

## Clinical Presentation, Management and Outcome of Gestational Trophoblastic Diseases Admitted in Chittagong Medical College Hospital

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### Abstract

**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 study aimed to determine the clinical presentation management options and outcome of GTD in patients admitted in a tertiary hospital of Bangladesh.

**Materials and methods:** This prospective observational study included 50 patients with GTD from the Obstetrics and Gynaecology Department of Chittagong Medical College Hospital, during the period of July 2013 to December 2013. The demographic profile, clinical presentation, management, outcome and complications were studied.

**Results:** Mean age was  $25.40 \pm 8.34$  years with most of the patients (46%) were in age group 20 - 29 years. 42% participants were primigravida. The commonest symptom after bleeding per-vaginum (94%) was amenorrhea (90%). Maximum cases (80%) were of complete hydatidiform mole. Rate of progression to invasive mole and choriocarcinoma were found 6% and 10% respectively. Suction evacuation and hysterectomy were the treatment option. One patient (2%) expired due to excessive bleeding.

**Conclusion:** The majority of cases are cured by simple suction uterine curettage. Regular follow up is important to estimate the true incidence of this disease.

**Key words:** Gestational trophoblastic diseases; Molar pregnancy; Outcome.

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Submitted on : 12.11.2021

Accepted on : 23.12.2021

### Introduction

The first description of Gestational Trophoblastic Disease (GTD) was by Hippocrates around 400 BC. Marchand discovered the association of this disease with pregnancy in 1895. Healthy trophoblastic tissue penetrates the endometrium, which creates a rich uterine vasculature, leading to a close connection between the fetus and the mother, which is called the placenta. Invasion is characteristic of malignant tissue, and fortunately, the malignant behavior of the healthy trophoblast is well controlled. Nevertheless, in gestational trophoblastic disease, the regulatory mechanisms become dysfunctional, resulting in highly invasive, vascular and metastatic tumors. GTD involves both benign and malignant entities that include hydatidiform mole (Complete and partial) choriocarcinoma, invasive mole, Epithelioid Trophoblastic Tumor (ETT) and Placental Site Trophoblastic Tumor (PSTT). The last four are known as Gestational Trophoblastic Neoplasia (GTN) all can metastasize and can be fatal if not treated.<sup>1,2</sup>

The reported prevalence of choriocarcinoma differs significantly worldwide and GTD is found more frequently in Asia compared to North America or Europe.<sup>3,4</sup> Maternal Mortality Ratio (MMR) in Bangladesh is still quite high; thus, a priority health and development issue.<sup>5</sup> The data regarding the outcome of GTD from developing countries are scant. In this context, this study was aimed to determine the clinical presentation, management and outcome of GTDs admitted in a tertiary teaching hospital of Bangladesh.

### Materials and methods

This prospective observational study was conducted in the Gynecology and Obstetrics Department of Chittagong Medical College Hospital from January 2013 to December 2013. Hospitalized patients who had a confirmed diagnosis of GTD and provide written informed consent were included in the study. Patients with persistent trophoblastic diseases and Choriocarcinoma following term pregnancy, abortion and ectopic pregnancy were excluded.

Ethical approval was taken from the Ethical and Review Committee of Chittagong Medical College. Written informed consent was obtained from the patients after explaining the detail study procedure.

Data regarding age, parity, gestational age, per vaginal bleeding, passage of vesicles, constitutional symptoms were collected with a pretested structured case record form. Then detailed general and clinical examination was done. Size of the uterus per abdomen was compared with gestational age and ascertained if it corresponded to the weeks of gestation. Per-speculum and per vaginal examination was also done. Relevant haematological and radiological investigations which included Hb%, blood grouping and Rh typing, thyroid function test, serum  $\beta$ -hCG, USG and chest X-ray were undertaken. Cross matching samples were drawn for blood transfusions, if and when required.

Suction and evacuation were done for all patients as a primary mode of management. The samples so obtained were sent for histopathological examination. Blood transfusions were done according to requirement of the patient either preoperatively, intraoperatively or in the post-operative period. Anti-D was given to Rh-negative women. The serum  $\beta$ -hCG was repeated 48 hours after evacuation. Then the patients were counseled regarding need for follow up and use of contraception during the entire period of follow up. Follow up was done with two weekly  $\beta$ hCG until 12 weeks.

