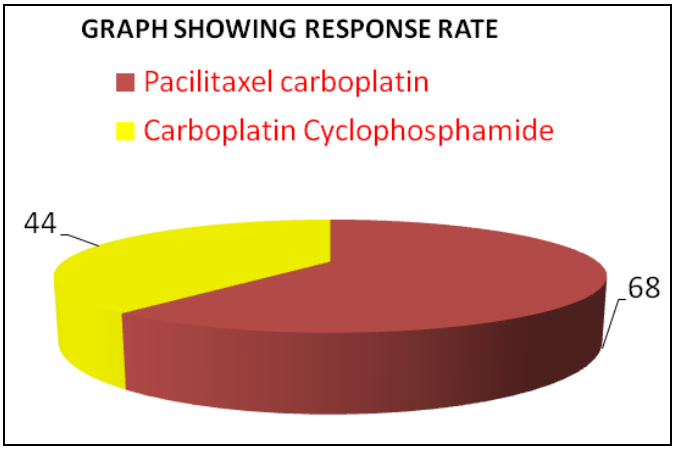

FIG.5: RESPONSE RATE

Response to combination chemotherapy was observed in 68 % and 44 % with Paclitaxel carboplatin and carboplatin cylophosphamide regimens respectively. (**Fig. 5**)

Fifteen patients in paclitaxel group and ten patients in cylophosphamide did not show any response to treatment. Four patients relapsed during treatment in paclitaxel group. Recurrence observed in 40 (58%) of cases.

Platinum resistant cases were 12 (17%). Remaining 28 (42%) cases were platinum sensitive. Second line chemotherapy was given in 30 cases. Six patients refused to further treatment. Further treatment was not advised in three cases due to poor performance status. One patient died due to disseminated disease.

TABLE 2: SECOND LINE CHEMOTHERAPY REGIMEN

Sr. No	Chemotherapy	n=30	%
1	Pegylated Doxorubicin (Single Agent)	13	43
2	Carboplatin and Gemcitabine	9	30
3	Carboplatin and Paclitaxel	6	20
4	Oral Gefitinib	2	7

Twenty eight cases (41%) were disease free up to last follow up. Fifteen cases receiving IIIrd line oral cytotoxic therapy in form of Tab Gefitinib. Twenty cases had residual disease. Seventeen cases developed metastases during course of treatment

DISCUSSION: It has been shown from various studies that epithelial ovarian cancers are not a single disease but are composed of a diverse group of tumors that can be classified based on distinctive morphologic and molecular genetic features.[8] These tumors are known for having large differences in histopathologic features, varying clinical and biological behavior. It is a fifth leading cause of death from cancer and leading cause of death from gynecological malignancies.[1, 2]

Incidence of age reported in various studies to be above 40 years and incidence increased with increasing age. [5], [9] Majority of epithelial ovarian carcinomas are diagnosed in peri or post-menopausal women with a mean age of 63 years. [10] In present study the peak incidence of ovarian cancer was in 6th decade accounting for 46 %, followed by 5th decade and 7th decade. Median age of presentation was 63 years.

More than 90% of ovarian cancers are derived from ovarian surface epithelium.[11] Surface epithelial tumors histologically commonest and are constitute 48.8% and 63.5% of all ovarian tumor. [12, 13] Histopathological analyses in this study showed

82% surface epithelial tumors, followed by 13 % of germ cell tumor and 5% sex chord stromal tumors. Similar findings were observed in various studies. Sarwar et al in their study observed the hospital prevalence of epithelial tumors 83.3%. [14] In another study, the prevalence of epithelial ovarian cancer was reported to be 90%. [15]

Histopathological grading is one of the prognostic indicators particularly in predicting recurrence.[16] Whereas the stage at presentation of these malignancies is major prognostic indicator and has the largest influence on the treatment outcome.

Most of patient presented in advanced stage probably due to lack of effective screening programs. Approximately 70% of patients with epithelial ovarian cancers are already having stage III or IV disease reported in various studies. [17] In present series 65 % and 17% were in stage III and IV respectively. Overall 82% of patients were in advanced stage in this study.

Treatment modality of ovarian cancer includes surgery, radiotherapy and chemotherapy and more recently targeted therapies. Surgery for staging and optimal cytoreduction followed by adjuvant chemotherapy is cornerstone of management for patients of advanced ovarian carcinoma. The maximal surgical cytoreduction includes total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy and omentectomy.

Eighty seven percent patients in this series underwent surgical procedure includes exploratory laparotomy for staging and primary removal of tumor. (**Fig.2**) The optimal cytoreduction is possible in few percentages of patients with advanced ovarian cancer.

There are advances in adjuvant chemotherapy in ovarian cancers with high response rates to front line chemotherapeutic agents. The standard regimens include taxens with a platinum combination with documented overall response rate 70% for patients with suboptimal debulked disease, and over 80% for patients with optimal cytoreduction. [18, 19]

Major fraction of patient in present study (86%) received adjuvant combination chemotherapy. A higher proportion of patient (47%) received Paclitaxel and carboplatin followed by carboplatin and Cyclophosphamide (14 %). Three patients did not receive treatment; two patients (3%) kept on follow up only due to low risk disease. Five patients (7%) receive only single agent chemotherapy considering poor performance status.

Advanced epithelial ovarian cancer is well known for high chemosensitivity. In the present study the response to combination chemotherapy was observed in 68 % and 44 % with Paclitaxel carboplatin and carboplatin Cyclophosphamide regimens respectively.

Stage at diagnosis and histological grade are strongly associated with prognosis [20] and Extent of residual tumor at primary surgery and sensitivity to platinum based therapy have major determinant of clinical outcome.[21] Despite high chemosensitivity and improvement of overall response rate, outcome of patients with advanced ovarian tumors remains poor due to recurrence. Long term follow ups recommended assessing response to initial therapy.

CONCLUSIONS: Epithelial ovarian carcinoma is one of most common gynecologic malignancy, usually diagnosed late when disease is in an advanced stage. The delay in diagnosis may be mostly explained by the lack of effective screening. In the present series, serous cystadenocarcinoma were the commonest epithelial histology. Most of patients were in 6^{th} decade of life and locally advanced stage. Majority of patient received Paclitaxel based chemotherapy. Patient showed significant response to adjuvant taxens based chemotherapy. However long terms follow up is recommended for evaluation the response to therapy.

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How to cite this article:
Kaur P, Khurana A, Chauhan A and Singh G: The Clinicopathological Profile in Patients with Epithelial Ovarian Carcinoma. Int J Pharm Sci Res 2016; 7(2): 868-72.doi: 10.13040/IJPSR.0975-8232.7(2).868-72.