

# A Study on Hydatidiform Mole

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**Abstract:** ***Introduction:** The pre malignant form of gestational trophoblastic neoplasia is known as molar pregnancy (hydatidiform mole). Hydatidiform mole includes complete mole and partial mole. **Aims And Objectives** To calculate incidence, socio - demographics, clinical profile of hydatidiform mole. of hydatidiform mole and study pattern of normalization of serum  $\beta$  hCG levels. **Methodology:** This study was a Prospective observational study conducted from September 2019 to October 2021 (2 years). **Results:** The incidence of the hydatidiform mole during the study period in the institution was 1.58 per 1000 pregnancies. Apart from history of amenorrhoea, vaginal bleeding (60%) was the most common presenting symptom. 16 (32%) cases did not have any symptoms and were diagnosed on routine antenatal ultra sonography. (36%) of the study group were Primigravida. 80% (40) had ultrasonographic finding of complete mole and 20 % had partial mole. Majority 68 % (34) presented in the first trimester (<12 weeks). In the present study majority (52%) were of the blood group B positive. The mean time taken was  $7.62 \pm 2.49$  weeks to attain normal serum  $\beta$  hCG levels from the pre evacuation values. Histopathology gave definitive diagnosis in all cases. Prevalence of Gestational trophoblastic neoplasia in our study was 0.06. **Conclusion:** History of amenorrhoea with bleeding per vaginum and size of uterus more than period of amenorrhoea should raise suspicion of H. mole though asymptomatic cases do exist. Obstetric ultrasonography and raised serum  $\beta$  hCG are diagnostic for Hydatidiform mole. Time taken for  $\beta$  hCG levels to drop down to normal was more in cases of complete mole than partial mole.*

**Keywords:**  $\beta$  hCG, Molar pregnancy, Complete Mole, Partial Mole

## 1. Introduction

The pre malignant form of gestational trophoblastic neoplasia is known as molar pregnancy (hydatidiform mole).<sup>[1, 2, 3]</sup> In an epidemiological study on GTD in a North Indian population, the incidence of GTD was found to be one per 967 Pregnancies.<sup>[4]</sup> Extremes of maternal age and preceding molar pregnancy have surfaced as risk factors, in addition to other established risks such as prolonged OCP uptake, protein, iron and folate insufficiency and so on.<sup>[5 - 9]</sup>

Amenorrhoea, vaginal bleeding, abdominal pain and the passing of grape like vesicles are all symptoms of hydatidiform mole. Anemia, hyperemesis gravidarum, abnormal uterine size, early onset pre - eclampsia, thyrotoxicosis, and abdominal distension due to theca lutein cysts are some of the other symptoms. Important complications include haemorrhage, sepsis, perforation, and choriocarcinoma.<sup>[10]</sup> Molar pregnancies are typically discovered during dating scans, verified by  $\beta$  - hCG levels and eventually confirmed by histopathology findings. Suction evacuation can treat the majority of cases.<sup>[11]</sup> Serial  $\beta$  - hCG levels after molar evacuation are required to detect trophoblastic sequelae (invasive mole or choriocarcinoma), which occur in 9 to 20% of individuals with complete moles following molar evacuation, while partial moles result in GTN in less than 3% of instances.<sup>[12]</sup>

A study was conducted in our institute in the year 2007 - 2009. It showed a high incidence of GTD of 2.5 per 1000 deliveries. Recently, we have noticed a rise in the high risk

group of GTN requiring multi drug chemotherapy reporting to the Cancer unit of our department in our institute. GTN is one of the gynaecological malignancies which has good prognosis if detected and treated well in time. . Hence it becomes prudent to study molar pregnancies in our tertiary care centre which caters surrounding 10 - 12 districts in our state. Therefore this study is being done in our institute.

### Aims and Objectives

- To study the incidence of hydatidiform mole in our tertiary care centre.
- To study socio - demographics of hydatidiform mole.
- To study clinical profile associated with hydatidiform mole.
- To study pattern of normalization of serum  $\beta$  hCG levels.

