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Incidence and clinical outcome of Gestational Trophoblastic diseases in a tertiary care hospital

***Anita Madan, **Sitara Soni, ***Upasana, ****Krati Agrawal, *****N.S. Neki**

*Assistant Professor,**Senior Resident, ***Lecturer, ****Junior Resident, Department of Obstetrics & Gynaecology, Govt. Medical College, Amritsar, India, 143001
*****Professor Medicine, Govt. Medical College, Amritsar, India, 143001
Corresponding Author: **Dr. Anita Madan,** Assistant Professor, Dept. of Obstetrics &Gynaecology, Govt. Medical College, Amritsar, India, 143001
E-mail: *dranitapuri@gmail.com*

Abstract

Introduction: Gestational trophoblastic disease (GTD) consists of group of disorders having pathology of abnormal trophoblastic proliferation ranging from hydatidiform mole to gestational trophoblastic neoplasia. Based on differences in morphology, histopathology, karyotype and clinical features, hydatidiform mole can be categorized into partial and complete moles. Molar pregnancy incidence varies across countries. The incidence of molar pregnancy in Asia is 1:100-300, choriocarcinoma 1:1000-2000 of live born children.

Aim: To determine the incidence, clinical outcome and management of women with gestational trophoblastic disease (GTD) at tertiary care hospital during a study period of 6 months.

Materials and Methods: This is an observational descriptive study conducted over a period of 6 months. In our study, total 18 cases were diagnosed with GTD, based on ultrasound, biochemical and histological examination.

Results: During study period, total patients delivered were 3610, out of which 18 cases had GTD. The overall incidence of GTD was 1/200 pregnancies, including cases of partial mole, complete mole, choriocarcinoma, and invasive mole. Highest incidence was found in extremes of age. 77.7% of cases presented in the first trimester, while 22.3% of cases presented in the second trimester. 77.7% of cases were complete mole, 11.1% were partial mole, and 11.1% were diagnosed as gestational trophoblastic neoplasm. Majority of cases (94.4%) presented with vaginal bleeding; pregnancy induced hypertension and preeclampsia was present in 16.6% of cases, 66.6% had abdominal cramps, 44.4% presented with signs of dehydration due to hyperemesis gravidarum, 22.2% had hyperthyroidism. Ultrasound was diagnostic in 95% cases, while histopathological examination was diagnostic in 100% of the cases. The incidence of GTDs in our hospital (1 in 200) is comparable to the incidence in Middle East and Far Eastern countries.

Conclusion: In our study, we found a high incidence of GTD in primigravidas. Most patients who had been diagnosed with GTD on USG were in first trimester.

Keywords: Gestational trophoblastic diseases, Hydatidiform mole, Gestational trophoblastic neoplasia.

Introduction

Incidence of gestational trophoblastic disease (GTD) varies greatly in different parts of world. In developing countries, incidence ranges from 1/100 to 1/1500 pregnancies. It forms a heterogenous group of disorders, comprising of hydatidiform mole- complete or partial and gestational trophoblastic neoplasia(GTN).

Hydatidiform mole is characterised by atypical hyperplastic trophoblasts and hydropic villi. Although persistent GTD follows molar pregnancy,it may follow any type of gestation as term pregnancy, abortion or ectopic pregnancy[1].Recurrent hydatidiform mole occurred in approximately 0.5-2.5% women in subsequent pregnancy.The risk of invasive mole or choriocarcinoma is substantially increased in these women[2].The evidence for a role of other factors; including diet, ethnicity, endogenous estrogen level, ABO blood group and environmental toxins , is weaker[3]. The role of high parity in the GTDs is unclear[4].

Abnormal bleeding and transvaginal ultrasonography(TVS) is the key to early diagnosis; and the frequent use of HCG assays is the key to follow up of these patients.The first symptom is vaginal bleeding and lower abdominal cramps. The blood may contain hydatid vesicles; and it may also be associated with hyperemesis, and preeclampsia. Other complications of GTD may include anemia, infection, trophoblastic embolism, uterine perforation, and choriocarcinoma[5].

In many cases of hydatidiform mole the ovary contains multiple theca-lutein cysts .These may vary from microscopic size to 6cm or more in diameter, their surfaces are smooth, often yellowish, and lined with lutein cells. The incidence of cysts in association with a mole is reported to the tune of 25 to 55%. They are thought to be resulting from over stimulation of lutein element by large amount of hCG secreted from proliferating trophoblastic cells.

The classic ultrasonographic image is of snowstorm pattern representing the hydropic chorionic villi. High resolution ultrasonography shows a complex intrauterine mass containing many small cysts[6].

Beta HCG is a glycosylated heterodimer protein produced predominantly by syncytiotrophoblst cells; consists of the alpha and beta units held together non-covalently.The alfa sub unit is similar to those of other pituitary glycoprotein hormones, but beta subunit is specific to hCG alone[1]. With intrauterine pregnancy, βhCG levels are found to increase by least 66% in 48 hours. Excessively high serum βhCG levels are found with GTDs (20 times the normal values)[3]. Spontaneous elimination of HCG from circulation following molar pregnancy evacuation predict a good outcome with minimum chances of future malignany.

