ORIGINAL ARTICLE

# GESTATIONAL TROPHOBLASTIC DISEASE

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**Background:** Molar pregnancy represents a significant burden of disease on the spectrum of Gestational Trophoblastic Disease (GTD). The incidence appears to be quite high in South Asia. The objective of this study was to determine the frequency of GTD, and clinical presentation, management and outcome of patients with molar pregnancy. **Methods:** This retrospective, descriptive study was conducted at Nuclear Institute of Medicine and Radiotherapy (NIMRA), Jamshoro from 1st Jan to 31st Dec 2009. All patients diagnosed and registered as GTD were included in the study. The clinical records of all molar patients were reviewed regarding presentation, treatment, and follow-up. **Results:** There were a total of 167 patients presenting with different female genital tract neoplasia at NIMRA during the study period, including 39 (29.35%) cases of GTD. Hydatidiform mole was seen in 33 (84.61%) patients. Complete mole in 31 (79.48%), partial mole in 2 (5.12%) patients, invasive mole in 1 (2.56%) patient, and choriocarcinoma in 5 (12.82%) patients. The mean age of the patients was 27±9.8 years. The highest incidence was found in nulliparous and para 1. Thirty-two patients had suction evacuation and 1 patient underwent hysterectomy. Patients received chemotherapy, 17 (54.54%) patients followed protocol for 3–6 months. **Conclusion:** Frequency of molar pregnancy was high, more common in low-parous, poor socioeconomic class women, and usually presented late.

**Keywords:** Gestational trophoblastic disease, Hydatidiform mole, management, outcome, women

## INTRODUCTION

Gestational Trophoblastic Disease (GTD) consists of a group of disorders arising from tissues of placental origin. They ranges from benign entity like hydatidiform mole, i.e., complete and partial mole to Gestational Trophoblastic Tumours (GTT) including invasive mole, choriocarcinoma and placental site trophoblastic tumors.[1] GTD accounts for less than 1% of female reproductive system cancers.[2] The worldwide incidence of GTD varies considerably, with relatively high frequency in South-east Asia compare to the West. Hydatidiform moles occur in approximately 1:2000–3000 in UK and USA, in India 1:160, and China 1:150. The incidence of choriocarcinoma in the UK and USA is of the order of 1:50,000–70,000 pregnancies and it is ten times more common in South-east Asia. The likewise malignant potential of this disease is higher in these regions (10–15% compared to 2–4% in the western countries).[3]

The exact incidence in Pakistan is not known, however in one study the reported frequency of GTD was 28 per 1000 live births.[4] GTD is unique for its genetic origin. In spite of high malignant potential, it is often curable due to high sensitivity to chemotherapy, with preservation of fertility.[5] The existence of ideal tumour marker –BhCG and ultrasound examination are the reliable tool for its diagnosis. The type of chemotherapy chosen whether single or multiple drug therapy are depends upon associated risk factors, extent of disease and previous treatment taken.[6] In different parts of the world there is decline in frequency of GTD and survival is improved due to early diagnosis and treatment. However it is still challenging problem in our country as most of the patients seek medical help very late and follow the treatment poorly. Few epidemiological and clinical studies have been conducted to compute the data regarding true prevalence rate and its sequel.

The purpose of our study was to determine the frequency of GTD, and its clinical presentation, management and outcome of molar patients.

## PATIENTS AND METHODS

This study was conducted at Nuclear Institute of Medicine and Radiotherapy (NIMRA) for a period of 1 year from 1st Jan to 31st Dec 2009. All cases of GTD referred from Liaquat University Hospital of Hyderabad and Jamshoro, Isra University Hospital Hyderabad, Nawabshah Medical College and private clinics of the region were included. The clinical records of molar patients were reviewed regarding mode of presentation, investigations, management, and follow-up. Basic investigations included blood grouping, complete blood picture, Serum β-hCG level, Ultrasonograpghy, and X-ray chest. In patients who received chemotherapy, haematology and biochemistry profile including complete blood count, Renal and Liver function tests and Chest X-ray was done before each course. Follow-up included clinical presentation and investigations including Ultrasound examination and X-ray chest, and serial β-hCG levels, initially fortnightly for 1–6 weeks or until Serum β-hCG level were normal, then monthly for 1–6 months, 3 monthly for 7–12 months. The data were analysed on SPSS-16.

## RESULTS

A total of 167 women with genital tract neoplasia were registered with NIMRA during the study period. Out of these, 39 cases (23.35%) were of GTD. Thirty-three (84.61%) had Hydatidiform mole; 31 (79.48%) complete mole and 2 (5.12%) partial mole, 1 (2.56%) case of invasive mole, and 5 (12.82%) choriocarcinoma. Majority (18, 54.54%) of cases were encountered in their twenties, with mean age of 27±9.8 years. Only 4 (10.25%) patients were above 40 years of age. Nulliparous and low parity women were affected more, and molar pregnancy was found in 14 (42.42%) while 10 (30.30%) were para 2–4 and 9 (27.27%) had more than 4 children (Table-1).

Women with poor socioeconomic status were affected more; 29 (87.87%) of patients belonged to income group <5000 rupees per month, 3 (9.09%) patients had income between 5000–10,000 rupees/month and only 1 patient (3.03%) had income above 10,000 rupees/month. At the time of presentation uterine size was larger than dates in 19 (57.57%) cases, while normal sized in 11 (33.33%) and smaller for dates in 3 (9.09%) cases. Most common presenting symptoms was vaginal bleeding (27, 81.81%), followed by pain in lower abdomen (10, 30.30%), hyperemesis gravidarum with fever (3, 9.0%) and passage of moles in 1 (3.0%) patient. Pre-treatment serum β-hCG level was elevated in all patients and was more than 50,000 IU/L in 87.87% cases. It was <100,000 IU/L in 13 (39.39%) patients, 100,000–200,000 IU/L in 7 (21.21%) patients, and >200,000 IU/L in 13 (39.39%) patients.

