



STUDY OF GESTATIONAL TROPHOBLASTIC DISEASES

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ABSTRACT

Introduction: Gestational trophoblastic disease (GTD) is a group of conditions that arise from trophoblastic tissue after fertilization. Published literature on GTD from the Indian subcontinent is minimal. Hence there is a need to evaluate the risk factors, complications, management, outcome of the condition.

Methods: It is a retrospective study of GTD managed at our hospital from April 2015 to October 2016.

Results: The incidence was 0.27%. 7 were complete, 3 partial, 2 invasive moles, 1 PSTT and 1 choriocarcinoma. Age group of presentation ranged from 20-36 years. 28.57% primigravidae, 35.7% presented in first trimester. 10 had vaginal bleeding, 4 were detected incidentally, 4 cases had vomiting and 3, pain abdomen. Anaemia, theca lutein cysts, hyperthyroidism, hypertension and mortality were reported. Treatment options were surgical and medical.

Conclusion: GTD has a rising incidence. With the use of better diagnostic modalities, the condition can be detected early and treated appropriately.

KEYWORDS : GTD, Molar pregnancy, BhCG, Amenorrhoea, Maternal mortality, Methotrexate

INTRODUCTION

Hippocrates was probably the first to describe gestational trophoblastic disease around 400 BC in his description of dropsy of the uterus.¹ Gestational trophoblastic disease (GTD) is a spectrum of cellular proliferations arising from the placental villous trophoblast encompassing 4 main clinicopathologic forms: hydatidiform mole (complete and partial), invasive mole, choriocarcinoma, and placental site trophoblastic tumour (PSTT) (Table). The term "gestational trophoblastic neoplasia" (GTN) has been applied collectively to the latter 3 conditions, which can progress, invade, metastasize, and lead to death if left untreated. GTD was historically associated with significant morbidity and mortality. Hydatidiform moles were often accompanied by serious bleeding and other medical complications prior to the development of early detection and effective uterine evacuation means in the 1970s. The outcomes for GTN were likewise poor before the introduction of chemotherapy into their management 50 years ago. The mortality rate for invasive mole approached 15%, most often because of hemorrhage, sepsis, embolic phenomena, or complications from surgery. Choriocarcinoma had a mortality rate of almost 100% when metastases were present and approximately 60% even when hysterectomy was done for apparent nonmetastatic disease. Gestational trophoblastic neoplasms are now some of the most curable of all solid tumours, with cure rates 90% even in the presence of widespread metastatic disease.²⁻⁴

Methods

It is a retrospective study of cases with Gestational Trophoblastic Diseases (GTD) managed at a tertiary care centre in Mumbai from April 2015 to October 2016 (1.5yrs). All patients diagnosed with GTD (by clinical examination, USG and B HCG) were included in the study.

Aims and objectives**To study**

1. The incidence of GTD
2. The risk factors, clinical presentations of GTD
3. Various modalities of management of GTD

Inclusion criteria

All patients presenting to the OPD/casualty with the diagnosis of GTD, (diagnosed clinically, by radiological imaging and BHCG).

Exclusion criteria

Intrauterine viable or non-viable pregnancies without any clinical, biochemical or radiological evidence of GTD.

Results

14 cases of GTDs have been reported out of 5034 total confinements during the period of study, the incidence being 0.27%.

Table 1: Type of GTD

Type	Number of cases	Percentage
Complete mole	7	50%
Partial mole	3	21.42%
Invasive mole	2	14.28%
PSTT	1	7.14%
Choriocarcinoma	1	7.14%

50% (7 cases) were complete moles, (3 cases) 21.42% partial moles, 14.28% (2 cases) invasive moles, 7.14% (1 case) each of Placental Site trophoblastic tumour and choriocarcinoma (Table 1).

