Open Access

Original Article

Treatment Patterns and Outcomes of Ovarian Cancer in Different Centres of Karachi

Perwasha Kerio, Ghulam Haider, Kalil Ahmed, Saima Zahoor, Hina Perveen, Muhammad Hayat

Jinnah Postgraduate Medical Center, Karachi Pakistan

ABSTRACT

Objective: To evaluate the treatment pattern i.e. either upfront surgery followed by adjuvant chemotherapy or upfront neoadjuvant chemotherapy followed by surgery and outcomes of advance ovarian cancer in different hospitals of Karachi.
Study Design: observational study.
Place and Duration of Study: Oncology Department, Jinnah Postgraduate Medical Center, Karachi, from Mar 2019-Sep 2020.
Methodology: All females of age 18-70 years with diagnosis of epithelial ovarian cancer (stage III-IV) and who had received chemotherapy or on chemotherapy in upfront or in adjuvant setting from another hospital and came to Jinnah Postgraduate Medical Center in mid of treatment due to exhaustion of
financial resources, as ovarian cancer treatment costs high and oncology department Jinnah Postgraduate Medical Center provides free treatment.
Results: Of 170 patient, 119(70%) patients received adjuvant chemotherapy after surgery, while 51(30%) received neoadjuvant chemotherapy followed by surgery. Among 51 patients who received neoadjuvant (upfront) chemotherapy, 30(58.8%) had partial and 13(25.5%) had complete clinical response, whereas 42(82.4%) had partial and 9(17.6%) had complete pathological response. About 38(74.5%) had complete and 13(25.5%) had partial biochemical response. Each patient followed for one and half year to see recurrence rate. Patients who underwent surgery 45(48.4%) had recurrence, 38(40.9%) completed the treatment plan and 10(10.7%) died. In patients who underwent neoadjuvant chemotherapy 12(41.4%) showed recurrence, 11(37.9%) completed the treatment plan and 6(20.7%) died.
Conclusion: To date most of the centers in Karachi following the pattern of upfront surgery followed by adjuvant chemotherapy. More disease recurrences are seen in upfront surgery group and more patient died in upfront chemotherapy group after follow up for one and half years.

Keywords: Clinical Response, Ovarian Cancer, Partial Response, Pathological Complete Response, Surgery.

How to Cite This Article: *Kerio P, Haider G, Ahmed K, Zahoor S, Perveen H, Hayat M. Treatment Patterns and Outcomes of Ovarian Cancer in Different Centres of Karachi. Pak Armed Forces Med J 2025; 75(SUPPL-I): S11-S15. DOI: https://doi.org/10.51253/pafmj.v75iSUPPL-I.5677*

INTRODUCTION

Worldwide, ovarian cancer (OC) is the 6th prevalent cancer and 7th leading cause of death in women.[1,2] In United States in 2018, almost 22,240 females were diagnosed with OC and 14,070 females died due to it.[3]. Epithelial ovarian cancer (EOC) is predominantly a cancer of the elder age group (55-64 years) with median age at the time of diagnosis 63 years, which indicates that 50% of the females are younger than 63 years and 50% are more than 63 years of age at diagnosis.[4] In Pakistan, EOC is the 4th most prevalent malignancy in women.[5]

There are various types of EOC; the most common pathologic type of EOC is high grade serous carcinoma, accounting for 80%. It occurs mostly in the age group 50-60 years. Nearly 75% of the females diagnosed with epithelial EOC have advanced stage of tumor (stage III or IV). Overall five-year survival rates for stage III is 28% to 50% whereas for stage IV is 13%.[6]

Correspondence: Dr Perwasha Kerio, Jinnah Postgraduate Medical Center, Karachi Pakistan.
Received: 12 Nov 2020; revision received: 03 Feb 2021; accepted: 05 Feb 2021

The standard treatment of EOC depends on stage. Females with advanced stage of EOC are being treated with cytoreductive surgery followed by platinum and taxane-based chemotherapy. However, if primary cytoreduction is not possible due to severity of the disease or poor performance status, patients can be managed with neoadjuvant chemotherapy followed by interval debulking surgery and adjuvant chemotherapy.[7-10]

In Pakistan, the treatment of stage III and IV EOC is not uniform among all oncology centers and oncologist. Upfront debulking surgery followed by adjuvant chemotherapy has been the common practice since long time. For the few years, this pattern is now changing with upfront chemotherapy followed by interval debulking surgery and remaining cycles of chemotherapy in adjuvant setting.[8] Proponents of this pattern of treatment are of the opinions that intact vasculature in pre-operative setting could yield better chemotherapy response and pathologic response can better predict long term survival. Therefore, we conducted this study to assess the treatment patterns

and outcomes of stage III & IV EOC in different hospitals of Karachi.

