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**Original Research Article**

# A clinicopathological study of gestational trophoblastic diseases in a tertiary healthcare centre

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## ABSTRACT

**Background:** Gestational trophoblastic diseases are marked by abnormal proliferation of various trophoblastic cells during placentation. It includes hydatidiform mole, invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT) and epithelioid trophoblastic tumor (ETT). GTNs are among the rare human tumours that can be cured even in the presence of widespread dissemination. Aims of present study was to assess histomorphological features of GTD along with its clinical correlation.
**Methods:** It was an observational cross-sectional study conducted in the Department of Pathology, at tertiary healthcare centre in South Gujarat over a period of 5 years from January 2019 to December 2023. Histological finding of all cases were recorded and clinical correlation done.
**Results:** Out of 50 analysed cases of GTDs, 47 cases (94%) were Hydatiform mole and 3 cases (6%) were choriocarcinoma. The incidence of gestational trophoblastic diseases is found to be 1 in 799 pregnancies. Age ranged from 18-35 years. The most commonly affected age group was 20-25 years with 29 cases (58%). Most cases were presented in the first trimester. Most common clinical presentation was bleeding per vagina in 34 cases (68%) followed by abdominal pain. The majority of GTD cases belonged to 50,000 to <1,00,000 mIU/ml beta-HCG level.
**Conclusions:** Hydatidiform mole is most prevalent gestational trophoblastic disease. Present study signifies the importance of routine histopathological examination of products of conception to rule out microscopic molar changes, since there is an higher incidence of molar pregnancies progressing to choriocarcinoma, a highly metastasizing neoplasm.

**Keywords:** Beta-hCG, Choriocarcinoma, Gestational trophoblastic disease, Hydatidiform mole

## INTRODUCTION

Gestational trophoblastic diseases (GTD) is one of the most interesting of all gynecological neoplasms. They are marked by abnormal proliferation of various trophoblastic cells during placentation.[1] Histologically it includes benign lesions such as hydatidiform mole (both complete and partial) as well as malignant lesions like invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT) and epithelioid trophoblastic tumor (ETT).[2] The incidence of GTD varies widely throughout the world being greatest in Asia.[3] According to WHO, incidence of hydatidiform moles highest in south-eastern Asia (3.8-13 cases per 1000 pregnancies), the Middle East (3.2-5.8 cases per 1000 pregnancies) and South America (4.6 cases per 1000 pregnancies) and lowest in western Europe and North America (0.8-1.5 cases per 1000 pregnancies).[4] Although GTNs commonly follow a molar pregnancy, they can develop following any gestational event, including induced abortion, spontaneous abortion, ectopic pregnancy or term pregnancy.[5] Recognition and separation of individual categories of Gestational Trophoblastic Diseases is essential as each disease entity has distinctive clinical manifestations and necessitates different therapeutic approach.[3] GTD are a source of significant morbidity as well as increased risk of mortality due to their

complications if not identified and treated early enough.[6] Histopathological examination is helpful for confirmation and to prevent the occurrence of metastatic consequences in majority of cases. Purpose of present study is to assess histomorphological features of GTD along with its clinical correlation.

## METHODS

Present study was an observational cross-sectional study conducted in the Department of Pathology at Government Medical College and New Civil Hospital, Surat over a period of 5 years from January 2019 to December 2023. Specimens obtained from uterine evacuation, dilatation and curratage, retained product of conception and hysterectomy specimens of all clinically suspected and histologically confirmed cases of GTDs were included in the study. The non-gestational tissue, poorly preserved specimens and cases of missing records were excluded from the study.

A total of 50 cases diagnosed as GTDs on histopathology were included in this study. Specimens were received in surgical pathology section, Pathology department along with their requisition form. Detailed clinical history including the age, presenting symptoms, parity status, per speculum and per vaginal examination findings, routine investigations, biochemical estimation of beta-HCG (whenever available), radiological examination by USG (transabdominal/ transvaginal) were noted from histopathology requisition form and case records and utilized during analysis.

Grossing of specimen were done according to standard guideline. The specimens were fixed in 10% formalin. Sections were taken from different area representing lesion. Tissue processing were done in routine tissue processor. Block preparation were done. Thin sections of 4-5 microns thickness were cut and then slides were prepared. All the histological sections were stained with H and E stain and mounted. All the histological sections will be examined microscopically. Histological findings and diagnosis were recorded.

