International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2023: 1.843

Clinical Outcomes of Gestational Trophoblastic Neoplasia Patients Treated in a Tertiary Care Centre

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Abstract: ***Gestational Trophoblastic Neoplasia (GTN) is a rare but highly curable condition arising from abnormal placental tissue. This retrospective study, conducted at Calicut Medical College, Kerala, from 2016 to 2019, evaluated the clinical and demographic profile, treatment outcomes, and fertility impacts in 25 patients diagnosed with GTN. Most patients were aged 20 - 35 years, with multiparous women showing a higher risk. Complete hydatidiform mole was the most common histopathological finding (60%), and 84% of patients were diagnosed at an early stage. Low - risk GTN cases responded well to single - agent chemotherapy, primarily Methotrexate, with a 100% treatment success rate. High - risk cases required more intensive regimens and occasional surgical interventions. Fertility outcomes were promising, with 72% of patients able to conceive post - treatment, though many experienced anxiety and depression during care. This study highlights the need for early diagnosis, effective treatment, and comprehensive psychosocial support to optimize outcomes for GTN patients. Further research is needed to explore long - term effects and improve awareness of this condition***

Keywords: Gestational trophoblastic neoplasia, Hydatiformmole, Invasive mole

1. Introduction

Gestational trophoblastic neoplasia (GTN) is a rare but potentially life - threatening condition that arises from abnormal placental tissue.1This disease spectrum includes various entities, such as complete and partial hydatidiform mole, invasive mole, choriocarcinoma, epithelioid trophoblastic tumour and placental site trophoblastic tumor[1]. Understanding the clinical features and management of gestational trophoblastic neoplasia is crucial, as it is the gynecologic malignancy with the highest cure rate when properly diagnosed and treated. The management of gestational trophoblastic neoplasia often involves a multidisciplinary approach, including gynaecologic oncologists, medical oncologists, and reproductive specialists.1 Patients may require chemotherapy, surgical interventions, and close monitoring of human chorionic gonadotropin levels to ensure complete remission. Recurrence of gestational trophoblastic disease is a significant concern, with a 1 - 2%risk of developing a second hydatidiform mole after the first molar pregnancy and a 20% risk after two molar pregnancies.2The aim of the study to describe the clinical and demographic profile of patients diagnosed with GTN. To describe the outcome of pregnancies following GTN treatment.

This study was undertaken to evaluate the long - term outcomes of patients diagnosed with gestational trophoblastic neoplasia at a tertiary care center in India, Kerala. Many factors can influence the prognosis and management of gestational trophoblastic neoplasia. Previous studies have reported that older maternal age, higher pretreatment human chorionic gonadotropin levels, and advanced disease stage are associated with poorer outcomes[3]

