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RESEARCH ARTICLE

Gestational trophoblastic neoplasia: treatment outcomes from a single institutional experience

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Abstract
Purpose To report the outcomes of gestational trophoblastic neoplasia (GTN) at a single institution and to determine the factors affecting response to chemotherapy and survival.
Methods/Patients From 1979–2010, we retrospectively reviewed the data of 221 patients treated at our center. GTN Patients were assigned to low-risk (score ≤ 6) or high-risk (score ≥ 7) based on the WHO risk factor scoring system. Overall survival (OS) probabilities were estimated using Kaplan–Meier method. Logistic regression was applied to study the impact of different factors on the response to initial therapy.
Results Patients' OS rate was 97 %. Median age at diagnosis was 37 year. 131 (59 %) patients had low-risk and 88 (40 %) cases had high-risk GTN. Complete remission rates to initial chemotherapy in low-risk group were 53 % and 87 % for single-agent methotrexate or dactinomycin, respectively. In high-risk group, 94 % achieved complete remission to initial chemotherapy with etoposide, methotrexate, dactinomycin, cyclophosphamide, and vincristine (EMA-CO). Etoposide, cisplatin, and dactinomycin as primary therapy in high-risk patients was successful in 70 %, while bleomycin, etoposide, and cisplatin (BEP) was successful in 53 % of cases. Salvage chemotherapy, surgical intervention or radiation therapy resulted in overall complete remission of 90 % in low-risk and 73 % in high-risk groups. Factors associated with resistance to initial chemotherapy were advanced-stage III/IV ($p = 0.005$), metastatic site other than lung or vagina ($p = 0.005$) and high-risk prognostic score ($p = 0.05$). OS was significantly influenced by the type of antecedent pregnancy (molar 98 % vs. others 93 %; $p = 0.04$), FIGO stage (I, II 100 % vs. III, IV 94 %; $p = 0.02$), score (low-risk 100 % vs. high-risk 92 %; $p = 0.01$), and site of metastasis (lung/vagina 98 % vs. others 85 %; $p = 0.002$).
Conclusions GTNs have excellent prognosis if properly treated at experienced centers. Single-agent dactinomycin seems more effective for low-risk GTN. EMA-CO remains the preferred primary treatment regimen for high-risk group. The excellent outcome reflects the success of salvage therapy.

Keywords Gestational trophoblastic disease · Chemotherapy, treatment · Survival · Clinical outcomes · Salvage therapy

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Introduction

The proliferative process arising from an aberrant fertilization event that has potential to develop into invasive malignant neoplasm is known as gestational trophoblastic disease (GTD). This includes hydatidiform mole (complete and partial) and gestational trophoblastic neoplasia (GTN), which encompasses persistent/invasive mole, choriocarcinoma, placental site trophoblastic tumors, and epithelioid trophoblastic tumor [1].

Most commonly, GTN is diagnosed following molar pregnancy, but it can also occur after any gestation including miscarriages and term pregnancies. Any form of GTN can metastasize and the most common metastatic site is lung (80 %) followed by vagina (30 %), brain and liver (10 %). GTN is highly sensitive to chemotherapy and most curable cancer with success rate exceeding 90 % [2]. It represents one of the only cancers for which single-agent chemotherapy is still in wider use.

Therapeutic decision is based on the International Federation of Gynecology and Obstetrics (FIGO) anatomic staging and prognostic scoring index. The low-risk group (prognostic score ≤ 6) can be treated with single-agent chemotherapy resulting in the survival rate approaching 100 %. The high-risk group (prognostic score ≥ 7) requires initial multi-agent chemotherapy with or without adjuvant radiation therapy and surgery to achieve a survival rate of 80–90 % [3, 4].

The King Faisal Specialist Hospital & Research Center (KFSHRC) has been a natural referral center and many patients were directed to our institution from all around the Kingdom of Saudi Arabia. The aim of this study was to review our clinical experience in the treatment of malignant GTN over the past 30 years at KFSHRC, to evaluate complete response rate to chemotherapy, and to analyze the risk factors affecting patients' response and overall survival.

