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Original Article

Gestational Trophoblastic Diseases at a Tertiary Care Hospital in Nepal: A Five Years Retrospective Study

Nikita Gautam[1], Ramesh Makaju[1], Dipika Basnet[1], Binita Lama[1], Prem Bahadur Maharjan[1], Sunila Shakya[2]

[1]*Department of Pathology, Dhulikhel Hospital, Kathmandu University Hospital, Dhulikhel, Nepal*

[2]*Department of Obstetrics and Gynaecology, Dhulikhel Hospital, Kathmandu University Hospital, Dhulikhel, Nepal*

ABSTRACT

Introduction: Gestational trophoblastic diseases, because of their diverse presentation and the malignant lesions being associated with recurrence, metastasis, and mortality, early diagnosis is important with the help of ultrasonogram preoperatively, serial Beta human chorionic gonadotropin, and histopathological examination for prompt treatment and timely management of the patients. The study aimed to identify the overall prevalence and relative frequencies of Gestational trophoblastic diseases and to assess the association of different gestational trophoblastic diseases with maternal age, parity, and gestational age.

Materials and Methods: This is a retrospective cross-sectional study conducted for five years from January 2016 to December 2020 in the Department of Pathology, and Department of gynecology and obstetrics of Dhulikhel Hospital, Kavre Nepal. This study included a spectrum of gestational trophoblastic diseases. All the details were obtained from the patient's record file and register book.

Results: Out of 65 cases, the most common was Hydatidiform mole with 59 (90.78%) cases. Bleeding per vagina was the most common clinical presentation. The most commonly affected age group was 21-25 years. Most of the gestational trophoblastic diseases were detected in the first trimester and primigravida.

Conclusion: Any pregnant woman presenting with abnormal uterine bleeding should be evaluated for the presence of underlying Gestational trophoblastic disease. Beta-hCG is a sensitive marker, however, histopathology remains a gold standard modality for the detection of gestational trophoblastic diseases. The judicious use of ultrasonograms and appropriate clinicopathological approach helps the clinician to decide the treatment modalities, especially between evacuation and hysterectomy.

Keywords: Beta-hCG; Gestational trophoblastic disease; Hydatidiform mole

Correspondence:

Dr. Nikita Gautam, MD
Department of Pathology, Dhulikhel Hospital, Kathmandu University Hospital
ORCID ID: 0000-0002-3970-9223
Email: urs.nikki5@gmail.com

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INTRODUCTION

Gestational trophoblastic disease (GTD) is a group of rare pregnancy-related tumors that occurs in 1 in 40000 pregnancies globally. However, the disease is more prevalent among Asians with 0.5-3/1000 pregnancies. GTD is characterized by abnormal trophoblastic proliferation inside the uterus soon following conception resulting from abnormal fertilization. The spectrum of GTD includes heterogeneous groups of interrelated histologically distinct diseases: [1-3]

- Hydatidiform moles (complete, partial, and invasive moles)
- Trophoblastic tumor-like lesions (exaggerated placental site and placental site nodule)
- Gestational Trophoblastic Neoplasia /GTN (Choriocarcinoma, Placental site trophoblastic tumor, and Epithelioid trophoblastic tumor),
- Abnormal (non-molar) villous lesions such as hydropic abortions, chromosomal trisomy syndromes, and placental mesenchymal dysplasia.

Among the spectrum of GTD, Hydatidiform moles are most common and detected in almost 80% of GTD suspected specimens while the incidence of gestational choriocarcinoma (CCA) comprises < 1% of all gynecological malignancies.

Risk factors for gestational trophoblastic disease include chromosomal abnormalities, extreme reproductive age, endogenous estrogens, high beta carotene diet, high animal fat diet, ethnicity, environmental toxins, smoking, alcohol consumption, herbicide exposure, after normal pregnancies, history of miscarriage, ectopic pregnancies or abortion.[5]

To distinguish moles from non-molar gestations, recognition of extravillous trophoblast (EVT), identifications of early moles, and differentiation of different forms of GTD are challenging in Pathology but histopathology is the gold standard to confirm the diagnosis which is extremely important because each GTD has its nature of disease progression. Such as the risk of persistent trophoblastic disease is greater after a complete mole (15-20%) than in a partial mole (<5%). Five percent of complete moles develop metastasis (choriocarcinoma) to the lungs or vagina. Likewise, the recurrence rate of moles in future pregnancies is 1-2% from both the complete and partial moles.[6, 7]

