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Original Research Article

Study of Gestational Trophoblastic Diseases at a Tertiary Care Hospital in Chhotanagpur Area

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Abstract

Aim: Study of gestational trophoblastic diseases at a tertiary care hospital in India

Methods: This observational study conducted in the Department of Obstetrics and Gynecology, RIMS, Ranchi, Jharkhand, India, the study population consisted of all the pregnant women registered at the study centre. Due to low incidence of gestational trophoblastic disease, all the diagnosed cases of GTD reporting to the tertiary care hospital were included. The data for total number of GTD cases, total number of pregnancies and live births in the hospital were taken from hospital registries. Following selection criteria were adopted for the present study. All the cases diagnosed as GTD either histologically or sonographically which included complete mole, partial mole, invasive mole, choriocarcinoma, PSTT and ETT.

Results: There were total 21000 deliveries at the study centre during study period. A total of 53 cases out of these were diagnosed to have GTD. These 53 patients were considered as participants for final analysis. Regarding symptoms of the participants, amenorrhea was seen in all 53 (100%) patients. The commonest symptom was bleeding per-vaginum which was seen in 40 (75.5%) of patients. The classic symptom of passage of grape like vesicles was seen in 5 (9.4%) of patients only. On evaluation of cases with ß-hCG, majority (70%) had pre-evacuation ß-hCG values between 1,00,000- 10,00,000 IU/L, with remaining 30% having ß-hCG values between 10,000-1,00,000 IU/L (mean pre- evacuation ß-hCG- 1.89±1.70 lakhs IU/L). The values changed post-evacuation (24 hours) to a mean of 0.62±0.54 lakh IU/L. Total 18 (90%) patients were followed till they attained first normal value of β hCG and the mean time taken for the same was observed to be 9.2±2.31 weeks. With respect to thyroid status, 15% of CHM were hyperthyroid whereas 45% of PHM patients were hyperthyroid. The need for blood transfusion was more in cases of CHM (80%) with average 1.6 units required per person compared to PHM where 80% required blood transfusion with an average of 2 units per person.

Conclusion: In conclusion, it can be said that early diagnosis and treatment is the key in GTD. Regular follow up of the patients is critically important for ensuring complete remission.

Keywords: Gestational Trophoblastic Diseases, Blood Transfusion, Thyroid Status.

Introduction

The gestational trophoblastic diseases encompass a wide range of conditions that vary in their clinical presentation, their propensity for spontaneous resolution, local invasion and metastasis and their overall prognosis. Gestational trophoblastic diseases are the lesions of trophoblasts with varying proliferative capacities ranging from Non-neoplastic hydatidiform mole (complete hydatid form mole, partial hydatid form mole, invasive mole) to bonafide neoplastic conditions gestational choriocarcinoma, placental site trophoblastic tumour and Epithelioid trophoblastic tumour[1,2]. In addition, two tumour like conditions are also included i.e exaggerated placental site reaction and placental site nodule or plaque[3]. The highest incidence of hydatidiform mole per 1000 pregnancies is seen in South East Asia with rates ranging from 13 in Indonesia, 8 in Taiwan, 5 in Philippines and 3.8 in Japan.[4,8] North America[9,11] Europe, and Oceania have the lowest incidence with approximately 0.5-1.84/1000 pregnancies[12,13] The incidence of choriocarcinoma varies from 1 in 40,000 pregnancies in North America to 3.2/40,000pregnancies in South East Asia and Japan[3] The aim of this study was to review all molar pregnancies admitted at our institution and to study the incidence, clinical presentation, management, complications and outcome of molar pregnancies.

Material and Methods

This observational study conducted in the Department of Obstetrics and Gynecology, RIMS, Ranchi, Jharkhand, India, after taking the approval of the protocol review committee and institutional ethics committee. The study population consisted of all the pregnant women registered at the study centre. Due to low incidence of gestational trophoblastic disease, all the diagnosed cases of GTD reporting to the tertiary care hospital were included. The data for total number of GTD cases, total number of pregnancies and live births in the hospital were taken from hospital registries. Following selection criteria were adopted for the present study.

Inclusion criteria

- All the cases diagnosed as GTD either histologically or sonographically which included complete mole, partial mole, invasive mole, choriocarcinoma, PSTT and ETT.

Exclusion criteria

- All other intrauterine pregnancies
- Unwillingness to give consent for the study.

