ORIGINAL ARTICLE

An Analysis of Frequency and Histopatohologies of Gestational Trophoblastic Neoplasia at Tertiary Care Hospital Peshawar, Khyber Pukhtoonkhwa (KPK)

SHANDANA BAWAR, TANVEER SHAFQAT, SONIA RAFIQ, SANODIA AFRIDI, REHANA RAHIM
Department of Obstetrics & Gynecology, Lady Reading Hospital, Peshawar, Pakistan
Correspondence: Dr. Shandana Bawar, e-mail: shandanabawar@hotmail.com

ABSTRACT

Background: Gestational trophoblastic disease (GTD) encompasses pregnancy related disorders arising from abnormal trophoblast tissue. It consists of premalignant conditions, complete and partial hydatidiform mole and malignant conditions that include invasive mole, choriocarcinoma, placental site trophoblastic tissue and rare epitheliod trophoblastic tumors. The malignant conditions collectively are termed as gestational trophoblastic neoplasia (GTN) or persistent trophoblastic disease (PTD).

Objective: To determine the frequency and histopathology of gestational trophoblastic neoplasia, its clinical presentation and management options of this malignant condition.

Subjects and Methods: The study was a prospective study conducted at Gynae B Unit, PGMI Lady Reading Hospital, Peshawar from October 2010 to October 2013. Inclusion criterion was, all the patients with history of irregular vaginal bleeding following molar pregnancy, miscarriages, ectopic or term pregnancy or irregular PV bleeding after repeated evacuations, with raised serum beta human chorionic gonadotropin (βhCG). They were evaluated with transvaginal ultrasound, chest x-r ay and Full blood count. After confirmation of molar pregnancy patients were registered, underwent suction evacuation and were counseled regarding disease and disease complications, with stress on contraception with barrier methods and 2 weekly follow up with serum βhCG from same laboratory. Patient's contact number and home address was taken for sending reminders of follow-up. On follow- up if patient was symptomatic for hemorrhage, pain abdomen, respiratory distress, raised or static serum βhCG, patient was readmitted and further evaluation was done for Gestational trophoblastic neoplasia with full blood count, liver function tests, renal function tests, MRI pelvis, CT chest. Patient was scored to low risk i.e. <6 and high risk >6, according to prognostic FIGO scoring. Low risk patients were started on single agent methotrexate/Folinic acid (MTX/FA) and high risk patients were treated in collaboration with clinical oncologist for commencement of multiagent chemotherapy, usually EMA/CO.

Results: Total of 123 patients with gestational trophoblastic diseases were included. The mean age was 27±8 years. The gravidity ranged from primi gravida to grand multi gravida, average conception rate being 3.9. The mean gestational age of patients with gestational trophoblastic disease at time of diagnosis and suction evacuation was 12.05±4.5 weeks. Total number of complete hydatidiform moles were found to be 60 (48.7%), partial hydatidiform moles were 14 (11.3%), gestational trophoblastic neoplasia 38 (30%) and in case of 11 (8.9%) follow-up was missing and histopathologies could not be retreated. Among 38 cases of gestational trophoblastic neoplasia, confirmed histopathology suggested 13 (34%) were complete H-moles, 7(18%) were found to have parital H-moles and retained product of conception, each. Eleven (28.9%) clinically and biochemically behaved as invasive mole, with massive haemorrhage and were followed and treated according to serum βhCG.

Conclusion: The frequency of gestational trophpblastic neoplasia is high among patients with gestational trophoblastic disease.