Table 2: Age at presentation

Age group	Number of cases	Percentage
20-25 years	7	50%
26 -30 years	4	28.57%
31-35 years	2	14.28%
> 35 years	1	7.14%

The youngest patient was 20 years of age (a case of complete mole) and the oldest patient, 36 years (a case of placental site trophoblastic tumour), the mean age at presentation being 26.14 years

Table 3: Obstetric score at presentation

Parity	Number of cases	Percentage
G1	5	35.71%
G2	4	28.57%
G3	3	21.42%
>G3	2	14.28%

Most of these cases were primigravida (28.57%) .

Table 4: Time of presentation

	Number of cases	Percentage
First trimester	5	35.71%
Second trimester	9	64.29%

35.7% (5 cases) presented in the first trimester while 64.28% (9 cases) presented in the 2nd trimester.

Table 5: Symptoms

Symptoms	Number of patients
Bleeding per vagina	10
Vomiting	3
Pain	2
Incidental	4

10 cases presented with bleeding per vagina, 4 cases were detected incidentally during a routine ultrasonographic examination. In addition to bleeding per vagina, 4 cases also presented with vomiting and 3 cases with pain abdomen.

Table 6: Complications

Complication	Number of cases
Anaemia	10
Need for blood transfusions	8
Theca lutein cyst	5
Hyperthyroidism	4
CCU admission	2
Hypertension	1
Mortality	1

The complications noted were anaemia (10 cases), theca lutein cysts (5 patients), hyperthyroidism (4 cases), and hypertension (1 case). Out of 10 cases presenting with anaemia, 8 required blood transfusion.

Table 7: Details of patients requiring admission to critical care unit

Details	Patient 1	Patient 2
Age	21yrs	35yrs
Parity	Nullipara	P4L4
Type of GTD	Complete mole	Complete mole
Period of gestation	10wk	15wk
Other co-morbidities	Nil	Nil
Complaints	Bleeding P/V and vomiting	Bleeding P/V
Uterus size	20weeks	26wk
BhCG levels on admission	428885	>10 lakh
Anaemia	+	+
Hyperthyroidism	+	+
Hypertension	-	+
Need for blood transfusion	+	+
Need for CCU admission	Persistent tachycardia? Thyroid storm	Persistent tachycardia? Thyroid storm
Duration of stay in CCU	1 day	1 day
BhCG after evacuation	44021	157002

There were 2 cases that required intensive monitoring in the Critical care unit.

Table 8: Modality of management

Management	Number of cases
Suction and Evacuation	5
Suction & evacuation + chemotherapy	7
Hysterectomy	2

Only suction and evacuation sufficed for 5 cases, Suction, evacuation with single agent chemotherapy was required for 7 cases, whereas hysterectomy was warranted in 2 cases.

An average fall of serum Beta human Chorionic Gonadotropin levels immediately post evacuation was by 86.5%

One mortality was reported. The case was a 30year, nullipara, who came with complaints of bleeding per vagina and an outside ultrasound showing fibroid uterus. She was severely anaemic with haemoglobin of 5gm%. Urine pregnancy test was positive and therefore an emergency curettage was done. Due to non-declining symptoms, a repeat ultrasound was done which showed retained products of conception, and BhCG: 5, 75,120. A repeat Suction & Evacuation was done, post which BhCG > 10 lakh and histopathology suggestive of choriocarcinoma. CXR PA s/o small nodular opacities in left upper zone of lung s/o? Infective etiology, Metastasis. HR CT was done which multiple metastatic nodules in lung. She was started with chemotherapy. However, she succumbed due to multiple metastases.

Clinical profile of patients requiring hysterectomy

Case1: This was a 24year, P2L2A1, with initial B HCG 125455 IU/ml, aborted a male foetus of 200g with moles of weight 1.25kg. Post abortal ultrasound was suggestive of an invasive mole confined to the uterus with no extension into the pelvis (endometrium not visualised with loss of endomyometrial differentiation). MRI also showed an enlarged uterus with loss of endomyometrial junction and abnormal soft tissue lesion in endometrial cavity extending into myometrium more into anterior wall than posterior wall. She was given 2 cycles of chemotherapy, post which B HCG was 2486, MRI findings remaining the same. To eradicate the active disease a non-descend vaginal hysterectomy was done, post which BhCG was 51.3. Histopathology report of this case showed invasive mole