Materials and methods

From 1979 to 2010, a total of 221 patients with GTN (invasive mole and choriocarcinoma, excluding placental site and epithelioid trophoblastic tumor) were treated at the primary institution. The diagnosis of GTN was made by both clinical and histopathologic criteria. Post-molar GTN was diagnosed using the following criteria: 1) plateau of human chorionic gonadotropin (hCG) levels for four consecutive tests over at least 3 weeks, 2) a rise in hCG levels by ≥ 10 % for three or more values over at least 2 weeks, 3) persistent of hCG 6 months after the molar evacuation, 4) histologic identification of choriocarcinoma, or 5) presence of metastatic disease. Invasive mole was diagnosed by pathologic confirmation or, if tissue was not available, after the molar pregnancy when there was rising or plateau in the hCG level or detection of metastatic disease in the absence of histologic diagnosis of choriocarcinoma. Patients were diagnosed with choriocarcinoma based on histologic findings of hyperplastic and dysplastic trophoblast in the absence of villi or if GTN developed following a non-molar pregnancy, thus excluding the possibility of an invasive mole.

The inclusion criteria were patients diagnosed to have GTN post-molar, abortion or full-term pregnancy using the FIGO anatomic staging and prognostic scoring index. Exclusion criteria were cases with the diagnosis of placental site trophoblastic tumor or epithelioid trophoblastic tumor.

After the diagnosis of GTN was made, staging work-up was performed. Along with complete history and physical examination, patients underwent laboratory tests: complete blood counts, quantitative serum hCG level, renal and liver function tests. Chest X-ray with computed tomography (CT) scan of the chest, abdomen, and pelvis were regularly performed, as well as either CT scan or magnetic resonance imaging (MRI) of the brain if other scans showed metastatic disease.

Based upon the staging work-up, patients with GTN were categorized according to the FIGO anatomic staging and the World Health Organization (WHO) scoring system called the prognostic scoring index. The WHO risk factor scoring system was determined by age, antecedent pregnancy, interval from antecedent pregnancy, pre-treatment hCG level, largest tumor size, site of metastasis, number of metastasis, and previous failed chemotherapy. Patients with score <7 were considered low-risk, whereas patients with score 7 or more were considered high-risk group.

At our primary institution, the first-line chemotherapy for patients with low-risk, including metastatic and non-metastatic disease, was usually started with single-agent chemotherapy consisting of methotrexate 1 mg/kg intramuscular (IM) weekly ($n = 59$) or an 8-day regimen of methotrexate (1 mg/kg IM every other day for four doses; $n = 13$). An alternative regimen of dactinomycin 1.25 mg/m^2 intra-venous (IV) every other week was given as initial therapy to 19 patients; and three patients received dactinomycin 0.5 mg IV daily for 5 days. Dactinomycin was given to 11 patients who developed methotrexate resistance or toxicity. Patients who failed single-agent chemotherapy received combination chemotherapy, including bleomycin, etoposide, and cisplatin (BEP) in 12 patients; etoposide, methotrexate, dactinomycin, cyclophosphamide, and vincristine (EMA-CO) in eight patients; and methotrexate, dactinomycin, and either chlorambucil or cyclophosphamide (MAC) in three patients. Other combination regimens used were etoposide, cisplatin, dactinomycin in two

patients, and vinblastine, ifosfamide, and cisplatin (VeIP) in two patients.

Patients with high-risk GTN were initially managed with combination chemotherapy, including EMA-CO in 16 patients, BEP in 19 patients (between 1994 and 2003), and etoposide, cisplatin, and dactinomycin in 20 patients (between 1987 and 1993). Seven patients were treated with MAC (from 1982 to 1983). Patients who developed resistant or relapsed disease were treated with salvage combination chemotherapy included EMA-EP (EMA-CO, but cyclophosphamide and vincristine were replaced by etoposide and cisplatin) in two patients, VeIP in eight patients, and etoposide, ifosfamide, and cisplatin (VIP) in four patients. Other salvage therapy used was taxane/platinum in two patients.