Patient's comprehensive history including age, address, chief presenting complaints, gravidity, gestational age, outcome of previous pregnancies, menstrual history were noted for all participants. Size of the uterus per abdomen was compared with gestational age and ascertained if it corresponded to the weeks of gestation. Per-speculum and per vaginal examination was also done. Relevant haematological and radiological investigations which included Hb%, blood grouping and Rh typing, thyroid function test, serum ß-hCG, USG and chest X-ray were undertaken. Cross matching samples were drawn for blood transfusions, if and when required. Suction and evacuation were done for all patients as a primary mode of management. The samples so obtained were sent for histopathological examination. Blood transfusions were done according to requirement of the patient either preoperatively, intraoperatively or in the post-operative period. Anti-D was given to Rh-negative women. The serum ß-hCG was repeated 48 hours after evacuation.

Follow up was done with weekly ß- hCG until normal for 3 consecutive weeks followed by monthly determination until the levels were normal for 6 consecutive months. The normal level of ß-hCG was taken to be less than 10 IU/L. At each follow up visit detailed history was taken

regarding irregular vaginal bleeding, pain abdomen, headache, cough, haemoptysis, and fever etc. Clinical examination, per speculum and per vaginal examination was done to look for signs of GTN. The time to achieve the first normal ß-hCG after evacuation was noted. USG as well as colour Doppler were done when clinically indicated. GTN was diagnosed during follow up either on the basis of a rise in serum ß- hCG levels or histopathology or with evidence of metastasis. Those diagnosed as GTN were classified as low risk or high risk using FIGO scoring system for GTN and were duly treated with chemotherapy[14].

Statistical analysis

The data was entered and analysed using MS excel software and chi-square test was applied. $p<0.05$ was considered as being significant. Data confidentiality was thoroughly ensured, and no individual finding was shared anywhere ever.

Results

There was total 21000 deliveries at the study centre during study period. A total of 53 cases out of these were diagnosed to have GTD, providing an incidence rate of 2.52/1000 deliveries. These 53 patients were considered as participants for final analysis.

Table 1: Presentation of clinical symptoms

Symptoms	Cases	Percentage
Amenorrhoea	53	100%
Per-vaginum bleeding	40	75.5%
Pain in abdomen	16	30%
Passage of grapes like vesicles	5	9.4%
Hyperemesis	5	9.4%
Hyperthyroidism features	5	9.4%

Age of the relatively young participant group ranged between 18 to 36 years (mean- 24.64±2.89 years). A total of 60.3% (32/53) participants were primigravida in the study. 16 (30%) of patients had previous history of full- term pregnancy while 13 (24.5%) had at least one abortion. Maximum number of patient (55%) presented in the first trimester (≤12 weeks), 40% presented between 13-20 weeks and only 1(5%) patient presented after 20 weeks, the mean gestational age at presentation being 12.7±3.86 weeks. Majority (55%) of the patients had uterine size larger than the period of gestation; 25% had uterine size corresponding to the period of gestation and 20% had uterine size smaller than the period of gestation.

Table 2: Diagnostic distribution of cases

Typing of case	Cases	Percentage
On histopathology report		
Complete mole	37	70%
Partial mole	13	24.5%
Invasive mole	3	5.6%
On USG report		
Complete mole	45	84.9
Partial mole	8	15.1%

Regarding symptoms of the participants, amenorrhea was seen in all 53 (100%) patients. The commonest symptom was bleeding per-vaginum which was seen in 40 (75.5%) of patients. The classic symptom

of passage of grape like vesicles was seen in 5 (9.4%) of patients only (Table 1).

The commonest blood group associated with GTD was A Rh-positive (45%), with AB Rh-positive (5%) being the least common. Rh-negative blood groups were not encountered in this study. The mean pre-treatment Hb% was 8.85±1.46 gm%. Only 5 (9.4%) patients had severe anaemia with Hb% less than 6.9 gm%. A total of 42 (79.2) patients required blood transfusion with mean requirement being 1.82 units of blood per patient. Out of 53 cases, 13 (24.5%) were hyperthyroid, while majority were having normal thyroid function functions 37 (70%) 3 was hypothyroid. All the study participants underwent chest X-ray and it was found to be normal in all of them.

Table 3: Distribution of cases by pre-evacuation ß- hCG level.

