

## Evaluation of clinical profile, management and outcomes of molar pregnancy

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### Abstract

**Introduction:** Hydatidiform mole is benign form of gestational trophoblastic disease characterized by hydropic swelling of the chorionic villi and proliferation of the trophoblasts. The majority of Hydatidiform mole is cured by simple surgical intervention. The disease can re-occur. The patients are followed up with serial serum BhCG till the normal level is achieved. With raised, plateau level of serum  $\beta$ -hCG values, persistent GTD is diagnosed. So the proper monitoring and follow up of gestational trophoblastic disease is a must. It reduces both the morbidity and mortality of the women. This study details the clinical profiles and outcome of molar pregnancy.

**Methods:** This is an observational study conducted in Department of Obstetrics and Gynaecology at Tribhuvan University Teaching Hospital from 1st May 2015 to 30th April 2017(2 years). Patients with the provisional diagnosis of molar pregnancy during the study period were included. After all required investigations, cases were managed according to the diagnosis. And were followed up with serial serum B- hCG. Further required treatment was given according the histopathological diagnosis.

**Results:** Total 46 cases of gestational trophoblastic disease (GTD) were diagnosed and it accounted for 4.9 per 1000 deliveries. Majority of patients belonged to age group of 20-40 years, presented during second trimester with amenorrhoea and per vaginal bleeding. Among these patients 93% (n=43) had suction evacuation, 5 % (n=2) had total abdominal hysterectomy with bilateral salphingo ophorectomy (TAH BSO), 2 % (n=1) had suction evacuation and laparotomy with untwisting of twisted theca luteal cyst. Thirteen patients developed persistent gestational trophoblastic tumour (PGTT) and six patients were diagnosed as gestational trophoblastic neoplasia (GTN) and managed with multiagent chemotherapy.

**Conclusions** Any deviation from normal norms in pregnancy or post delivery, gestational trophoblastic disease has to be thought of. Along with proper diagnosis and management, counseling regarding follow up should also be emphasized, which not only reduces morbidity but also reduces the mortality.

**Keywords:** Beta hCG, GTD, Choriocarcinoma, PGTT

### Introduction

Gestational Trophoblastic Disease (GTD) refers to a wide spectrum of interrelated conditions ranging from benign [Complete molar pregnancy (CMP) or Partial molar pregnancy(PMP)] to malignant(Invasive mole, choriocarcinoma, Placental site trophoblastic tumour, Epitheloid tumour) forms.<sup>1</sup> Hydatidiform mole is an abnormal pregnancy characterized by the presence of hydropic swelling of the chorionic villi and proliferation

of the trophoblasts.<sup>2</sup> It is an important pregnancy related disorder with incidence of 1 in 400 in Asia and Latin America.<sup>1-2</sup>

The majority of benign trophoblastic diseases are cured by simple surgical intervention. And then followed up with serial serum B hCG. The diagnosis of persistent GTD is made usually on raised serum  $\beta$ -hCG values. If the serum levels of  $\beta$ -hCG during the follow up interval levels plateau for 3 or more consecutive weeks,

rise, or persist for eight weeks following evacuation, a diagnosis of persistent GTD is made.<sup>2</sup> The diagnosis of GTN is made histopathologically. Unlike other gynecology malignancy, fertility can be preserved and normal pregnancy can be anticipated. However the disease can re-occur and proper monitoring and follow up of cases is must.

# Methods

This is an observational study, conducted in Department of Obstetrics and Gynaecology in Tribhuvan University Teaching Hospital from 1<sup>st</sup> May 2015 to 30<sup>th</sup> April 2017(2 years). Patients with provisional diagnosis of molar pregnancy were included during the study period after informed consent. Suction and evacuation was done and tissue sent for histopathological examination. Serum B hCG was sent pre-evacuation and subsequently after 24 hours and weekly then after. Patients were followed up weekly till three consecutive serum B hCG normalizes. If level of hCG platued or rose or persisted over the period of 8 weeks then it was considered as PGTT. Gestational trophoblastic neoplasia were managed according to treatment protocol. Low risk group with single agent and high risk group with multi agent chemotherapy. The clinical profile, management and outcome of molar pregnancy were recorded in preformed performa sheet. Data were collected and analyzed using SPSS version 20.

# Results

During the study period 9325 deliveries were conducted at our center and 46 cases of GTD were diagnosed which comes out to 4.9 per 1000 pregnancies.

**Table1. Age distribution of patients with GTD (n=46)**

<19 yrs	3	7%
20-40yrs	37	80%
>40yrs	6	13%

Mean age was 29 yrs. The disease was mostly seen on women from Mongolian community constituting 42% of total study population. Forty-eight percentage of patients (n=22) were primi gravid and fifty two percentage (n=24) were multi gravid. Among them, 39% had history of one abortion and 13% had two or more abortions.

**Table 2.Period of gestation at presentation**

<12wks POG	16	35%
13-20wks POG	27	59%
>20wks POG	3	7%

Mean age of presentation is 14 weeks POG. Amenorrhea and vaginal bleeding were the most common presentations.