Gestational Trophoblastic Neoplasm (GTN) also called malignant gestational trophoblastic diseases; refers to invasive mole, choriocarcinoma, and placental site trophoblastic tumor. Approximately half of cases follow a hydatidiform mole, 25 percent follow an abortion, and 25 percent develop after an apparently normal pregnancy[7].

Hydatidiform mole, a pathological condition, affects the course of a normal pregnancy[8].Approximately 15-25% of moles developed into invasive moles, and 3-5% into a choriocarcinoma[9]. Gestational choriocarcinoma was preceded by hydatidiform mole in 30-60% of cases which was 1000 times greater than after a normal pregnancy.The presence of androgenetic cell lines, particularly in those with a purely androgenetic complete hydatidiform mole component, warrants follow up because of some risk of persistent gestational trophoblastic disease[10].

This study was undertaken to know the incidence, characteristic symptoms, and management of patients diagnosed with GTD in a tertiary care centre in a time period of 6 months.

Materials and Methods

This is an observational study done in patients of GTD reporting to a tertiary care centre over a period of 6 months. Diagnosis of molar pregnancy was done by history, gynecological and ultrasound examination, serum β HCG levels and histopathology of uterine contents.

During this period, there were total 3610 pregnant patients admitted in our hospital,out of which, total 18 cases were diagnosed as GTD. These patients were studied using parameters such as last menstrual cycle, parity, socioeconomic status, obstetrics and gynaecological history, history of prior molar pregnancy, antecedent pregnancy, and clinical features like vaginal bleeding, abdominal pain, passage of cysts vaginally, headache, tremor, palpitation, anxiety, sweating (symptoms of hyperthyroidism), excessive vomiting and anorexia to the extent of causing dehydration (symptoms of hyperemesis gravidarum).

Investigations were done for each patient, such as complete hemogram; thyroid profile; hCG level; urine complete examination (for cases with hyperemesis gravidarum and preeclampsia), pelvic and abdominal ultrasound examination, chest X ray; and histopathological examination for the products of conception after suction and evacuation of the uterus done in every patient. Follow up with HCG levels are done with repeat dilatation and curettage after 1 week and weekly till date.

Results

During the period of the study (6 months), 3610 pregnant women were admitted to tertiary hospital. Out of which, 18 cases were found to have GTD (1 in every 200 pregnant women).

Table (1): The incidence of GTD in different age group

AGE(YEARS)	GTD(N-18) NO.(%)	No.of pregnant patient	INCIDENCE
≤20	1	254	1/254
21-25	7	1010	1/144
26-30	3	986	1/329
31-35	2	546	1/273
35-40	1	498	1/498
≥40	4	316	1/79
TOTAL	18	3610	1/200

Out of total 3610 pregnant women admitted to the hospital, 254 (7%) were in the age group of less than 20 years, 3040 (84.2%) were in the age group of the 20-39 years and 316 (8.7%) were above 40 year.

Table 2: Distribution of cases according to parity

PARITY	NO.OF CASES	PERCENTAGE
Primigravida	5	27.8
2-3	9	50
≥4	4	22.2
TOTAL	18	100

The highest incidence was found in primigravida(27.8%) and 50% cases of GTD had parity of (2-3), while 22.2% cases had parity ≥4.

Table 3: Distribution of cases according to socioeconomic state.

SOCIOECONOMIC STATUS	NO.OF CASES	PERCENTAGE
High Socioeconomic status	6	33.3
Low Socioeconomic status	12	66.6
TOTAL	18	100

Twelve cases (66.6%) were of low socioeconomic status, while six cases (33.3%) of high socioeconomic state, as per modified Kuppuswamy scale.

Table 4: Distribution of cases according to Gestational age

Gestational age	frequency	percentage
1st trimester	14	77.7
2nd trimester	4	22.3
TOTAL	18	100

The GTD was most commonly (77.7% of cases) diagnosed in the first trimester while 22.3% of cases were diagnosed in second trimester.

Table 5: Distribution of cases according to type of molar pregnancy

TYPE OF MOLAR PREGNANCY	NO.OF CASES	PERCENTAGE
COMPLETE MOLE	14	77.7
PARTIAL MOLE	2	11.1
GTN	2	11.1
TOTAL	18	100

Out of 18 cases of GTD; 14 cases (77.7%) were complete molar pregnancy, 2 cases (11.1%) were partial hydatidiform mole, and the remaining 2 cases (11.1%) were gestational trophoblastic neoplasm (GTN)

Table 6: Different clinical manifestations in cases presenting with GTD

SYMPTOMS	NO.OF CASES	PERCENTAGE
1.vaginal bleeding	17	94.4
2.anemia	14	77.7
3.abdominal cramps	12	66.6
4.hyperthyroidism	4	22.2
5.hyperemesis	8	44.4
6.preeclampsia	1	5.5
7.passage of cysts	5	27.7

94.4% of the cases presented with vaginal bleeding, 59.4% had just spotting, while 35% presented with massive hemorrhage. 66.6% of the cases presented with abdominal cramps, 44.4% of the patients diagnosed with hyperemesis gravidarum.22.2% cases presented with marked elevation of T3 and T4 hormones (hyperthyroidism).Pregnancy induced hypertension (PIH) occurred in 11.1%, with 5.5% cases had preeclampsia.