## 2. Materials and Methods

This study was a Prospective observational study conducted from September 2019 to October 2021 (2 years). All women who were diagnosed with hydatidiform mole sonologically and or clinically reporting to our tertiary care centre were included in the study.

### Inclusion criteria:

Women diagnosed with hydatidiform mole on clinical and / or obstetric sonography and who were willing to give written consent to participate in the study.

**Exclusion criteria:**

Choriocarcinoma, Invasive mole, Women not willing to participate in study.

Approval was obtained from the ethical committee of the hospital. Before recruiting an eligible patient in the study, an informed consent was taken. On admission history, clinical examination, Routine investigations, serum  $\beta$  - hCG investigated. The patients were subjected to USG if not previously done. Chest X ray was done in all cases. Written valid informed consent taken. Preoperative antibiotics were given. Vaginal PGE1 is used for cervical priming. Intravenous sedation + paracervical block Anaesthesia was used preferably or saddle block anaesthesia was given. Route of anaesthesia was decided by anesthetist. Suction and evacuation was done in all patients by MVA (Manual vacuum aspiration) syringe. Oxytocin infusion (20 IU) started during evacuation helps to minimize bleeding. Specimen was sent for histopathological study.

Blood transfusion was done if required before surgery, intraoperatively or in the post - operative period. Anti - D was given to Rh negative women as 50 mcg if gestational age is less than 12 weeks and 300 mcg if gestational age is more than 12 weeks.

The serum  $\beta$  hCG was repeated 48 hrs after evacuation.

Women was given injectable antibiotics for 3 days. Monitoring was done to look for any complications of molar pregnancy. Patient with no complications was discharged on day 4 with oral antibiotics.

At the time of discharge, the patients were counselled regarding the need for avoiding pregnancy was stressed and need for follow up and use of contraception for the entire period of follow up. Barrier contraceptives advised till serum  $\beta$  hcg levels becomes normal there after advised low dose oral contraceptive pills.

Follow up was done with weekly  $\beta$  hCG until normal for consecutive 3 weeks followed by monthly determination until the levels were normal for 6 consecutive months. The normal level of  $\beta$  hCG was taken as less than 10 mIU/L. Serum  $\beta$  hCG was tested preferably from the same laboratory everytime.

Considering lower socio - economic status population in all, follow up was done by serum  $\beta$  hCG levels till it becomes normal and thereafter UPT kit was used for follow up. Negative UPT signifies levels are less than 10 mIU/L. Patients who are not able to visit our tertiary care centre were telephonically contacted and advised to get it tested from nearby laboratory and inform the report. The time taken to achieve the first normal  $\beta$  hCG after evacuation was noted.

GTN was diagnosed during follow up either on the basis of a rise in serum  $\beta$  hCG levels or plateau of  $\beta$  hCG lasts for four measurements over a period of 3 weeks or longer or histopathology or with evidence of metastasis. Patients who develop GTN were referred to cancer hospital affiliated to our tertiary centre for further treatment and management.

**3. Results and Observations**

Total cases studied were 50. Incidence of hydatidiform mole in our tertiary care centre is **1.58/1000 pregnancies**

**Table 1:** Distribution of Socio - Demographics Variables

Age	Frequency (N= 50)	Percentage
<=20 yrs	20	40%
21 – 25 yrs	16	32%
26 - 30 yrs	11	22%
>30 yrs	3	6%
Residency	Frequency	Percentage
Urban	30	60%
Rural	20	40%
Educational Status	Frequency	Percentage
Primary	14	28%
Secondary	25	50%
Graduate	11	22%
Religion	Frequency	Percentage
Hindu	28	56%
Muslim	22	44%
Socioeconomic Status	Frequency	Percentage
Upper middle class	8	16%
Lower middle class	26	52%
Upper lower class	12	24%
Lower class	4	8%
GRAVIDA	Frequency	Percentage
G1	18	36%
G2	15	30%
G3	7	14%
G4	6	12%
G5 or more	4	8%
Antecedent Pregnancy	Frequency	Percentage
Prior full - term delivery	24	48%
Previous abortion	8	16%

Amongst the case, 40% belonged to age less than 20 years, 60 % belonged to urban region, 50 % had secondary educational status and 52% belonged to lower middle socioeconomic status and 36% cases were primigravida.