METHODOLOGY

This was an observational study conducted at the department of Medical Oncology, Jinnah postgraduate medical center, Karachi from March 2019-Sep 2020. Sample size was estimated as 206 using open epi sample size calculator by taking statistic of optimal debulking surgery as 20.3%, margin of error as 5.5% and 95% confidence level.1 The non-probability consecutive sampling technique was used to enroll the patients.

Inclusion Criteria: All females of age 18-70 years with confirmed diagnosis of EOC (stage III-IV) and who had received chemotherapy or on chemotherapy in upfront setting or in adjuvant setting, no other concomitant malignancy and who were presented to our department for treatment were included.

Exclusion Criteria: Patients with comorbids, who were poor candidates for completion of chemotherapy and standard surgery were excluded.

As oncology department of JPMC is providing free treatment to cancer patients therefore significant number of patients, after having received few cycles of chemotherapy came to JPMC for continuation of treatment due to exhaustion of financial resources. Also gynecology department of JPMC offering free of cost surgery, therefore significant number of patients come for interval debulking surgery after having received few cycles of pre-operative chemotherapy at private centers and clinics. Patients already having surgery from different hospitals were also included and those having optimal surgery (to achieve maximal debulking to less than 1 cm or resection all visible disease) was concluded from their medical records including surgical notes, radiologic reports and histopathologic reports. The details regarding socio-demographics, medical history, pathology, tumor markers, chemotherapy regimens, number of cycles and response evaluation during chemotherapy were recorded on predesigned proforma. Clinical response to chemotherapy was evaluated after 3 to 4 cycles of chemotherapy. Clinical response is measured by radiologic evaluation with CT scan chest abdomen and pelvis with contrast with RECIST 1.1 by radiologist, partial clinical response is reduction in more than 30% of total tumor size and complete clinical response is disappearance of all clinical lesions. Pathologic response is measured after neoadjuvant (upfront) chemotherapy on surgical ovarian, omental and lymph node tissue histopatholoogically. Partial pathologic response is multifocal tumor regression but easily identifiable residual tumor and complete pathologic response is no residual tumor in histopathologic material. Biochemical response measured by serum CA-125 level (reference range 0-35 u/mL). Partial biochemical response is decrease in CA-125 level following treatment but not reaching upto normal level and complete biochemical response is normalization of CA-125 level after treatment.

The ethical review board approval was taken before initiation of study (NO.F.2-81-IRB/2019-GENL/1755/JPMC). The written informed consent was taken from all the eligible patients before data collection from patient.

SPSS version 23 was used to analyze data. Mean and SD were reported for numeric variables. Frequency and percentage were computed for categorical or nominal variables.

RESULTS

Total 250 patients were enrolled in this study but 70 patients were excluded due to incomplete information and other pathologies including non-epithelial types of OC. Of remaining 170 patients who fulfilled all criteria of them the mean age of females was reported as 47 years. Majority of the females belonged from rural area 99(58.2%), illiterate 77(45.3%), had monthly income 15,000-30,000 93(54.7%), married 134(78.8%) and housewives 159(97.6%). The females who were married, majority of them had 1-4 parity 76(44.7%). About 16(9.4%) had positive family history of breast cancer whereas 44(25.9%) had positive family history ovarian among second-degree relatives. Out of 170 patients, 123(72.4%) had high grade serous histology followed by endometroid histology 14(8.2%).

Patients were divided into 7 groups based on where treatment started, 11 patients from Kiran hospital (6.5%), 16 patients from Agha khan university hospital (9.4%), 6 patients from Dr. Ziauddin hospital [ZU], 6 patients from Liaquat national hospital (LNH) (3.5%), 78 patients from JPMC (45.9%), 10 from Civil hospital Karachi (CH) (5.9%) and 43 patients reported from miscellaneous centers (MC) (25.3%). Of 170 patient, 119 patients had upfront surgery (70%), while 51(30%) received upfront chemotherapy followed by interval debulking surgery. Out of 170 patients, 11 patients had optimal surgery (6.4%) and 108 had suboptimal surgery (63.5%). Center-wise most of the

patients had suboptimal surgery at Kiran hospital (63.6%), miscelleneous (95.3%), JPMC (62.8%) and CHK (80%) respectively. In CHK 9 (90%), in ZH 4 (66.7%), in JPMC 49(62.8%), in Kiran hospital 6(54.5%) had adjuvant chemotherapy after cytoreductive surgery, whereas in AKUH 9(56.3%) and in LNH 3(50%) received upfront chemotherapy followed by interval debulking surgery. (Table-I)

