

**Original article:**

## **Gestational trophoblastic disease: study on incidence and management at a tertiary centre**

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### **ABSTRACT:**

**Background:** Gestational trophoblastic disease encompasses an intriguing group of interrelated diseases derived from placental trophoblasts with an varying incidence worldwide.

**Objectives:** (1) To study the profile and incidence of cases attending the tertiary hospital. (2) To identify various cases of gestational trophoblastic diseases, their presentation and associated complications.

**Methodology:** A retrospective study was conducted over a period of two years (January 2014- December 2015) at a tertiary care hospital and data was analysed using hospital records.

**Results:** The incidence of gestational trophoblastic disease is 2.23 per 1000 deliveries. Molar pregnancy constituted 22 cases and 6 cases of gestational trophoblastic neoplasia.

**Conclusion:** Emphasis on health education, early diagnosis with ultrasound and serum beta HCG levels and proper follow up is required.

**Keywords:** gestational trophoblastic disease, serum beta HCG, gestational trophoblastic neoplasia, chemotherapy.

### **INTRODUCTION:**

Gestational trophoblastic disease is the term used to describe the heterogenous group of interrelated lesions that arise from abnormal proliferation of placental trophoblasts. Benign lesions consist of hydatidiform moles, complete and partial, whereas malignant lesions consist of invasive mole, placental-site trophoblastic tumor and choriocarcinoma.<sup>(1)</sup> Incidence of molar pregnancy vary in different regions of the world. . Incidence of molar pregnancy in India is 19.1 per 10,000 deliveries (Pai) according to hospital based studies. <sup>(2)</sup>The higher incidence is attributed to socioeconomic and nutritional factors. Maternal age influence the rate of molar pregnancy. Ova from older women may be susceptible to abnormal fertilisation leading to complete hydatidiform mole.<sup>(1)</sup> Ultrasound and serum beta HCG have a key role in diagnosis and follow up of gestational

trophoblastic disease. Prophylactic chemotherapy, prevents metastasis and reduces the incidence and morbidity of local uterine invasion.

### **MATERIALS AND METHODS:**

A retrospective study based on medical records of patients of gestational trophoblastic disease over a period of two years from January 2014-December 2015 was conducted at King George Hospital, Visakhapatnam. A total of 28 cases of gestational trophoblastic disease were recorded during the period of two years.

### **OBSERVATIONS AND RESULTS:**

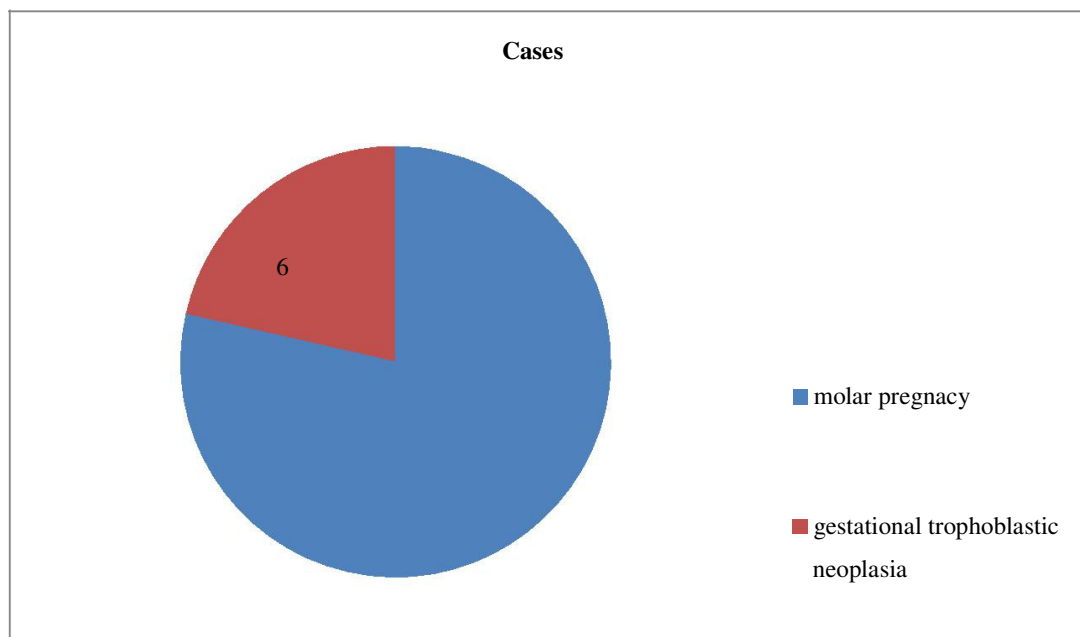
There were 12,274 deliveries conducted from January 2014 to December 2015 and 28 cases of gestational trophoblastic disease during the same period. Incidence of gestational trophoblastic disease in our observatory period is 2.23 per 1000 deliveries.