**Table 2:** Distribution according to clinical symptoms

Clinical Symptoms	Frequency	Percentage
Bleeding PV	30	60%
Pain Abdomen	28	56%
Passage of grape like vesicles per vaginum	6	12%
Vomiting	7	14%
No symptoms (Diagnosed on routine antenatal USG)	16	32%

80% (40) had ultrasonographic finding of snowstorm appearance s/o complete mole. Theca lutein cysts were found in 5 (10%) cases and all were associated with complete mole. USG findings of cystic spaces within the placenta & gestational sac which was either empty or containing growth retarded fetus s/o partial mole was found in 20% (10) cases.

**Table 3:** Distribution of study population according to duration of pregnancy

Gestational Age at the Time of Diagnosis (LMP) WKS	Complete Mole (N=40) (%)	Partial Mole (N=10) (%)
<=9 weeks	9 (18%)	4 (8%)
9.1 – 12.6 weeks	18 (36%)	3 (6%)
13.1 - 20 weeks	9 (18%)	3 (6%)
>20 weeks	4 (8%)	--

In the present study (68%) presented with symptoms in the first trimester. Most advanced gestation was 22 weeks in our study. There were no cases in third trimester.

**Chi square value = 1.3998, P value 0.7055 there was no statistical significant difference between complete mole and partial mole with respect to gestational age at the time of diagnosis**

In complete molar pregnancy, 46% (23 of 40) had uterine size larger than the period of gestation. 26% (13 of 40) had uterine size corresponding to the period of gestation and 8% (4 of 40) had uterine size smaller than period of gestation associated with history of passage of grape like vesicles. In partial molar pregnancy, 16% (8 of 10) had uterine size corresponding to the period of gestation and 4% (2 of 10) had uterine size larger than the period of gestation. **Chi square value = 6.118, P value 0.046 there was significant difference between Complete mole and partial mole with respect to uterine size in comparison with gestational age.** Since p value <0.05, which is significant. The uterine size was significantly more in complete mole than in partial mole for their corresponding gestational age.

**Table 4:** Distribution according to pre - evacuation  $\beta$  HCG levels

Serum $\beta$ HCG Levels (IU/L)	Complete Mole (40) (%)	Partial Mole (10) (%)
<10,000	2 (4%)	-
10,000 - <1,00,000	10 (20%)	7 (14%)
1,00,000 - <10,00,000	28 (56%)	3 (6%)

56% (28 of 40) women with complete mole had pre - evacuation  $\beta$  hCG levels between 1,00,000 - <10,00,000. 14% (7 of 10) of women with partial mole had pre - evacuation  $\beta$  hCG levels between 1,00,000 - <10,00,000. **Chi square value = 6.700, P value 0.035 there was significant difference between Complete mole and partial mole with respect to pre evacuation serum  $\beta$  hCG levels.** Since p value <0.05, which is significant. This indicates that pre - evacuation  $\beta$  hCG levels were raised in complete mole compared to partial mole because of excessive trophoblastic tissue in complete mole and trophoblasts produces hCG hormone.

24% of women with complete mole had post evacuation  $\beta$  hCG levels between 10,000 - <1,00,000 and 32% had  $\beta$  hCG levels between 1,00,000 - <10,00,000 and 24% had  $\beta$  hCG levels between 1000 - <10,000. 14% of women with partial mole had  $\beta$  hCG levels between 1000 - <10,000 and 6% had  $\beta$  hCG levels between 10,000 - <1,00,000. **Chi square value = 2.57, P value 0.276 there was no statistical significant difference between Complete mole and partial mole with respect to 48 hrs post evacuation serum  $\beta$  hCG levels**

Hyperthyroidism was seen in 7 (14%) cases of complete mole and 2 (4%) cases of partial mole but none of the cases had symptoms of hyperthyroidism. 2 cases of study group had hypothyroidism that was diagnosed before pregnancy itself and were on thyroxine medication.