Discussion

Ultrasonographic scan in the first trimester has made the early diagnosis of GTD easy. However, in any patient where hyperemesis persists beyond first trimester, possibility of GTD should always be kept in mind. If GTDs is suspected on clinical grounds and ultrasonic scanning; quantitative estimation of serum βhCG should be carried out to confirm the diagnosis.

The incidence of GTDs in the current study (1/200 pregnancies) is comparable to the incidence in Middle East and Far Eastern countries. The highest incidence of GTD was in 1in 100 pregnancies from Indonesia, 1 in 200 pregnancies in Mexico, and 1 in 250 in Philippines. The lowest incidence was found in North America and Europe to the tune of 1:500. The incidence was 1:2000 pregnancies in Paraguay[3]. Netherlands showed an increasing trend of GTD most likely due to an increase in migrant Asian women giving birth[11].

Regarding the age distribution; in the current study, the highest frequency rate was found in the age group of 40 years and above (1 case / 79 pregnant women), while the lowest frequency rate was in the age group of 35-40 years (1 case/498 pregnant women),which is comparable with other studies such as: a study done in the state of Victoria/ Australia by Beischer et al revealed that the incidence of GTDs and its complications was higher in patients over 40 years of age[12]. A study done in USA by Hayash et al showed that the highest rate of molar pregnancy was found among women 40 years and older, and the second highest rate among women aged 15-19 year[13].The current results are also coinciding with the results of a study done in Mexico by Moore EL, where the GTDs were more common at the extremes of reproductive age.

Women in their early teenage or perimenopausal years are most at risk, women older than 35 years have a 2-fold increase in risk, women older than 40 years experience a 5-to 10-fold increase in risk compared to younger women[14].Another study done in Iran by Shamshiri-Milani which revealed that 76.6% of GTD cases were at age group of 20-39 years and 23.3% in the age group of below 20 years[15] .A study was done in Malaysia by Aye and Karali, which showed that 78.5% of HM at the age group of 20-40, 15.5% at the age group of below 20 years, the remaining (5.8%) was for above 40 years[16].

In our study, 67% of cases of GTDs were of low socioeconomic state while 33% of the cases were of high socioeconomic status,as per modified Kuppuswamy scale. Nutritional and socioeconomic factors appear to be important risk factors for molar pregnancy in some populations[13].

77.7% of the cases of GTD in our study were diagnosed in first trimester which is comparable to study done in Malaysia by Aye and Karali, showing that 75% of cases of GTDs were diagnosed at first trimester[17].

Vaginal bleeding remained the most common presenting symptom, occurring in 94.4% of cases which is comparable with a study done in USA by Soto-Wright et al showing that 84% of cases presented with vaginal bleeding[17]. A study done by Coukos et al, revealed that 75% of patients presented with abnormal vaginal bleeding[18].

Hyperemesis gravidarum was one of the presenting symptoms in 44.4% of the cases in the current study, while study done by Felemban et al reported that the hyperemesis gravidarum occurred in 29% of cases[18].

In our study, 5.5% of cases of GTD presented with pre-eclampsia, whereas a study done in USA by Soto-Wright et al which showed that only 1.3% GTDs cases presented with pre-eclampsia[18].

The possible explanation for this difference may be the nutritional status of the third world population.

22.2% of the patients in current study presented with elevated T3, T4 hormones, but studies by Felemban et al, showed only 3.3% cases, and study done in USA reported 10% cases. The reason is unknown.
Two cases (7.5%) out of 18 cases had GTN in current study. One case was diagnosed as choriocarcinoma, and other one as invasive mole, which was comparable to the study done by Al-Mulhim which reported 10% cases, out of which invasive mole (6.7%), choriocarcinoma(3.3%)[19] .A study in Finland done by Loukovaara et al revealed that 49% of choriocarcinoma identified during the study period were associated with a preceding hydatidiform mole.

Due to early diagnosis of GTDs by ultrasound and serum hCG level, early management with uterine evacuation and medical management was possible. Hence there were no complications reported in our study. Although preliminary results are promising, a great limitation to the study is incomplete information, commonly encountered in clinical care and program evaluation in similar settings[20,21,22]. Both incomplete information and incomplete documentation affect appropriate risk stratification, a challenge in GTN management that has been noted in cancer centers in low-resource settings[23].

Conclusion

The incidence of GTDs in BNMCC hospital is 1/200 pregnancies. Highest incidence rate was at the age group 40 and above and age group less than 25 years. The most common presentations were abnormal vaginal bleeding in early pregnancy, hyperemesis gravidarum, passage of cysts and the presence of hyperthyroidism. Malignant gestational trophoblastic condition was found in 7.5% cases.

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