The normal level of  $\beta$ -hCG was taken to be less than 10 IU/L. At each follow up visit detailed history was taken regarding irregular vaginal bleeding, pain abdomen, headache, cough, haemoptysis and fever etc. Clinical examination, per speculum and per vaginal examination was done to look for signs of GTN. The time to achieve the first normal  $\beta$ -hCG after evacuation was noted. USG as well as colour Doppler were done when clinically indicated. GTN was diagnosed during follow up either on the basis of a rise in serum  $\beta$ -hCG levels or histopathology or with evidence of metastasis. Those diagnosed as GTN were classified as low risk or high risk using FIGO scoring system for GTN and were duly treated with chemotherapy.<sup>6</sup>

Data were processed and analyzed by using computer based Microsoft excel software. Data were presented in frequency and percentage or mean and standard deviation. Results and observation were presented in tables.

### Results

Out of 50 patients with GTD, majority (46%) were in the age group of 20-29 years with a mean age of  $25.40 \pm 8.34$  years. Twenty one (42.0%) patients were primi and rest were 29 (56.0%) were multigravida. Among multi gravid patients 16 (32.0%) were 2<sup>nd</sup> gravida, 10 (20.0%) were 3<sup>rd</sup> gravida and 03(06.0%) were found 4<sup>th</sup> gravida. Regarding presenting complains amenorrhoea, per vaginal bleeding, history of passage of grape like vesicles and constitutional symptoms were found in the study. Almost 94% of patients had per vaginal bleeding. Enlarged uterus with open os found in about 30(60%) patients. Only 5(10%) patients presented with adenexal cyst and nodules in pouch of douglus and vagina found in only 6% of patients. Serum  $\beta$ hCG was in between 1-2 lac in the 40% of the patient. About 30% patients had Serum  $\beta$ hCG <1 lac and 30% patients had >2 lac (Table I).

**Table I** Baseline characteristics of the patients (n=50)

Variables	Frequency	Percentage (%)
Age, Years		
<20 years	15	30.0
20-29 years	23	46.0
30-39 years	9	18.0
40 years	3	6.0
Mean $\pm$ SD (Range)	25.40 $\pm$ 8.34 (17-45)	
Gravida		
Primigravida	21	42.0
2 <sup>nd</sup> gravida	16	32.0
3 <sup>rd</sup> gravida	10	20.0
4 <sup>th</sup> gravida	3	6.0
Presenting complaint <sup>†</sup>		
History of Amenorrhea	45	90.0
Per vaginal bleeding	47	94.0
Expulsion of Grape like vesicles	34	68.0
Constitutional symptoms*	42	82.0
Per-vaginal examination findings <sup>†</sup>		
Enlarged uterus with os open	30	60.0
Adnexal cyst	5	10.0
Nodules in pouch of douglus	3	6.0
Nodules in vagina	3	6.0
P/v bleeding	47	94.0
Pre-evacuation $\beta$ hCG level.		
50,000-1,00,000 IU/L	15	30.0
1,00,000-2,00,000 IU/L	20	40.0
>2,00,000 IU/L	15	30.0

\*Nausea, vomiting, loss of appetite, weight loss. <sup>†</sup>Included multiple responses.

Table II shows distribution of clinical diagnosis where out of 50 patients 42 (84.0%) were diagnosed as cases of molar pregnancy, 5(10%) were choriocarcinoma and 3 (6.0%) were diagnosed as cases of invasive mole. Among the cases of molar pregnancy 40 were complete mole and 2 were partial mole. No cases of PSTT or ETT were seen in the study.

**Table II** Distribution of the patients according to the diagnosis

Diagnosis	Frequency	Percentage(%)
Complete mole	40	80.0
Partial mole	2	4.0
Invasive mole	3	6.0
Choriocarcinoma	5	10.0

Table III shows the distribution patients according to the treatment given. Out of 50 patients 40(80.0%) were treated by suction curettage and 02 (04.0%) were treated by hysterectomy. Among patients of hysterectomy one was done due to perforation during suction curettage and another one was molar pregnancy with age 40 with completed family. Eleven patients (22%) were treated by chemotherapy. Invasive mole (03) Choriocarcinoma (05) and 03 patients of persistent mole were in this group. Forty (80%) patients completely cured. Persistence of disease was found in about 06 (12%) patients. Out of 50 patients about 03 (0.6%) patients were lost from the study. One patient was died due to irreversible shock with H/O excessive vaginal bleeding.