During the therapies, history and physical examination, complete blood counts, chemistry profiles, and hCG were done at first day of each course of the treatment. Patients were considered to be responding by the decrease in hCG levels. Complete remission was defined when three consecutive weekly hCG levels were within the normal range (<5 mIU/mL). Additional two courses of chemotherapy were usually given after the first normal hCG level. After the complete remission was achieved, serum hCG level was measured monthly for one year with the use of oral or barrier contraception to prevent pregnancy. Relapse was defined when the hCG level rose after an initial complete remission. Surgery was considered to either excise sites of bulky and/or resistant tumor or less frequently to treat complications such as tumor hemorrhage or infection.

The clinical data about the patient and disease characteristics, including age, antecedent pregnancy, interval from pregnancy, clinico-pathologic diagnosis, pre-treatment hCG, extent of tumor and treatment were descripted. Descriptive statistics included medians and ranges for continuous variables and frequencies for categorical variables. Overall survival probabilities were calculated using Kaplan–Meier method. Survival curves were compared using log-rank test. A univariate analysis was utilized using logistic regression to study the impact of each risk factor on the response to initial therapy. Significant level was set to 0.05. Statistical analysis was done using SPSS version 20 (IBM, Chicago, IL).

Results

A total of 221 patients with GTN were treated at our primary institution from the year 1979 through 2010. The patient and disease characteristics are presented in Table 1. The median age of patients at the time of diagnosis was 37 years (range 14–55). The overall survival rate for the patients was 97 % (Fig. 1). Most patients developed GTN

Table 1 Patients and disease characteristics

Demographics	Number = 221
Median age (range)	37 years (14–55)
<40 years	135 (61 %)
≥40 years	86 (39 %)
Antecedent pregnancy	
Hydatidiform mole	157 (71 %)
Abortion	27 (12 %)
Term pregnancy	30 (14 %)
Other	7 (3 %)
Interval	
<4 months	130 (59 %)
4–6 months	39 (18 %)
7–12 months	14 (6 %)
12 months	31 (14 %)
Unknown	7 (3 %)
Pre-treatment hCG level	
<1,000	29 (13 %)
1,000–<10,000	43 (20 %)
10,000–<100,000	72 (33 %)
≥100,000	69 (31 %)
Unknown	8 (4 %)
Clinico-pathologic type	
Persistent/invasive GTN	103 (46.6 %)
Choriocarcinoma	117 (53 %)
Unknown	1 (0.4 %)
Previous chemotherapy outside	
No	175 (79 %)
Yes	46 (21 %)
FIGO stage	
I	91 (41 %)
II	17 (8 %)
III	86 (39 %)
IV	27 (12 %)
Prognostic score	
Low-risk	131 (59 %)
High-risk	88 (40 %)
Unknown	2 (1 %)
Radiation therapy	
Yes	17 (8 %)
No	203 (92 %)
Unknown	1 (0.4 %)
Surgery	
No	16 (7 %)
Yes	203 (92 %)
Uterine evacuation	158 (71 %)
Hysterectomy	69 (31 %)
Metastatectomy	8 (4 %)

hCG human chorionic gonadotropin, *GTN* gestational trophoblastic neoplasia, *FIGO* International Federation of Gynecology and Obstetrics

following the molar pregnancy (71 %), had disease duration from antecedent pregnancy of less than 4 months (59 %), and had the pre-treatment hCG level of ≤100,000 IU/L (65 %). The lung ($n = 112$, 51 % cases) was the most common site of metastasis, followed by brain ($n = 15$, 7 %), vagina ($n = 14$, 6 %), and liver ($n = 11$, 5 %). The diagnosis was based on histopathologic evidence in 86 (39 %) cases and elevated hCG levels with history consistent with GTN in 135 (61 %) patients. The median follow-up period was 39 months.

