ORIGINAL ARTICLE

PREGNANCY OUTCOMES AFTER CHEMOTHERAPY FOR GESTATIONAL TROPHOBLAST NEOPLASIA

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ABSTRACT

Objective: To find out the outcomes of pregnancy and safety of chemotherapeutic regimen in women who conceived after chemotherapy for the treatment of Gestational Trophoblastic Neoplasia.

Materials and Methods: A Prospective cohort study was done at the Department of Obstetrics and Gynecology, Hayatabad Medical Complex, Peshawar. Ninety women were followed up for pregnancy outcomes after being diagnosed with Gestational Trophoblastic Neoplasia and treated with standard chemotherapeutic regimens between June 2005-2014. After treatment, patients were followed up for a period of five years. The patients` demographic profile, FIGO score, type of chemotherapy, treatment, and pregnancy outcomes were recorded on predesigned Performa and a computerized record was kept. Data analysis was done through SPSS-16.

Results: The mean age of patients was 28.2 years (±12.5) and the mean parity was 3.39 (±1.49). Out of 90 patients diagnosed with Gestational Trophoblastic Neoplasia, 59 (65.6%) patients were of low risk and 31 (34.4 %) were in the high-risk category. Overall survival was 100% after chemotherapy in the low-risk category and 70.58% in the high-risk category. The pregnancy rate among women with the desire to conceive was 97%. The term live birth in 42 pregnancies was 85.7%, without any congenital abnormality. Five (10.2%) women had miscarriages, 1 woman (2%) had a repeat molar pregnancy, and 4 women experienced live twin birth after chemotherapy.

Conclusions: Women who underwent treatment for Gestational Trophoblastic Neoplasia can be assured positively about their pregnancy outcomes and fertility prospects in the future. Chemotherapy regimens currently used globally are highly effective and preserve fertility.

Key Words: Gestational Trophoblast Neoplasia, FIGO Prognostic score, Pregnancy outcomes

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INTRODUCTION

Gestational trophoblastic disease (GTD) is a spectrum of disorders associated with highly abnormal trophoblastic tissue. At one end of the spectrum we have premalignant forms consisting of complete and partial hydatidiform mole, while at the other end, there are malignant forms collectively termed Gestational Trophoblastic Neoplasia consisting of invasive mole, choriocarcinoma, placental site trophoblastic tumors, and epithelioid trophoblastic tumor. Human chorionic gonadotrophin produced by trophoblast cells is a useful biomarker for monitoring response to treatment and surveillance for detecting resistance or relapse.[1]

The plateaued or increasing human chorionic gonadotrophin that occurs in 0.5–1% of Partial Moles and 15–29% of complete moles, denotes progression of previously benign molar pregnancy into gestational trophoblastic neoplasia .[2] Gestational Trophoblastic Neoplasia can occur after a molar pregnancy, term pregnancies and ectopic pregnancy. Since most women who develop gestational trophoblast neoplasia are of childbearing age, preservation of fertility becomes an important consideration.[3] Worldwide, GTNs are considered to most curable amongst all gynecologic tumours, having survival rates approaching 100%, with preservation of fertility[4, 5].

Single-agent or multiagent chemotherapy can be used empirically in the treatment of post molar gestational trophoblastic neoplasia and choriocarcinoma based on International Federation of Gynecology and Obstetrics (FIGO) prognostic scoring system.[6] This system incorporates risk factors like age, antecedent pregnancy, chorionic gonadotropin levels, number, site, and size of

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metastasis. Women scoring 0-6 receive single agent chemotherapy and those scoring ≥ 7 require multi-agent chemotherapy from the outset.[7,] It is a unique gynecologic tumor with overall cure rate approaching 100% in low-risk gestational trophoblast neoplasia and almost 90% in a high risk category.[8-11]

Our study aimed to evaluate the reproductive outcomes of women in the first pregnancy, who conceived during the first year of follow-up or afterward, and to establish the safety of the chemotherapeutic regimen used for the treatment of Gestational Trophoblastic Neoplasia in women of reproductive age.

