

## GESTATIONAL TROPHOBLASTIC DISEASE: EXPERIENCE AT NAWABSHAH HOSPITAL

Khairunnisa Nizam, Gulfaeen Haider\*, Nizamuddin Memon\*\*, Ambreen Haider<sup>†</sup>

Department of Obstetrics and Gynaecology, Nawabshah Medical College Hospital, Nawabshah, \*Department of Obstetrics and Gynaecology, Isra University Hospital, \*\*Department of Radiology, <sup>†</sup>Department of Cardiology, Liaquat University of Medical Health Sciences Hospital, Hyderabad, Pakistan

**Background:** Gestational Trophoblastic Disease (GTD) is a heterogeneous group of diseases that includes partial and complete hydatidiform mole, invasive mole, choriocarcinoma and placental site trophoblastic tumour. The incidence of GTD varies in different parts of the world. The malignant potential of this disease is higher in South East Asia in comparison to western countries. Objectives of study were to determine the frequency, clinical presentation and management outcomes of GTD. This retrospective, descriptive case series was conducted in the Department of Obstetric and Gynaecology Nawabshah Medical College Hospital, from 1<sup>st</sup> Jan 2007 to 30<sup>th</sup> Dec 2007. **Methods:** The case records of all the gestational trophoblastic cases during study period were analysed regarding their history, clinical examination, investigations, treatment and follow-up. The main outcomes were measured in terms of duration, antecedent pregnancy, investigations, treatment and the follow-up. **Results:** There were a total of 1056 Obstetric admissions during the study period, which included 30 cases of trophoblastic disease with a frequency of GTD was 28 per 1000 live births. Of these 30 cases, 21 (70%) patients had hydatidiform mole, 7 (23.3%) patients had invasive disease and 2 (6.6%) patients had choriocarcinoma. Twenty three patients (76.6%) received chemotherapy while 25 (83.3%) patients had suction evacuation and 4 (13.3%) patients underwent hysterectomy. Among all patients, 29(96.7%) fully recovered and 1 (3.3%) died because of extensive disease; metastasis extending up to brain. **Conclusion:** Frequency of GTD was higher compared to national and international studies. The disease was common in extremes of ages, low para and grand multiparous women. Hydatidiform mole was the commonest type of trophoblastic disease in these patients. Most common presenting complaint was bleeding per vagina followed by pain in lower abdomen.

**Keywords:** Gestational trophoblastic disease, Hydatidiform mole, Management.

### INTRODUCTION

Gestational Trophoblastic Disease (GTD) is a heterogeneous group of diseases that includes partial and complete hydatidiform mole, invasive mole, choriocarcinoma and placental site trophoblastic tumour. In recent years, new entities like epithelioid trophoblastic tumour have been added.<sup>1</sup> The incidence of GTD varies in different parts of the world, for example, in Japan, the incidence is 2/1000 deliveries while in Malaysia, the incidence of molar pregnancy and gestational trophoblastic neoplasia is 2.8/1000 and 1.59/1000 deliveries respectively.<sup>2,3</sup> Meanwhile, in North America, its incidence is reported up to 2.5/1000 pregnancies.<sup>4</sup> Highest incidence of 12.1/1000 deliveries is reported from Turkey.<sup>5</sup> The malignant potential of this disease is higher in South East Asia where it is as high as 10–15% in comparison to 2–4% in the western countries.<sup>6</sup>

The exact incidence in Pakistan is not known but only one study has reported it to be 0.68/1000 births.<sup>7</sup> Common clinical presentations include vaginal bleeding in early trimester, uterus larger than gestational age and absence of foetal parts after 20 weeks of gestation. Ultrasonography is a reliable non-invasive tool for diagnosis of GTD in the clinical setting.

Since this group of disorders is now one of the highly curable neoplasms, early diagnosis and prompt treatment is necessary. The rates of GTD are decreasing and survival has dramatically improved in different parts of the world.<sup>8,9</sup>

In Pakistan, few studies have been conducted in Lahore and Karachi to find out the incidence of GTD, with an objective to compute the epidemiological and clinical data in these areas.

The objective of this study was to find out the frequency, common presentation, type of the GTD, extent of the disease, treatment modalities and the outcome in a cohort of local population.