Key words: Gestational trophoblastic disease, Persistent trophoblastic disease, Serum beta hCG

INTRODUCTION

Gestational trophoblastic disease (GTD) encompasses pregnancy related disorders arising from abnormal trophoblast tissue. It consists of premalignant conditions, complete and partial hydatidiform mole and malignant conditions that include invasive mole, choriocarcinoma, placental site trophoblastic tissue and rare epitheliod trophoblastic tumors. The malignant conditions collectively are termed as gestational trophoblastic

neoplasia (GTN) or persistent trophoblastic disease (PTD). Trophoblasts are cells that arise from the outer cell mass of an embryo and develops into placenta.[1,2]

World wide the incidence of Gestational trophoblastic disease is 0.5 and 8.3 cases per 1000 live births, the incidence is twice as high in some Asian countries and Asian woman in UK and America.[3] The exact incidence in Pakistan is not known, however in one study the reported frequency of GTD was 28 per 1000 live births.[4,5] Molar pregnancy can arise from any type of gestation including miscarriage, ectopic pregnancy and term pregnancy. The disease produce a hormone human chorionic gonadotrophin, which is important in diagnosis, management and follow up of disease, hence making it an ideal tumor marker.[6,7] In proportion of patients, 10% in UK, the trophoblastic disease persists with symptoms of irregular vaginal bleeding/massive haemorrhage, abdominal pain, breathlessness, cough, respiratory failure or neurological symptoms and or elevated serum βhCG and is termed as GTN. The rationale of this study was to determine the frequency of GTN and histopathologically proven antecedent pregnancies that evolved into gestation trophoblastic neoplasia, its clinical presentation and management.

SUBJECTS AND METHODS

The study was a prospective study conducted at Gynae B Unit PGMI Lady Reading Hospital, Peshawar from October 2010 to October 2013. After informed consent, the subject were enrolled as per inclusion criteria. The Inclusion criterion was, all the patients with history of irregular vaginal bleeding following molar pregnancy, miscarriages, ectopic or term pregnancy or irregular PV bleeding after repeated evacuations, with raised serum βhCG. They were evaluated with transvaginal ultrasound, chest X-ray and full blood count. After confirmation of molar pregnancy patients were registered, underwent suction evacuation and were counselled regarding disease and disease complications, with stress on contraception with barrier methods and 2 weekly follow up with serum βhCG from same laboratory. Patient's contact number and home address was taken for sending reminders of follow-up. On follow-up if patient was symptomatic for hemorrhage, pain abdomen, respiratory distress, raised or static serum βhCG, patient was readmitted and further evaluation was done for gestational trophoblastic, neoplasia with full blood count, liver function tests, renal function tests, MRI pelvis and CT chest. Patient was scored to low risk i.e. <6 and high risk >6, according to prognostic FIGO scoring. Low risk patients were started on single agent methotrexate/Folinic acid (MTX/FA) and high risk patients were treated in collaboration with clinical oncologist for commencement of multiagent chemotherapy, usually EMA/CO.

RESULTS

Total of 123 patients with gestational trophoblastic disease were registered in Gynae B Unit, PGMI Lady Reading Hospital Peshawar, in period of 3 years. The mean age of these patients was 27±8 years. The gravidity ranged from primi gravida to grand multi gravida, average conception rate being 3.9. The mean gestational age of patients with gestational trophoblastic disease at time of diagnosis and suction evacuation was 12.05 ±4.5 weeks. These patients came from almost all the districts of KPK and some of them were from Afghanistan. Total number of complete hydatidiform moles were found to be 60 (48.7%), partial hydatidiform moles were 14 (11.3%), gestational trophoblastic neoplasia 38 (30%) and in case of 11(8.9%) follow-up was missing and histopathologies could not be retreated. Among 38 cases of gestational trophoblastic neoplasia, confirmed histopathology suggested 13 (34%) were complete H-moles, 7 (18%) were found to have parital H-moles and retained product of conception each. Eleven (28.9%) clinically and biochemically behaved as invasive mole, with massive haemorrhage and were followed and treated according to serum βhCG (Tables 1-3).