MATERIALS AND METHODS

Ninety patients with the diagnosis of GTN were treated in the Department of Obstetrics and Gynecology, Hayatabad Medical Complex, Peshawar between June 2005-2014. Patients were diagnosed with gestational trophoblast neoplasia based on clinical, biochemical, and histopathologic criteria. International Federation of Gynecology and Obstetrics (FIGO) prognostic scoring system was used to categorize patients into low-risk and high-risk groups. Low-risk patients with a score of ≤6 were given single-agent chemotherapy comprising methotrexate and folinic acid, whereas high-risk groups with a score of ≥7 were managed with combination chemotherapy, including EMA-CO (Etoposide, Methotrexate, Actinomycin, Cyclophosphamide, and Vincristine). Falling chorionic gonadotrophin levels indicated response to treatment with patient labeled as having achieved complete remission, with weekly normal hCG levels in the first month after the last chemotherapy course. In the follow-up period, serum hCG level was measured 3-monthly in the first year with the use of oral or barrier contraception to prevent pregnancy. Patients were followed up 6-monthly in the second year after chemotherapy and then advised to follow up with serum hCG levels done every year for the rest of their life.

The clinical data about the patients` age, parity, clinicopathological diagnosis, response to treatment, conception if any during follow-up, and pregnancy outcomes were recorded on predesigned Performa and a computerized record was kept.

RESULTS

The mean age of the sample was 28 years (±12.5) and the mean parity was 3.39 (±1.49). Amongst 90 patients diagnosed and treated for GTN, 59 (65.6%) patients were low risk and 31 (34.4 %) were in the high-risk category. Overall survival was 100% after chemotherapy in the low-risk category and 70.58% in the high-risk category. The pregnancy rate among women with the desire to conceive comprised 49 women and 48 pregnancies was 97%. The term live birth in 42 pregnancies was 85.7% without any congenital abnormality. Five (10.2%) women had miscarriages, 1 woman (2%) had a repeat molar pregnancy and 4 women experienced live twin birth after chemotherapy.

Pregnancy outcome measure or variable was not applicable in 41 patients that included 9 patients that died during treatment/chemotherapy, 15 patients that developed resistance to chemotherapy, and 10 patients who had hysterectomy during treatment, while 7 patients were lost to follow-up.

Table 1: Demographic Characteristics of participants

Characteristics	Value
Mean Age (Years)	28.2 years (±12.5).
Mean Parity	3.39 (±1.49).
Mean BMI (Kg/m2)	22±3.39
Nationality	70% Pakistani
	20% Afghani

Table 2: Clinical Characteristics of participants

Clinical Characteristics	Frequency	Percentages
FIGO low risk category	59	65.6%
FIGO high risk category	31	34.4%
Survival in low risk category	59	100%
Survival in high risk category	22	70.9%
No of women pregnant in follow up period	48	97%
Pregnancy outcomes in 48 patients		
Singleton and twin live births	42	85.7%
Miscarriage	5	10.2%
Repeat Molar Pregnancy	1	2%

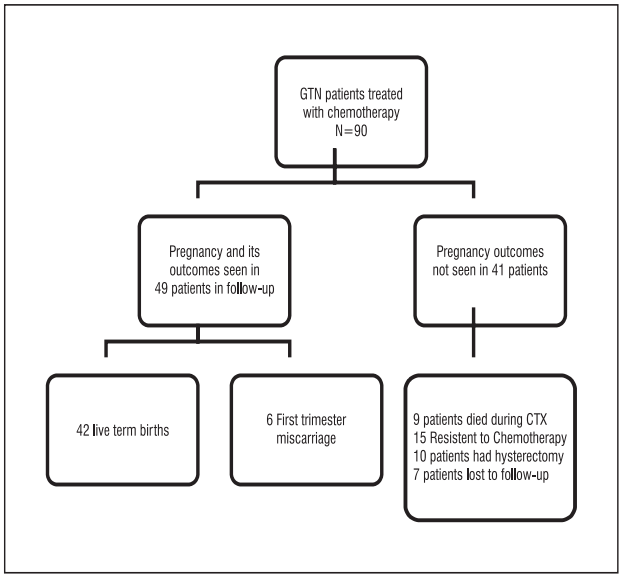

Fig 1: Follow-up and Pregnancy outcome in women treated for Gestational Trophoblast Neoplasia

