

Clinical Presentation and Management of Hydatidiform Mole in a Peripheral Tertiary Hospital

JAGLUL HAIDER KHAN¹, JANNATUL FERDOUS², SAMIYAALAM³

Abstract:

This study was conducted in Faridpur Medical College Hospital, Faridpur, from January 2008 to December 2008 among fifty patients, diagnosed as a case of molar pregnancy. Incidence of molar pregnancy was 8.27 per thousand pregnancy. Sixty percent of the patients were multiparous and eighty percent of low socio economic status. B positive blood group was prevalent (36%) in this study. Sixty percent (60%) of the patients presented with amenorrhoea and abnormal vaginal bleeding. Most of the patients (72%) were treated with suction evacuation and curettage. Of them hemorrhage was the most common immediate complication (80%). Complication like shock and perforation during evacuation was 14% and 4% respectively. Three patient (6%) developed Persistent Gestational Trophoblastic Disease (GTD) and one (2%) patient developed choriocarcinoma with lung metastasis and died. Thirty two (64%) patients attended for regular follow up but ten patients (20%) had attended irregularly and eight patients (16%) had dropped out. This study shows that follow up for molar pregnancy cases is not satisfactory in a district medical college hospital. Further improvement can be done by increasing awareness of the patients.

Aims and Objectives:

1. To analyze the pattern of clinical presentation of molar pregnancy in a peripheral tertiary referral hospital.
2. To evaluate pattern of complications presented with and the complications that arises during and after treatment.
3. To evaluate the management including follow up in a peripheral tertiary hospital.

Introduction:

Gestational trophoblastic neoplasia is a pregnancy related disorder that has been applied to describe the different pathological appearance of trophoblastic tissue. It includes hydatidiform mole, invasive mole, placental site trophoblastic tumors and choriocarcinoma. Among them hydatidiform mole is the most common. It develops from the placental tissue during early pregnancy in which the embryo fails to develop normally. Microscopically mole may be identified by three classic findings¹ 1. Edema of villous 2. Avascular villi. 3. Nest of proliferating syncytiotrophoblast and cytotrophoblast element surrounding villi.

In about half of all cases of choriocarcinoma and 10 to 15% of invasive mole the antecedent pregnancy is hydatidiform mole. Regardless the method of termination close follow up with serial beta HCG titer is essential for every patient because the incidence of malignant disease commonly thought to be 20-30% and the cure rate of properly treated metastatic gestational trophoblastic neoplasia is approximately 90%¹. This trophoblastic disease has got a wide range of complications. It may be persistent resulting metastatic or nonmetastatic malignant disease and may recur in subsequent pregnancy.

Molar pregnancy occur most frequently in South East Asia like Malaysia, Singapore, Hong Kong, Indonesia, Philippines and China². Incidence in Philippines is 1 in 80, in India is 1 in 400³. The exact etiology of the disease is yet unknown, but it appears to be related to the ovular defect as it some times affects one ovum of a twin pregnancy. There is an increased risk in teenagers and woman over 35 years. The rate rises to 10 fold after the age of 40 years¹. Patients with higher parity are at higher risk in under developed countries⁴. No parity effect was found in two studies

1. Assistant professor, Obstetric & Gynaecology, Dhaka Medical College
2. Associate professor, Gynaecological Oncology, BSMMU
3. Assistant register, Obstetric & Gynaecology, FMCH

done by Jonathan Buckley 1984⁵. More than 95% of complete mole are female (46xx). The partial mole is usually triploid. The prevalence appears to vary with race and ethnic origin. More common in certain racial groups. Blood group A woman mating with group A man are at least risk & risk is 10 fold greater if mate with group O man. Women with group AB have relatively poor prognosis³. It occurs especially in rice eater and in those whose diets are deficient in protein, folic acid and carotene. The occurrence of a trophoblastic tumor can be regarded as the result of a breakdown in what must be a complicated host invader balance. There are also reports of matching leucocytic HLA types between the woman and her partner. The lack of ability to control trophoblastic activity has two possible basis an inherent or immunological one and one which results from malnutrition and debility. Gestational trophoblastic tissue may suppress the maternal immune response via such factors as interleukins and tumor necrosis factor. Rise of gamma globulin level in absence of hepatic disease. Increase association of ABO blood group which possesses an ABO antigen².