After one year 122 patients who underwent for first line chemotherapy. Patients who underwent surgery 45(48.4%) had recurrence, 38(40.9%) completed the treatment plan and 10(10.7%) died. In patients who underwent neoadjuvant chemotherapy 12(41.4%) showed recurrence, 11(37.9%) completed the treatment plan and 6(20.7%) died (Figure- 2).

Table-I: Center-Wise Distribution Of Upfront Treatment And Surgery (N=250)

	Kiran hospital	Agha khan university hospital	Dr. Ziauddin hospital	Liaquat national hospital	Miscellaneous centers	Jinnah postgraduate medical center	Civil hospital Karachi
	n=11(6.5%)	n=16(9.4%)	n=6(3.5%)	n=6(3.5%)	n=43 (25.3%)	n=78(45.9%)	n=10(5.9%)
Upfront treatment							
Upfront chemotherapy followed by Interval debulking surgery followed by remaining cycles of chemotherapy (n=51)	5(45.5%)	9(56.3%)	2(33.3%)	3(50%)	2(4.7%)	29(37.2%)	1(10%)
Upfront surgery (n=119)	6(54.5%)	7(43.8%)	4(66.7%)	3(50%)	41(95.3%)	49(62.8%)	9(90%)
Optimal surgery (n=11)	0	7(43.8%)	2(33.3%)	2(33.3%)	0	0	0
Suboptimal surgery (n=108)	7(63.6%)	0	2(33.3%)	1(16.7%)	41(95.3%)	49(62.8%)	8(80%)
Adjuvant chemotherapy (n=119)	6(54.5%)	7(43.8%)	4(66.7%)	3(50%)	41(95.3%)	49(62.8%)	9(90%)

The most common chemotherapy regimen was carboplatin+paclitaxel (Table-II).

Table-II: Comparison of Adjuvant and Neoadjuvant Chemotherapy and Regimen (n=250)

Upfront treatment	Chemotherapy regimen		
	03 weekly carboplatin and paclitaxel	Weekly carboplatin and paclitaxel	Dose dense carboplatin and paclitaxel
Neoadjuvant chemotherapy	22(43.2%)	25(49%)	4(7.8%)
Adjuvant chemotherarpy	93(78%)	24(20%)	2(2%)

Out of 170 patients, 90(52.9)% had clinical stage IIIC followed by stage IV (21.8%). After upfront surgery, 79(46.55%) had stage IIIC, 49(28.8%) had stage IIIA, 27(15.9%) had stage IIIB and 15(8.8%) had stage IV.

Among 51 patients who received neoadjuvant (upfront) chemotherapy, 30(58.8%) had partial and 13(25.5%) had complete clinical response, whereas 42(82.4%) had partial and 9(17.6%) had complete pathological response. About 38(74.5%) had complete and 13(25.5%) had partial biochemical response. (Figure-1).

Out of 170 patients, 83 patients (48.8%) had recurrence and the median recurrence time was 6 months with interquartile range of 3 to 9 months.

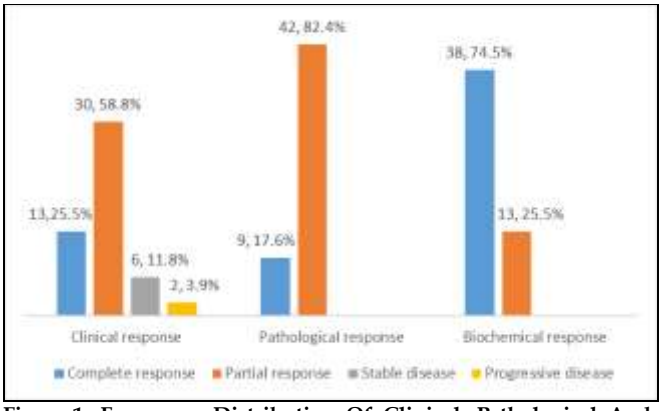

Figure-1: Frequency Distribution Of Clinical, Pathological And Biochemical Response