DISCUSSION

Chemotherapeutic regimens used for GTN are safe and preserve fertility. [8] Worldwide survival rate of almost 100% in the FIGO low-risk category, and around 80–90 % for the high-risk category, have been reported. Our unit employed time-tested chemotherapeutic regimens that gave favorable cure rates approaching 86.7%, which are similar to local and regional figures quoted in national and international literature. However, cure rates of 100% are also being reported in western countries which are ahead of our cure rates. Lack of centralized care, late diagnosis, advanced presentation, funding, and financial constraints are the factors that impair statistics of GTN centers like ours that ran on philanthropist aid and zakat funds. Nevertheless, cure rates of 86.7% and live birth rates of 85.7% are reassuring, amidst all these constraints.

In our study, the mean age of patients was 28±12.5 years which seems similar to what is published in the western studies. [12] In this age group, women have to confront potentially life-threatening diagnoses, delays in future childbearing, and overall anxiety and negative perceptions on fertility and conceiving again in the future. [9, 10] All women treated in our study were advised to avoid pregnancy for at least 12 months after clinical remission to avoid the expected teratogenicity, and circumvent confusion between a new pregnancy and relapsed disease as the cause of rising chorionic gonadotrophin values, by using combined oral contraceptive pills or barrier methods. Contraceptive failure, lack of compliance, and psychosocial pressure for early conception were factors that led to conception in 9 women within the first year of follow up but reproductive outcomes were good and comparable to what is being reported by William J. [13]

Overall, 48 out of 90 patients with GTN conceived after treatment. 50.8% of the low-risk category and 45% of the high-risk category conceived, in contrast, to a study by Wong JM[14] that reported 85% conception in the low-risk category and 53% in the high-risk category. But live birth rates were more than 70% in both studies. A Brazilian study also showed no difference in subsequent pregnancies in patients who received single-agent methotrexate or combination chemotherapy. [15]

In our study, 48 out of 90 GTN patients that conceived after successful treatment, 42 (85.7%) had live term births that also included 4 live twin births as well without any newborn showing congenital abnormality. Live term birth rates in women in our study are more than what is reported in Berkowitz RS study of 68.6%, and 70% by Gadduci A, possibly due to differences in knowledge, attitude, and practices regarding contraception use, family size, in western and eastern or developing country women. [16 and 17]

An Indian case series showed 9 out of 52 patients with GTN conceived after treatment, in contrast to our results. [18] In contrast to our study, documented lower fertility rate in Indian study is likely due to completion of the family at a younger age in their community and effective adherence to contraceptive advice. The possibility of ineffective follow-up for a long time can't be ruled out in this study. In contrast to our study, the New England Trophoblastic Disease Center showed a 1.3% increase in stillbirth in a subsequent pregnancy after treatment for GTN. [19]

Our study showed that five women (10.2%) had a spontaneous miscarriage and one had a repeat molar pregnancy for which she underwent suction and curettage. A Saudi Arabian study showed abnormal pregnancies in 18 % of patients who conceived after treatment. [20] Another study by Lan Zet al showed that 4 out of 22 that conceived had a miscarriage, one repeat molar pregnancy, and one stillbirth. This Japanese study showed that 11.3% of pregnancies after chemotherapy for GTN end in spontaneous miscarriage. [21]

A few limitations of this study should be considered. The sample size was small and it was a single-centre study involving only the Pathan population. The study was dependent on verbal information about pregnancy outcomes in the follow-up period. Further multicenter studies should validate the safety of chemotherapy in such patients. Such patients should be followed up lifelong and properly registered in a specialized and centralized treatment center at provincial levels.

CONCLUSIONS

Current chemotherapeutic regimens used in the management of Gestational Trophoblastic Neoplasia are highly effective, safe, and preserve fertility. Women should be counseled to expect normal reproductive outcomes comparable with the general population after chemotherapy for gestational trophoblast neoplasia.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Bangash AG: Data collection, literature search, writing up.

Tabassum S: Data analysis

Afridi F: Conceived the idea

Zahoor F: Bibliography

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.