**Table 1: Distribution of gestational trophoblastic disease**

Cases	Number	Percentage
Molar pregnancy	22	78.57%
Gestational Trophoblastic Neoplasia	6	21.43%
Total	28	100%

Out of the 28 cases 22 had molar pregnancy and 6 cases had gestational trophoblastic neoplasia. Of the 22 cases of molar pregnancy there are only 2 cases of partial mole.

**Figure1**



**Table 2: Age wise distribution of cases**

Age	No.of cases	Percentage
<20 years	13	46.43%
20-35 years	13	46.43%
>35 years	2	7.14%
Total	28	100%

The cases below the age of 20 years were 46.43% and equal numbers were in the age group 21-35 years. Only 7.14% cases were above 35 years of age. By parity there were equal number of primigravidae and multigravidae that is 50% in the study. This observation could be attributed to early marriage and thus pregnancies.

**Table3: Gestational age at presentation of molar pregnancy**

Gestational Age	No. of cases	Percentage
<8 weeks	4	18.19%
8-20 weeks	18	81.81%

Majority of the molar pregnancy cases 81.81% cases have been detected in the second trimester and only 4 cases in the second month of gestation. Average gestational age of diagnosis is 14-16 weeks. No cases were detected after 20 weeks gestation.

**Table 4: Associated features with Gestational Trophoblastic Disease**

Risk factors	No. of cases	Percentage
Beta HCG>100000mIU/ml	15	68.2%
Neoplasia	6	21.43%
Theca leutin cysts	2	9.10%

Hyperthyroidism	2	9.10%
Anaemia	26	92.85%
Excessive uterine size	17	77.27%
Recurrent mole	1	4.54%

Excessive uterine size was noted among 77.27% and in 68.2% of the cases beta HCG levels were greater than 100000mIU/ml. These features indicated marked trophoblastic proliferation, considered as high risk mole. Majority 92.85% had anaemia and required blood transfusions. Hyperthyroidism was noted in 9.10% of cases but

didn't require treatment for the same. Theca lutein cysts were noted in 9.10% of cases. One case of recurrent molar pregnancy had a second molar pregnancy 8 months after treatment of first molar pregnancy.

**Table 5: Clinical presentation of cases**

Presentation	No.of cases	Percentage
Bleeding per vaginum	12	42.85%
Amenorrhoea	7	25%
Pain abdomen	5	17.85%
US finding	4	14.29%

Most common clinical presentation was bleeding per vaginum constituting 42.85% of cases. Incidental US finding after a routine obstetric scan was 14.29% of cases.

**Management of gestational trophoblastic disease**

Suction evacuation was done in all cases of molar pregnancy and tissue was sent for histopathology. Prophylactic chemotherapy was given in 40.9% of cases. An average of 4 cycles of chemotherapy

was given. Chemotherapy was given till 3 consecutive values of HCG were normal. Chemotherapy given was single agent methotrexate alternating with folinic acid. Total leucocyte count, haemoglobin, liver function tests, renal function tests and X ray chest were monitored. Most common side effect noted was nausea and vomiting. Prophylactic chemotherapy reduced relapse and progression as well as helped in follow up of cases.

**Table 6: Gestational Trophoblastic Neoplasia presentation and treatment**

	Case 1	Case2	Case3	Case4	Case5	Case6
Age	19	23	25	24	30	20
Beta HCG	200000	974000	35284	82664	341	69220
US features	Uterus with lesions in junctional zone at fundus	Trophoblastic tissue invading myometrium	4*5cms nodule invading myometrium	Necrotic and trophoblastic tissue in uterus	4*4cm lesion invading myometrium	7*6cms lesion with thinned out myometrium
Treatment	9 cycles of MTX chemotherapy	Hysterectomy with one cycle of chemotherapy	Hysterectomy	Hysterectomy followed by chemotherapy	hysterectomy	hysterectomy
Diagnosis	Invasive mole	Invasive mole	Invasive mole	Choriocarcinoma	Invasive mole	Invasive mole
Stage	1	1	1	1	1	1

Invasive mole was the histological diagnosis in 5 cases of GTN, among them one case was treated with single agent chemotherapy methotrexate for 9 cycles on the advice of oncologist. Rest all cases were treated with hysterectomy as a definitive treatment. Choriocarcinoma was the histological diagnosis in 1 case and following hysterectomy patient was referred to oncologist. One case of invasive mole had a successful

uneventful full term pregnancy after one year of completion of chemotherapy. Rest of the cases of molar pregnancy lost follow up.