Out of 33 molar pregnancies, 32 (96.96%) patients underwent primary suction evacuation at their respective hospitals, only 1 case of (3.0%) molar pregnancy was diagnosed on histopathology examination of hysterectomy specimen carried out for irregular vaginal bleeding. Eighteen (54.54%) patients received no adjuvant therapy. Chemotherapy as single agent (Methotrexate and folinic acid rescue regimen) was given to 15 (45.45%) patients, and was well tolerated. The side-effects reported were stomatitis, nausea, and vomiting in 3 (9.09%) patients.

Serial measurement of serum β-hCG level was used to monitor the behaviour of resident trophoblastic tissue after evacuation. Initially it was carried out fortnightly till the serum β-hCG level was undetected, then monthly for 6 months. Only 17 (51.51%) patients followed the protocol, 16 (48.48%) patients for 3–6 months and 1 for one year. Sixteen patients discontinued their protocol before it had been completed, i.e., after second to third visit. In patients having benign hydatidiform mole the serum β-hCG level was undetectable within three month period.

**Table-1: Demographic characteristics and symptoms**

| Characteristic | Number (%) |
|---|---|
| **Age** | |
| <20 years | 5 (15.15%) |
| 20–29years | 18 (54.54%) |
| 30 >30 years | 10 (30.30%) |
| **Parity** | |
| 0–1 | 14 (42-42%) |
| 2–4 | 10 (30.30%) |
| >4 | 9 (27.27%) |
| **Amenorrhoea** | |
| 3 Months | 10 (30.30%) |
| 4 Months | 9 (27.27%) |
| >4 Months | 14 (42.42%) |
| **Vaginal bleeding** | 27 (81.81%) |
| **Pain in lower abdomen** | 10 (30.30%) |
| **Passage of moles** | 1 (3.0%) |
| **Fever with vomiting** | 3 (9.0%) |

## DISCUSSION

Worldwide GTD is reported to be highest in Asian countries[7,] with a relatively higher risk for blacks[8]. Extremes of reproductive life are important risk factors associated with molar pregnancy. In present study highest incidence was found in age group 20–29 years, and similar results were reported from Karachi[9]. The mean age of patients was 27±9.8 years, nearly similar results have been reported from an African study[10]. The frequency of molar pregnancy was found to be the highest in para 0 and para 1. Talati NJ from Karachi also found the nulliparity as a risk factor.[11] Vaginal bleeding was the most common presenting symptom like in other studies.[10–12] The clinical presentation of patients was similar to those in other studies, but the time of presentation was much later to that in the West. Majority (23, 69.69%) patients presented after the 1st trimester, while 10 (33.33%) patients presented within 1st trimester in our study. Berkowitz RS *et al*[13] reported majority of patients diagnosed within 1st trimester often before classical clinical sign and symptoms develop. Late presentation resulted in uteri being larger than dates and appearance of theca lutein cysts in our patients. Low literacy, lack of antenatal care and low socioeconomic conditions remain major contributory factors for late presentation.

The diagnosis of GTD was based on clinical examination, ultrasonography, β-hCG level, and on histopathological features. Routine ultrasound examination in 1st trimester of pregnancy would be helpful in early diagnosis of GTD while the use of Colour Doppler has made it possible to determine the extent of disease in the uterus, assessing the disease recurrence, and monitoring the efficacy of chemotherapy.[14–16]

Ultrasound and serum β-hCG are considered as sensitive detectors of GTD. The patients who had markedly elevated β-hCG levels and uteri larger than dates before evacuation are categorised as high risk for

subsequent malignantchange.[17] Chemotherapy as single agent (Methotrexate and folinic acid rescue regimen) was well tolerated. The side-effects reported were stomatitis, nausea, and vomiting, but none had toxicity whatsoever to stop the therapy. Serial measurement of serum β-hCG level is used to monitor the behaviour of resident trophoblastic tissue after surgical evacuation. Only 17 patients (51.51%) followed protocol for 3–6 months. Sixteen (48.48%) patients discontinued their protocol before it had been completed. In patients having benign hydatidiform mole the serum β-hCG level was undetectable within three months. Poor compliance and lack of follow-up remained the limitation of our study, which is a challenge in rest of our country.[18] The study conducted by Batorfi J, *et al*[19] also reported that at least 43% of patients discontinue their protocol it has been completed. Low socioeconomic status, low literacy rates, and inability to understand the importance of follow-up are the major contributing factors in our region. Majority of our patients were from remote areas and lack of proper facilities to reach the tertiary care hospitals and late antenatal care are also contributory factors for delayed presentation and poor follow-up. Given our institutional setting and demographics, we would advocate prophylactic chemotherapy for the high-risk group since the follow-up is not entirely reliable.

## CONCLUSION

Molar pregnancies were more common in low parous women, belonging to poor socioeconomic class and presenting late, vaginal bleeding being the commonest symptom. Proper antenatal care helps to improve the prognosis and outcome by early diagnosis and treatment of these women. Improving literacy rate, and awareness regarding nature of disease and its risk of malignancy needs special emphasis.

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