The symptom which most often calls attention to the abnormality is recurrent uterine bleeding. Nausea, vomiting have been reported in 14-32 % of patients of hydatidiform mole and may be confused with nausea and vomiting of early pregnancy. In over 80% of cases the first evidence of hydatidiform mole is the passage of vesicular tissue, bleeding and brown discharge.

The uterus is too large for the period of amenorrhoea. is present in only 50% of cases. Sometimes the uterus is smaller than normal, especially if the mole dies. Enlargement of both ovaries seen in 25-30% of molar pregnancy. Suction evacuation and curettage is the preferred method of choice regardless of uterine size. When a large hydatidiform mole (>12wks size) is evacuated by suction curettage a laparotomy set up should be readily available as hysterotomy, hysterectomy, or bilateral hypogastric artery ligation may be necessary if perforation or hemorrhage occur¹. In all cases even if the mole has been removed by hysterectomy regular observation of patient is essential to detect the first sign of remaining or reawakening chorionic activity³. Follow up is done with serial beta HCG estimation, gynecological examination & Chest radiography. Approximately 70% patients develop a normal beta HCG within 8 weeks post evacuation. Another 15% demonstrate continuous

decline in titer and ultimately achieve normal titer without treatment. Rest 15% who have elevated titer at 8 weeks postevacuation demonstrates rising titer or plateau. Nearly half of these patients will have histological evidence of invasive mole and the other half will have choriocarcinoma.

Materials and Methods:

It was a prospective type of descriptive cross sectional study. conducted in the department of obstetrics and gynecology of Faridpur Medical College hospital from January 2008 to December 2008. Fifty consecutive patients who were admitted in the Obstetric and Gynae department of Faridpur Medical College Hospital and diagnosed as Hydatidiform mole had been taken as the study population. Diagnosis was made by ultrasonographic findings & serum BhcG assay. Histopathology was done in all the patients.

Study size (n) - $n = Z^2 \frac{pq}{d^2}$, Here, - Z = 1.96, P = 50, q = 50, d = 10 % of p - 5 % (Here actual prevalence is not known)

$$n = 1.96^2 \frac{50 \times 50}{0.05^2} = 384$$

Therefore the required sample size n = 384, but due to the reduced patient attendant it was not possible to collect required number of sample. After fulfillment of eligibility criteria 50 cases were collected during the study period. Sampling technique was purposive consecutive sampling.

Measurement of out Come Variable

Following outcome variables were studied

- Demographic variables- Age, Parity, Socio economic Condition, Blood group, Obstetric history & previous history of molar pregnancy.
- Clinical variables- Presentation at admission like amenorrhoea, pervaginal bleeding, pervaginal passage of vesicles, lower abdominal pain & exaggerated sign symptoms of pregnancy, and gestational period at admission. Ultrasonography & Serum BhcG assay were the main diagnostic tool in this study.
- Other variables were mode of treatment, complications, followup and prognosis of the patients

Data were collected in a preformed questionnaire and from direct clinical evidence. All datas are presented in tables. After collection of required information data were checked and processed manually, researched,

analysed and edited by computer and simple statistical calculation were done by using percentage. Ethical clearance was taken from ethical committee of Faridpur Medical college hospital.

Results:

During the study period total 5625 pregnant patients and 350 patients with abortion and 75 ectopic pregnancies were admitted in this hospital. Among them 50 were suffering from Gestational trophoblastic disease. So incidence of Gestational trophoblastic disease was 8.27 per thousand pregnancies. Eighty percent (40) of the patient were in low socioeconomic group and 16% (8) from middle and only 4% from upper class. Thirty six percent (18) of the patients blood group were B+ve, 30% O+ve, 26% A+ve, and 8% AB+ve. None of them were negative blood group. In the study population 60% of patient presented with amenorrhea and per vaginal bleeding. Twenty percent (10) presented in addition with passage of vesicles, 4% (2) presented with amenorrhea with exaggerated sign symptoms of pregnancy and 4% (2) had no symptoms other than amenorrhea (table-1). Among 50 patients 72% came before 16 weeks of gestation at the time of presentation and no patients after 24 weeks of gestation (table-2). In this study 72% patients were diagnosed with clinical suspicion and confirmed by USG. In 4% cases diagnosis was accidental during routine USG. Histopathology was done in all patients. Out of 50 patients 80% were complicated with hemorrhage, 8% were complicated with shock 4% were complicated with sepsis and 8% presented with no complications (table-3). Thirty patients (60%) were between 20-29 years of age and only 4 (8%) were above 40 years. Forty percent (20) of patients were nulliparous and 40% were of low parity and 20% were grand multipara