The gestational trophoblastic disease presents with varying clinical and histological features ranging from benign lesions to frank malignancy with evidence of distant metastasis. Early pregnancy vaginal bleeding is the most common clinical presentation along with elevation of B-hCG (usually >10,000 mIU/ml). [4]Though the disease is more prevalent in Asian countries, there is limited information on GTD from Nepal. Till now there is no published data on the magnitude of the GTD problem among women admitted at Dhulikhel hospital. Therefore, the current study will contribute to finding out the prevalence and relative frequencies of different GTDs.

MATERIALS AND METHODS

A five-year retrospective study was conducted in the Department of Pathology at Dhulikhel Hospital - Kathmandu University Hospital from January 2016 to December 2020, following ethical approval by the KUSMS-Institutional Review Committee (IRC no: 81/2021). A total of 65 gestational-related biopsies received from the Obstetrics and Gynecology Department were processed as mentioned below and findings were entered into the record system. Biopsies were fixed in 10% formalin for 24 hours before the tissue was processed for paraffin blocking. Five-micron sections were cut and the prepared slides were stained with H&E stain. The histopathological features were studied in detail by the pathologists and diagnoses were made as per the recent WHO classification of GTD 2014. Information on the patient's age, parity, gestational age in weeks, clinical features, Serum B-hCG levels, and clinical diagnosis were obtained from the patient's record file and register book at the pathology department where all the entries were done on reception of the specimen along with its histopathology form. The needed information was retrieved from the record book at the OB/GYN department. The collected data were entered into Microsoft Excel, and descriptive statistical analysis using Statistical Package for Social Sciences (SPSS) 20.0 software was carried out.

RESULTS

The total number of deliveries during the period of five years from January 2016 to December 2020 was 14,742, out of which 65 cases of GTD were diagnosed. The overall prevalence of GTD in this tertiary care hospital during the study period was 65/14742= 0.004 with its occurrence 4 per 1000 deliveries (0.4% or 1:227 deliveries). Out of the received 65 specimens at the pathology department with the clinical diagnosis of GTD, 62 (95.38%) specimens were obtained from the suction evacuation procedure which includes clinical diagnosis-Hydatidiform mole (complete and partial) along with Hydropic abortus, two (3.08%) salpingectomy specimen of ruptured tubal ectopic pregnancy and one (1.54%) was hysterectomy specimen of choriocarcinoma case. In the histopathological study, the most common GTD was Hydatidiform mole with 59 (90.78%) cases followed by Hydropic Abortus three (4.61%) and Choriocarcinoma with three (4.61%) cases (Table 1).

Table 1: Distribution of Gestational Trophoblastic Diseases according to histopathological examination (N=65)

Types of GTD		No. of cases n (%)
Hydatidiform mole	**Partial**	41 (63.1)
	Complete	18 (27.7)
Hydropic Abortus		03 (4.6)
Choriocarcinoma		03 (4.6)

Among the case of hydatidiform mole, 41(63.08%) cases were of partial mole and 18(27.70%) cases were of complete mole. The most common clinical presentation was bleeding per vagina in 37 (56.92%) cases followed by amenorrhea and passage of grapes-like vesicles in 34(52.31%) and 32(49.23%) cases each, with the combination of one or more symptoms (Table 2). The most commonly affected age group was 21-25 years with 28(43.08%) cases followed by 26-30 years with 14(21.54%) cases (Table 3). Most of the cases of GTD presented in this study were in the first trimester as seen in 44(67.69%) cases and 20(30.77%) cases were in the second trimester. (Table 4).