### PATIENTS AND METHODS

This retrospective, descriptive case review was conducted at the Department of Gynaecology and Obstetrics, Nawabshah Medical College Hospital, from 1<sup>st</sup> Jan 2007 to 30<sup>th</sup> Dec 2007. The case records of all these patients who were admitted with trophoblastic disease and neoplasm were analysed retrospectively regarding the age, parity, signs and symptoms, duration of previous treatment, histopathology, investigations, type of trophoblastic disease, type of surgical treatment, chemotherapy, follow-up and mortality associated with this disease. All those patients having trophoblastic disease with

elevated  $\beta$ -HCG, ultrasonic or histopathological evidence of the disease were included in the study. Brain metastasis was detected through CT Scanning of the patients. Patients having irregular bleeding per vagina without any evidence of trophoblastic disease were excluded. Socioeconomic status of patient was labelled as poor class if monthly income was up to rupees 10,000 per months, middle class if income is up to 20,000 per months and upper class if monthly income was more than 20000 rupees per months. Data was analyzed using SPSS version 11.0.

## RESULTS

There were total 1056 Obstetrical admissions during the study period which included 30 cases of GTD. Hence, the frequency of GTD was 28 per 1000 live births in this study.

Majority of the patients were of more than of 38 year age 16 (53.3%) (Table-1). Out of these 30 patients, 15 (50%) were para one, while 12 (40%) were para more than four (Table-2).

The most common presenting symptom was bleeding per vaginum 11 (36.3%) followed by pain in lower abdomen 7 (23.3%), passage of moles 5 (16.6%), hyperemesis gravidarum 4 (13.3%) and dyspnoea in 3 (10.0%).

The antecedent pregnancy was hydatidiform mole in 19 (63.3%) patients, abortion in 9 (30%) and full term pregnancy in 2 (6.6%) patients.

The gestational period in 18 (60%) patients, in which disease was diagnosed was between 2–5 months, in 9 (30%) patients, it was between 1–2 months, and in only 3 (10%) patients, it was more than 5 months.

Hydatidiform mole was diagnosed in 21 (70%) patients, invasive mole in 7 (23.3%) and choriocarcinoma in 2 (6.6%) patients. No patient had placental site trophoblastic tumour.

Out of 30 patients, 29 underwent surgical treatment. In 25 (83.3%) patients, suction evacuation was done and 4 (13.3%) cases underwent hysterectomy. Indication of hysterectomy was emergency presentation with heavy bleeding.

Seven (23.3%) patients received no adjuvant chemotherapy. Twenty three (76.6%) patients received chemotherapy. Among them 19 (82.6%) patients received single drug therapy (methotrexate alternate with folinic acid) and 4 (17.3%) received multiple drug therapy (EMA-CO regime). Before starting chemotherapy, opinion from oncologist in Atomic energy department was taken regarding type and dosage of chemotherapy. Chemotherapy was given for 3–6 months. Among the 30 patients, 29 (96.7%) fully recovered and 1 (3.3%) died because of extensive disease (metastasising up to brain). Follow-up of the patients was carried out by clinical examination and

investigations such as serum  $\beta$ -HCG level, ultrasound examination and X-ray chest. Initially, it was carried out monthly, then after every 3 months till the  $\beta$ -HCG level was not detectable. In patients having benign hydatidiform mole, the serum  $\beta$ -HCG level was undetectable within 3 months period.

**Table-1: Socio-demographic data**

Parameters	Number of Patients	Percentage
<b>Age</b>		
<20	10	33.1
21–38	4	13.31
>38	16	53.3
<b>Parity</b>		
0–1	15	50
2–4	3	10
>4	12	40
<b>Education</b>		
Illiterate	19	63.3
Primary	8	26.6
Middle	2	6.6
Graduation	1	3.33
<b>Socioeconomic condition</b>		
Low	22	73.3
Middle	7	23.3
High	1	3.3

**Table-2: Clinical presentation**

Symptoms	Number of Cases	Percentage
Bleeding P/V	11	36.6
Pain in lower abdomen	7	23.3
Passage of moles	5	16.6
Hyperemesis gravidarum	4	13.3
Dyspnoea	3	10

**Table-3: Type of gestational trophoblastic disease**

Type of GTD	Number of Cases	Percentage
H. Mole	21	70
Invasive mole	7	23.3
Choriocarcinoma	2	6.6

## DISCUSSION

Gestational Trophoblastic Disease (GTD) is characterised by the secretion of a distinct tumour marker, the  $\beta$ -HCG. This condition is curable even in the presence of metastasis. The major well-established risk factors for the disease are advanced maternal age and a past history of GTD.<sup>10</sup> Frequency of GTD in our study is 28 per 1000 live births, which is quite significant. This frequency is also higher within our country if compared to hospital based studies from Peshawar<sup>11</sup> and Karachi.<sup>12</sup> The reason for the high frequency of the GTD in this study might be the fact that the hospital is a major referral centre with large catchment area.

