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Original Research Article

A Prospective Investigation of the Clinical and Epidemiological Aspects of Molar Pregnancy in a Tertiary Care Center

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Abstract:

Background and Objectives: Gestational trophoblastic diseases (GTD) refers to a spectrum of pregnancy related trophoblastic abnormalities. The objective of this study was to determine the incidence of molar pregnancies in DMCH, along with the demographics and risk factors associated and to evaluate its management and outcome.

Methods: The study was a prospective epidemiological study which includes fifty eight patients with gestational trophobastic diseases treated at the gynecological ward, Darbhanga medical college and Hospital Laheriasarai, Darbhanga. Study duration is Two years.

Conclusion: Incidence of molar pregnancies in this study was much higher as this hospital is the referral centre for Southeastern Odisha. However, proper reporting and follow up can prevent mortality associated with malignant transformation.

Keywords: Beta HCG, Chemotherapy, Gestational Trophoblastic Disease, Hydatidiform Mole, Molar Pregnancy.

Introduction

Gestational trophoblastic disease (GTD), the heterogeneous group of interrelated lesions that arise from abnormal proliferation of placental trophoblast. It includes Hydatidiform mole (complete or partial), invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT) and epithelioid trophoblastic tumor. Despite the problems of classification, it is normal to regard hydatidiform mole as the benign form of the trophoblastic disease, which as a potentially malignant condition may progress to choriocarcinoma. Hence GTDs are regarded as a spectrum of diseases. The incidence and etiologic factors contributing to the development of GTD have been difficult to characterize which is attributed to a number of factors, like inconsistencies in case definitions ,no centralized data bases and lack of proper control groups for comparison. 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 incidence was as high as 2.0 per 1000 pregnancies in South East Asia and Japan [1]. Extremes of maternal age and prior history of molar pregnancy are most important risk factors associated with molar pregnancy, apart from prolong use of contraceptive pill, β-carotene deficiency and racial factors. Vaginal bleeding is usually the commonest presenting symptom which was preceded by varying period of amenorrhoea. Hyperemesis, hyperthyroidism, preeclampsia and theca luteal cysts are usually associated with markedly elevated hCG value. More than 90% of patients with partial moles have symptoms of incomplete or missed abortion; the diagnosis is usually made after histological review of curettage specimens [2]. Serial quantitative serum β- hCG assays are helpful in diagnosis and follow of molar pregnancy.

Suction and evacuation is the preferred method of treatment independent of uterine size, for patients wishing to maintain fertility [3]. Clinical findings of prompt uterine involution, ovarian cyst regression, and cessation of bleeding are all reassuring signs but definitive follow-up requires serial serum quantitative hCG measurements.

Materials and Method

This is a prospective epidemiological study to determine incidence, demographics, management and outcome of molar pregnancies after a follow-up of six months. It includes fifty-eight patients with molar pregnancies treated at the gynaecological ward, Darbhanga medical college and Hospital Laheriasarai, Darbhanga. Ethical approval was obtained from the institutional ethical committee and informed consent was obtained from all patients.

Inclusion Criteria:

1. Women diagnosed with molar pregnancies sonologically or histopathologically.

2. Willing to give written informed consent to participate in the study

Predesigned Performa was filled at the time of presentation. Enquiry was made regarding bleeding per vaginum, hyperemesis gravidarum, pain abdomen, features of eclampsia, expulsion of grape like vesicles, respiratory difficulties and features of hyperthyroidism like tremor or tachycardia. General physical examination and detailed systemic examination was done. Height of the uterus and its consistency was ascertained. Perineum was inspected for bleeding per vaginum or expulsion of moles. Vagina was examined to exclude nodularity. Bimanual examination was done and condition of the cervix was also noted.

Routine laboratory investigations were done for each patient. Quantitative serum β-hCG level was determined to facilitate therapy and follow up. Ultrasonography of abdomen and pelvis was done to confirm the diagnosis and to know the ovarian status. Chest X-ray P-A view was done to detect presence of pulmonary embolization or metastasis.