Case2: A 36year, multipara, referred from a local health centre with menorrhagia and an ultrasound showing focal lesion in posterior wall of uterus. She had undergone a diagnostic Hysteroscopy, dilatation and curettage there, wherein they found a lesion on left lateral wall of uterine cavity, in-situ. A biopsy of this lesion showed placental site trophoblastic tumour, and was hence referred to our set up for further management. A repeat ultrasound at our tertiary health centre showed an ill-defined lesion in upper endometrial cavity with loss of posterior endomyometrial junction, suggesting invasion of posterior myometrium. MRI showed focal lesion seen within the endometrial cavity near the fundus, which could not be separated from the fundal and lateral wall of the uterine cavity. There was disruption of adjacent junctional zone with invasion of myometrium along fundoposterior wall reaching upto serosa. BhCG was minimal of 600.7 IU/ml. This case was subjected to a Total Abdominal Hysterectomy with Bilateral Salpingo-oophorectomy. Histopathology suggested Placental Site Trophoblastic Tumour.

Discussion

In our study, 14 cases of GTDs have been reported out of 5034 total deliveries during the period of study, the incidence being 0.278% or 2.78 in 1000 deliveries. In a study carried out by Mayun⁵ in Gombe, North-eastern Nigeria reported a frequency of 6 in 1000 deliveries, which is comparatively higher than the frequency found in our study.

The incidence and etiologic factors contributing to the development of GTD have been difficult to characterize. Epidemiologic studies have reported wide regional variations in the incidence of hydatidiform mole.⁶ Estimates from studies conducted in North America, Australia, New Zealand, and Europe have shown the incidence of hydatidiform mole to range 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 pregnancies.⁷

Investigations into possible ethnic and racial differences leading to an increased incidence of hydatidiform mole among American

Indians, Eskimos, Hispanics, and African Americans as well as various Asian populations have not been able to attribute them to genetic traits, cultural factors, or simply differences in reporting.⁸⁻¹⁰

In Europe and North America, choriocarcinoma affects approximately 1 in 40,000 pregnancies and 1 in 40 hydatidiform moles, whereas in Southeast Asia and Japan choriocarcinoma rates are higher at 9.2 and 3.3 per 40,000 pregnancies, respectively. The incidence rates of both hydatidiform mole and choriocarcinoma have declined over the past 30 years in all populations.¹¹⁻¹²

In our study, the commonest type of GTD were complete moles, followed by partial moles and then invasive moles, least common being Placental Site trophoblastic tumour and choriocarcinoma which is similar to what is known and published in standard texts of histopathology and gynaecologic pathology from the Western world.¹³ Mayun *et al.* in Zaria reported choriocarcinoma represented 37% of GTDs and the entire molar pregnancies constituted 63%. Among the molar gestations CHM was the most common type representing 60.7%, while PHM and invasive mole each accounted for 35.7% and 3.6%, respectively.

In our study, the youngest patient was 20 years of age (a case of complete mole) and the oldest patient, 36 years (a case of placental site trophoblastic tumour), the mean age at presentation being 26.14 years. This is quite similar to the age range of the Gombe study population (Mayun *et al.*) which was between 15 and 44 years with a mean age of 26.5 years. Ebonyi by Anuma *et al.*,¹⁴ reported an age range of 19–55 years, however, a mean age of 33.4 ± 7.4 years.

Most of the cases in our study were primigravida (28.57%) in our study. In a descriptive case series from 2001 to 2007 in Bharatpur, Nepal showed that in 15.5 % of cases of molar pregnancy had occurred among primigravida and same proportion had positive past history of molar pregnancy¹⁵ while large proportion (36.7 %) of primigravida suffered from molar pregnancy in another study¹⁶. However, studies have also shown that there is no real association of gravidity with molar pregnancy when corrected for age¹⁷.

