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Research Article

CLINICAL PROFILE OF GESTATIONAL TROPHOBLASTIC DISEASE IN A TERTIARY CARE CENTRE IN SOUTH INDIA

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ABSTRACT

Background: .Gestational Trophoblastic Disease is a group of heterogeneous premalignant and malignant lesions in reproductive age of women which are curable with acceptable morbidity. This study aims to assess the clinical profile and outcomes of GTD patients treated in the GTD clinic conducted by Department of Medical Oncology, Government Rajaji Hospital, Madurai Medical College .

Methods: Records of 172 patients registered from January 2016 to May 2022 were analyzed. Demographic and clinical details of all patients were collected from the records.GTN was diagnosed by serial analysis of serum beta human chorionic gonadotrophin levels.The incidence of GTD and response to treatment were analyzed.

Results: Among 117 patients registered in GTD clinic 46 developed GTN majority being low risk (85%). 37% of low risk cases treated with methotrexate in first line experienced failure.All of them were cured with subsequent line of therapy. 6 out of 7 high risk patients achieved complete response with EMACO regimen while one patient was lost to followup.9 patients reported back with successful pregnancy including those treated with chemotherapy.

Conclusions: Gestational Trophoblastic Neoplasia is extremely chemosensitive and it can be cured with low morbidity .Treatment with chemotherapy in addition to high response rates does not hamper the fertility.

INTRODUCTION

Gestational Trophoblastic Disease (GTD) are a heterogeneous group of lesions arising from the trophoblastic epithelium of the placenta following an abnormal fertilization. Placental trophoblastic cells can proliferate, escape host's immune response, invade and metastasize to different organs.[1]

Gestational Trophoblastic Disease can be either pre-malignant (partial and complete hydatidiform mole) or malignant (Gestational Trophoblastic Neoplasm-comprising invasive mole, choriocarcinoma, placental site trophoblastic tumour and epitheliod trophoblastic tumour.[2]

Huge variations in the incidence have been reported in different regions ranging from 23 per 100,000 deliveries to 1,299 per 100,000 deliveries.[3,4,5]

The pre-malignant trophoblastic lesions usually disappear after evacuation in majority. However there is a risk of progression to invasive malignant lesions with risk of persistence in the uterus and dissemination to various organs. Serum beta human chorionic Gonadotropin (βHCG) is a sensitive marker aiding in diagnoses and evaluation of treatment response of Gestational Trophoblastic Neoplasia.[6,7]

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Gestational Trophoblastic Neoplasia is extremely chemosensitive and it can be cured with low morbidity in most patients.[8]

OBJECTIVE

This retrospective observational study aims to assess the clinical profile and outcomes of GTD patients treated in the GTD clinic conducted by Department of Medical Oncology, Government Rajaji Hospital, Madurai Medical College from January 2016 to May 2022.

METHODS AND MATERIALS

Medical records of 172 patients registered in the GTD Clinic of Government Rajaji Hospital from January 2016 to May 2022 were analyzed. Demographic and clinical details of all patients were collected from the records.GTN was diagnosed by serial analysis of serum beta human chorionic gonadotrophin levels.

Patients were evaluated, monitored and treated as per the GRH Protocol for GTD. Serum beta hcg is repeated in all patients after evacuation procedure every two weeks until normal value. Thereafter beta hcg values are monitored every month for one year during which all patients receive oral

contraceptives. After one year of followup patients are advised to review during their next pregnancy routinely.

Persistent Trophoblastic Disease is diagnosed when there is

1. Plateauing of HCG values during followup (2 to 3 values)
2. Bleeding per vaginum either intermittent or continuous
3. Persistent theca leutin cysts >6 cm for >6 weeks
4. Occurence of metastases during follow up

Patients with persitent trophoblastic disease are further investigated with

1. Ultrasonography of abdomen and pelvis with doppler study of uterine vascularity
2. Chest X-ray PA view
3. Blood tests- CBC,RFT,LFT
4. If lung metastases-Computed Tomograpy of chest abdomen, CT/MRI brain
5. PET CT scan in selected patients.

Risk assessment is done using WHO scoring system .For low risk (<6) Injection Methotrexate is given weekly at a doe of 50mg/m^2.Beta hcg values are checked every alternate weeks and one additional dose is given after value become normal. Patients are then followed up with hcg values every month for one year along with administration of oral contraceptives.

