

Original Research Article

A clinicopathological study of gestational trophoblastic disease in a tertiary care centre of southern Assam

Sailendra K. Thakuria*, Monoj K. Deka, Shah A. Sheikh

Department of Pathology, Silchar Medical College and Hospital, Silchar, Assam, India

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*Correspondence:

Dr. Sailendra K. Thakuria,

E-mail: sailendra.gmch@gmail.com

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ABSTRACT

Background: Gestational trophoblastic disease (GTD) covers a wide spectrum of benign and malignant conditions that arise from pregnancies with abnormal trophoblastic tissue development. It is a source of significant morbidity as well as increased risk of mortality from their complications if not identified and treated early enough. Our study aimed at the various clinicopathological features of GTDs along with their prevalence in a tertiary care centre.

Methods: It was a retrospective cross-sectional study conducted over a period of 3 years from January 2017 to December 2019. All GTD cases were retrieved from department registries and analysed.

Results: Out of 60 diagnosed cases of GTDs, 57 cases (95%) were Hydatiform mole. Invasive mole and choriocarcinoma were 2 cases (3%) and 1 cases (2%) respectively. Age ranged from 18-37 years. The most commonly affected age group was 20-25 years with 33 cases (55%). Most cases were presented in the first trimester presenting with bleeding per vagina. The majority of GTD cases belonged to blood group A and 50,000-<1,00,000 mIU/mL beta HCG level.

Conclusions: Histopathological examination is helpful for confirmation of diagnosis. It is very important to follow up of such patients for early diagnosis of malignant trophoblastic tumors.

Keywords: Beta hCG, Choriocarcinoma, Gestational trophoblastic disease, Histopathology, Hydatiform mole, Invasive mole

INTRODUCTION

Gestational trophoblastic disease (GTD) represents a spectrum of lesions characterized by an abnormal proliferation of trophoblasts, including complete mole, partial mole, invasive mole, choriocarcinoma, and placental site trophoblastic tumors (PSTT). All forms develop in association with pregnancy. These diseases share several characteristics such as arise in the fetal chorion, produce beta-human chorionic gonadotrophin (β -hCG), and respond well to chemotherapy.¹

Hertig has referred to gestational trophoblastic neoplasms as "God's first cancer and man's first cure".² Broad

variations in the incidence of GTD have been reported in different parts of the world.^{3,4} The various risk factors include endogenous oestrogens, extreme reproductive age, multiparity, past history of spontaneous abortions, high beta carotene diet, high animal fat diet, ABO blood group, environmental toxins, ethnicity, smoking, alcohol consumption, socioeconomic status, etc.⁴

The importance of gestational trophoblastic neoplasms derives not only from the diagnostic and obstetric management problems they bring but also from the association of the complete mole with choriocarcinoma and with much more frequent residual post-evaluation trophoblastic disease.

It is accordingly important to distinguish between complete and partial moles for their separate modes of behavior.⁵

The introduction of cytotoxic chemotherapy has drastically revolutionized the prognosis of gestational trophoblastic tumors with the overall survival rate has jumped from 19%, in the era of surgery alone to 90% and more in the era of chemotherapy.⁶ Thus, the present study on GTD provides an insight into clinicopathological evaluation with its clinical correlation.

METHODS

The present study was a retrospective, cross-sectional descriptive study conducted in the Department of Pathology at Silchar Medical College and Hospital, Silchar over a period of 3 years from January 2017 to December 2019.

A total of 60 cases diagnosed as GTDs on histopathology were included in this study. Detailed clinical history, biochemical estimation of serum assay for beta-hCG level and radiological assessment by USG was done for diagnosis.

Histopathological analysis was carried out on 10% formalin fixed, paraffin embedded tissue sections which were stained with hematoxylin and eosin stain (H and E) and examined under microscope. Samples were collected using stratified random sampling technique. All the datas were analyzed using Microsoft excel 2013 and figures were drawn using Microsoft word 2013.

Inclusion criteria

All clinically diagnosed and histopathologically confirmed cases were included in the present study.

Exclusion criteria

The nongestational tissue was not included.

RESULTS

During our study period, total 20,403 vaginal deliveries were performed in our hospital. Out of which 200 retained products of conceptus and a total of 60 GTD cases were diagnosed histopathologically. The prevalence of GTDs in our study was 0.3% i.e. 3 GTD cases per 1000 deliveries.