Table-I
Clinical presentation of the cases (N=50)

Presenting symptoms	Number of patients	Percentage (%)
Amenorrhea with vaginal bleeding	30	60
Amenorrhoea with vaginal bleeding & passage of vesicles	8	16
Amenorrhea with lower abdominal pain	8	16
Amenorrhea with exaggerated sign symptoms of pregnancy	2	4
Amenorrhea was the only symptom diagnosed during routine USG	2	4

Table-II
gestational period at the time of presentation (N=50)

Period of amenorrhea at the time of presentation	Number of patients	Percentage, (%)
<12 weeks	13	26
12-16 weeks	23	46
17-20 weeks	10	20
21-24 weeks	4	8
>24 weeks	0	0

Table-III
Immediate complications in study cases (N=50)

Immediate complications	Number of patients	Percentage, (%)
Hemorrhage only	40	80
Hemorrhage and shock	4	8
Sepsis	2	4
Without any complications	4	8

Seventy two percent (36) patients received first line treatment with suction evacuation & curettage, 12 (24%) patients were treated by D&C due to incomplete evacuation earlier and 2 patients needed laparotomy followed by hysterectomy due to uterine perforation (table-4). Among 50 patients 28% had incomplete evacuation and 14% developed shock and 4% had uterine perforation managed by resuscitation by blood transfusion followed by laparotomy and hysterectomy (table -5). In this study 64% of patients appeared for regular follow up for one year. 20% appeared irregularly and 16% dropped out. (Table-6).

Table-IV
Surgical treatment of the cases (N=50)

Treatment received by the patients	Number of patients	Percentage, (%)
Suction evacuation and curettage	36	72
D&C	12	24
Suction evacuation followed by total abdominal hysterectomy	2	4

Table-V*immediate postoperative complications (N=50)*

Complications	Number of patients	Percentage, (%)
Incomplete evacuation	14	28
Shock	7	14
Perforation	2	4

Table-VI*Follow up of patients (N=50)*

Follow up	Number of patients	Percentage, (%)
Regular follow up	32	64
Irregular follow up	10	20
No follow up	08	16

Among the regular followed up patients 2 (6.25%) patients develop Persistent Gestational Trophoblastic Disease(GTD) and 30 patients(93.75%) did not develop any late complications and completely cured. Among the 18 patients who had failed regular follow up one patient (5.5%) developed Persistent Gestational Trophoblastic Disease(GTD) (table-7). 8 patients received no follow up and one of the dropped out patient later presented with severe anemia and respiratory distress and diagnosed choriocarcinoma and died. So 60% patients cured completely and one patient died due to severe complication due to failed follow up (table-8).

Discussion:

In this study the incidence of molar pregnancy was 8.27 per thousand pregnancies that is 1 in 121 pregnancies. Study by Nahar (20005-2006) in FMCH &BSMMU showed incidence of molar pregnancy to be 1 in 141 pregnancy that is 7.08 per thousand pregnancy⁶. Another study by Khatoon RA 1993 in DMCH it was found that the incidence was 1 in 107 pregnancies e.g. 9.3 per thousand⁷. Study by Akhter 1978-1980 at SSMC and Mitford Hospital showed that incidence of molar pregnancy was 1 in 144 delivery that is 6.9 per thousand⁸. Study by Mungan E. 1996 showed much lower incidence 1.84 per thousand pregnancies⁹. Another study in India by Reddy and Rajeswari during 1989-91 showed an incidence of 4.08 per thousand pregnancies¹⁰. In this study maximum number of patients (60%) were in 20-29 yrs age group. Study by Nahar (2005-2006) at FMCH & BSMMU