Ethical clearance for the study was obtained from the Human Research Ethics Committee of the Medical College and the hospital of the present study setup.

## RESULTS

In the present study a total of 50 cases analyzed during study period from January 2019 to December 2023, out of which 46 (92%) were dilatation and evacuation (D and E) material, 3 (6%) were hysterectomy specimen and 1 (2%) was received as placenta with anomalous fetus. Histopathological examination of these specimens revealed 47 (94%) cases of hydatidiform mole and 3 (6%) cases of choriocarcinoma (Figure 1). Among 47 cases of hydatidiform mole, 34 (72.34%) cases were complete hydatidiform mole and 13 (27.65%) cases were partial hydatidiform mole. A clinicopathological analysis was carried out.

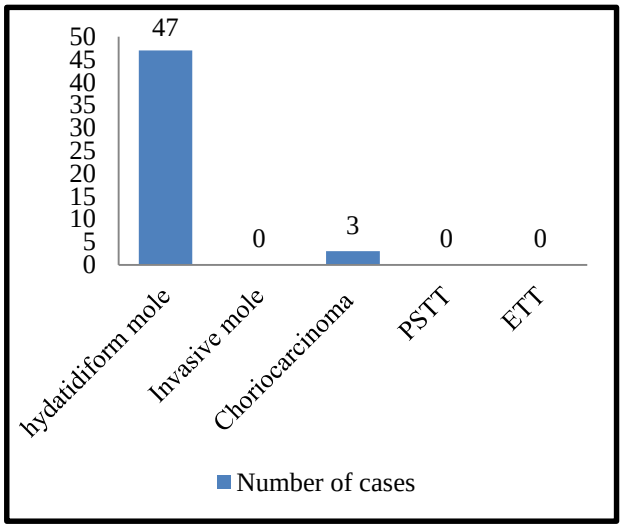


**Figure 1: Spectrum of gestational trophoblastic diseases (n=50).**

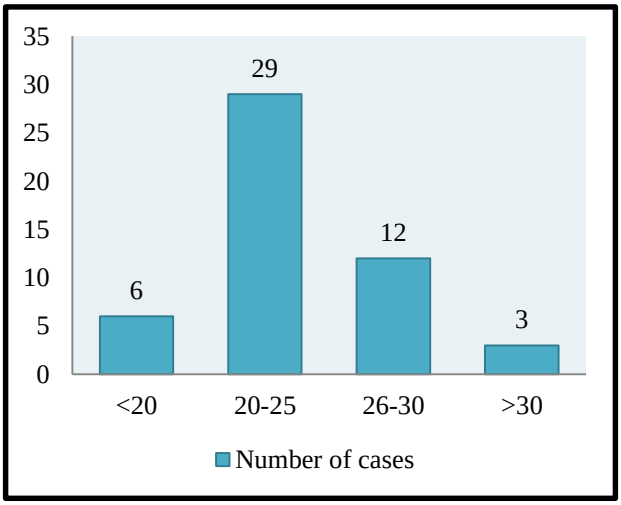


**Figure 2: Age wise distribution of GTD cases (n=50).**

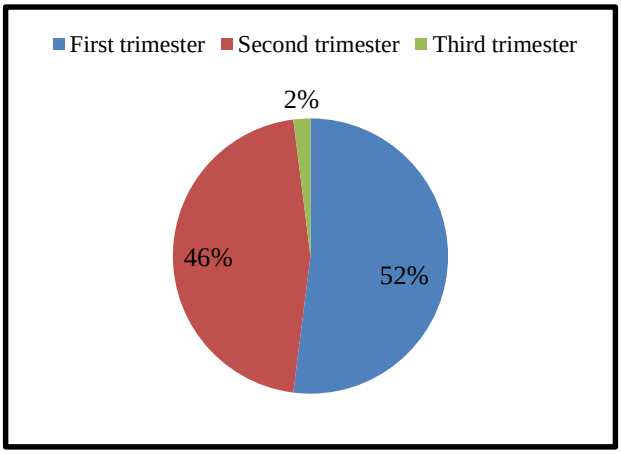


**Figure 3: Distribution of GTD cases according to trimester.**

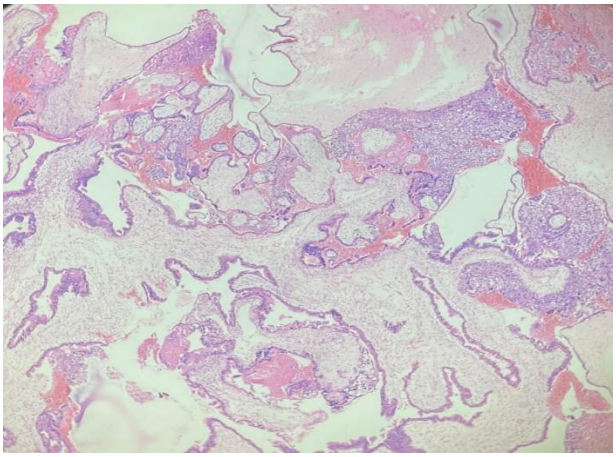

**Figure 4: Microphotograph of complete hydatidiform mole showing hydropic chorionic villi and circumferential trophoblastic hyperplasia(H&E,4X).**

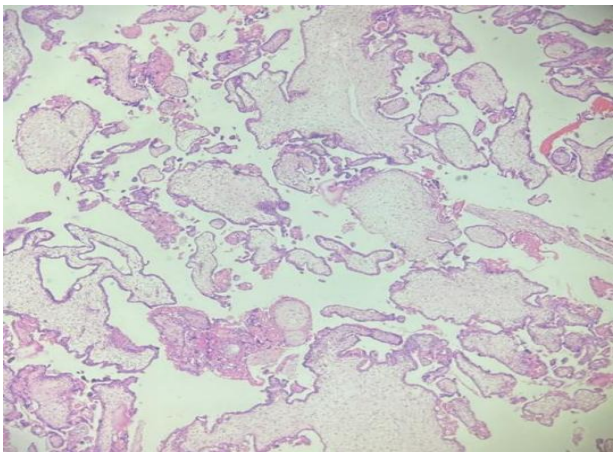

**Figure 5: Microphotograph of partial hydatidiform mole showing two population of villi, enlarged hydropic vilii and small fibrotic villi with minimal trophoblastic hyperplasia(H&E,4X).**

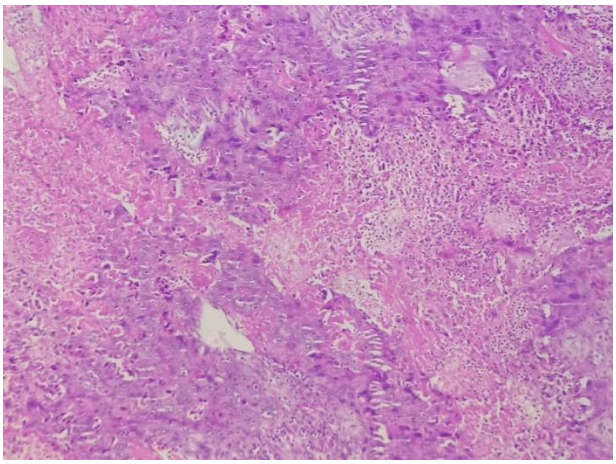