Out of 60 cases of gestational trophoblastic diseases, 57 cases (95%) were diagnosed as hydatiform mole (40 cases of complete mole and 17 cases of partial mole). Rest 3% and 2% cases were diagnosed as invasive mole and choriocarcinoma respectively. No single case of PSTT was found (Figure 1). In our study, the age ranged from 18-37 years. Most common age group affected was 20-25 years with 33 cases (55%). In this age group, we

found only hydatiform mole, no other GTD cases were found. This age group was followed by 25-30 years with 19 number of cases (32%) consisting of 18 cases of hydatiform mole and 1 case of invasive mole respectively. We got 4 number of cases in <20 years and >30 years age group.

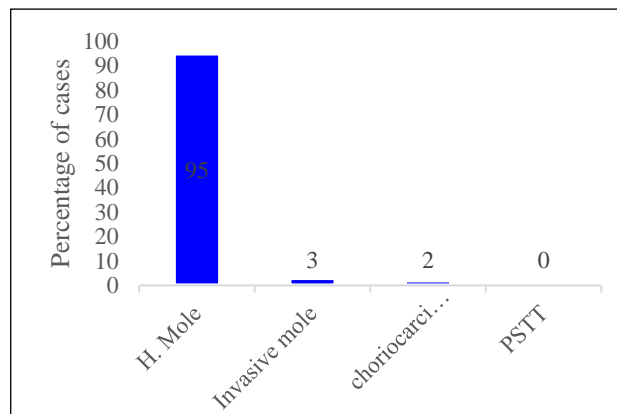


Figure 1: GTD cases according to histopathological diagnosis.

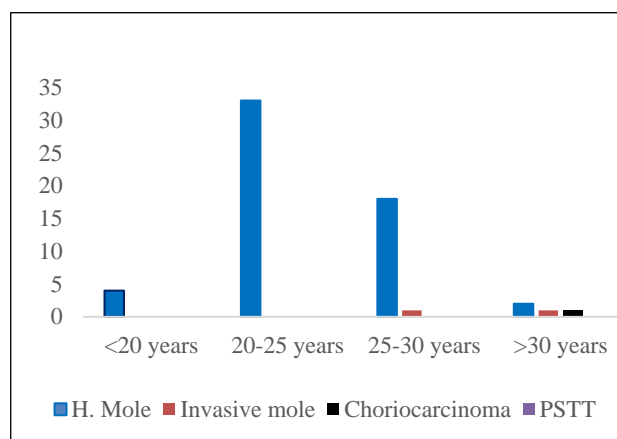


Figure 2: Distribution of GTD cases according to age group.

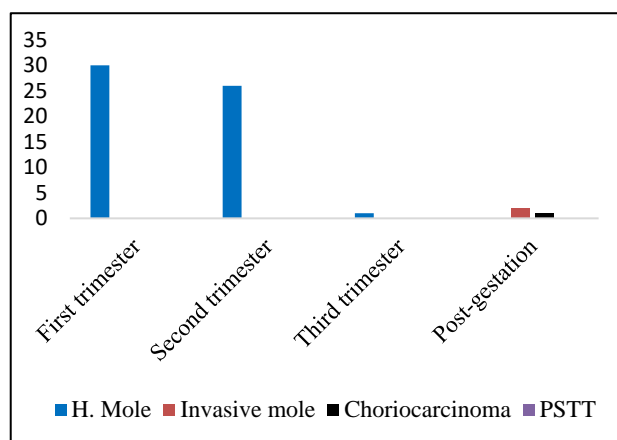


Figure 3: Distribution of GTD cases according to trimester.

We distributed GTD cases according to trimester. We found maximum number of cases in the first trimester. All 30 cases of first trimester were hydatiform mole with no single case detected in the other categories. This trimester was followed by second trimester with 26 cases of hydatiform mole. Single case of hydatiform mole was detected in the third trimester. However, in the post-gestational period, we got total 3 number of cases

consisting of 2 invasive mole and 1 PSTT respectively. Out of 60 GTD cases in our study, most common clinical presentation was bleeding per vagina with 55 cases (91.7%). Most of the H. Mole cases showed this symptom i.e. 91.2% (52 out of 57 cases). This clinical presentation was followed by amenorrhea (88.3%). Here also, the majority of H. Mole cases showed this symptoms (91.2%; 52 out of 57 cases).

Table 1: Various clinical presentations of GTD cases.