Table 1: Demographical features of patients with GTN

Age group (years)	No.	%
≤20	6	15.7
21-30	18	47.3
31-40	11	28.9
>40	3	7.8
District-wise distribution		
Peshawar	9	23.6
Charssada	8	21.0
Mardan	3	7.8
Bannu	2	5.2
Nowshehra	2	5.2
Dir	2	5.2
Afghanistan	3	7.8
Miscellaneous	9	23.6

Table 2: Clinical presentation among patients with GTN (n = 38)

Presenting symptoms	No.	%
Irregular PV bleeding	25	65.0
Repeated evacuations	5	13.1
Pain abdomen	2	5.0
Shock	6	15.7

Table 3: Type of chemotherapy received by patients of GTN (n = 32)

Chemotherapy	No.	%
MTX/FA	28	73.0
EMA/CO	4	10.5

DISCUSSION

Trends in gestational trophoblastic disease are on rise and frequent in Asians and asian population in UK. In present study the frequency of GTD was found to be 0.68% among obstetrical patients which makes about 123 patients with GTD in 3 years, which is far more as compared to a recent study from Malaysia which found 102 patients with same disease in 6 years. It is seen that out of 123 patients 38 (30%) had malignant transformation into persistent trophoblastic disease or gestational trophoblastic disease, during follow-up. This is very high as compared to same study from Malaysia which showed frequency of gestational trophoblastic disease to be 3.9%.[8] Gestational trophoblastic neoplasias are seen in higher frequency in South East Asian as compared to Far East Asians.[9] This is often attributed to low socioeconomic status and poor nutritional status.

Gestational trophoblastic neoplasia developed in 13 (34%) complete hydatidiform mole (CHM) and 7 (18%) partial hydatidiform mole and retained product of conception each. Recent study by Schmitt et al[10] suggested the risk of GTN however, to be 0.34% (6/1747), 0% (0/593) after a partial HM (PHM), 0.36% (4/1122) after a complete HM (CHM). While studies from Australia and England suggested 1.7% and 5.6 % of partial HM underwent malignant transformation respectively.[11,12] This vast difference is due to, firstly the studies have been carried out in different hospital based communities, secondly the antecedent pregnancies have been diagnosed by different methods. In our study histopathologies were considered while in other studies immunostaining was the choice for diagnosis. Histopathology of molar and non-molar hydropic pregnancies at early gestations are often misinterpreted and there is also an interobserver difference.[13,14] The mean gestational age of GTD at time of diagnosis and suction evacuation in our study was found to be 12.05±4.5 weeks. For this reason it is now recommended that genetic studies including DNA analysis and immunostaining should be carried to confirm the genotype of molar pregnancy.[10,13] In our study it was noted that 7 (18%) of antecedent pregnancy were found to have histopathology of retained product of conception which is far less as compared to the study from Nigeria, which explains abortion (46.7%) to be predisposing factor to choriocarcinoma.[15] Eleven (28%) of patients came with massive hemorrhage for which emergency hysterectomy was done and the specimen uteri showed invasive moles, therefore histolopathological diagnosis of antecedent pregnancies could not be made out. After hysterectomy these patients were followed with weekly serum βhCG till normalization. Only 5 of them received single agent chemotherapy (MTX/FA) for plateued or rising serum βhCG.

Frequency of chemotherapy among GTN patient was found to be 32 (84%) out of 38 patients. Six (15.6%) patients had life saving hysterectomies who were subjected to weekly follow up with serum βhCG till normalization and then according to protocol lifelong. Out of 32 patients receiving chemotherapy, 28 received single agent chemotherapy MTX/FA. Four patients received multiagent chemotherapy EMA/CO. Out of those 4 patients, 2 patient received EMA/CO after developing resistance to MTX/ FA. While 2 of them were subjected to EMA/ CO as they fell into high risk group with ≥6 score.[2] High risk patients developed GTN after term pregnancy and after evacuation of complete hydatidiform mole. Only 1 patient died whose follow-up was lost and subsequently came with metastatic disease to lungs as well as CNS. Patients who developed resistance to single agent chemo should be treated with multiagent chemotherapy containing drugs like platinum agent or etoposide.[16,17] Chemotherapy was continued until serum βhCG values were normal for three consecutive chemotherapy cycles, after which the patients are being followed for life time according to protocol.

CONCLUSION

Frequency of gestational trophoblastic neoplasia is high among gestational trophoblastic disease. Multicenter, community-based studies are needed

to present the real incidence of gestational trophoblastic disease as disease has a potential to develop into malignant forms which are highly curable. A national register is must for strict follow up of patients. Follow up is mandatory with counseling of patients and family about the disease with financial and psychological support.

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