**Figure 6 : Microphotograph of choriocarcinoma showing large area of necrosis with biphasic mixture of cytotrophoblastic and syncytiotrophoblastic cells(H&E,10X).**

Since the incidence of gestational trophoblastic diseases is generally expressed in relation to total number of pregnancies rather than total population, incidence of gestational trophoblastic diseases in recent study is calculated according to it. The total number of pregnancies encountered in the five years period was 39,971. The gestational trophoblastic diseases form 0.13% of pregnancies. Thus, the incidence of gestational trophoblastic disease is 1 in 799 among the cohort of pregnant women over the five-year period. Hydatidiform mole form 0.12% (1 in 850) and choriocarcinoma form 0.007% (1 in 13,324 pregnancies) (Table 1). During a five-year period, the total number of live births was 38,761. Consequently, the incidence of GTD in this cohort of live births is 1 in 775.

The youngest case encountered in this study was 18 years old and oldest was 35 years. 58% of cases of GTD occurred in the age group of 20-25 years, followed by 24% cases which occurred in the age group of 26-30 years, followed by 12% cases below 20 years of age and 6% cases above 30 years of age (Figure 2). Hydatidiform mole was found to be highest in the age group of 20-25 years (61.7%) whereas choriocarcinoma was widely distributed in the age group of 25-30 years.

We distributed GTD cases according to trimester. We found maximum number of cases in the first trimester (26 cases) comprising of 24 cases of hydatidiform mole and 2 cases of choriocarcinoma. This followed by 23 cases in second trimester comprising of 22 cases of hyadatidiform mole and single case of choriocarcinoma. Single case of partial hydatidiform mole was detected in the third trimester (Figure 3).

