



Original Article

Clinico-Epidemiology Profile of Molar Pregnancy in Tertiary Care Centre: A Retrospective Review of Medical Records

Authors

Dr Vinod^{1*}, Dr Kalpana Mehta², Dr Vimla Choudhary³, Dr Ramniwas⁴, Dr Anusha⁵

¹3rd Year Resident, ²Senior Professor & Unit Head, ³Assistant Professor, ^{4,5}2nd Year Resident

Department of Obstetrics and Gynaecology, MDM Hospital, Dr. S. N. Medical College, Jodhpur, Rajasthan

*Corresponding Author

Dr Vinod

Department of Obstetrics and Gynaecology, MDM Hospital, Dr. S. N. Medical College, Jodhpur, Rajasthan

Abstract

Background: Gestational trophoblastic disease (GTD) includes a series of disorders that are characterized by an abnormal proliferation of trophoblastic tissue with varying tendency to spontaneous remission, local invasion and metastasis. The incidence of GTD varies greatly in different parts of the world. Hydatidiform mole presents with amenorrhea, painless vaginal bleeding and spontaneous passage of grape-like vesicles, high serum and urinary β human chorionic gonadotrophin (β HCG) levels.

Objective: To study epidemiology & clinical profile of Gestational Trophoblastic Disease and to evaluate its management and outcome.

Material and Methods: A retrospective study was conducted over a period of five years in MDM Hospital, Jodhpur. A total of 39301 pregnancies were recorded during the period of five years. The demographic profile, clinical presentation, management and complications were studied.

Results: There were 60 patients of GTD with an incidence of 1.52 per 1,000 pregnancies. Among these 60 cases, 45 (75%) cases had complete H mole. Most of the patients (63.3%) were in age group of 21-30 years and majority in nulliparous women (38.3%). Majority of the molar pregnancy cases 83.3% cases have been detected in the second trimester. The most common clinical presentation was bleeding per vaginum constituting 58.3% of cases. Majority (85%) of the patients were treated by suction and evacuation.

Conclusion: Gestational Trophoblastic Disease requires early diagnosis, treatment and strict monitoring to be 100% curable. Routine check-up helps to timely management of the GTDs thereby preventing their progression to GTN.

Keywords: Gestational Trophoblastic Disease, Hydatidiform Mole, Molar Pregnancy, Neoplasia, Serum beta HCG.

Introduction

Gestational trophoblastic disease (GTD) includes a series of disorders that are characterized by an abnormal proliferation of trophoblastic tissue with varying tendency to spontaneous remission, local

invasion and metastasis¹. It encompasses several distinct clinical entities, from benign complete and partial hydatidiform moles to malignant invasive moles, choriocarcinoma, placental site trophoblastic tumour (PSTT), and epithelioid

trophoblastic tumor; malignant forms of GTD are grouped together under the term gestational trophoblastic neoplasia (GTN)². Hydatidiform mole is the most common GTD^{3,4}.

The incidence of GTD varies greatly in different parts of the world, with 0.4 per 1000 birth in United States of America to 12.5 per 1000 births in Taiwan⁵. In Nepal, hospitals in Kathmandu valley have recorded its incidence as 5.1, 2.9, 2.8, and 4.1 per 1000 live births⁶. These 10–20fold variations in the incidence of molar pregnancy might be overestimated by reporting biases, such as population-based and hospital-based data⁷. In addition, incidence rates may be based on the total number of pregnancies, deliveries or live births. Furthermore, under registration of GTD might occur¹. The incidence of GTD in India was found to be one per 967 pregnancies in an epidemiological study on GTD in a North Indian population⁸. Incidence of molar pregnancy in India is 19.1 per 10,000 deliveries (Pai) according to hospital based studies⁹.

Clinically hydatidiform mole presents with amenorrhoea, painless vaginal bleeding and spontaneous passage of grape-like vesicles, high serum and urinary β human chorionic gonadotrophin (β HCG) levels. There may also be hyperemesis gravidarum, doughy uterus, inappropriate uterine size, bilateral theca lutein cyst and rarely, features of thyrotoxicosis and pre-eclampsia in the first half of pregnancy¹⁰⁻¹². Hydatidiform mole is a relatively common gynecological problem which could present like spontaneous abortion, one of the most common gynecological emergencies. Ultrasonography is a simple non-invasive examination which can correctly identify the placental molar transformations in-utero. Currently with widespread use of first trimester ultrasonography a significant proportion of patients with molar pregnancy are asymptomatic at the time of diagnosis. Careful and reliable human chorionic gonadotropin monitoring is essential for the early detection of post molar persistent gestational trophoblastic tumor. Therefore we conducted a

study to determine the epidemiology & clinical profile of Gestational Trophoblastic Disease and to evaluate its management and outcome.