Table 2: Clinical presentations of women diagnosed with different Gestational Trophoblastic Diseases (n=65)

Clinical presentations[a]	Hydatidiform mole	Hydropic Abortus	Choriocarcinoma	No. of cases n(%)
Bleeding per vagina	32	03	02	37 (56.9)
Amenorrhea	34	00	00	34 (52.3)
Pain	13	00	03	16 (24.6)
Passage of grapes-like vesicles	32	00	00	32 (49.2)
Acute Abdomen	00	00	02	02 (3.1)

a: women presented with one or a combination of symptoms

Table 3: Age distribution of women diagnosed with Gestational Trophoblastic Diseases

Age group (Years)	Partial mole	Complete mole	Hydropic Abortus	Choriocarcinoma	No. of cases n(%)
<20	05	06	00	00	11 (16.9)
21-25	17	09	01	01	28 (43.1)
26-30	08	03	02	01	14 (21.5)
31-35	06	00	00	01	07 (10.7)
>35	05	00	00	00	05 (7.7)

Table 4: Distribution of Gestational Trophoblastic Disease in terms of Gestational age (N=65)

Trimester (Weeks of Gestation)	Partial mole n (%)	Complete mole n (%)	Hydropic Abortus n (%)	Choriocarcinoma n (%)	No. of cases n (%)
First trimester	29 (44.62)	09 (13.85)	03(4.61)	03(4.61)	44 (67.69)
Second trimester	11(16.92)	09(13.85)	00	00	20 (30.77)
Third trimester	01(1.54)	00	00	00	01 (1.54)

In majority of cases(27, 41.54%) beta-hCG levels were between 100,000 to <5, 00,000 mIU/mL followed by <50,000 mIU/mLin 23(35.38%) cases. (Table 5)

Table 5: Distribution of Beta-HCG levels in different GTD

Beta-HCG levels(mIU/mL)	No. of cases (n)	Frequency (%)
<50,000	23	35.38
50,000-<1,00,000	06	9.23
100,000-<5,00,000	27	41.54
5,00,000-<10,00,000	07	10.77
>10,00,000	02	3.08

DISCUSSION

Gestational trophoblastic disease (GTD) is a group of rare pregnancy-related tumors that occurs in 1 in 40000 pregnancies globally. However, the disease is more prevalent among Asians with 0.5-3/1000 pregnancies.[4]

The total number of deliveries during the period of five years from January 2016 to December 2020 was 14,742, out of which 65 cases of GTD were diagnosed. So, the prevalence of GTD in this tertiary care hospital was 4 per 1000 deliveries (0.4% or 1:227 deliveries). A similar study conducted by Vaithy KA et al, Jagtap SV et al, and Koirala A et al showed an incidence of 4 per 1000 deliveries.[4,5,8] However, the incidence of GTD varies significantly across the world with 0.4 per 1000 birth in the United States of America, 12.5 per 1000 births in Taiwan to 9.46 per 1000 patients in Gambia, West Africa. [8,9] Likewise, in our country, Nepal, considering the data of various hospitals within the Kathmandu valley, the incidence of GTD is ranging from 2.8 to 5.1 per 1000 deliveries.[8]

The most common GTD was Hydatidiform mole with 59 (90.78%) cases followed by Hydropic Abortus and Choriocarcinoma with three (4.61%) cases each. Among the case of hydatidiform mole, 41(63.08%) cases were of partial mole and 18(27.70%) cases were of complete mole. This was similar to the study conducted by Vaithy KA et al, where out of 160 cases of GTD, 92(57.5%) cases were of partial mole and 32(20%) cases of complete mole, 13(8.1%) cases of choriocarcinoma and 17(10.6%)cases of Placental site trophoblastic tumor.[4] Likewise, in a study conducted by Jaiswal P et al, out of 141 cases, 110 (71.0%) were partial mole, 15(9.7%) complete mole, 12(7.7%) invasive mole, three (1.9%) persistent mole and one (0.6%) choriocarcinoma.[10]However, this was in contrast to the study conducted by AuroreF et al, Veeraraghavan G et al, Koirala A et al, Singh J et al where complete mole outnumbered partial mole.[2,3,8,11]

With regards to combinations of one or more clinical manifestations, bleeding per vagina was the most common clinical presentation with 37 (56.92%) cases followed by amenorrhea and passage of grapes-like vesicles with 34(52.31%) and 32(49.23%) cases each. The observations are in concordance with the findings done by Vaithy KA et al, Jagtap SV et al, Koirala A et al, Anyanwu M et al and Pritam A et al. [4,5,8,9,12]