Clinical presentation	H. Mole	Invasive mole	Choriocarcinoma	PSTT	Total (%)
Bleeding per vagina	52	2	1	0	55 (91.7)
Amenorrhea	52	1	0	0	53 (88.3)
Pain	42	0	1	0	43 (71.7)
Hyperemesis gravidarum	7	2	1	0	10 (16.7)
Passing grape like vesicle	7	0	0	0	7 (11.7)

Other clinical presentations were pain (71.7%), hyperemesis gravidarum (16.7%) and passing grape like vesicles (11.7%) respectively. Various clinical presentations of GTD cases were shown in Table 1. In the present study, we distributed the various GTD cases according to blood groups of individual patients irrespective of their Rh status. We observed that among

the 4 ABO blood group types, blood group A had the maximum number of cases with 44 cases (73.3%). The second most common blood group was O with 10 cases (16.7%). T

his was followed by blood group B (8.3%) and AB (1.7%) respectively. Distribution of cases according to various blood groups were shown in Table 2.

Table 2: Distribution of cases according to various blood groups

Diagnosis	Blood group (ABO type)			
	A	B	AB	O
H. Mole	42	5	1	9
Invasive mole	1	0	0	1
Choriocarcinoma	1	0	0	0
PSTT	0	0	0	0
Total (%)	44 (73.3)	5 (8.3)	1 (1.7)	10 (16.7)

Table 3: Beta-hCG levels among various GTD cases

Beta hCG levels (mIU/mL)	H. Mole	Invasive mole	Choriocarcinoma	PSTT
50,000-<1,00,000	54	0	0	0
1,00,000-<5,00,000	2	1	0	0
5,00,000-<10,00,000	1	1	1	0
Total (%)	57 (95)	2 (3)	1 (2)	0

In the present study, we distributed GTD cases according to beta-hCG level into three categories i.e 50,000-<1,00,000 mIU/mL, 1,00,000-<5,00,000 mIU/mL and 5,00,000-<10,00,000 mIU/mL respectively. No single case was detected below 50,000 mIU/mL and above 10,00,000 mIU/mL beta hCG level in this study. However, we found 54 cases in the range 50,000-<1,00,000 mIU/mL, all of which were hydatiform mole. We got 3 number of cases each in the range 1,00,000-<5,00,000 mIU/mL and 5,00,000-<10,00,000 mIU/mL respectively. Beta hCG levels of various GTD cases were shown in Table 3. Photomicrograph in the Figure 4

showing chorionic villi in complete mole with predominant stromal edema and marked trophoblastic proliferation in a circumferential pattern.

Mild cytologic atypia is present. There is also presence of cistern formation in the villi.

Photomicrograph in Figure 5 showing partial mole with dual population of villi. There is presence of edematous hydropic villi inclusion and small fibrotic villi. Enlarged villi are irregularly shaped with scalloped borders and presence of mild trophoblastic hyperplasia.

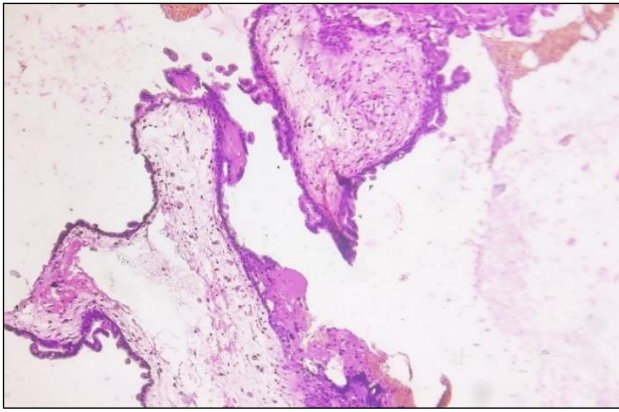


Figure 4: Complete mole (10x, H and E).

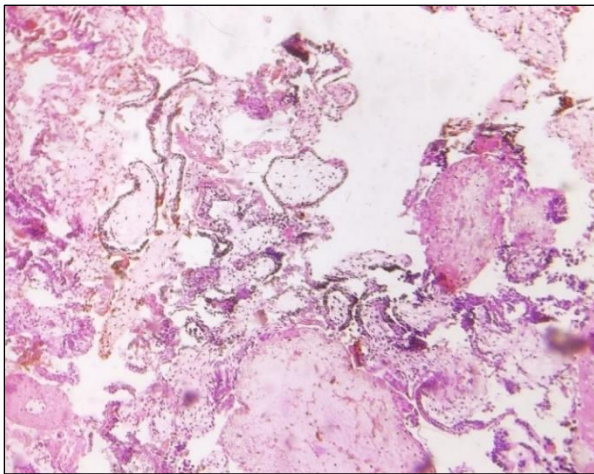


Figure 5: Partial mole (10x, H and E)

DISCUSSION

A gestational trophoblastic disease (GTD) consists of a wide spectrum of cellular proliferation and arises from the placental villous trophoblast. It consists of 4 main clinicopathologic forms: hydatidiform mole (complete and partial), invasive mole, choriocarcinoma, and placental site trophoblastic tumor (PSTT).