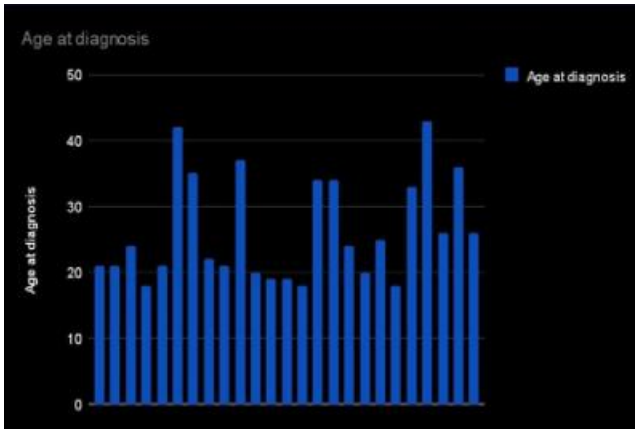
2. Materials and Methods

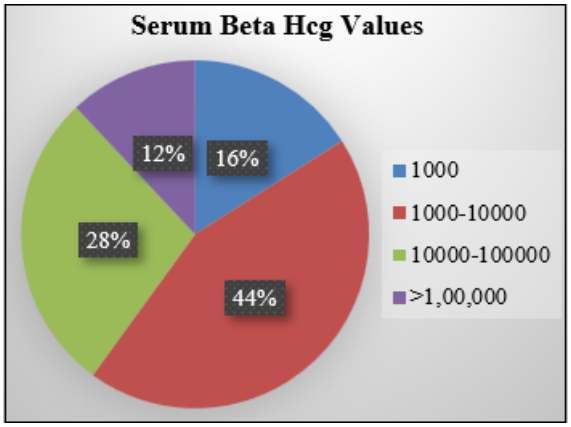
This was a Retrospective cohort study conducted at, Institute of Maternal and Child, Calicut inpatients who were histologically diagnosed as Gestational Trophoblastic neoplasia during the year 2016 - 2019. All patients were called up and interviewed using a set of Variables. Details regarding antecedent pregnancy, bhcglevels, histopathology, types of chemotherapy, number of cycles, complications of chemotherapy, resistance, psychological impact of chemotherapy, type of Gestational trophoblastic neoplasia, pregnancy after Gestational trophoblastic neoplasia, use of contraception, atypical presentations and complications. Data was collected from GTN registry and by phone calls and analysed with simple percentage method. IEC approval taken on 24/5/2024

3. Results

Total number of deliveries were 62964 at medical college, Kozhikode over 2016 - 2019, of which we had 25 patients diagnosed with GTN.

Maternal age is significant risk factor for GTN, with higher risks is observed in very young and older mothers. In our study while most of the patients were between 20 - 35 years (60%) during diagnosis. Oldest women with GTN was 43 years old.





Multiparous women were observed to have high risk factor for developing GTN, 56% were multigravida while 9% were primigravidas and 8% were grand multi gravida.

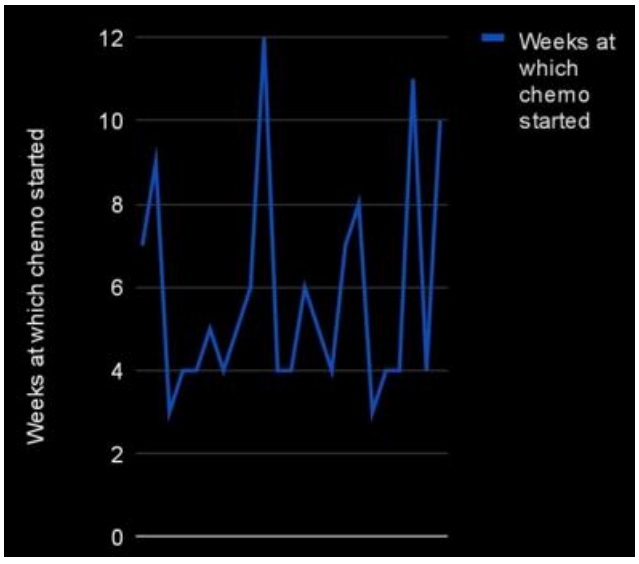
On Histopathologic examination 60% had complete hydati form mole, 12% choriocarcinoma, 8% invasive mole, 16% partial mole, 4% PSTT.24% patients had plateauing bhcg while 72% were having with rising bhcg.

Pretreatment Beta Hcg values were recorded and44% had Beta Hcg between 1000 and 10000.24% had plateauing Beta Hcg while 72% had rising Beta Hcg.

84% were stage 1 at diagnosis.88% were low risk GTN, and was treated with Methotrexate with leucovorinand 100% response to chemotherapy, subsequent normalisation of Beta Hcg. Mean chemotherapy cyles were 6.

12% belonged to high-risk group and mean chemotherapy cycles were 8. RAll patients were given consolidation plus chemotherapy. Invasive mole, Choricarcinoma, and PSTT in one patient. Hysterectomy was done in 3 patients, one was PSTT, and 2 were Invasive mole. All belonging to high-risk group.

Risk X Chemo drugs					
	Chemo drugs				
	Actinomycin D	EACO	MTX	MTX, Actinomycin D, EMACO	MTX, EMACO
LOW RISK	1	0	21	0	0
	4.5%	0.0%	95.5%	0.0%	0.0%
HIGH RISK	0	1	0	1	1
	0.0%	33.3%	0.0%	33.3%	33.3%



Regarding Chemotherapy, side effects were alopecia in 20% of patients, 16% had vomiting, Altered LFT 12%, Anorexia 12%, Tiredness in 12%, Skin rashes in 8%. Neutropenia and loose stools in 4%, anaemia and lung consolidation in 4%.