Complete hydatidiform mole were found more common in the primigravida followed by para 2 and para 1. Whereas partial hydatidiform mole were found more common in para 1 followed by primigravida and para 2. All choriocarcinoma cases were found in para 2 patients.

Out of 50 GTD cases in our study, most common clinical presentation was bleeding per vagina in 34 cases (68%) followed by abdominal pain in 11 cases (22%). Other clinical presentations were amenorrhea (20%), vomiting (12%), passage of grape like structure (4%) and others (Table 2).

Among 50 cases of GTD, pelvic ultra-sonographic (USG) findings were available in 43 cases. Correlation of USG finding with histopathological finding were shown in Table 3.

Pre-evacuation beta-hCG were available in 33 cases. In the present study, distribution of GTD cases was done according to beta-hCG level into five categories i.e., <50,000, 50,000-<1,00,000 mlU/ml, 1,00,000-<5,00,000 mlU/ml, 5,00,000-10,00,000 mlU/ml and >10,00,000 respectively. In majority of cases(46%) beta-hCG levels were between 50,000–1,00,000 mIU/ml, followed by beta-

hCG levels between 1,00,000–5,00,000 mIU/ml in 11 cases. In 3 cases beta-hCG level were <50,000 mIU/ml. 3 cases had beta-hCG level in the range of 5,00,000-<10, 00,000 mlU/ml and single case had beta-hCG above >10,00,000 mlU/ml. Beta hCG levels of various GTD cases were shown in Table 4.

**Table 1: Incidence of hydatidiform mole and choriocarcinoma in relation to total no. of pregnancies (39,971).**

| Type of GTD | No. of cases | Incidence |
|---|---|---|
| **Hydatidiform mole** | 47 | 1 in 850 |
| **Choriocarcinoma** | 3 | 1 in 13,324 |
| **Total GTD** | 50 | 1 in 799 |

**Table 2: Various clinical presentations of different GTD cases (n=50).**

| Clinical presentations | CHM | PHM | Choriocarcinoma | No. of cases | % |
|---|---|---|---|---|---|
| **Bleeding per vagina** | 24 | 10 | | 34 | 68 |
| **Abdominal pain** | 7 | 2 | 2 | 11 | 22 |
| **Amenorrhea** | 8 | 2 | | 10 | 20 |
| **Vomiting** | 6 | | | 6 | 12 |
| **Passage of grapelike structure** | 2 | | | 2 | 4 |
| **Nausea** | 1 | | | 1 | 2 |
| **Chest pain** | | | 1 | 1 | 2 |
| **Weight loss, anorexia** | | | 1 | 1 | 2 |
| **Fever, diarrhoea** | | | 1 | 1 | 2 |

**Table 3: Correlation of USG finding with histopathological findings (n=43).**

| | Histopathological findings | | | |
|---|---|---|---|---|
| **Usg findings** | **CHM** | **PHM** | **Choriocarcinoma** | **Total** |
| **Molar pregnancy** | 15 | 6 | | 21 |
| **Complete molar pregnancy** | 14 | | | 14 |
| **Partial molar pregnancy** | 2 | 3 | | 5 |
| **Neoplastic etiology** | | | 2 | 2 |
| **Hemoperitoneum, free fluid in abdomen** | | | 1 | 1 |

**Table 4: Relation of beta-hCG level and GTD (n=33).**

| Beta hCG levels (mlU/ml) | CHM | PHM | Choriocarcinoma | No. of cases |
|---|---|---|---|---|
| **<50,000** | | 3 | | 3 |
| **50,000-1,00,000** | 10 | 4 | 1 | 15 |
| **1,00,000-5,00,000** | 9 | 2 | | 11 |
| **5,00,000-10,00,000** | 3 | | | 3 |
| **>10,00,000** | 1 | | | 1 |
| **Total** | 23 | 9 | 1 | 33 |

## DISCUSSION

GTD encompasses a spectrum of tumours and tumour like conditions characterized by proliferation of pregnancy associated trophoblastic tissue, which can potentially progress to malignancy.[7] It comprises four main clinicopathologic forms: hydatidiform mole(both complete and partial), invasive mole, choriocarcinoma and placental site trophoblastic tumor (PSTT). The term "gestational trophoblastic neoplasia"(GTN) is collectively used for the latter three conditions, which can progress, invade, metastasize and potentially lead to death if not treated appropriately.[6] In present study a total 50 cases of GTD were analyzed over period of 5 years. All these cases were of uterine GTD. Extra-uterine gestational trophoblastic disease were not included in present study.