**Table III** Management and outcome of the patients

Parameters	Frequency	Percentage (%)
Treatment modalities		
Suction evacuation and curettage	40	80.0
Suction evacuation followed by total abdominal hysterectomy	2	4.0
Received chemotherapy	11	22.0
12 weeks outcome		
Completely cured	40	80.0
Persistence of disease	6	12.0
Lost from the study	3	6.0
Died	1	2.0

## Discussion

Majority of the patients belonged to age group 20-29 years (46%), similar to the study by Smith & Kumar et al with the mean ages being similar as well.<sup>7,8</sup> FIGO and WHO criteria states age more

than 39 years as a high-risk factor, but this was not reflected in the present study as there were only three (6%) patients with age more than 40 years. This could be due to the small sample size, early age at marriage in the Bangladesh and attainment of maximum fertility at lower age itself. Fifteen patients (30%) were less than 20 years of age. Age less than 20 years is not considered as a risk factor by WHO, though some experts have observed both extremes (35 years) to be at increased risk of disease.<sup>9-12</sup>

Twenty one (42%) of the cases was primigravida. The study from Pakistan observed 36.5% of patients to be primigravidas.<sup>11</sup> The other study from northern part of India had 21% primigravida among all patients and 26% had a history of abortion in antecedent pregnancy.<sup>8</sup> However the Nigerian study had 48% of the patients with previous history of at least one abortion.<sup>10</sup>

In the present study the commonest symptom after per vaginum bleeding is amenorrhea, seen in 90% of patients. The clinical study from Dubai reported incidence of vaginal bleeding in 29% patients only.<sup>13</sup> However, Fatima et al noted bleeding per vaginum to be the commonest symptom seen in as many as 94.2%.<sup>11</sup> One of the most classical symptom i.e passage of grape like vesicles per vaginum was seen in 68% of patients in the present study; while in the Nigerian study by Ocheke et al, it was found in 60% cases.<sup>10</sup>

In the present study 80% of the patients showed complete mole, and in 4% patients showed partial mole. These proportions were not consistent with the published literature. The Malaysian study by Nirmala et al observed 46.1% patients to have complete mole and 53.9% having partial mole.<sup>14</sup> Lybol et al observed 30.2% having complete mole, 44.5% of patients having partial mole and in rest 11.6% the histopathology was unspecified.<sup>15</sup> Eighty percent cases were treated by suction and curettage and hysterectomy was needed in two cases. Suction curettage of the uterus is clearly the best means of management in most cases but is associated with higher rates of chemotherapy. This is probably due to a higher rate of incomplete evacuation.<sup>16, 17</sup>

Complications usually associated with GTD include haemorrhage, fever, septicemia, tumour embolization and uterine perforation.<sup>2</sup> These were minimal in the present study. One patient died due

to excessive hemorrhage with shock. Two (4%) patient had uterine perforation and had laparotomy followed by hysterectomy. Among 84% patients of molar pregnancy, spontaneous remission was occur in 88% of patient where 12% patients became persistent mole. About 3(6%) patients were lost due to lack of education, lack of health awareness, and poor socio-economic status and inadequate motivation.

The incidence of development of Choriocarcinoma in this study was high (10%) and another 6% case had invasive mole. In a study from Malaysia 3.9% patients developed persistent trophoblastic disease.<sup>14</sup> However in the study by Kumar et al 23% of the patients developed invasive mole and 14% developed choriocarcinoma.<sup>8</sup>

### Limitations

Small sample form a single center and short follow-up period are some of the limitations of the present study.

### Conclusion

In conclusion, maximum cases of GTD were of complete hydatidiform mole. Suction evacuation and hysterectomy were the treatment option. Rate of progression to invasive mole and choriocarcinoma were found 6% and 10% respectively.

### Recommendations

Further, a multi-centric study is essential in Bangladesh to determine the true incidence and overall outcome of molar pregnancy, which will help in the understanding exact burden of the disease. Because of paucity of population-based studies in India, there is imminent need to establish a centralized disease specific registry to ensure availability of unbiased and representative data.

### Acknowledgement

Authors expressed their heartiest thanks to all respondents.

### Contribution of authors

NJ-Conception, acquisition of data, drafting & final approval.

SC-Design, critical revision & final approval.

MMUM-Data analysis, critical revision & final approval.

SA-Interpretation of data, drafting & final approval.

NS-Acquisition of data, data analysis, critical revision & final approval.

SMSS-Interpretation of data, drafting & final approval.

DB-Acquisition of data, drafting & final approval.

### Disclosure

All the authors declared no competing interests.

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