Treatment outcomes of low-risk group of GTN patients are shown in Table 2 [131 (59 %) patients falling into the low-risk (0-6 FIGO prognostic score)]. The overall complete remission rate to the initial chemotherapy regimen (CRI) was 69.5 % (91/131). We observed a complete remission in 53 % of patients treated with single-agent methotrexate (39/73), while the remission rate was 87 % in patients treated with single-agent dactinomycin (20/23). Thirty-five patients received combination chemotherapy regimen as first-line therapy because nine cases had failed the single-agent chemotherapy outside the KFSHRC, four had hCG level of more than 100,000 IU/L and the remaining cases with no clear reason(s). The group subjected to combination regimen had remission rate of 91 % (32/35).

Thirty-three (25 %) patients required second-line salvage therapy. The complete remission rate to sequential single-agent dactinomycin for the low-risk group was 82 % (9/11). Two patients with resistant to first-line dactinomycin were treated with single-agent methotrexate and one patient achieved complete remission. Twenty patients received a multi-agent chemotherapy as second-line therapy. Finally, eight patients required third-line treatment, four patients required fourth-line treatment, and only one patient required fifth-line treatment. The overall complete remission to sequential chemotherapy, initial and salvage chemotherapy, for low-risk disease was 90 % (118/131) as summarized in Table 2.

Thirty-six (27.5 %) low-risk patients underwent hysterectomy. Hysterectomy was performed either as prior to initial chemotherapy in 13 patients, due to persistent disease in 15 patients, because of acute bleeding in 5 patients, or unknown reason in 3 patients. Seven of 15 patients (47 %) who had hysterectomy for persistent disease achieved complete remission without further salvage chemotherapy. Two patients underwent thoracotomy for resistant focus. One patient received radiation therapy to pelvis. The overall survival rate of the low-risk patients was 100 %.

Treatment outcomes of high-risk group of GTN patients are shown in Table 3 [88 (40 %) patients of the study population falling into the high-risk group]. The overall complete remission rate to the initial multi-agent chemotherapy was 57 % (50/88). We observed a complete remission in 94 % of patients treated with EMA-CO regimen (15/16), while the remission rate was 70 % in patients treated with etoposide, cisplatin, and dactinomycin (14/20). Of the 19 high-risk patients who received BEP regimen, 10 (53 %) patients achieved the complete remission. The MAC regimen was administered to seven patients with remission rate of 28.5 % (2/7).

Thirty (34 %) patient required second-line therapy. Only 47 % (14/30) of patients achieved complete remission to secondary chemotherapy resulting in an overall complete

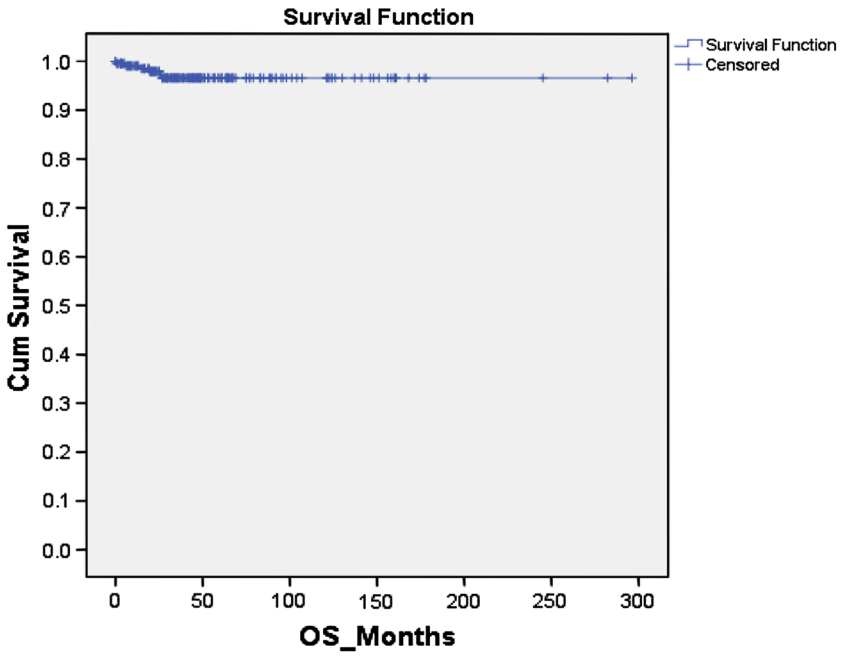

Fig. 1 Overall survival in patients with gestational trophoblastic neoplasia (GTN) as determined by Kaplan–Meier analysis