76% of patients had either anxiety or depression during treatment and main concern was future fertility.84% of patients regained normal menstruation after normalisation of Beta Hcg.

72% of patients were able to conceive. Out of this 20 delivered live babies and 2 (10%) only resulted in abortion. HTN complicating 12.5% cases of pregnancies following GTN. Severe preeclampsia in 6.25%.

Only 72% of patients had knowledge about the disease. Contraception was advised for all patients and all of them complied.1 patient had premature menopause. Marital conflicts was seen only in patients who had premature menopause, decreased libido and anger.

Regarding the case of PSTT, she was 22 yr old lady presented with 3 years of amenorrhea following last child birth. Bhcg was 40 - 50. She was diagnosed as a case of high risk GTN. MRI was taken. She underwent extrafascial hysterectomy with bilateral salpingectomy and PLND, HPR came as PSTT. She was kept under Bhcg follow up. Later USG showed ovarian metastasis. Bhcgpost surgery was below 30. She received 6 cycles of EMACO and was on follow up 6 monthly. She was being suspected with extensive bone metastasis and she expired 2 years later.

4. Discussion

Gestational trophoblastic neoplasia (GTN) is a rare but highly curable group of conditions that arise from placental cells. Our study provides insights into the clinical presentation, treatment outcomes and fertility outcomes of

gestational trophoblastic neoplasia patients treated at a tertiary care centre in India.1

The majority of patients in our study were between 20 - 35 years old, consistent with previous studies that have shown gestational trophoblastic neoplasia to predominantly affect younger women of reproductive age.

Most patients in our study had an antecedent molar pregnancy, which is the most common precursor condition for gestational trophoblastic neoplasia[2].

The rate of lower pre- treatment hCG levels (<10, 000 IU/L) was high in our cohort, similar to findings from other studies in the region [1]. This could be related to delays in seeking medical attention or differences in biological factors between populations.

The majority of patients in our study were low - risk, as determined by the FIGO staging system, and were able to be treated with single - agent chemotherapy, consistent with the high cure rates associated with gestational trophoblastic neoplasia.

Fertility outcomes were generally favourable, with over 70% of patients able to conceive again after treatment. However, a significant proportion of patients experienced anxiety and depression related to their diagnosis and treatment, highlighting the need for comprehensive psychosocial support.

Our study had some limitations. The sample size was relatively small, and the retrospective nature of the data collection may have introduced biases. Additionally, long - term follow - up data on pregnancy outcomes and recurrence rates were not available for all patients.

Overall, our study demonstrates that with appropriate management, patients with gestational trophoblastic neoplasia can have excellent prognosis and fertility outcomes, though the psychological impact of the disease requires careful consideration.

Gestational Trophoblastic Neoplasia (GTN) is a rare yet significant condition with distinct epidemiological and clinical patterns. The present study conducted at Calicut Medical College provides valuable insights into the demographics, clinical presentations, and outcomes of GTN, and allows for meaningful comparisons with previous studies.

Our study found that the majority (60%) of GTN patients were between 20 - 35 years, with the oldest patient being 43 years old. This is consistent with prior research indicating that GTN is more common in women of reproductive age, but can also occur at the extremes of reproductive age. For instance, a study by Seckl et al. (2010) observed that the incidence of GTN is highest in women under 20 and over 40 years of age.

We observed a higher incidence of GTN among multigravida women (56%), compared to primigravida (9%) and grand multigravida (8%). This aligns with the findings of Altieri et al. (2003), which demonstrated that the risk of GTN increases with higher parity.

In our study, 44% of patients had Beta HCG levels between 1000 and 10000 at admission. This range is critical as higher levels of Beta HCG are often associated with more severe disease and worse prognosis, as documented in previous studies like those by Ngan et al. (2018).

The distribution of histopathologic types in our study showed 20% complete hydatidiform mole, 12% choriocarcinoma, and 4% PSTT, among others. These findings are generally consistent with the literature, where complete moles are the most common precursor lesions for GTN. The proportion of PSTT in our study (4%) is slightly higher than the typical 1 - 2% reported in other studies, potentially indicating a higher detection or referral rate at our institution.

Most patients (72%) presented with rising BhCG levels, and 84% were diagnosed at Stage 1. Early - stage diagnosis is critical for favorable outcomes, as highlighted by studies from the International Society for the Study of Trophoblastic Diseases (ISSTD). Our findings suggest effective early detection and referral processes in place at our center.

