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ROLE OF CHEMOTHERAPY IN THE MANAGEMENT OF ADVANCED MALIGNANT OVARIAN TUMOURS

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ABSTRACT:

OBJECTIVE: *To assess the role of adjuvant chemotherapy after surgical management of advanced malignant ovarian cancers in prognosis and survival of patients*
METHODOLOGY: *This prospective observational study was performed to analyse the treatment of all cases of Malignant ovarian tumours, diagnosed and treated at the department of Gynaecology and obstetrics, Jinnah Postgraduate medical centre, in collaboration of Oncology department Jinnah Postgraduate medical centre Karachi, during January 2001 till June 2002. After obtaining informed consent, patients with diagnosed malignant ovarian tumors were enrolled in the study, patients with co-morbidities or failed to give consent were excluded from the study. The profile consists of a thorough history, physical examination, investigations and diagnosis as were recorded in Performa. Data was analyzed by SPSS version 17.*
RESULTS: *During the study period, total 16 cases of ovarian malignancy were diagnosed and treated. Total Gynaecological malignancies admitted during this study period were 70. Among these ovarian malignancy was the second commonest with 22.85% incidence rate following cervical cancers (i.e, 54.28%). All the patients underwent laparotomy supported by adjuvant chemotherapy in majority of cases. All patients were followed for a minimum period of six months*
CONCLUSION: *Majority of the patients are reported with advanced disease at the time of diagnosis, i.e that is why these patients cannot be treated with surgery alone. Consequently, adjuvant chemotherapy has become a major treatment modality for this disease in advance stages.*

KEY WORDS: Ovarian cancers, laparotomy, laparoscopy, chemotherapy, radiotherapy, Intra peritoneal chemotherapy.

INTRODUCTION:

Ovarian Cancer is among one of the most lethal gynaecological cancers. For more than two decades, epithelial carcinoma of the ovary has been the number one killer of U.S Women.[1] Approximately one in 70, American women develop ovarian carcinoma accounting for 4 % of all cancers in women. In United Kingdom, the incidence is 14.0 per 100,000 women.[2] White females had considerably higher rates of ovarian cancer than the black race. Similarly its rates are high in North America and Northern Europe and low in Japan.[3] In a study of gynaecological cancer in Faisalabad (Pakistan), Ovarian cancer was the most frequently found gynaecological cancer, incidence rate is 38.0%.[4] S. Jamal at el, (1993) also reported ovarian cancer as the commonest gynaecological malignancy in their study.[5]

The primary treatment for early stage ovarian cancer is surgery, which should entail a total abdominal hysterectomy in addition to bilateral salpingo-oophorectomy, and with or with out lymph nodes removal with complete surgical staging of the disease. In situations of borderline ovarian cancers, where future fertility is important, a unilateral oophorectomy may be an option. For these patients and patients with stage I a well differentiated tumours, no additional therapy is indicated. These patients have a 10 years relapse rate of only 10%.[6]

More than two third of cases are advanced at the time of diagnosis, i.e, stage III and IV,[7] and these patients cannot be cured with surgery alone. Consequently an adjuvant chemotherapy has become a major treatment modality for this disease. Cytoreductive

surgery to reduce the diameter of the largest residual mass to less than 1-2 cms results in better response to chemotherapy.

With cisplatin and cyclophosphamide treatment, long term control may be expected in less than 10% of women with incompletely resected stage III and less than 5% of women with stage IV disease.[8] The prognosis for patients with advanced ovarian cancer remains poor with reported 5 years survival rates ranging between 15-20%.[9]

Comparison of combination of paclitaxel & Cisplatin with previous treatment at that time i.e cisplatin and cyclophosphomide, as first line chemotherapy in women with sub optimally debulked stage III,or stage IV ovarian cancer demonstrated a significantly higher major response rate(25% versus 19%), and a 14 month over all advantage in survival in favour of the paclitaxel containing arm.[10]

Recent efforts are focused on evaluating Carboplatin combination with paclitaxel.[11]

Another taxanes docetaxel, which has shown response rates of over 20% in relapsed ovarian cancer is currently being studied in combination with cisplatin in clinical trials.