Table 2 The overall treatment results for the low-risk group of patients with GTN

Disease category/chemotherapy	Number of patients	Complete remission (%)
Low-risk	131	CRI: 91 (69.5 %)
Single-agent methotrexate	73	39 (53 %)
Single-agent dactinomycin	23	20 (87 %)
Combination chemotherapy (EMA-CO or BEP or MAC)	35	32 (91 %)
Low-risk: salvage chemotherapy		
Single-agent dactinomycin	11	9 (82 %)
Single-agent methotrexate	2	1 (50 %)
EMA-CO	8	6 (75 %)
MAC	3	1 (33 %)
BEP or EP	12	7 (58 %)
VeIP	2	2 (100 %)
VIP	2	1 (50 %)
		Overall CR: 118 (90 %)

GTN gestational trophoblastic neoplasia, *CRI* complete remission to initial chemotherapy, *EMA-CO* etoposide, methotrexate, dactinomycin, cyclophosphamide, and vincristine, *MAC* methotrexate, dactinomycin, and either chlorambucil or cyclophosphamide, *BEP* bleomycin, etoposide, and cisplatin, *EP* etoposide and cisplatin, *VeIP* vinblastine, ifosfamide, and cisplatin, *VIP* etoposide, ifosfamide, and cisplatin, *CR* complete remission

Table 3 The overall treatment for high-risk group for patients with GTN

Disease Category/Chemotherapy	Number of Patients	Complete Remission (%)
High-risk	88	CR1: 50 (57 %)
EMA-CO	16	15 (94 %)
BEP	19	10 (53 %)
Etoposide/cisplatin/actinomycin	20	14 (70 %)
MAC	7	2 (28.5 %)
High-risk: salvage chemotherapy		
EMA-CO	6	3 (50 %)
EMA-EP	2	2 (100 %)
BEP or EP	7	5 (71 %)
MAC	8	1 (12.5 %)
VeIP	8	1 (12.5 %)
VIP	4	2 (50 %)
		Overall CR: 64 (73 %)

GTN gestational trophoblastic neoplasia, *CRI* complete remission to initial chemotherapy, *EMA-CO* etoposide, methotrexate, dactinomycin, cyclophosphamide and vincristine, *MAC* methotrexate, dactinomycin, and either chlorambucil or cyclophosphamide, *BEP* bleomycin, etoposide, and cisplatin, *EP* etoposide and cisplatin, *VeIP* vinblastine, ifosfamide, and cisplatin, *VIP* etoposide, ifosfamide, and cisplatin, *CR* complete remission

remission rate to sequential chemotherapy, initial and salvage chemotherapy, in high-risk patients of 73 % (64/88) as summarized in Table 3.

Thirty-two (36 %) high-risk patients underwent hysterectomy, 14 of whom had hysterectomy prior to or with the initiation of chemotherapy. The others had this procedure either to persistent disease in 11 patients or due to acute bleeding in six patients. Two high-risk patients had lung resection of resistant focus and got complete remission without any further chemotherapy. Two patients underwent craniotomy and one patient had bowel resection for the persistent disease. Radiation therapy was given to 16 (18 %) patients, 13 of whom received whole brain radiation therapy for brain metastasis. Three patients were required pelvic radiation and one patient was given radiation to the lung. Most of the patients who received radiation therapy were earlier cases before the year 2002. The overall survival for the high-risk patients was 92 %.