**Table 3.Size of theca luteal cyst(n=46)**

Not detected	42	91%
<6cm	1	2%
>6cm	3	7%

Theca luteal cysts were not detected clinically as well as radiologically in forty two patients (91%).

Thirteen patients (28%) with PGTT had larger uterine size (more than four weeks) than period of gestation with variable level of serum B hCG level.

Ten patients (28%) had serum B hCG level >1,00,000 miu/ml ( 1-chorioca,1-invasive mole,3-PGTT,5-CMP). Two patients with CMP had B hCG level 50,000-1,00,000 miu /ml and one patient with PMP had serum B hCG <50,000 miu/ml. All were diagnosed as persistent trophoblastic disease, concluding larger uterine size indicate more chances for persistant disease than do levels of B-hCG.

**Table 5 .Treatment modalities**

Suction Evacuation	43	93%
TAH BSO	2	4%
Laparotomy and SE	1	2%

Repeat evacuation due to retained molar tissue was done only in one patient.

**Table 5 .Histopathology**

Complete mole	30	66%
Partial mole	10	21%
Choriocarcinoma	5	11%
Invasive mole	1	2%
PSTT	-	-

**Table 6. Chemotherapy**

None	33	69%
Single	7	15%
Multi	6	13%

Out of forty-six patients of gestational trophoblastic disease, thirty three (69%) did not require further interventions after evacuation. Thirteen patients (28%) were managed with chemotherapy. There were 5 cases of choriocarcinoma, three of them had antecedent term vaginal delivery and the longest last-delivery to disease diagnosis interval being 2.5 years, one had history of manual vacuum aspiration for missed abortion and one had history of molar pregnancy. Both of them had irregular pervagial bleeding.

Eighteen percent of patients (n=7) were in low risk group, managed with single agent chemotherapy and 15% of patients (n=6) were in high risk group, managed with multi agent chemotherapy regime. Among high risk group five (5/6) were choriocarcinoma, one (1/6) was invasive mole, all were diagnosed histopathologically. Among the five cases of choriocarcinoma, two (2/5) had history of receiving multiagent chemotherapy previously and both presented to our institute with per rectal bleeding, seizures and shortness of breath. Among them one patient (1/5) left the hospital against medical advice & the other patient (1/5) had brain metastasis with right eye involvement. She was referred to oncologist, later followed up and found to be improved after treatment. Rest three cases (3/5) were managed with multiagent chemotherapy and had favourable outcome. The low risk regime consists of Methotrexate and folinic acid and high risk regime consist of Etoposide, Methotrexate, Actinomycin, Cisplatin and Vincristine.

## Discussion

The purpose of the study was to find the occurrence of gestational trophoblastic disease and also to explore the clinical behavior, complications and management of the disease at our center. The marked difference in incidence of hydatidiform mole among countries is widely acknowledged, and attributed to genetic, environment and host-related factors. Literature shows various incidences in different countries, ranging from 11.5/1000 deliveries in Indonesia to less than 1/1000 deliveries in the US. Incidence appears much higher in Asia, Africa, and Central America than in the US, Europe, or Australia.<sup>3</sup>

At our center, there were 46 cases of GTD among 9325 deliveries in the study period of two years. The occurrence was 4.93 per 1000 deliveries. The disease was more common in Mongolian community in Nepalese society. Sivaneuratnam et al. reported the incidence of molar pregnancy as 2.8 per 1000 deliveries and had shown that the disease is common among Chinese compared to others like Malayas and Indian community in Malasia.<sup>4</sup>

Maternal age is the most consistent risk factor for hydatidiform mole in every region and ethnic group in which it has been studied, with most studies showing a significant increase in risk in women delivering above age 35 and a further 10-fold increase beyond age 40. The available evidence suggests that H. mole arises as a consequence of defective ova. It is premature in young and postmature in old ages.<sup>5</sup> However, in this study maximum number of patients were from young age group between 20-40 years (77%, n=30) and this was consistent with the study by Dinesh kumar et al.<sup>6</sup> As maximum number of conception occur during reproductive age so as the maximum number of gestational trophoblastic disease occur in young age group.

Amenorrhea, vaginal bleeding and pain in lower abdomen were common presentation as in study by Mahrukh Fatima et al.<sup>7</sup> Nausea was present in only two women. Studies have shown hydatidiform mole is more common in primigravidas.<sup>8</sup> However here not much difference was noted between primigravida 48% (n=22) and multigravida 52% (n=24). Patient of para one (P1) and above were affected more in comparison with nulliparous. Tariq Y et al. had found maximum cases of in Para 1-4, about 42%.<sup>9</sup>

The reported obstetrics risk factor for both CMP & PMP is history of spontaneous abortion, giving women a 2 to 3 fold increased risk of a molar pregnancy compared to women without history of miscarriage.<sup>10</sup> Fifty two percent patients had one and more abortions. Among 46 cases of GTD, the range of parity was from 0 to 8. Gravida above 5 apparently is considered as a poor prognostic sign.<sup>11</sup>