The present study showed cases of GTD ranged from 17-41 years. The most commonly affected age group was 21-25 years with 28(43.08%) cases followed by 26-30 years with 14(21.54%) cases. Above 35 years, we noted 05(7.69%) cases. The findings were similar to the studies conducted by Jagtap SV et al, with the age ranging from 19-38 years, the most affected age group was 20-25 years with 44 (57.14%)cases.[5]Similarly, 20-30 years

the most commonly affected age group in the study conducted by Pritam A et al.[12]Unlike in a study conducted by Singh J et al, GTD was common at extreme of reproductive ages mostly in more than 35 years of age with 22 (44%) cases and less than 20 years of age with 17 (34%) cases.[11] This was consistent with findings in the study conducted by Nizam and Jaffer. [11]

The mean age of presentation in this study was 25.4 years which was in concordance with other studies by Jagtap SV et al and Veeraraghavan G et alwith 24.5, and 23.5 years respectively.[2,5] However, a study conducted by Koirala A et al showed a mean age of 22 years.[8]Early age of marriage may be related to early occurrence of GTD in this region.[5]

In context to the gestation period, GTD was commonly detected in the first trimester as seen in 44(67.69%) cases and 20(30.77%) cases were in the second trimester. Singh J et al and Pritam A et al in their study of 50 and 37 cases respectively reported the first and mid-second trimester to be the most common gestational period of presentation.[11,12] This was in discordance with the study conducted by Koirala A et al in their study of 64 cases, which reported the second trimester to be the most common gestational period of presentation.[8] Increase availability of ultrasonogram, gynaecological and histopathological examinations has helped in the early detection of disease.

Similarly, the cases of GTD were more common in a primigravida with 28(43.08%) cases with decreasing frequencies in subsequent gravida, second gravida, third gravida, fourth gravida, and fifth gravida as 22(33.85%) and nine(13.85%), four(6.15%), two(3.07%) cases respectively. These findings were similar to various studies conducted by Vaithy K et al, Jagtap SV et al, Tanwar RK et al.[4,5,7] However, this was in contrast to the study conducted by Anyanwu M et al and Pritam A et al, where GTD was more common in multigravida with 16 (80%) cases and 23 (62.16%) cases respectively.[9, 12]

In this study, suction and evacuation were performed in almost all cases of hydatidiform moles and hydropic abortus, whereas a hysterectomy was done in one case of choriocarcinoma. However, two patients presented with acute abdomen. Laparotomy was done for suspicion of ruptured ectopic pregnancy. Right salpingectomy was performed and a histopathological examination of the fallopian tube revealed choriocarcinoma in both cases. This was similar to the study conducted by Veeraraghavan G et al.[2] In their study, the patient presented with suspicion of ruptured ectopic pregnancy, however, histopathological examination failed to reveal molar tissue. Post-operatively, after 1 month, the patient had rising beta-hCG levels so single-agent chemotherapy was started. With a persistent rise in beta-hCG levels and multiple pulmonary nodules on the CT chest, metastasis from choriocarcinoma was diagnosed and the patient was treated with multi-agent chemotherapy following which beta-hCG values returned to their baseline levels. Similarly, a patient presented with ectopic pregnancy was diagnosed to have choriocarcinoma on histopathological examination in the study conducted by Tanwar RK et al. [7]

Among the cases of GTD, the lowest beta-hCG level was 46.84 mIU/mL and a majority of cases27(41.54%) had beta-hCG levels between 100,000 to <5,00,000 mIU/mL followed by <50,000 mIU/mL in 23(35.38%) cases. This was in contrast to the study conducted by Pritam A et al where serum beta-hCG levels were between 50,000-100,000mIU/mL in 22(59.46%) cases followed by <50,000 in 11(29.73%) cases.[12] Likewise, a study conducted by Antaratani RC et al, showed serum beta-hCG levels to be >200,000, <50,000, 1,00,000-200,000, and 50,000-100,000 mIU/mL in 51.61%, 22.58%, 14.51% and 11.29%cases respectively.[13]

CONCLUSIONS

The present study provides the prevalence of Gestational trophoblastic disease among women admitted to the maternity department of a tertiary-level hospital. Among the diagnosed case of GTDs, Hydatidiform mole was the most common. The most commonly affected age group was 21-25 years of age, mostly detected in primigravida during the first trimester. Among the Hydatidiform mole, the partial mole was the commonest. The most common clinical presentation was bleeding per vagina with the combination of one or more symptoms. In the majority of cases, beta-hCG levels were between 100,000 to <5, 00,000 mIU/mL. The multifocal approach in its diagnosis such as increasing the use of ultrasonography in the first trimester and easy availability of beta-hCG helps in the early identification of the disease. Histo-morphological study remains the gold standard means for diagnosis and identification of the spectrum of GTD which guides the clinicians further in proper planning of treatment modalities to initiate appropriate therapy and timely management of the patient as well as to predict the prognosis of GTD.