Material and Methods

Study Population: A retrospective study was conducted in the Department of Obstetrics and Gynecology, MDM Hospital under Dr S N Medical College, Jodhpur, Rajasthan over a period of five years from January 2015 to December 2019. There were 39301 pregnancies were enrolled from gynaecological outpatient clinic of MDM Hospital. The study was approved by the Institute Ethics Committee.

Methodology: A total of 39301 pregnancies were recorded during the period of five years and 60 patients were diagnosed as having GTD. All women under study were subjected to a detailed history as per the preset proforma including age, address, chief presenting complaint, gravidity, gestational age, outcome of previous pregnancies, menstrual history were noted for each case.

The clinical examination included nutritional status, height, weight, BMI calculation, pallor, oedema, PR, BP, thyroid swelling. Size of the uterus per abdomen was noted to check if it corresponded to the weeks of gestation. A difference of at least 4 weeks between uterine size and gestational age was considered significant. Per speculum and per vaginal examination was done. CVS and RS examined.

Blood samples collected for investigations which included Hb%, blood grouping and Rh typing, thyroid function test, serum beta-hCG. Cross matching samples were drawn if blood transfusion required. Urine samples collected for albumin, sugar and microscopy. The patients were subjected to USG if not previously done. As a primary mode of management suction and evacuation done for all patients followed by gentle curettage was done. The samples obtained sent for histopathological examination. The serum beta hCG was repeated 48 hrs after evacuation. Post evacuation USG was done if the patient complained of excessive or irregular bleeding per

vaginum. Repeat evacuation was done if there was evidence of retained molar tissue on post evacuation USG.

Then the patients were counselled regarding the need for follow up and use of contraception for the entire period of follow up. Follow up was done with weekly beta hCG until normal for 3 consecutive 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.⁷² At every follow up visit history regarding irregular vaginal bleeding, pain abdomen, headache, cough, hemoptysis, fever was taken and clinical examination which included CVS, RS, per abdomen, per speculum, per vaginal examination done to look for signs of GTN. The time 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 histopathology or with evidence of metastasis. Women diagnosed with persistent trophoblastic disease or GTN were scored according to modified WHO scoring system [Table- 1]¹³

Results

A total of 39301 pregnancies were recorded during the period of four years and 60 patients were diagnosed as having Gestational trophoblastic disease. This gives an incidence of 1.52 per 1,000 pregnancies. Among these 60 cases, 45 (75%) cases had complete H. mole, 12 (20%) cases had partial H. mole and 3(5%) cases had GTN at the time of presentation. During follow up 2(4%) more patients of complete mole turned into GTN. The incidence of GTN was found to be 0.07 per 1000 pregnancies (4 out of 28,301 pregnancies) (Table-2).

Most of the patients (63.3%) were in age group of 21-30 years. In this study H. mole was more common in nulliparous women (38.3%) while the least was 6.7% in women with parity four and above. Majority of the molar pregnancy cases 83.3% cases have been detected in the second

trimester while 16.6% cases have been detected in the second month of gestation. No cases were detected after 20 weeks gestation. (Table 2)

Majority 86.6% of the cases had anaemia and required blood transfusions. Excessive uterine size was observed among 78.4% of the cases while 70% of the cases had beta HCG levels were greater than 100000mIU/ml. These features indicated marked trophoblastic proliferation, considered as high risk mole. Hyperthyroidism was seen in 8.3% of cases. Theca lutein cysts were observed in 10% of cases. (Table 3)

The most common clinical presentation was bleeding per vaginum constituting 58.3% of cases while the least common clinical presentation was Incidental US finding after a routine obstetric scan was 5% of cases.