showed that 64% patients were in 20-29 yrs age group⁶. A study by Khatoon RA in 1993 at DMCH showed that 63.75% patients were in 21-30 yrs age group⁷. Another study of 287 patients was done in Pusan, Korea¹¹ which showed highest number patients (70%) were below 30 yrs of age. In a study of 38 cases from the department of Obstetrics and Gynecology, Pennsylvania Hospital, maximum (60%) patient was between 20-30 years. Findings of this study are comparable of the previous observations. In present series most of the patients (60%) were multipara. also a large percentage (40%) of patients were nulliparous.

The study of 50 cases of GTD at Tripur Maternity Hospital India by Reddy and Rajeshwari showed that 70% patients were of 1-3 parity where as the study of 310 cases by Mungan et al (1996) differ from present study in that multiparty was found to be strongly associated with hydatidiform mole in 60% cases. So findings of present study were consistent with other study but it differed from the study by Mungan et al (1996)⁹.

In present series most of the patients with molar pregnancy had blood group B (36%). In the study of Nahar most of the patients with molar pregnancy had blood group A (32%). The study of Reddy and Rageshwari (1994) showed 52% of molar pregnancy patients had blood group O. Study by Nahar in FMCH & BSMMU Hospital (2005-2006) showed abnormal vaginal bleeding and amenorrhea were the commonest (60%) complaints⁶. According to Gold Stein DP, Berkowitz RS (1994) the most common presenting symptom in patients was bleeding (97%)¹³. A study by Curry SL from North Carolina USA of 347 patients 89% of patients had abnormal bleeding¹⁴. In this study (Table-1) 60% patients presented with abnormal vaginal bleeding with amenorrhea, 16% presented in addition with passage of vesicles, 4% of patients were diagnosed accidentally by USG and had no symptom except amenorrhea.

Out of 50 patients 46% patients were at 12-16 weeks of gestation at the time of admission (Table-2) which is consistent with the study of Nahar with (40%) patients with 12-16 weeks of gestation at admission⁶. No patients presented beyond 24 weeks and 26% patients presented before 12 weeks in this series. In the present study diagnosis was confirmed by USG 72% and pre evacuation serum beta HCG in (20%), 4% was diagnosed by USG without any symptom. Histopathology was done for all patients.

Most of the patients (80%) in this series came with hemorrhage as the immediate complication, 8% presented with shock 4% presented with no complication, no patient presented with preeclampsia. In Nahar study 80% presented with hemorrhage as immediate complication, 12% presented with shock, no patients had preeclampsia. A study of 327 patients by Curry S.L. from North Carolina showed that 80% had abnormal uterine bleeding, 12% developed preeclampsia. So our study correlates with both the studies in that maximum presentation was as hemorrhage as immediate complication, but other severe complication like shock is comparatively low in this series probably because of early presentation & early intervention than previous which can also explain that some patient also had no complication at diagnosis.

Among the treated patients 14 (28%) patient had incomplete evacuation and treated with D&C. Seven (14%) patients developed shock and managed with blood transfusion and other measures. Two (4%) patient had uterine perforation and had laparotomy followed by hysterectomy (Table-4). Among the three patients (6%) who developed persistent mole (Table-7) had no evidence of metastasis. Two of them were treated with chemotherapy and one was treated with total abdominal hysterectomy. One patient (2%) who attended no follow up developed choriocarcinoma and presented with severe anemia & lung metastasis and died. Follow up of the patients were done by clinical examination, serum beta HCG, X-ray chest (where indicated) and USG (where indicated) for a period of 1 year. In this series (Table-6) 32 (64%) patients of GTD attended for regular follow up, 20% had irregular follow up, 16% had dropped out. In the study of Nahar Shamsun 70% patients attended for regular follow up, and 30% dropped out. In her study no patient had attended irregularly for follow up.