In case of methotrexate failure either single agent Actinomycin-D or combination chemotherapy with EMACO regimen is given.

For high risk patients (>6) combination chemotherapy with EMACO regimen is started.HCG is repeated every cycle and two additional cycles are given after normal HCG levels are attained.Patients are then followed up with hcg values every month for two years along with administration of oral contraceptives.

In case of EMACO failure EMAEP or PEB or PVB regimens are given.

RESULTS

Among the 172 patients registered in GTD clinic during the study period majority of them were below 30 years (89.6%). 73.3% patients were in age group of 20-30.Only 2.3% patients were above 40 years of age.

Age	Number	Percentage
<20	28	16.3%
20-30	126	73.3%
31-40	14	8.1%
>40	4	2.3%

50.6% of women never had children while 32.2% had one child before developing GTD.

Previous Children	Number	Percentage
NIL	87	50.6%
1	56	32.6%
2	20	11.6%
>/= 3	09	5.2%

60% of women had symptoms at presentation with majority having bleeding per vaginum (42% of total patients and 70% of symptomatic patients). Hyperemesis and abdominal pain were other reported symptoms. Some patients had a combination of these symptoms.

Two patients had presented with respiratory distressed (probably due to trophoblastic thromoembolism) one among them was intubated, started on chemotherapy, successfully extubated and cured subsequently.

One patient had presented with neurological deficit with seizures after a term delivery and was found to have choriocarcinom with brain metastases.

Clinical Presentation	Number	Percentage
Asymptomatic By Rouitne Usg	69	40%
Symptomatic Presentation	103	60%

Symptom	Number	Percentage
Bleeding Per Vaginum	72	70% (42%)
Hyperemesis	18	17% (10%)
Abdominal Pain	15	14% (9%)
Respiratory Distress	2	1.9% (1%)
Neurological Symptoms	1	0.9% (0.5%)

Usg Findings	Number	Percentage
Ovarian Cyst	12	7%
Blighted Ovum	3	2%
Uterine Artery AVM	2	1%
Subchorionic Haemorhage	2	1%
Pregnancy +Mole	1	0.5%

64.5% patients had presented before 12 weeks of gestation while 96.5% had been diagnosed before 16 weeks of gestation. 56% of patients had an elevated beta hcg of more than one lakh at presentation.

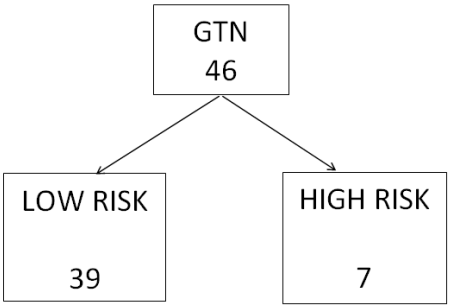
Gestational Age At Presentation	Number	Percentage
</=8 weeks	59	34.3%
8- 12 weeks	52	30.2%
13-16 weeks	55	32%
>16 weeks	6	3.5%

Pre Evacuation Hcg	Number	Percentage
< 1,000	11	6%
1,000-10,000	20	12%
10,000-1,00,000	45	26%
>1,00,000	96	56%

Among the 172 patients, 46 patients (26.7%) developed Gestational Trophoblastic Neoplasia. 85% had a low risk disease and 37% had pre-treatment HCG value above one lakh.

Who risk	Number	Percentage
LOW	39	85%
HIGH	7	15%

Pre Treatment Hcg	Number	Percentage
< 1,000	3	6%
1,000-10,000	12	26%
10,000-1,00,000	14	31%
>1,00,000	17	37%