Majority (85%) of the patients were treated by suction and evacuation. Hysterotomy was done in a patient who was diagnosed on USG with single live intrauterine fetus of 21 weeks with bulky cystic placenta completely covering the internal os (partial mole with placenta praevia). Three (5%) patients underwent subsequent total abdominal hysterectomy when they were found to have GTN in their follow up (including two post evacuation patients referred from peripheral centers). Secondary curettage was done in one patient in their first follow up visits when they complained of excessive bleeding per vaginum & their USG showed echogenic material in endometrial canal and retained products of conception was found in histopathology. Majority (90%) of patients had spontaneous remission defined as three consecutive β -hCG value undetectable. 8.33% patients progressed to GTN in present study. One patient lost to follow up (1.6%). Among the 05 cases of GTN, 3 developed invasive mole and 1 developed choriocarcinoma while one of them showed rising titres without any other specific sign & symptom, so was categorized persistent trophoblastic disease and was referred to oncology department for chemotherapy. Because of small number of patients in present study there is higher percentage of GTN [Table-5].

Table 1 Modified WHO prognostic scoring system for GTN as adopted by FIGO

SI No.	Risk Factor	Risk Score			
		0	1	2	4
1	Age (years)	< 40	>40	-	-
2	Antecedent pregnancy	Mole	Abortion	Term	-
3	Interval from antecedent pregnancy to chemotherapy (months)	< 4	4-6	7-12	>12
4	hCG concentration (mIU/ml)	< 10 ³	10 ³ - <10 ⁴	10 ⁴ - 10 ⁵	>10 ⁵
5	Number of metastasis	0	1-4	4-8	>8
6	Site of metastasis	Lung	Spleen, Kidney	Gastrointestinal Tract	Brain, Liver
7	Largest tumour mass diameter(cm)	-	3-5	>5	-
8	Previous failed chemotherapy drugs	-	-	Monotherapy	Combined therapy

Table 2 Demographic profile, Risk Factor and Clinical presentation of Gestational Trophoblastic Disease

SI No.	Demographic variable	Range	Number	Percentage
	GTD	Complete and Partial H. mole; and GTN	60	1.52/1000 Pregnancies
1	Age	< 20 years	08	13.3
		21-30 years	38	63.3
		31-40 years	10	16.6
		>40 years	04	6.7
2	Gestational Period	<8 weeks	10	16.6
		8-20 weeks	50	83.4
3	Parity	Nullipara	23	38.3
		Para 1	19	31.6
		Para 2	09	15
		Para 3	05	8.3
		Para 4 and above	04	6.7

Table 3 Associated features with Gestational Trophoblastic Disease

SI No.	Risk factor	Number of cases	Percentage
1	Beta HCG>100000mIU/ml	42	70
2	Neoplasia	10	16.7
3	Hyperthyroidism	05	8.3
4	Anaemia	52	86.6
5	Excessive uterine size	47	78.4
6	Recurrent mole	02	3.3
7	Theca leutin cyst	06	10

Table 4 Clinical presentation of cases

SI No.	Presentation	Number of cases	Percentage
1	Bleeding per vaginum	35	58.3
2	Amenorrhoea	12	20
3	Pain abdomen	10	16.7
4	US finding	03	5

Table 5 Diagnosis, Management and Outcome of Molar Pregnancy

Sl. No			No. of cases	Percentage
1.	Primary Diagnostic Modality	Radiological finding (dating scan for early pregnancy) + β hCG level thereafter	57	95
		Histopathology(Clinically & radiologically diagnosed as Missed abortion)	03	5
2	Preevacuation β hCG level (mIU/ml)	<10 ³	05	8.33
		10 ³ - 10 ⁴	21	35
		10 ⁴ – 10 ⁵	10	16.66
		>10 ⁵	24	40
3	Treatment Modalities	S + E	51	85
		D & C	02	3.33
		Hysterotomy	02	3.33
		S + E f/b Hysterectomy	04	6.66
		S + E f/b Secondary evacuation	01	1.66
4	Post evacuation Outcome	Spontaneous Remission	54	90
		GTN	05	8.33
		Lost to follow up	01	1.66
5	Antecedent Pregnancies Among GTN cases	Mole	05	100
		Abortion	0	0
		Term pregnancy	0	0

Discussion

Gestational trophoblastic disease (GTD) encompasses a spectrum of pregnancy related trophoblastic abnormalities which include complete and partial moles, placental site trophoblastic tumours, choriocarcinomas, and invasive moles. Molar pregnancies (hydatidiform mole) represent a significant burden of disease on the spectrum of GTDs. The incidence rates of Gestational Trophoblastic Disease vary significantly between different regions of the world.