Another reason is that our patients had low socioeconomic and poor educational status (73.3% of patient had monthly income less than Rs. 10,000).

A Korean study proved this fact by decreasing the rate of incidence from 4.4 (1960s) to 1.6 (1990s) with improvement in medical care and to socioeconomic and educational changes.

Improvement in nutrition in another study did not support the suggestion of protein deficiency as an etiological factor.<sup>13</sup>

Another study conducted by Tham stated that the high incidence in Asia is generally attributed to low socioeconomic status and malnutrition.<sup>14</sup> Maternal reproductive age is the most consistent risk factor for hydatidiform mole in every region and ethnic group. In this study, disease was more common in the extreme of reproductive ages. It is consistent with the findings of studies from Singapore<sup>6</sup> and Karachi<sup>12</sup>.

The available evidence suggests that hydatidiform mole arises as a consequence of defective ova.<sup>15</sup> It is premature in young and post mature in old ages. Antecedent pregnancy in invasive mole was hydatidiform mole while in choriocarcinoma both the patients had full-term pregnancy one year back.

Vaginal bleeding was the most common presenting symptom in this study and it is also reported by other studies such as Kim<sup>16</sup> and Zalel *et al*<sup>17</sup>. Another study conducted by Moodley *et al*, have also reported the same findings.<sup>2</sup>

The diagnosis of trophoblastic disease was based on clinical and histopathological features,  $\beta$ -HCG, ultrasonography, especially by using high resolution vaginal ultrasonography that could diagnose the disease much earlier. Ultrasonography and serum  $\beta$ -HCG are the sensitive detectors of trophoblastic disease. These tests are simple, non invasive, inexpensive and yield quick result. Ultrasonography and Doppler imaging are helpful in diagnosing gestational trophoblastic disease, in determining whether invasive disease is present, in detecting recurrent disease, and in following the effectiveness of chemotherapy.<sup>18</sup> Most of the patients in this study were having hydatidiform mole while 29.9% were having malignant trophoblastic disease in the form of choriocarcinoma and invasive mole. Choriocarcinoma is a potentially fatal disease but current management protocol has turned the prognosis highly favourable. Izhar<sup>19</sup> from Peshawar has also reported cure rate of 80%. Like other studies, in this study, majority of patients with molar pregnancy were treated with suction curettage, i.e. 83.3% and only 4 patients needed hysterectomy; seven had invasive mole and other had persistent vaginal bleeding, which did not settle with evacuation and chemotherapy. Patients with malignant trophoblastic disease were treated with multiple agent chemotherapy and those who had increased serum  $\beta$ -HCG or those with persistent bleeding per vagina, after evacuation, were treated with single drug chemotherapy. The duration of treatment ranged from 3–6 months with three doses

of chemotherapy till the serum  $\beta$ -HCG level was undetectable.

Overall complete cure was achieved in 96.7% patients in this study. However, 1 patient (3.3%) died during therapy. Main reasons of death in this patient was extensive disease (metastasising up to brain) and poor general health.

## CONCLUSION

In this series, frequency of GTD was higher compared to national and international literature. The disease was common in extremes of ages, low para and grand multiparous women. Hydatidiform mole was the commonest type of trophoblastic disease in these patients. Most common presenting complaint was bleeding per vagina followed by pain in lower abdomen. Patients with regular follow-up recovered fully while mortality was associated with complications, delay in recovery and receiving no proper treatment. Proper management in the early stages strongly influences the outcome of the diseases. Hence, emphasis should be given to detect the disease in its early stage to decrease the mortality and morbidity from this condition.

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**Address for Correspondence:**

**Dr. Gulfareen Haider**, B/No: 530-A, Block C, Unit 8 Latifabad, Hyderabad, Pakistan. Cell: +92-300-9379794

**Email:** gfareen@yahoo.com