ß-hCG	Cases	Percentage
<10,000 IU/L	0	0%
10,000-1,00,000 IU/L	16	30%
>1,00,000 IU/L	37	70%

On histopathological examination, 37 (70%) were reported to be cases of complete hydatidiform mole (CHM) and 13 (24.5%) were partial hydatidiform mole (PHM). The specimen of uterus of 3 patients (5.6%) who underwent hysterectomy showed hydropic villi invading myometrium suggestive of invasive mole. No cases of choriocarcinoma, PSTT or ETT were seen in the study. Of the 53 patients who got ultrasound done, 45 (84.9%) showed picture of complete mole (Table 2).

On evaluation of cases with ß-hCG, majority (70%) had pre-evacuation ß-hCG values between 1,00,000- 10,00,000 IU/L, with remaining 30% having ß-hCG values between 10,000-1,00,000 IU/L (mean pre-evacuation ß-hCG- 1.89±1.70 lakhs IU/L). The values changed post-evacuation (24 hours) to a mean of 0.62±0.54 lakh IU/L. Total 48 (90.5%) patients were followed till they attained first normal value of β hCG and the mean time taken for the same was observed to be 9.2±2.31 weeks (Table 3).

Table 4: Comparison of complete mole versus partial mole

Variables	CHM (Mean±SD)	PHM (Mean±SD)	p value
Maternal age (years)	23.41±3.31	24.7±6.36	0.55
Gestational age (weeks)	12.43±2.19	15.18±7.50	0.19
ß-hcg (lakh IU/L)	1.82±1.89	1.94±0.86	0.87
48 hours repeat ß-hcg (lakh IU/L)	0.64±0.63	0.93±0.87	0.27
Time for ß-hcg normalization (weeks)	9.67±2.50	7.9±1.4	0.15
Blood transfusion (units)	1.60±1.19	2.10±1.97	0.47

According to prognostic scoring scale (PSS), 40% patients were in low risk and 60% patients were in high risk group in the study. Patients in high risk were then enrolled for chemotherapy for complete recovery. Suction evacuation was the primary mode of treatment and was undertaken in 90% of patients. 5.6% patient underwent hysterectomy in view of uterine perforation during suction evacuation with moribund status. 1 patient, who was at 26 weeks with partial mole, underwent preterm vaginal delivery. Complications were minimal in the present study. 15% patients had febrile morbidity. 3 (5.6%) patient had haemorrhage and one underwent hysterectomy.

Clinical characteristics were compared between patients of complete mole and partial mole. In all the studied parameters only, non-significant difference was observed between the groups. Although the pre-evacuation ß-hCG level and gestational age at presentation was higher in CHM patients compared to PHM, the difference was not statistically significant. The mean time taken for ß-hCG to return to normal levels after suction evacuation was 9.67±2.50 weeks in CHM and 7.9±1.4 weeks in PHM which was also not statistically significant, though it was higher in CHM.

With respect to thyroid status, 15% of CHM were hyperthyroid whereas 45% of PHM patients were hyperthyroid. The need for blood transfusion was more in cases of CHM with average 1.6 units required per person compared to PHM where required blood transfusion with an average of 2 units per person (Table 4).

Out of 53 cases, 3 (5.6%) was diagnosed as GTN. She underwent hysterectomy for uterine perforation during evacuation and histopathology of uterus showed hydropic villi invading myometrium suggestive of invasive mole. She belonged to high-risk category according to FIGO score and was started with single drug (methotrexate) chemotherapy.

Discussion

Because of wide geographical variations in the incidence of gestational trophoblastic disease as a result of differences in methodology, classifications of mole, case detection and definition of the denominator; the comparison of incidence of GTD among countries has been difficult[15]. The recent attempts at standardization of histopathological and clinical nomenclature has improved uniformity in the different epidemiological studies across the world.[15,16] Unlike few of the western countries, as India does not have the disease specific registry for gestational trophoblastic disease, only institution based studies are supposed to provide some light on the epidemiological data. Hence this study is an effort to understand the incidence, demographics, treatment and outcome of hydatidiform mole patients in a tertiary care government hospital.