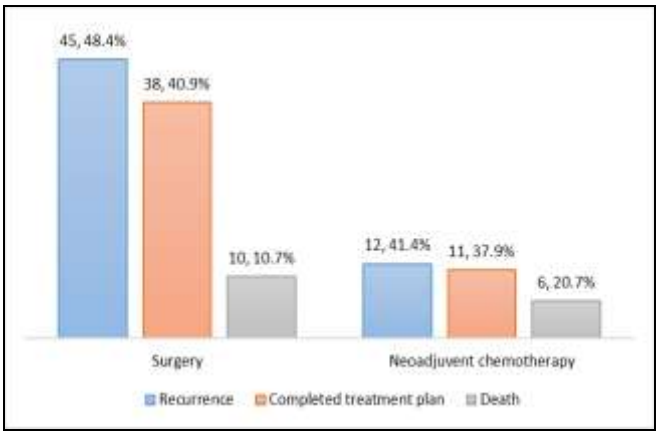

Figure-2: Treatment Outcomes In Surgery Versus Neoadjuvent Chemotherapy Groups

DISCUSSION

OC is the 6th prevalent cancer and leading cause of mortality from gynecological malignancies.[1-11] Most of the EOC patients present at late stage III and IV. In the present study, most of the females had high grade serous (72.4%), followed by endometroid (8.2%) and mucinous (6.5%) respectively. In a study by Sarwar *et al.,* serous cystadenocarcinoma was the frequent histology (29%), followed by mucinous cystadenocarcinoma (13%) and endometroid adenocarcinoma (7%) respectively. 12 In our study, we found 52.9% had clinical stage IIIC followed by stage IV (21.8%). Whereas, Sawar *et al.,* found 44% presented with stage III and 22.4% with stage IV.[12]

Currently, the primary treatment for EOC patients with advanced stages is cytoreduction followed by chemotherapy. While, neo-adjuvant chemotherapy followed by interval debulking surgery is considered as alternative therapy when patient is unable to undergo for complete resection during primary debulking surgery. [13] In a research by Lim *et al.,*, out of 279 females with bulky stage III or IV of EOC, 51% were treated with extensive primary debulking surgery whereas 49% were treated with neoadjuvant chemotherapy.[14] In our study, we found 63.5% of the patients underwent for suboptimal surgery, 30% interval debulking surgery and 6.4% had optimal surgery. In most of the centers like KH, MC, JPMC and CH suboptimal surgery was common. Several researches have explained the association with complete cytoreduction and survival.[7, 8] Ryu *et al.,* in their study showed that a cytoreduction of <1cm conferred a statistically better disease-free survival (p<0.05) as well as overall survival (p<0.05). 15 In the current study, 70% of the patients were being treated with adjuvant chemotherapy after cytoreductive surgery. In different hospitals like CH, ZH, JPMC and KU, the adjuvant chemotherapy after cytoreductive surgery was common whereas, in AKUH and LNH, neoadjuvant chemotherapy followed by surgery was common. Inciura A *et al.,,*. in their study found median progression-free and overall survival in patients treated with neoadjuvant chemotherapy and adjuvant chemotherapy was same for stage III and IV (p<0.05).[16]

EOC is most sensitive tumors to cytotoxic drugs, with more than 80% of the females show response to standard chemotherapy combined with platinum and taxane.[17,18] In the present research, most common chemotherapy regimen was carboplatin combined with paclitaxel. Further, 51 patients who received neoadjuvant (upfront) chemotherapy followed by surgery, 17.6% had partial and 7.6% had complete clinical response, whereas 24.7% had partial and 5.3% had complete pathological response. Out of 170 patients, 81.2% had complete and 18.8% had partial biochemical response.

CONCLUSION

To date most of the centers in Karachi following the pattern of upfront surgery followed by adjuvant chemotherapy. More disease recurrences are seen in upfront surgery group and more patient died in upfront chemotherapy group after follow up for one and half years.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

The following authors have made substantial contributions to the manuscript as under:

PK & GH: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

KA & SZ: Data acquisition, data analysis, approval of the final version to be published.