It is known that molar pregnancy can recur.<sup>11</sup> Following a single CHM or PHM, the overall re-occurrence risk of HM in a subsequent pregnancy is about <2%.<sup>12-14</sup> The risk increases to 15–23% after  $\geq 2$  consecutive CHMs. Within this group there is likely to be a proportion of women who have familial recurrent HM for whom the

chance of a successful pregnancy out-come is likely to be very much lower.<sup>15-17</sup> However, in this study one case (2%) out of 46 had history of one previous molar pregnancy which comes in same range in study conducted by Sebire et.al.<sup>18</sup>

In this study majority of patients (46%) had presented in 2nd trimester. Koirala et al in their study of 64 cases reported 2nd trimester as the most common period of presentation.<sup>19</sup> This is probably due to increase in gynaecological, sonographic and histopathological services over the years which have led to early recognition of the molar pregnancy.

Excessive uterine size is one of the classic signs of GTD. It is noted that patient with uterine size four weeks larger than date and presence of theca lutein cyst of >6 cm have a 50% risk of persistent disease.<sup>20</sup> In our study, 28% (n=13) patients had uterine size  $\geq 4$  weeks larger than date and three (3/13) were diagnosed as PGTT (2 cases of CMP & 1 case of PMP) & received single chemotherapy. Three (3/13) patients had gestational trophoblastic neoplasia diagnosed histopathologically and managed with multiagent chemotherapy. However, larger uterine size in seven patients (7/13) was normal after evacuation and follow ups.

Palpable theca luteal cyst is common in GTD<sup>21</sup> and they mostly regress spontaneously within 8 weeks. Different studies have quoted the incidence of theca lutein to be between 20 - 46% with molar pregnancy.<sup>22-23</sup> However this study shows only 9% (n=4) had palpable theca lutein cysts, this can be due to patients presenting during earlier weeks in second trimester. Nowadays larger sizes of theca lutein cysts and larger uterine sizes have become less common, may be due to the advent and frequent use of ultrasound. Mungan C et al. had reported presence of theca lutein cysts in about 39% of the cases; none of them needed emergency surgery for torsion. This percentage was similar to another series from Turkey, however one patient needed emergency surgery for torsion.<sup>24</sup> In our study, we found one patient of MP with acute abdomen, and suction evacuation followed by laparotomy with untwisting of right sided theca lutein cyst and partial untwisting of left theca cyst done.

Suction evacuation was preferred method of evacuation of GTD, independent of uterine size. Ninety three percentage (n=43) of patients were managed with suction evacuation in present study. Hysterectomy is an alternative to suction evacuation if child bearing has

been completed. The adnexa may be left intact even in presence of theca lutein cysts. In addition to evacuating the molar pregnancy hysterectomy provides permanent sterilization and eliminates the risk of local myometrial invasion as a cause of persistent disease. Four percent of patients had elective hysterectomy with bilateral salphingoophorectomy. Because of potential risk for metastatic disease even after hysterectomy, the risk of post molar GTN still remain at 3-5% there by requiring continued hCG follow up.<sup>25</sup>

After evacuation, most molar pregnancies required no additional treatment. Mc Neishia et al. had shown in about 15% of complete moles and 1% of partial moles, the abnormal trophoblast cells persist and proliferate, requiring further treatment primarily with chemotherapy, which produces cure rates approaching 100%.<sup>26</sup> In our study, 22% of CMP and 10% of PMP required further treatment with chemotherapy. Similar finding were noted in the study done by Tasneem H et al.<sup>26</sup>

Gestational trophoblastic neoplasias (GTN) are no longer a grave threat it used to be. The advent of chemotherapy has drastically reduced the mortality rate. The survival rate approaches 100% in low risk GTN (WHO score  $\leq 6$ ). Chemotherapy has been so effective that the survival rate for high risk GTN (WHO score  $\geq 7$ ) is more than 90% even in the presence of distant metastases.<sup>27</sup> When managed appropriately, mortality can be significantly low. However GTN is notorious for its late recurrence. In this setting, the post diagnostic follow up and the importance of beta- hCG levels cannot be overemphasized.<sup>28</sup> However in a populous country like Nepal, follow-up could prove to be a challenge.

## Conclusions

Post diagnostic work up of gestational trophoblastic disease should involve close monitoring and follow up of patients with beta-hCG values, clinical presentation as any abnormal per vaginal bleeding following any gestational events (delivery, abortions, ectopic pregnancy, molar evacuation) should be properly evaluated. Suspicious pregnancy event should be followed up with beta-hCG values at 6 weeks postpartum. In cases of gestational trophoblastic neoplasia, WHO/ FIGO scoring should be done and managed according to the risk assessment. The importance of contraception and follow up should be emphasized to patients. In order to reduce the rate of defaulters, a national level registry could be started to monitor the patients follow



up, because trophoblastic neoplasia could prove to be rapidly fatal, unless managed appropriately with chemotherapy.

**Conflict of interest:** None declared

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