The incidence of GTD in this study is observed to be 2.52 per 1000 deliveries. This is comparable to the rates observed in previous hospital-based studies in Dubai (2.5 per 1000 live births) and Malaysia (2.6 per 1000 deliveries). The only institute based similar study from India showed incidence rate of 1.31 per 1000.[17,18,9] In a study conducted across races in Northern England and Wales, the incidence of gestational trophoblastic disease in the Asian population was found to be 1.95 times higher than in the non-Asian population (1 per 387 live births versus 1 per 752 live births).[20] Majority of the patients belonged to age group 20-25 years (60%), similar to the study by Kumar N et al; with the mean ages being similar as well.[19] FIGO and WHO criteria states age more than 39 years as a high-risk factor; but this was not reflected in the present study as there were no patients with age more than even 36 years. This could be due to the small sample size, early age at marriage in the Indian society and attainment of maximum fertility at lower age itself. More than half of the patients were found to be below the age of 25 years. Age less than 18 years is not considered as a risk factor by WHO, though some experts have observed both extremes (<20 years and >35 years) to be at increased risk of disease.[21,24]

In the present study the commonest symptom after amenorrhea is per vaginum bleeding, seen in 75.5% of patients. The clinical study from Dubai reported incidence of vaginal bleeding in 29% patients only.[5] However, Fatima et al, noted bleeding per vaginum to be the commonest symptom seen in as many as 94.2%[23]. One of the most classical symptoms i.e. passage of grape like vesicles per vaginum was seen in only 9.4% of patients in the present study; while in the

Nigerian study by Ocheke AN et al, it was found in 60% cases.[22]

The antecedent pregnancy was an abortion in 24.5% of patients. These numbers were comparable with many other studies. The study from Pakistan observed 36.5% of patients to be primigravidas[14]. The other study from northern part of India had 21% primigravida among all patients and 26% had a history of abortion in antecedent pregnancy.[19] However the Nigerian study had 48% of the patients with previous history of at least one abortion.[22]

The mean gestational age during diagnosis in the present study was 12.7±3.86 weeks. This is comparable with many other recent studies, like Nirmala et al. having observed a mean gestational age of 11±3 weeks during presentation.[18] However Ocheke AN et al, reported a mean gestational age of 17 weeks during diagnosis.[22] This is probably because the routine use of ultrasonography for the evaluation of early pregnancy has led to earlier diagnosis and the mean gestational age at presentation has decreased.

In the present study a total of 29 (54.7%) women had a uterus larger than dates, which was similar to previous similar studies[17,19,22,23,24]. The usually high prevalence of anaemia and subsequent requirement of blood transfusion in GTD cases was also observed, with 80% patients having Hb of <10 gm% at the time of presentation and 79.2% participants requiring blood transfusion.

In the present study, the pre-evacuation β-hCG level was higher in complete mole group (1.94±1.86 lakhs IU/L) compared to partial mole group (1.82±1.89 lakhs IU/L), however the difference did not meet statistical significance (p=0.87), probably because of small sample size. Some similar studies with larger samples did note mean pre-evacuation serum β-hCG level to be significantly higher in the complete mole.[25,26]

The difference for number of weeks until the serum β - hCG level became undetectable was statistically not significant between complete and partial mole in this study (p=0.142), numerically higher in complete mole group though. Similar observations were made by Nirmala et al.[18]

In the present study histopathology examination (HPE) of 24.5% of the patients showed partial mole, and in 70.5% patients HPE showed complete mole. These proportions were not consistent with the published literature. The Malaysian study by Nirmala et al observed 46.1% patients to have CHM and 53.9% having PHM.[18] Lybol et al, observed 30.2% having CHM, 44.5% of patients having PHM and in rest 11.6% the HPE was unspecified.[27]

Complications usually associated with GTN include haemorrhage, fever, septicemia, tumour embolization and uterine perforation. These were minimal in our study. 3(5.6%) had haemorrhage. One underwent hysterectomy in view of uterine perforation. Only one (5%) patient developed GTN, that being invasive mole. Similar proportions were reported in the Malaysian study, where 3.9% patients developed persistent trophoblastic disease.[18] However in the study by Kumar et al, 23% of the patients developed invasive mole and 14% developed choriocarcinoma.[19]

Conclusion

In conclusion, it can be said that early diagnosis and treatment is the key in GTD. Regular follow up of the patients is critically important for ensuring complete remission. Further, a multi-centric study is essential in India to determine the true incidence and overall outcome of molar pregnancy, which will help in the understanding exact burden of the disease. Because of paucity of population-based studies in India, there is imminent need to establish a centralised disease specific registry to ensure availability of unbiased and representative data.

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