RECOMMENDATION

Baseline beta-hCG levels are required to compare with post-evacuation values in the case of molar pregnancies. As per FIGO recommendations, weekly beta-hCG levels are to be monitored till it becomes undetectable post-evacuation. This is followed by monthly monitoring of beta-hCG levels for 6 months and then every 2 months for further 6 months. Pregnancy should be avoided for 6 months post normalization of beta-hCG levels so oral contraceptive pills are advised as trophoblastic neoplasia is fatal unless managed timely and appropriately with chemotherapy.

LIMITATIONS OF THE STUDY

As it is a small-scale retrospective study, certain socio-demographic factors such as blood group, ethnicity, socio-economic status, and occupation could not be assessed because of a lack of information in the medical records. Cytogenetic studies and molecular analysis were not performed due to limited resource facilities. Despite the limitations, this study provides baseline information on Gestational trophoblastic disease in our settings and enlightens us with further research that could be carried out in the future.

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REFERENCES

1. Hui P, Baergen R, Cheung A.N.Y et al. Gestational trophoblastic disease. In: Kurman RJ, Carcangiu ML, Herrington CS, Young RH: WHO Classification of Tumors of Female Reproductive Organs. Fourth Edition. IARC: Lyon; 2014.p.155-167.
2. Veeraraghavan G et al. A 3 year retrospective study on gestational trophoblastic disease in a government obstetrical tertiary care centre. Int J Reprod Contracept Obstet Gynecol.2 016; 5(12):4405-9. Crossref
3. Aurore F, Khadidja B, Ginette R et al. Gestational trophoblastic disease in Switzerland: retrospective study of the impact of a regional reference centre. Swiss Med Wkly.2021; 151:w20406. Crossref
4. Vaithy K et al. Analysis of histomorphological spectrum of gestational trophoblastic diseases: Clinico-Radio-Pathological correlation at a tertiary care teaching hospital. IP Journal of Diagnostic Pathology and Oncology. 2021; 6(1):62-8. Crossref
5. Sunil Vitthalrao Jagtap et al. Gestational Trophoblastic Disease-Clinicopathological Study at Tertiary Care Hospital. Journal of Clinical and Diagnostic Research.2017; 11(8):27-30. Crossref
6. Heller DS. Update on the pathology of gestational trophoblastic Disease. APMIS 2018; 126:647-54. Crossref
7. Tanwar RK, Saxena B, Garg Radha, Goyal Harsh et al. Gestational Trophoblastic Neoplasia: A Retrospective Study of 23 Cases. Cancer Research Journal.2020; 8(3):45-50. Website
8. Koirala A, Khatiwada P, Giri A, Kandel P, Regmi M, Upreti D. The Demographics of Molar Pregnancies in BPKIHS. Kathmandu Univ Med J. 2011; 36(4):298-300. Crossref
9. Anyanwu M, Bah K. A cross sectional descriptive study on hydatidiform mole at Gambian tertiary hospital. MOJ Women's Health. 2020; 9(1):1-5. Crossref
10. Jaiswal P, Shrestha S, Dwa Y, Manandhar S. Correlation of ultrasound imaging with histopathological findings in gestational trophoblastic disease. Journal of Patan Academy of Health Sciences. 2020; 7(3):41-46. Crossref
11. Singh J, Sharma S, Kour K, Bashir S. Prevalence of molar pregnancy (a three-year retrospective study) in a tertiary care hospital. Annals of Applied Bio-Sciences. 2016; 3(1): 34-6. Crossref
12. Pritam A, Singh P, Sinha A. Analysis of Molar Pregnancy in a Tertiary Care Centre of Muzaffarpur, Bihar: A two years Retrospective Study. Journal of Medical Science and Clinical Research. 2019; 7(2):715-9. Crossref
13. Antaratani RC, Shruthi M. Study of gestational trophoblastic diseases at a tertiary care hospital in India. Int J Reprod Contracept Obstet Gynecol. 2018; 7(4): 1622-7. Crossref