In present study, we found that hydatidiform mole was the most common form of GTD accounting for 47 out of 50 cases (94%), followed by 3 cases of choriocarcinoma (6%). These findings are comparable with other studies like Sankaran et al, Jagtap et al, Thakuria et al and Madan et al, found 87.3%, 96.10%, 95% and 88.8% cases of hydatidiform mole respectively.[1,6-8] 6% cases of choriocarcinoma were found in present study, while study done by Sankaran et al and Madan et al, found 9.5% and 5.55% cases of choriocarcinoma respectively.[1,8] No single case of invasive mole and placental site trophoblastic

tumor was found in present study. The incidence of gestational trophoblastic disease was found to be 1 in 799 pregnancies. Karim et al reported an incidence of 1 in 314 pregnancies and Sankaran et al, reported an incidence of 1 in 550 pregnancies.[1,9] The incidence of gestational trophoblastic diseases is found to be slightly low in present study compared with others.

In the present study the incidence of gestational trophoblastic diseases with respect to live births constitute about 1.28 per 1000 which correlates with that of Sankaran et al, reported an incidence of 1.86 per 1000 live births.[1] The incidence of GTD exhibits a wide geographical diversity due to differences in methodology, classification of mole, case detection and definition of the denominator.[6] The present study showed cases of GTD ranged from 18 to 35 years, which is comparable with study done by Mulik et al and Kumar et al, which also show participant group ranged between 18 to 35 years.[10,11]

The peak incidence was found to be in the age group of 20-25 years (58%) which is similar to findings by Jagtap et al, (57.14%), Thakuria et al, (55%) and Kumar et al, (55%) which also show maximum number of cases in 20-25 years age group.[6,7,11] The mean age in present study was 24 years among all cases, which showed concordance with other study by Thakuria et al, (24%), Agrawal et al, (23.9%) and Jagtap (24.5%).[6,7,12] Obahiagbon et al and Mbamara et al, found mean age to be higher, 31.27 years and 31 years respectively.[13,14]

We found that most of the cases presented were in first trimester as seen in 26 (52%) cases, 23 (46%) cases were in second trimester and 1 (2%) case in third trimester which is in concordance with study by Thakuria et al and shrivastava et al, which had similar observation.[6,15] While study by Fatima et al, observed 48.2% cases in second trimester followed by 30.6% cases in first trimester and 21.2% cases in third trimester.[16]

In our study it was observed that primigravida were 42% and 58% were multiparous women. Among the multiparous women most of the patients were between 2nd and 4th gravida. Study by Agrawal et al and Benjapibal et al, had similar observations.[12,17] This study showed that the most common clinical presentation was bleeding per vagina with 34 (68%) cases, followed by abdominal pain with 11 (22%) and amenorrhea with 10 (20%) cases respectively. These findings were similar to results found in other studies like Thakuria et al, Jagtap et al and Mulik et al.[6,7,10] One of the most classical symptom i.e., passage of grape like vesicles per vaginum was seen in only 4% of patients in the present study, while in the done study by Ocheke et al, it was found in 60% cases.[18]

In present study, majority of cases (46%) had beta hCG level between 50,000-1,00,000 mIU/ml followed by 1,00,000-5,00,000 mIU/ml (33% cases). Similar results observed by Jagtap et al and Thakuria et al.[6,7] The serum beta hCG is the most sensitive and specific marker for diagnosis of the trophoblast-related conditions, i.e., pregnancy and the GTD. It also aids in assessing treatment response and recurrence of tumour.[7]

In present study, sample size was small as it was an institutional study. Also, follow up beta-hCG levels were not available for the study.

## CONCLUSION

Present study concluded that hydatidiform mole is most prevalent gestational trophoblastic disease. Complete hydatidiform mole are more common than the partial hydatidiform mole. Reproductive age group is most commonly affected age group in GTD.

Present study signifies the importance of routine histopathological examination of products of conception to rule out microscopic molar changes, since there is an higher incidence of molar pregnancies progressing to choriocarcinoma, a highly metastasizing neoplasm. Early recognition and treatment of choriocarcinoma with chemotherapy leads to 100% cure. There is the need for population-based studies on GTD with a view to determining a more accurate incidence and prevalence in our environment.

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