Collectively, the term “gestational trophoblastic neoplasia” (GTN) has been applied to the later 3 conditions, which can eventually progress, invade, metastasize, and lead to death if proper treatment has not been instituted.⁷ The incidence of GTD shows a wide geographical variation as a result of differences in methodology, classification of mole, case detection, and definition of the denominator. The incidence of GTD varies widely throughout the world.⁸

In the present study, we observed that a total of 60 cases of uterine GTD. No single case of extra-uterine gestational trophoblastic disease was found. The incidence of GTD in present study was 3/1000 deliveries. Other studies which was done in different parts of the world as well as in India like Yakasai et al, Agrawal et al,

and Koirala et al, showed incidence of GTD was 4.5, 5.17, and 3.94 per 1000 deliveries respectively.⁹⁻¹¹

However, Sekharan et al showed high incidence rate i.e, 5/1000 deliveries.¹² These variations in the incidence of GTD may be due to differences in methodology, classification of mole, case detection.

In our study, we found that hydatiform mole was the most common form of GTD accounting for 57 out of 60 cases (95%). This was followed by invasive mole 2 cases (3%) and choriocarcinoma 1 case (2%) respectively. No single case of placental site trophoblastic tumor was detected in our study. Jagtap SV, also mentioned in their study that hydatiform mole (96.10%) was the most common entity followed by invasive mole, choriocarcinoma, and placental site trophoblastic tumor.¹³ Another study conducted in Nigeria by Mayun et al, also found hydatiform mole was frequently found entity with 54 out of 56 cases.¹⁴

The present study showed cases of GTD ranged from 18 to 37 years. It was most commonly noted in the age group of 20-25 years with 33 cases (55%). Study by Jagtap et al., and Taboo et al, also found peak incidence of GTD in the 20-25 years of age group.^{13,15} The mean age in our study was 24 years among all cases, which showed concordance with other studies by Agrawal et al., and Jagtap et al. noted mean age of 23.9, and 24.5 years.^{10,13} Early occurrence of GTD may be due to early marriage in our study.

We found that most of the GTD cases, (30/60 cases, 50%) were in the first trimester followed by the second trimester with 26 cases (43.3%). Rest cases were in the third trimester and post-gestational period. Jagtap et al, presented in their study that 42 (59.15%) cases were in the first trimester and 29 (40.85%) cases were in the second trimester.¹³ Another study by Taboo et al., had a similar observations.¹⁵ While study by Fatima et al, observed 31.6% cases in the first trimester.¹⁶ Patients usually give a clinical history of vaginal bleeding, which often associated with symptoms of toxemia, and frequently there is a history of passage of grape-like structures per vaginum.⁴

The present study also showed that the most common clinical presentation was bleeding per vagina with 55 (91.70%) cases, followed by amenorrhea with 53 (88.3%) cases and pain abdomen 43 (71.7%) respectively. These findings were similar to results found in other studies like Jagtap et al, Taboo et al, and Berkowitz et al.^{13,15,17}

We have found that patients with blood group ‘A’ had the highest incidence of GTD followed by blood group ‘O’ and least were noted in blood group ‘B’. A study done by Parazzini et al, found that ABO blood groups were associated with the risk of GTD.¹⁸ Many studies mentioned that GTD was more prevalent with blood group A.⁴ Similar results were found in our study.

In the present study, most of the GTD cases showed serum beta hCG levels between 50,000-<1, 00,000 mIU/ml. We observed that the lowest level of beta hCG was 58940 mIU/ml. This level was observed in one partial mole case. Similar findings were noted in other studies.^{13,19} Monitoring serum beta hCG are most sensitive and specific for the diagnosis of the various trophoblast-related conditions, like pregnancy and the GTD. It is important to regularly monitor beta hCG levels during treatment and follow-up to make sure that the condition is improving in women diagnosed with complete or partial mole. Persistently, increasing the level of serum beta hCG is diagnostic of the invasive nature of the disease.

Limitations

The limitation of this study was that it was a hospital based study with small sample size. To validate our findings, further research with bigger sample size is needed.

CONCLUSION

Among all entities of gestational trophoblastic disease, hydatidiform mole was the most prevalent in our study. We have observed that the complete hydatidiform mole was the most common type. The most sensitive and specific for the diagnosis of GTD cases was the serum estimation of beta-hCG levels. For confirmation, histopathological examination with H and E stain is very helpful. Patients should be followed up and carefully monitored for early detection of malignant trophoblastic tumors and to reduce the mortality rate

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Ethical approval: The study was approved by the Institutional Ethics Committee

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