In this study we found that there were 60 cases of molar pregnancy and 10 cases of neoplasia amongst 39301 pregnancies which gives the incidence 1.52 per 1000 deliveries. Our findings are similar with Jethwani L et al¹⁴ who had reported the incidence rate 1.76 per 1000 pregnancies. In another study conducted by Rauf et al¹⁵ the incidence of GTD was 1 per 967 pregnancies in a hospital based study. When we compare our results with various studies we found that study conducted in North America, Australia, New Zealand, and Europe reported the incidence of H. Mole ranging from 0.57–1.1 per 1000 pregnancies, whereas studies in Southeast Asia

and Japan have suggested an incidence as high as 2.0 per 1000 pregnancies¹⁶.

In this study among these 60 cases of GTD, 45 (75%) cases had complete H. mole, 12 (20%) cases had partial H. mole and 3(5%) cases had GTN at the time of presentation. During follow up 2(4%) more patients of complete mole turned into GTN. Our findings are in accordance with the study done by Farhat Khanum et al¹⁷ where out of 45 cases of GTD 31(68.8%) were had complete H. mole , 7(15.5%) were had partial H. mole and 7 (15.5%) were had choriocarcinoma.

In this study most of the patients (63.3%) were in age group of 21-30 years which is in accordance with Ramesh Chandran et al¹⁸, Vaidya et al¹⁹ and Ocheiki et al²⁰. However Prazzini et al²¹ and Sebire et al²² reported complete mole was observed in teenager women and whose age is 36-40 years or above respectively. Occurrence of molar pregnancy represents the release of defective ova.

In this study we found that H. mole was more common in nulliparous women (38.3%) followed by para 1, para 2, para 3 while the least was women with parity four and above (6.7%). Our results are in concordance with Fatima et al²³ and Alteiri et al¹⁶ who also reported H. mole was more common in nulliparous women.

In this study majority of the patients 83.4% were gestational age at presentation was 8-20 weeks while 16.6% cases have been detected in < 8 weeks of gestation. No cases were detected after 20 weeks gestation. Our findings are consistent with Jethwani et al¹⁴, Madhuri et al²⁴ who all reported most of the cases were detected in 8-20 weeks of gestation. In another study Jangbhadur Singh et al²⁵ reported 52% of cases during 2-5 months gestational age. Detection by ultrasonography played a key factor in diagnosis of GTD.

In this study excessive uterine size was observed among 78.4% of the cases while 70% of the cases had beta HCG levels were greater than 100000mIU/ml which is in accordance with Madhuri et al²⁴ who reported 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 al²⁶, 57.57% of cases had uterine size larger than dates and 60.6% of the cases had beta HCG levels greater than 100000mIU/ml. 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 this study the most common clinical presentation was bleeding per vaginum constituting 58.3% of cases followed by Amenorrhoea 20%, Pain abdomen 16.7% while the least common clinical presentation was Incidental US finding after a routine obstetric scan was 5% of cases. Our results are similar with Madhuri et al²⁴ who reported bleeding per vaginum was the most common presentation in 42.85% of cases and incidental ultrasound diagnosis in 14.28% of cases. In another study conducted by Lakra P et al²⁷ 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 al²⁶ 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 this study the primary mode of diagnosis was USG which is in accordance with Santos Ramos²⁸, Benson CB²⁹ and Vaidya A et al¹⁹ who reported role of sonography in detecting molar pregnancy. In this study most (85%) of the patients were treated by suction evacuation. 6.6% of the patients treated by suction evacuation followed by hysterectomy. suction evacuation followed by secondary curettage was done in 3.33% who has excessive bleeding per vagina. Hysterotomy was done as primary treatment in patient who was diagnosed radiologically as partial H mole with complete placenta previa. The treatment modalities of molar pregnancy were well studied by Hancock B W³⁰, Tidy JA. Soper JT³¹.

Majority (90%) of patients had spontaneous remission defined. 8.33% of the patients who underwent evacuation for H mole progressed to GTN. One patient lost to follow up (1.6%). All cases with GTN were found as low risk GTN by modified WHO prognostic scoring system and achieved remission after single agent chemotherapy. Our findings are similar with Ramesh Chandran et al¹⁸, in their study 93.6% of patients were low risk and 6.4% were high risk and given multidrug chemotherapy to the patients who developed GTN.

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. Routine check up helps to timely management of the GTDs thereby preventing their progression to GTN. They require more vigilance and follow up of patients to prevent relapse and persistence of disease. Prophylactic chemotherapy in such cases is helpful.

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