Taxanes in various dose schedule achieve response rates of 10-50% with median overall survival of 10-12 months in patients with platinum refractory disease.[12] Other drugs such as topotecan, gemcitabine and doxorubicin have shown activity as second line treatment in platinum resistant ovarian cancer.[13]

Intraperitoneal chemotherapy delivered high concentration of drugs directly to the tumour in peritoneal cavity. It is most effective in patients with small sized residual tumour. Mitoxantrone and taxol are used in small volume in platinum refractory ovarian cancer.[14]

METHODOLOGY:

A prospective observational study to analyse the role of adjuvant chemotherapy in all cases of malignant ovarian tumours diagnosed and treated at department of diagnosed and treated at department of Gynaecology and obstetrics in collaboration with oncology department of Jinnah post graduate medical center Karachi, during January 2001 till June 2002 is undertaken. Patients were admitted through out patient's Department of Gynaecology and obstetrics, JPMC. In total 52 Patients had undergone surgical treatment for ovarian tumours, out of which 16 were found to have malignant ovarian tumours. Patient's profile consists of a detailed history including her age, parity, presenting complaints, associated complaints, duration of symptoms, any treatment taken

TABLE-I
INCIDENCE OF OVARIAN CARCINOMA

	Number	Percentages %
Total laparotomies benign	52	100.00
tumour malignant tumour	36	69.23
	16	30.76

TABLE-II
CLINICAL FINDINGS AT DIAGNOSIS

	Number	Percentages %
Mass	14	87.50
Ascites	6	37.50
Pleural effusim	1	6.25
Paedal oedema	2	12.50

TABLE-III
ADJUVANT TREATMENT FOLLOWING SURGERY

Treatment	Number	Percentage
Chemotherapy	14	62.50%
Radiotherapy	Nil	——

TABLE-IV
ADVERSE EFFECTS OF CHEMOTHERAPY

Side effects	Number	Percentage (%)
Gastrointestinal	6	37.50
Fever	5	31.25
Alopecia	3	18.75
Hepatotoxicity	4	25.00
Neurotoxicity	1	6.25%
Nephrotoxicity	1	6.25%
Haematologic toxicity	3	18.75%

TABLE-V
OUTCOME OF PATINETS WITH OVARIAN TUMOURS

Stage	Number	Follow up	Lost follow up	Expired
I	8	6	2	Nil
II	3	3	—	—
III	3	3	—	1
IV	2	2	—	2

for these complaints prior to admission. History of weight loss, anorexia and bowel habits, menstrual history, and family history of cancer were also recorded. Socioeconomic status of Patients was noted as well. A full general physical examination as well as systemic examination was performed with especial emphasis on abdominal and pelvic examination. Investigations include all the baseline investigations like complete blood count, liver and renal function tests, serum electrolytes etc. X ray chest, abdomen and pelvis, serum CA-125 levels, Intravenous pyelography, ultrasonography, Doppler imaging, C.T Scan and MRI etc were also performed.

After surgery patients were refered to oncology department where they were registered and chemotherapy was given to them as decided by oncologists. Afterward they were admitted for chemotherapy treatment further follow up was done in OPD. A specially designed proforma was used to record data which was analyzed by SPSS version 17 with descriptive statistics.

RESULTS:

Gynaecological malignancies admitted during the study period were 70. Among which cervical carcinoma was the most common cancer i.e, 54.28% ovarian cances ranked as the second most common gynaecologic malignancy with 22.85% (n=16). During this study period, 52 laparotomies were performed in total for ovarian tumours. Out of which 16 (30.76%) were malignant and 36 were found benign tumours. (Table I)

Age of the patients ranges between 15-80 years with 68.75% were below 40 years of age. Majority of patients (75.0%) were married and multi parous i.e, (43.75%) and 6 patients were nulliparous i.e (37.50%) only 4 patients (25.0%) were menopausal. Regarding clinical presentation of ovarian carcinomas, majority of the patients i.e, 14 patients(87.50%) were presented with pain in abdomen followed by abdominal distension in 8 patients (50.0%) Menstrual irregularities were present in 3 patients (18.75) while backache in 5 patients (i.e, 12.50%) each. Duration of symptoms was less than 6 months in most of the patients i.e, 10 patients (62.50%). Adenexal mass was the most common clinical finding in examination presented in 14 patients (87.50%), (Table II.)