As shown in Table 4, the factors that were significantly associated with resistant to the initial chemotherapy include advanced-stage disease (III and IV; odd ratio "OR" 0.4) as compared to the early-stage disease (I and II; OR 1.0) ($p = 0.005$). Patients with metastatic site other than lung or vagina had increased risk of resistance to initial chemotherapy when compared to metastatic disease localized to vagina and/or lung (OR 1.0 vs. 0.5; $p = 0.005$). Patients with high-risk prognostic score compared to the low-risk group showed an increased risk of resistant to the initial chemotherapy (OR 1.0 vs. 1.7; $p = 0.05$). Age, pre-treatment hCG level, antecedent pregnancy, and duration of disease from pregnancy did not significantly affect the resistance to initial chemotherapy in this study cohort.

The overall survival (OS) was also significantly influenced by the type of antecedent pregnancy (molar OS 98 % vs. other OS 93 %; $p = 0.04$). Patients with advanced-stage disease had poor survival when compared to the early-stage group (III and IV OS 94 % vs. I and II OS 100 %; $p = 0.02$). Patients with high-risk prognostic score compared to low-risk group showed poor outcome (OS 92 vs. 100 %; $p = 0.01$). Patients with metastatic site other than lung or vagina were associated with poor survival when compared to metastatic disease localized to vagina and/or lung (OS 85 vs. 98 %; $p = 0.002$).

There were six relapses that occurred after complete remission to the initial chemotherapy from the entire 221 patients giving an overall 3 % risk of relapse. The median time to relapse was 4 months. Three of the relapsed patients had low-risk prognostic score and were successfully cured with salvage chemotherapy. In contrast, only one of the three high-risk patients who relapsed was successfully cured with salvage therapy.

Table 4 Univariable logistic regression analysis of prognostic factors for complete response to initial chemotherapy and overall survival

Prognostic factors	Number (%)	OR for response to initial chemotherapy (95 % CI)	*p* value	Overall survival (%)	*p* value
Type of pregnancy					0.04
Molar	157 (71 %)	0.9 (0.5-1.8)	0.9	98	
Non-molar	64 (29 %)	1.0		93	
Metastatic sites					0.002
Lung or vagina	91 (41 %)	1.0	0.02	98	
Other sites	35 (16 %)	0.38 (0.87-1.74)		85	
Prognostic score					0.01
Low	131 (59 %)	1.7 (0.9-3.0)	0.05	100	
High	88 (40 %)	1.0		92	
FIGO stage					0.02
I–II	108 (49 %)	1.0	0.005	100	
III–IV	113 (51 %)	0.4 (0.2-0.7)		94	
Age (years)					0.7
<40	135 (61 %)	1.0	0.8	96	
≥40	86 (39 %)	0.9 (0.5-1.5)		97	
Pre-treatment hCG					0.6
<1,000	29 (13 %)	1.0	0.08	100	
1,000–<10,000	43 (20 %)	1.1 (0.3-3.2)	0.8	97	
10,000–<100,000	72 (33 %)	0.4 (0.1-1.08)	0.07	98	
≥100,000	69 (31 %)	0.67 (0.2-1.7)	0.4	95	
Interval					0.3
<4 months	130 (59 %)	1.0	0.2	98	
4–6 months	39 (18 %)	2 (0.8-4.6)	0.09	97	
7–12 months	14 (6 %)	0.6 (0.2-1.8)	0.3	92	
>12 months	31 (14 %)	1.1 (0.48-2.4)	0.8	90	
Chemotherapy outside					0.75
No	175 (79 %)	1	0.5	96.3	
Yes	46 (21 %)	1.1 (0.5-2.1)		97.5	

OR odds ratio, *CI* confidence interval, *FIGO* International Federation of Gynecology and Obstetrics, *hCG* human chorionic gonadotropin

With regard to fertility outcomes, 38 (17 %) patients became pregnant after the completion of chemotherapy. Thirteen of these pregnant women were of the high-risk group. Healthy babies without congenital malformation were delivered in 24 (63 %) pregnant patients. Abnormal pregnancies occurred in seven (18 %) patients that include miscarriage ($n = 5$), stillbirth ($n = 2$), and molar pregnancy ($n = 1$) patient. The remaining pregnant women had unknown outcome, if any.