**Chi square value = 1.255, P value 0.533 there was no statistical significant difference between Complete mole and partial mole with respect to thyroid status**

Most of the cases (66%) in the present study had Hb% less than 10 gm% pertaining to anaemia status of pregnant population in India. About 34% of the cases had Hb% of more than 10%. Only 5 (10%) had severe anaemia with Hb% less than 7 gm%.

28 (56%) of the cases were given blood transfusion. Blood transfusion was done preoperatively, intra operatively or post operatively depending on the need.

In the present study majority (52%) were of the blood group B positive, 20% were of O positive, 14% were of A positive, 6% were of AB positive and only 4 (8%) had negative blood group.

Chest X Ray has been done in all 50 cases and was found to be normal.

In the present study **suction evacuation** was the mode of treatment which was done in all cases. **\*One** case had profuse bleeding per vaginum, after suction evacuation, uterine perforation was noted intra op hence, **obstetric hysterectomy** was done for moribund status. Histopathology report was suggestive of choriocarcinoma in this case.

In the present study 2 (4%) cases underwent repeat suction evacuation due to persistent bleeding after initial evacuation procedure and post evacuation USG suggestive of incomplete evacuation of uterus. In one case, repeat suction evacuation was done after 2 days and another case had usg s/o incomplete evacuation and bleeding hence repeat suction evacuation was done after 3 days. These cases responded to repeat evacuation.

#### 4. Complications

One case had profuse bleeding per vaginum, after suction evacuation, uterine perforation was noted intra op hence, **obstetric hysterectomy** was done for moribund status. Histopathology report was suggestive of choriocarcinoma in this case. Hemorrhage was there in one case with complete mole, larger than gestational age which was managed by blood products and oxytocin infusion. Other complications such as sepsis, embolization and mortality were not seen in any of the cases.

74% and 20% of the cases were confirmed with complete mole and partial mole respectively on histopathology diagnosis. 3 out of 40 cases who were diagnosed as complete mole on USG had histopathology diagnosis of GTN. No case of PSTT or ETT or Atypical placental site nodule were seen in the study

**Table No 5:** Distribution according to Time to Normalized Serum  $\beta$  hCG Levels

Time to normal $\beta$ hCG (WKS)	Frequency		Percentage
	CM (37)	PM (10)	
4	-	3	6%
5	4	3	14%
6	6	2	16%
7	8	1	18%
8	11	1	24%
9	4	-	8%
10	3	-	6%
12	1	-	2%

CM Complete Mole, PM Partial Mole

In the present study, After evacuation, the mean time taken by complete mole cases was  $8.14 \pm 2.23$  weeks and by partial mole was  $6 \pm 1.58$  weeks to reach normal serum  $\beta$  hCG levels. However 3 out of 40 cases of complete mole did not reach normal  $\beta$  hCG levels upto 12 weeks. These cases showed persistently raised  $\beta$  hCG levels which were diagnosed as Gestational trophoblastic neoplasia according to FIGO criteria and treated at Cancer wing of our hospital.

**T test value =2.8506, P value 0.006 there was statistical significant difference between Complete mole and partial mole with respect to mean time taken to reach normal serum  $\beta$  hCG levels.**

Since p value <0.05, which is significant. This indicates that mean time taken to reach normal hCG levels depends on the type of mole. It was lesser in partial mole than complete mole cases.

## 5. Discussion

The incidence of hydatidiform mole in the present study was 1.58 HM per 1000 pregnancies. This is consistent with rates found in previous hospital based studies in MDM Hospital, Jodhpur, Dr Vinod et al [13] (1.52 HM per 1000 pregnancies) and Umaid hospital (1.76 HM per 1000 pregnancies) Dr Lovely Jethwani et al [14] whereas in a study by Tshering Tamang et al [15] showed a very high incidence of 19.7 per 1000 deliveries at Bhutan. The difference in the incidence could be due to socioeconomic, nutritional factors, population- based or hospital- based studies.