Low - risk patients in our study were successfully treated with Methotrexate, showing a 100% response rate, which mirrors the success rates reported in the literature. High - risk patients required more intensive regimens and had a mean chemotherapy cycle length of 8, aligning with treatment protocols recommended by FIGO and other authorities. The need for hysterectomy in 12% of our patients is consistent with the rates reported by Lurain (2010), who found that surgical intervention is occasionally necessary for treatment - resistant cases.

Chemotherapy side effects such as alopecia (20%) and vomiting (16%) were prevalent in our cohort, similar to other studies reporting these as common adverse effects. The high prevalence of anxiety or depression (76%) underscores the need for psychological support, as also emphasized by studies from the European Organisation for Research and Treatment of Cancer (EORTC).

Encouragingly, 72% of our patients were able to conceive post - treatment, with most pregnancies resulting in live births. This is in line with findings from studies by Lim et al. (2015) which report high rates of successful pregnancies following GTN treatment. The use of assisted reproductive technologies (ART) was minimal, highlighting the natural fertility preservation post - treatment.

Awareness about the disease (72%) and the use of condoms (60%) during follow - up indicate a reasonably good level of patient education and compliance, crucial for preventing recurrence and ensuring timely monitoring, as highlighted by Ngan et al. (2018).

The unique case of a 22 - year - old patient with PSTT, who developed ovarian metastasis and subsequently died, illustrates the aggressive nature of PSTT and the challenges in managing this rare subtype. This case aligns with the

findings of studies by Schmid et al. (2009), who noted poor prognosis in metastatic PSTT despite aggressive treatment.

Only 6 patients (24%) had substantial knowledge about GTN, while others had limited understanding, knowing it only as a form of cancer. This gap in patient education highlights the need for better informational resources and counseling, as emphasized by studies like Ngan et al. (2018), which recommend comprehensive patient education as a critical component of GTN management to improve compliance and outcomes.

The mean duration for the return of menses was 4 weeks post - treatment, indicating a relatively quick recovery of menstrual function in most patients. This is consistent with findings by Lim et al. (2015), which reported that menstrual cycles typically resume within a few weeks to months after completing GTN treatment.

All patients who used contraception opted for condoms, with no reported use of oral contraceptive pills. This contrasts with some previous studies that suggest a mix of contraceptive methods post - GTN treatment, including oral contraceptives, which are generally safe and effective in preventing pregnancy during the follow - up period (Seckl et al., 2010).

Of the pregnancies following GTN treatment, 14 were detected early, with BhCG monitoring at 6 and 10 weeks conducted in only 10 patients. Early detection of subsequent pregnancies is crucial for managing and monitoring potential complications, as supported by studies like those by Lurain (2010), which emphasize the importance of close follow - up and early intervention.

ART was required in only one patient to achieve pregnancy, indicating that natural fertility is generally well - preserved post - GTN treatment. This is consistent with previous research indicating that most women retain their fertility after GTN treatment and can conceive naturally (Lim et al., 2015).

Two patients reached menopause, with one patient not resuming menses after chemotherapy. All other patients reported regular menstrual cycles. This outcome aligns with studies that show premature menopause as a rare but possible side effect of GTN treatment, often associated with more aggressive therapies (Schmid et al., 2009).

Marital issues were reported only in the patient who experienced premature menopause, primarily due to decreased libido, anxiety, and anger. The psychological impact and sexual dysfunction following GTN treatment are significant concerns that need addressing, as highlighted by studies like those by Ngan et al. (2018), which advocate for psychological and sexual counseling as part of comprehensive GTN care.

5. Conclusion

Our study provides valuable insights into the clinical characteristics and outcomes of gestational trophoblastic neoplasia patients treated at a tertiary care centre in India. The majority of patients had favourable treatment responses and were able to conceive again post - treatment, though a significant proportion experienced mental health challenges. These findings underscore the importance of comprehensive, multidisciplinary care for women with gestational trophoblastic neoplasia to optimise both medical and psychosocial outcomes.

Further research is needed to better understand the long - term impacts of this disease and its treatment on the overall health and wellbeing of affected individuals.

Source of support: nil

Conflict of interest: none

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