Total abdominal hysterectomy bilateral salpingo-oophorectomy and Infracolic omentectomy with or without lymph nodes removal was the treatment in most of the patients (7 patients i.e 43.75%). Staging of the tumour shows that 8 patients (50%) were having stage I disease, 3 patients (i.e 18.75%) had stage II disease and stage III disease each. While 2 patients (12.5%) were presented with stage IVdisease. Histopathology showed predominance of epithelial tumours, found in 11 patients (i.e 68.75%). Majority of patients (14 patients i.e 87.50%) received chemotherapy after primary surgery. Chemotherapy was not advised to one patient with low risk malignancy. One patient with krukenberg tumour was planned to have chemotherapy but she expired before receiving it. (TableIII)

Most of the patients suffered from gastrointestinal problems like nausea, vomiting and diarrhoea (6 patients i.e, 37.50%). Five patients (31.25%) complaints of fever, while 4 patients had jaundice and disturbed liver function tests, so their chemotherapy was stopped till their tests become normal and then restarted again. Patients with haematologic toxicity presented with anemia, low white blood cell counts and low platelets count received blood or platelets transfusion accordingly (Table-IV).

Total 3 patients expired. All belonged to stage III and IV disease. Two patients of stage I lost follow up. Rest of the patients were regularly followed up in out patient clinics.(Table V)

Out of total 16 cases reviewed, two patients (12.50%) were lost to follow up. One patient was expired prior to chemotherapy. Of remaining 13 patients, 10 (62.50%) were alive. Most of these patients were presented with early stage disease. 3 out of 5 patients, who presented with FIGO stage III and IV, were died due to this lethal disease.

DISCUSSION:

Surgery is considered as the best treatment for the ovarian cancers. All our patients included in this study underwent surgery. Different procedures were performed according to extent of disease. These include recommended procedures of Total Abdominal Hysterectomy, bilateral salipingo-oophorectomy, Omentectomy with or without pelvic nodes removal to unilateral salpingo-oophorectomy etc. Histological distribution of ovarian cancers in our study showed the predominance of epithelial ovarian carcinoma accounting for 68.75% of all cases, which is consistent with other studies. Costa MJ[15], also described serous epithelial carcinoma as the most predominantly occurring epithelial carcinoma in their study (i.e, 65.4%). Following primary surgery, all of our patients received systemic intravenous combination chemotherapy mostly in 6 courses as prescribed by Oncologist. Patients were transferred to Radiology Department of Jinnah Post Graduate Medical centre, where they received systemic chemotherapy according to tumour grading and staging. Patients with tumour of low malignant potential were not subjected to chemotherapy. None of our patients received intraperitoneal chemotherapy.

Now days, Intra peritoneal chemotherapy is preferred over intravenous chemotherapy. Multiple studies have shown that regimens including intraperitoneal chemotherapy are superior with regard to progression free survival and overall survival in women with stage III, residual less than 1 cm epithelial ovarian cancer in the short and medium term compared to the standard 6 cycles of intravenous chemotherapy[16]. The long term disease survival rate at 8 years is however, remained unchanged.[17]

Dr. Joan L, Walker, MD and colleagues, [18] in a comparative study identifies the challenges associated with the administration of intraperitoneal chemotherapy in conjunction with intravenous chemotherapy. They conclude that intra peritoneal chemotherapy's success is dependent upon appropriate surgical resection, patients selection and training of physicians and nurses.

Regarding side effects, gastrointestinal disturbances including nausea, vomiting and diarrhea were the commonest. Some patients also complaints of abdominal distension which was developed due to ascites and metastasis in other organs, which is consistent with other studies, showing anemia, fatigue, dizziness, bowel symptoms, leukopenia, temporary hair loss and thrombocytopenia.

CONCLUSION:

Surgery is said to be the definite treatment for ovarian cancer but is not the complete treatment. Adjuvant chemotherapy has an important role in managing these patients side by side with surgical management. Now days, Intraperitoneal chemotherapy is more popular than the routine systemic intravenous chemotherapy. With the careful selection of the patients, intraperitoneal chemotherapy has been associated with increase in survival rates in the initial trials. Results of further trials will decide the optimal mode of chemotherapy in ovarian cancer treatment.

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