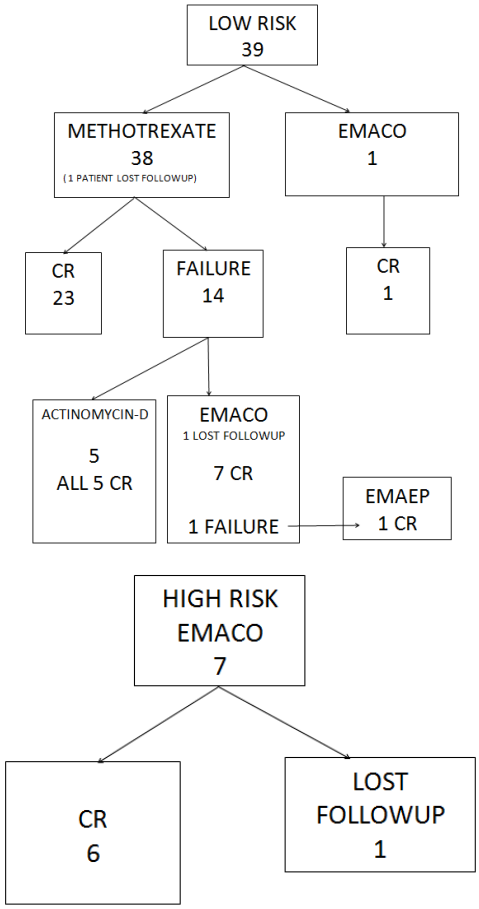
Among the 39 patients 38 received weekly methotrexate regimen. One patient received EMACO regimen and attained complete response. Among the 38 patients who received methotrexate 37% failed to achieve a complete response.

Subsequently 5 patients were treated with Actinomycin-D and achieved a complete response.7 patients were treated with EMACO regimen and 1 among them alone failed to achieve a response who responded to next line EMAEP regimen.

Six out of seven high risk patients who recieved EMACO regimen achieved a complete response while one patient lost followup.

9 out of 172 patients had reported back with a successful pregnancy so far after completing the protocol. One patient was treated with single agent methotrexate and two received EMACO regimen.

One patient who conceived before the completion of protocol developed a subsequent molar pregnancy.



DISCUSSION

Gestational Trophoblastic Tumours are extremely chemo sensitive tumours constituting <1% of gynecological malignancies. In view of chemosensitivity chemotherapy is the main modality of treatment with an overall cure rate is around 90-100%.

Early diagnosis of asymptomatic GTD is possible now with the advent of ultrasonogram-Doppler and sensitive beta HCG assays. In our study 64% of patients had been diagnosed in the first trimester with 40% been diagnosed asymptotically by ultrasonography

Advanced maternal age is considered as a risk factors for GTD. The mean age of GTD studies from observational studies in India were 23 to 24 years of age.[9][10] In our study only 10.4% of patients were above 30 years of age.Half of the study population was composed of primiparous women.

First line treatment of low risk GTN single agent chemotherapy with single agent methotrexate and actinomycin-D regimens have consistently produced high response rates and survival approaching 100%.[12][13]

Patients who fail with methotrexate based regimens are found to have a 75% complete response using secondary dactinomycin. Failure of both methotrexate and dactinomycin can be tackled with multi-agent salvage therapy.[14]

In our institution 63% patients treated with single agent methotrexate achieved a complete response.Second line actinomycin-D produced 100% response rate in the five patients treated. Only one patient progressed on EMACO regimen as second line who attained a complete response with EMAEP regimen.

Dose intensive multi-agent chemotherapy has been the standard of care for high risk GTN. Regimens such as EMACO, EMAEP have produced complete responses in range of 70%-94% with overall survival >85% in various studies.[15][16]

In our institution all high risk patients who completed EMACO regimen had a complete response.One patient had defaulted during treatment.

Subsequent pregnancy after GTD and GTN have been documented in literature with 67% being normal term deliveries and 1.3% being molar pregnancies.[17]. In our patients who became pregnant 9 had normal pregnancy.Only one patient who had become pregnant before completing followup as per protocol reported with a subsequent mole.

CONCLUSION

Gestational Trophoblastic Disaese is a group of heterogenous premalignant and malignant lesions in reproductive age of women which are curable with acceptable morbidity. Treatment with chemotherapy in addition to high response rates does not hamper the fertility.

Highly sensitive serum beta HCG assays have greatly aided in timely diagnosis and response assessment of treatment.

Patient compliance is of utmost importance in curing this entity with proper treatment. Adequate patient education from health care specialists can help achieve a good amount of patient compliance.

GTN is one great example of success story of chemotherapy in oncology which needs proper diagnosis risk stratification and timely treatment.

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