HP & MH: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Basu P, De P, Mandal S, Ray K, Biswas J. Study of 'patterns of care' of ovarian cancer patients in a specialized cancer institute in Kolkata, eastern India. Indian J Cancer. 2009; 46(1): 28-33. https://doi:10.4103/0019-509x.48592.
2. Momenimovahed Z, Tiznobaik A, Taheri S, Salehiniya H. Ovarian cancer in the world: epidemiology and risk factors. International journal of women's health. 2019; 11: 287-99. https://doi:10.2147/ijwh.s197604.
3. Torre LA, Trabert B, DeSantis CE, Miller KD, Samimi G, Runowicz CD, *et al.,* Ovarian cancer statistics, 2018. CA Cancer J Clin. 2018; 68(4): 284-96. https://doi:10.3322/caac.21456.
4. OCRA. Ovarian cancer research alliance 2020 [cited 2020]. Available from: https://ocrahope.org/patients/about-ovarian-cancer/statistics/#:~:text=Age%20of%20Ovarian%20Cancer%20Diagnosis,from%20ovarian%20cancer%20is%2070.
5. Malik IA. A prospective study of clinico-pathological features of epithelial ovarian cancer in Pakistan. J Pak Med Assoc. 2002; 52(4): 155-8.
6. Mostafa MF, El-etreby N, Awad N. Retrospective analysis evaluating ovarian cancer cases presented at the clinical oncology department, Alexandria University. Alexandria Journal of Medicine. 2012; 48(4): 353-60. https://doi.org/10.1016/j.ajme.2012.07.001.
7. Martín-Cameán M, Delgado-Sánchez E, Piñera A, Diestro MD, De Santiago J, Zapardiel I. The role of surgery in advanced epithelial ovarian cancer. Ecancermedicalscience. 2016; 10: 666. https://doi:10.3332/ecancer.2016.666.

8. Chishti U, Aziz AB. Primary debulking surgery versus neo-adjuvant chemotherapy in stage III/IV ovarian cancer: Comparison of perioperative morbidity and survival data in Pakistani women. J Pak Med Assoc. 2015; 65(3): 306-9.
9. Kobal B, Noventa M, Cvjeticanin B, Barbic M, Meglic L, Herzog M, *et al.,* Primary debulking surgery versus primary neoadjuvant chemotherapy for high grade advanced stage ovarian cancer: comparison of survivals. Radiology and oncology. 2018; 52(3): 307-19. https://doi:10.2478/raon-2018-0030.
10. Nakamura K, Kitahara Y, Nishimura T, Yamashita S, Kigure K, Ito I, *et al.,* Nadir CA-125 serum levels during neoadjuvant chemotherapy and no residual tumor at interval debulking surgery predict prognosis in advanced stage ovarian cancer. World J Surg Oncol. 2020; 18(1): 200. https://doi:10.1186/s12957-020-01978-6.
11. Reid BM, Permuth JB, Sellers TA. Epidemiology of ovarian cancer: a review. Cancer biology & medicine. 2017; 14(1): 9-32. https://doi:10.20892/j.issn.2095-3941.2016.0084.
12. Sarwar CM, Siddiqui N, Khokhar RA, Badar F. Epithelial ovarian cancer at a cancer hospital in a developing country. Asian Pac J Cancer Prev. 2006; 7(4): 595-8.
13. Santoiemma PP, Powell DJ. Tumor infiltrating lymphocytes in ovarian cancer. Cancer Biol Ther. 2015; 16(6): 807-20. https://doi:10.1080/15384047.2015.1040960.
14. Lim MC, Yoo HJ, Song YJ, Seo SS, Kang S, Kim SH, *et al.,* Survival outcomes after extensive cytoreductive surgery and selective neoadjuvant chemotherapy according to institutional criteria in bulky stage IIIC and IV epithelial ovarian cancer. J Gynecol Oncol. 2017; 28(4): e48-e. https://doi:10.3802/jgo.2017.28.e48.
15. Polom K, Roviello G, Generali D, Marano L, Petrioli R, Marsili S, *et al.,* Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for treatment of ovarian cancer. Int J Hyperthermia. 2016; 32(3): 298-310. https://doi:10.3109/02656736.2016.1149233.
16. Inciura A, Simavicius A, Juozaityte E, Kurtinaitis J, Nadisauskiene R, Svedas E, *et al.,* Comparison of adjuvant and neoadjuvant chemotherapy in the management of advanced ovarian cancer: a retrospective study of 574 patients. BMC Cancer. 2006; 6: 153. https://doi:10.1186/1471-2407-6-153.
17. Cortez AJ, Tudrej P, Kujawa KA, Lisowska KM. Advances in ovarian cancer therapy. Cancer Chemother Pharmacol. 2018; 81(1): 17-38. https://doi:10.1007/s00280-017-3501-8.
18. Sato S, Itamochi H. Neoadjuvant chemotherapy in advanced ovarian cancer: latest results and place in therapy. Ther Adv Med Oncol. 2014; 6(6): 293-304. https://doi:10.1177/1758834014544891.