In our study, 35.7% (5 cases) presented in the first trimester while 64.28% (9 cases) presented in the 2nd trimester. Nimisha *et al.*¹⁸ reported the period of gestation at presentation ranged from 8 to 34 weeks with a major proportion (66.4 %) having gestational age at time of evaluation more or equal to 13 week (early 2nd trimester). A study from Sweden also reported the mean gestational age at the time of USG was 12.4 weeks.¹⁹ According to New England Trophoblastic Disease Centre²⁰, the mean estimated gestational age at evaluation was 11.8 weeks (range 6–22)

The most common presentation of cases in our study was bleeding per vagina similar to Mayun *et al.* Honeycomb uterine appearance on pelvic ultrasound and passage of vesicles per vagina were reported as other modes of clinical presentation by Ocheke *et al.*²¹ in our study, 4 cases were detected incidentally during a routine ultrasonographic examination. In the last two decades, due to early diagnosis, there has been a change in the clinical picture of HM. Sun *et al.* reported fewer number of patients with CM presenting with vaginal bleeding. This was attributed to the implementation of early routine ultrasound for pregnant women in the region.²¹ In contrast, a majority of cases in our study presented with vaginal bleeding. The reason for this may be the labelling of any spotting and brownish vaginal discharge by a patient as vaginal bleeding.

In the recent years, patients rarely present with a compound theca-lutein cyst in the ovaries.²³ In this study, only 5 patients had ovarian enlargement. This low number is due to a policy to refer any patient with bleeding or hyperemesis in early pregnancy for ultrasound to exclude twins or molar pregnancy.

Pre-eclampsia in the second trimester, a typical feature of CM, is now rarely seen, (1 case) as the majority of cases are diagnosed early.

A study from Israel showed that although vaginal bleeding was the most common presenting symptom while 41 % of their patients were asymptomatic. Furthermore, systemic manifestations such as hyperemesis, pre-eclampsia, clinical thyrotoxicosis and respiratory distress were exceedingly rare in this study²⁴. It was seen from reports of a study done in Sweden that the current clinical presentation of complete mole has clearly changed compared to that of the classic type of mole with vaginal bleeding (77 %), abdominal pain (23 %) and hyperemesis (19 %) being the most commonly occurring symptoms. The clinical presentation of partial moles usually includes no typical symptoms. Rather, the signs and symptoms are those of incomplete abortion or missed abortion²⁵.

Nimisha *et al.* reported anaemia among 40.2 % of the patients, transfusion was done in 45.6 % of the patients, similar to our study wherein 71.43% cases were anaemic and 57.14% required blood transfusion. ICU admission and respiratory distress have been reported in other studies²⁶⁻²⁸ as well as ours

In the present study, the various management methods were suction evacuation, chemotherapy and hysterectomy. Combined treatment modalities were used among 50 % of patients. At a centre in Nepal, 13.3 % of patients were treated with suction evacuation, 62.2 % of patients underwent adjuvant chemotherapy among which 26.6 % received single agent chemotherapy and received EMA-CO regimen.²⁹

In our study, two patients have undergone hysterectomy as a modality of management. This modality of management is also seen in a study conducted in Pakistan³⁰, wherein, 12 out of 85 women underwent an elective hysterectomy as primary therapy for intact hydatidiform mole (HM); 5 of whom also underwent with bilateral salpingo-oophorectomy (BSO) and 4 with unilateral salpingo-oophorectomy. All these patients were noted to be older than 40 and had complete their family planning. In patients who underwent salpingo-oophorectomies, reason was noted to be the large size of associated ovarian cyst on one and/or both sides.

Conclusion

GTD has a rising incidence in today's world. With the use of better diagnostic modalities, the condition can be detected early and treated appropriately. However, as a silent disease, it presents with subtle signs and symptoms and hence can be easily misdiagnosed. Also, because of its subtle presentations, patients often present late in the course of the disease, wherein management of the condition can be sometimes life - saving. But once diagnosed accurately, it needs prompt treatment. Treatment however is easy and patients respond wonderfully with both medical and surgical management. However, it can be an important cause of maternal mortality.

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