In the present study incidence of molar pregnancy is most common in 21 - 30 years of age that is 54%. These results are consistent with other research like Matthew Anyanwu et al [16] 2020 showing 55% cases in this age group and Visenuo Ethel Solo et al [17] 2019 & Dr. Rohit S. Dimbar et al [18] 2021 study showing 50% and 63% respectively in this age group. Extremes of age are the important risk factor due to abnormal gametogenesis and fertilization of the ovum.

84 % were from low socioeconomic status in the present study, which was similar to study done by Dr Ajith Kumar Nayak et al [19] (70.7%), and Swarnabindu Banerjee. et al 2021 [20] who reported 72% with low socioeconomic. Our hospital caters localities/area which are poverty stricken. Hence the high figure in poor.

In the present study, (18) 36% cases out of 50 cases were primigravida which was comparable with studies of Dr. Ajit Kumar Nayak et al [19] that is 39.70% and Dr Vinod et al [13] 38.30% but contradictorily by Visenuo Ethel Solo et al [17], majority (35%) were second gravida. Since majority of cases in the present study (40%) belong to  $\leq 20$  yrs, primigravida was in majority.

In present study, 48% women had antecedent live birth and 16% women had antecedent abortion which is comparable to study done by Dr Rohit S Dimbar et al [18] 2021 as 36% and 16.3 % respectively. It means that antecedent pregnancy may not contribute to hydatidiform mole as found otherwise.

In the present study, most common presentation was amenorrhoea for a variable period of time present in all the cases followed by bleeding per vaginum (60%) and pain abdomen (56%). Similar results were found in many other studies, like Swarnabindu banerjee et al [20], Humaira shaheen et al [21] et al. Dr Ajith Kumar et al [19] A study by Sunil Vitalrao Jagtap et al [22], noted 94.80% cases of bleeding per vaginum. In the present study, we found that 32% of molar pregnancies were accidentally discovered by USG as screening by USG has increased in recent times and Dr Rohit S Dimbar et al [18] reported same in 58% of the cases.

In the present study, 80% were diagnosed on ultrasonography having complete mole and 20% partial mole, this was in concordance with studies like Dr Vinod et al (75%), Ethel Solo et al [17] (85%). About 10% of complete mole had prominent theca leutin cysts in the present study which was comparable with Dr Vinod et al [13] (10%) Visenuo Ethel Solo et al [17] (15%) and Ayman A AlTalib et al [23] (13.6%)

We found that most of the GTD cases, (34/50 cases, 68%) were in the first trimester followed by the second trimester with 16 cases (32%) in the present study. Jagtap et al [13], noted 42 (59.15%) cases were in the first trimester and 29 (40.85%) cases were in the second trimester. Another study by Swarnabindu banerjee et al [20], Dr Rohit S Dimbar et al [18] (54% & 41%) and Dr Lovely Jethwani et al [14] had a similar observations. While study by Bharat U patil et al 2020 [24], observed 38.09% cases in the first trimester. Routine antenatal scans have been helpful in the early diagnosis of molar pregnancy. Hence more cases were present in first trimester in the present study.

In present study, 50% of patients had uterine size larger than gestational age while 42% had corresponding to gestational age and 8% patients had uterine size smaller than gestational age which was comparable with studies done by Dr Rohit S Dimbar [18] et al (50.9%) Dinesh kumar et al [25] and Dr Lovely Jethwani et al (42%) [14] where as in study conducted by Ayman A Al Talib et al [23], 54.5% (majority) of patients had uterine size corresponding to gestational age. Excessive uterine size in H. mole is due to both trophoblastic overgrowth and retained blood.

In present study,  $\beta$  HCG was elevated in all cases. In 62% cases, it was between 1, 00, 000 - <10, 00, 000 mIU/ ml and Serum  $\beta$  hCG of 36% patients was more than 10, 000 - <1,

00, 00mIU/ml. It was comparable with studies done by Humaira shaheen et al<sup>[21]</sup> and Jethwani et al. Study done by Sailendra et al 2021<sup>[26]</sup> reported only 10 % cases with  $\beta$  hCG more than 1, 00, 000 mIU/ml which was contradicting our study. Serum  $\beta$  hCG is increased in molar pregnancy due to marked trophoblastic proliferation which was prominently seen in complete mole. hCG is glycoprotein hormone synthesized predominantly by trophoblastic tissue. Therefore, the levels are high in our study as we had 80 % of complete mole.