Thirty (60%) patients were cured by 6-8 weeks, 6% developed persistent mole which was evidenced by persistently increasing or plateau of beta HCG and 2% developed choriocarcinoma which was evidenced by presence of pulmonary metastasis and increasing or raised level of beta HCG. In comparison to Nahar study (2005-2006) in FMCH and BSMMU that showed 8.55% patients developed persistent mole and 5.7% patients developed choriocarcinoma, but cure rate was similar. In Boston 23% patients developed persistent trophoblastic disease¹⁶ and in Ankara Turkey (1996)

14.5% patients were diagnosed as persistent molar disease⁹.

Conclusions:

Incidence of GTDs in FMCH was 8.27 per thousand pregnancies, more common in multiparous women of low socioeconomic class and in B+ve blood group women. Incidence in nulliparous is also high. Maximum patients presented at 12-16 weeks of gestation with abnormal vaginal bleeding. Seventy two percent patients were treated with suction evacuation and curettage. Hemorrhage was most common complication. During one year of surveillance period 64% patients attended the follow up protocol regularly, 20% had irregular follow up and 16% dropped out. The incidence of Persistent Gestational Trophoblastic Disease (GTD) was 6% and choriocarcinoma was 2%. It seems that attendants for follow up can be raised by proper counseling and raising awareness of the patients. As prognosis of persistent GTD can only be improved by early diagnosis of the cases and by early administration of chemotherapeutic agents, only way to save these women by regular follow up. That is only possible by raising awareness and counseling.

References:

1. Decherney, Nathan, Current Obstetrics & Gynecologic Diagnosis & Treatment, 10th edition, 2007, McGraw-Hill, 885-894
2. Dutta D.C. Text book of Obstetrics, 6th edition, 2007, Typesetter and Printer, 28-36, 385-424
3. Kumer, Malhotra, Jeffcoate's principles of Gynecology, 7th edition, 2008, Jaypee Brothers, p-161-169.
4. Parazzaini F et al. Risk factors for gestational trophoblastic disease, a separate analysis of complete and partial moles. J Obstet Gynaecol, 1991; 78(6); 1039-1045
5. Buckley JD. The epidemiology of molar pregnancy and choriocarcinoma. J Clin Obstet Gynaecol 1984; 27(1): 153-156
6. Nahar, Molar pregnancy Analysis of 50 cases in FMCH & BSMMU, Dissertation FCPS examination, Dhaka, 2005.
7. Khatoon RA. Clinical profile of the patient admitted with hydatidiform mole in DMCH, Dhaka-A study of eighty cases. Dissertation FCPS examination, Dhaka 1995.

8. Akter. Hydatidiform mole. Dissertation ,FCPS examination, Dhaka 1981
9. Mungan T, Kuscu E, Dabakoglu T, Seroz S, Ugur M, Cabanoglu O ,Hydatidiform mole; clinical analysis of 310 patients. International journal of Obstel Gynaecol, 1996;25;233-238
10. Reddy T, Rajeshwari K, Epidemiology of gestational trophoblastic disease in Govt. Maternity hospital Tirupati,J. Obset Gynecology of India 1994;p565-569.
11. Martin BH, Kim JH. Changing face of gestational, trophoblastic tumor. Int J Obstel. Gynaecol ,1998;(60):111-120
12. Matsui H, Iitsuka Y , Yamazawa K , Tanaka N ,Seki K, Sekiya S, Changes in the incidence of molar pregnancies. Hum. Reprod. 2003 Jan;18(1):172-5.
13. Goldstein DP, BerkowitzRS. Current management of complete and partial molar pregnancy. J Reprod Med 1994;39(3);139-146.
14. Curry SL et al. Hydatidiform mole-Diagnosis, management and long term follow up of 347 patients.J Obstel Gynaecol 1984;27 (1):192-198.
15. Mangili G, Garavaglia E, Cavoretto P, Gentile C, and Scarfone G, Rabaiotti E. Clinical presentation of hydatidiform mole in northern Italy: has it changed in the last 20 years? Am J Obstel Gynecol.2008 Mar;198(3):302.
16. Soto Wright V. Bernstein M, Goldstein DP, Berkowitz RS. The changing clinical presentation of complete molar pregnancy.Obset Gynaecol 1995;264(5):775-779.
17. Gemer O, Sega S, Kopman A, Sasson E. The current clinical presentation of complete molar pregnancy. Arch Obstel Gynaecol, 2000;264(1):33-34.