**DISCUSSION:**

Author	Incidence per 1000 deliveries	age 21-35 yrs	primigravidae	Distended uterus	HCG levels >100000	GTN
Lakra et al (3)	2.3	92.1%	57.9%	54.6%	18.4%	5
Koirala A et al (5)	3.9					
Dinesh kumar et al (6)	4.565		30%			
Nousheen Aziz et al (8)		54.54%	42.42%	57.57%	60.6%	6
Jangbhadur Singh et al (7)		22%				
Present study	2.23	46.43%	50%	77.27%	62%	6

Gestational trophoblastic disease encompasses an intriguing group of interrelated diseases derived from placental trophoblasts. Variants differ in spontaneous resolution, local invasion and metastasis. The incidence rates of Gestational Trophoblastic Disease vary significantly between different regions of the

world. In the present study, there were 22 cases of molar pregnancy and 6 cases of neoplasia amongst 12274 deliveries. Incidence is 2.23 per 1000 deliveries. Similar observations were made in other studies, Lakra P et al (3) reported 2.3 per 1000 deliveries, Humaira et al (4) conducted a study

in Pakistan reported an incidence of 2.5 per 1000 deliveries and Koirala A et al <sup>(5)</sup> from Nepal reported an incidence of 3.9 per 1000 deliveries. Dinesh kumar et al <sup>(6)</sup> 4.565 per 1000.deliveries.

Early marriage is still a custom among the rural population, cases noted in the age group of < 20 years and 21-35 years was 46.43% each. Lakra P et al <sup>(3)</sup> reported 92.1%of cases in the age group of 20-34 years. Dinesh kumar et al <sup>(6)</sup> also reported an higher number of cases in the age group of 20-35 years.

Jangbhadur Singh et al <sup>(7)</sup> reported 34% of cases below 20 years and 22% in the age group of 21-35 years. Occurrence of molar pregnancy represents the release of defective ova.

In the present study, there were equal number of primigravidae and multigravidae. Similar findings were reported by Lakra P et al <sup>(3)</sup> 57.9% were primigravidae. While Dinesh Kumar et al <sup>(6)</sup> reported 70% of the cases being parity one and above. In the present study, 81.8% of cases were detected in 8-20 weeks of gestation. Similarly, Lakra P et al <sup>(3)</sup> reported a mean age of 13.84 weeks (8-23 weeks). Jangbhadur Singh et al <sup>(7)</sup> reported 52% of cases during 2-5 months gestational age. Detection by ultrasonography played a key factor in diagnosis of GTD.

In our study , excessive uterine size than the period of gestation was noted in 77.27% of cases and beta HCG levels greater than 100000mIU/ml in 68.2% of cases. Similar observation was made by Nousheen Aziz et al <sup>(8)</sup>, 57.57% of cases had uterine size larger than dates and 60.6% of the cases had beta HCG levels greater than 100000mIU/ml. Lakra P et al <sup>(3)</sup> reported 54.6%patients with uterine height more than the

period of gestation, while beta HCG levels greater than 100000mIU/ml were reported only in 18.4% of patients. Excessive uterine size and high levels of beta HCG indicate majority of cases were in the high risk group, thus requiring higher vigilance and follow up of patients.

In the present study bleeding per vaginum was the most common presentation in 42.85% of cases and incidental ultrasound diagnosis in 14.28% of cases. Findings of Lakra P et al <sup>(3)</sup> showed bleeding per vaginum (84.2%) and pain abdomen (89.5%) as the most common presenting symptoms, ultrasound diagnosis in 15.8% of patients. Nousheen Aziz et al <sup>(8)</sup> reported 81.81% patients with vaginal bleeding as presenting symptom. Hence, vaginal bleeding associated with pain abdomen is the most common presentation of symptoms and routine obstetric ultrasound helps in early detection of cases.

In the present study, 6 cases of GTN were reported. Among them, 5 cases were invasive mole and one case of choriocarcinoma. Main modality of treatment was hysterectomy followed by chemotherapy except in one case of invasive mole wherein chemotherapy was given. Follow up of all cases of GTN was good and a case had a subsequent full term pregnancy. Lakra P et al <sup>(3)</sup> reported 5 cases of GTN including one case of choriocarcinoma. Nousheen Aziz et al <sup>(8)</sup> reported 5 cases of choriocarcinoma and 1 case of invasive mole.

In the present study, 53.57% of molar pregnancy were given prophylactic chemotherapy with methotrexate alternating with rescue agent folinic acid. Considering high risk factors of the molar pregnancy and poor follow up patients prophylactic chemotherapy is advocated to

prevent relapse and progression to persistent disease. Nousheen Aziz et al<sup>(8)</sup>, Lakra P et al<sup>(3)</sup>, Dinesh kumar et al all have stressed on the importance of prophylactic chemotherapy because of prevailing conditions in India as patient compliance and follow up is poor.

**CONCLUSION:**

Gestational trophoblastic disease is an important reproductive health problem with 100% cure rate. Early detection by ultrasound and serum

beta HCG values is necessary for treatment of the disease. There are more number of high risk cases, thus requiring more vigilance and follow up of patients to prevent relapse and persistence of disease. Prophylactic chemotherapy in such cases is helpful. Education regarding GTD, its risk factors and need for follow up its treatment and contraception in high risk cases should be conducted.

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