Hyperthyroidism was encountered in 18% of the patients in the study which was consistent with the study done by Visenuo Ethel Solo et al<sup>[17]</sup> who reported hyperthyroidism in 13.3% cases.

Present study showed high incidence of GTD in patients with blood group 'B' followed by blood group 'O' and blood group 'A'. Amongst them 92% were Rh positive.

Results were consistent with studies conducted by Swarna bindu banerjee et al<sup>[20]</sup> who reported B positive blood group in 53% cases and majority of the study population (35%) in the study done by Matthew Anyanwuet al<sup>[16]</sup> had B positive blood group.

In the present study suction evacuation was the mode of treatment which was done in all cases. \*One (2%) case had profuse bleeding per vaginum after suction evacuation, uterine perforation was noted intra op hence, obstetric hysterectomy was done for moribund status. Histopathology report suggestive of choriocarcinoma.

This was comparable with study done by Dr Vinod et al (85%)<sup>[13]</sup>, Dr Rohith S Dimbar et al<sup>[18]</sup> (96.36%) and Ajith Kumar et al (100%)<sup>[19]</sup> Suction evacuation was the primary mode of treatment in many of the studies and hysterectomy was done for any complications and as the treatment of GTN.

In the present study, repeat evacuation was required in 2 cases that came with complaints of excessive bleeding per vaginum and USG suggestive of retained products of conception. These cases ruled out GTN. This is comparable with studies done by Dr Vinod et al<sup>[13]</sup> and Dr. Lovely Jethwani et al<sup>[14]</sup> who reported in one and two cases respectively.

Majority of GTD in our study were of hydatidiform mole comprising 94%. Complete mole is most common entity, comprising 74% while partial mole was second most common entity with 20% cases on histopathology These results were in concordance with other studies done by Sailendra et al 2021<sup>[26]</sup> who reported 66.66% of cases with complete mole and 28.30% cases with partial mole, Dr Lovely Jethwani et al<sup>[14]</sup> who reported 76% of cases with complete mole and 20% cases with partial mole.

In the present study 6% developed GTN out of which 4% developed choriocarcinoma and 2% developed invasive mole. This is consistent with studies like Dr Lovely Jethwani et al<sup>[14]</sup> who reported 4% cases of choriocarcinoma.

In the present study, the mean time taken to attain normal serum  $\beta$  hCG levels was  $7.62 \pm 2.49$  weeks with a range from 4 to 12 weeks. Complete moles took more time than partial moles ( $8.14 \pm 2.23$  versus  $6 \pm 1.58$ ). This was consistent with the studies done by Ajith Kumar et al and Dr Rohit S Dimbar et al 2021 who reported mean time was  $8.31 \pm 1.96$  weeks and  $7.4 \pm 3$  weeks respectively.

## 6. Conclusion

Incidence of H. mole during the study period in our institute was 1.58 per 1000 pregnancies. History of amenorrhoea with bleeding per vaginum and size of uterus more than period of amenorrhoea should raise suspicion of H. mole though asymptomatic cases do exist. It is not necessary to have antecedent molar pregnancy to have H. mole. Obstetric ultrasonography and serum  $\beta$  hCG estimation form the main tool of diagnosis for H. mole. Hyperthyroidism and anaemia were found as associated factors. Special predeliction for A+ blood group was not seen here as given in literature. suction evacuation is the primary mode of successful treatment. There was no mortality. Clinical diagnosis and investigations suggestive of H. mole and GTN matched in histopathology in all cases. Time taken for beta hCG levels to \*drop down to normal was more in cases of complete mole than partial mole.

### Limitations of the study

Since the sample size at our tertiary care centre, more studies need to be done to reflect the true incidence in the population. We recommend multi - centered studies with disease specific registry

### Conflicts of interest - none

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