Discussion

The majority of women diagnosed with GTN can be cured with overall worldwide survival rate of low-risk group approaching 100 %, and 80–90 % for high-risk group [5–9]. However, these tumors are rare in any individual hospital and most treatment recommendations are based on the observational studies from larger series. Our KFSHRC has become a referral center and many patients were directed to our center from all across the Kingdom of Saudi Arabia. In this large series of 221 patients spanning over 30 years of period, we confirm the previously reported highly curable rates of GTN when therapeutic decisions are based on FIGO anatomic stage and prognostic scoring index. The overall survival rate for patients with GTN treated at our center approached 97 %. The median age of women needing treatment in our study was 37 years which seem quite older than what is published in the peer-reviewed English literature (usually under the age of 35 years) [15]. This is presumably due to the greater number of cases getting pregnant in older age.

Patients with low-risk GTN can usually be treated successfully with single-agent chemotherapy. In our series of 131 low-risk patients, we observed a complete remission rate of 53 % to single-agent methotrexate and 87 % to single-agent dactinomycin. In keeping with our results, other peer-

reviewed studies have also reported the superiority of single-agent dactinomycin over methotrexate as a frontline therapy in low-risk patients. Randomized clinical trial comparing biweekly dactinomycin to weekly IM methotrexate has demonstrated a superior response rate for dactinomycin over methotrexate (69 vs. 53 %; $p = 0.015$) [10]. Retrospective review of 247 patients with low-risk GTN treated with single-agent therapy showed significantly higher primary remission rate with dactinomycin than with methotrexate regimen [11].

For patients who developed evidence of methotrexate resistant, we observed a successful salvage with single-agent dactinomycin (in 82 % of cases). Due to lower toxicity, decreased cost, and advantage of convenience of single weekly IM methotrexate and also successful salvage therapy with dactinomycin, we preferred to start treatment with methotrexate and keeping dactinomycin as secondary therapy in the presence of methotrexate resistance or as primary therapy when there is contraindication to methotrexate (effusion, renal or hepatic impairment). In our series, the overall complete remission rate to sequential chemotherapy and overall survival rate of low-risk GTN patients was 90 and 100 %, respectively.

The proportion of women with high-risk disease in our study was high due to the tertiary nature of the referrals. Among the patients with high-risk GTN, our data support the effectiveness of the combination chemotherapy. A large majority of patients (94 %) achieved complete remission with the first-line use of the EMA-CO regimen. Despite the absence of randomized trials to prove its superiority, EMA-CO has emerged as the current optimal primary treatment for the patients with the high-risk GTN [12–14]. The overall survival rate was 92 %, reflecting successful salvage of some non-responders with cisplatin-based chemotherapy.

Following the successful therapy of GTN, the overall relapse rate in our study is low (3 %), which is similar to other studies reported in the peer-reviewed literature [15, 16]. The median time from remission to relapse was 4 months. Most of the relapsed patients were successfully cured with additional salvage chemotherapy. Patients can anticipate subsequent pregnancy outcomes similar to the general population [17, 18].

Treatment of patients with GTN in specialized centers optimizes the opportunity for cure and minimizes for morbidity. Factors that are known to increase resistance to initial chemotherapy include high-risk prognostic score, advanced-stage (III and IV), metastatic disease other than lung or vagina, prior unsuccessful chemotherapy, had higher pre-treatment hCG level, antecedent term gestation, and clinico-pathologic diagnosis of choriocarcinoma [19, 20]. Our study confirms the lower outcomes in patients with advanced-stage disease, metastatic site other than the lung and vagina, high-risk prognostic score, and antecedent non-molar pregnancy.

In summary, our data confirm the previously reported high rate of remission and survival in both low-risk and high-risk GTN patients when using the FIGO staging criteria and the WHO prognostic scoring system. Referral of such patients to relatively more experienced centers is highly recommended for appropriate risk stratification and subsequent therapeutic management of patients with GTN.

Conflict of interest None.

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