In all cases of hydatidiform mole, suction and evacuation was done with wide-bore cannula, even if the uterus was 20 weeks or more. Patients with anemia (haemoglobin<8%) received blood transfusion. Cervical preparation with misoprostol was done in cases where os was closed. Oxytocin drip was started only after evacuation was complete to decrease the risk of trophoblastic embolisation. On histopathological examination, if a fetus or fetal tissue were present then mole was classified as partial otherwise it was considered complete. Cytogenetic analysis was not done. If serum β hCG levels fails to become normal or reelevation at 4-8 weeks or rising serum β hCG levels, single agent chemotherapy (MTX- FA regimen) was given. Those who failed to show response to MTX-FA were treated with combination chemotherapy (EMA-CO regimen). Each patient was followed for 6 months. The symptoms and signs of persistent molar pregnancy like amenorrhea, uterine enlargement, irregular bleeding, ovarian masses, difficulty in breathing, nodules in vagina and haemoptysis were looked in each patient. After molar evacuation, serum β-hCG levels were monitored at weekly intervals until these levels are normal for 3 consecutive weeks followed by monthly determination until the levels are normal for 6 consecutive months. All the patients were advised to avoid pregnancy during the entire interval of hormonal follow up by either oral contraceptive or by barrier methods.

Results

In present study, total 20294 deliveries enrolled from Two years. and 58 cases of molar pregnancies were diagnosed, treated and followed up for a period of 6 months. Incidence of molar pregnancies was found to be 2.85 in 1000 deliveries. Demographic properties are discussed in Table-I. Number of cases of complete mole was 53(91.4%), partial mole was 4 (6.9%) and invasive mole 1(%). There was no case of choriocarcinoma, PSTT and epitheloid trobloblastic tumor.

Table 1: different types of molar pregnancies (N=58)

Types	No of cases	Percentage
Complete mole	53	91.4
Partial mole	4	6.9
Invasive mole	1	1.7
Choriocarcinoma	0	0
Placental site trophoblastic tumor	0	0
Epitheloid trophoblastic tumor	0	0

Out of total 58 patients, majority were in 21-30 years age group (55.2%) (Table-II).70.7% belonged to low socioeconomic status (Table- III). Incidence of molar pregnancies was highest among primigravida (39.7%) (Table-IV). Most of the patients (66%) presented in second trimester with a mean gestational age of 12.8±2 weeks. Only 34% of patients presented in first trimester while no one presented in third trimester. 19 patients (32.8%) had molar pregnancies following term pregnancy and 15 patients (25.9%) had molar pregnancies following non- molar abortion (Table-V).

Table 2: Age Incidence (N=58)

Age group	No. of cases	Percentage
11-20 years	15	25.9
21-30 years	32	55.2
31-40 years	7	12
41-50 years	4	6.9
Above 50 years	0	0

Table 3: Socio-Economic Status (N=58)

Status	No. of cases	Percentage
High	2	3.4
Middle	15	25.9
Low	41	70.7

Table 4: Gravidity / Parity (N=58)

Gravida	No. of cases	Percentage
Primigravida	23	39.7
G2	9	15.5
G3	13	22.4
G4	10	17.2
≥G5	3	5.2

Table 5: Antecedent Pregnancy (N= 58)

Antecedent pregnancy	No.	Percentage
Term pregnancy	19	32.8
Non-molar abortion	15	25.9
Molar abortion	0	0

Amenorrhoea for a variable period of time was present in all cases followed by bleeding per vaginum (77.6%)(Table-VI). Least common symptoms were features of hyperthyroidism (1.7%). Though 47 patients had pallor and only 13.8% required blood transfusion. No case of preeclampsia/eclampsia and haemoptysis was detected.53 patients (91.3%) had enlarged uterus on examination.

Table 6: Signs And Symptoms Of Molar Pregnancies (N=58)

Clinical Features	No. of cases	Percentage
Amenorrhea for a variable period of time	58	100
Vaginal bleeding	45	77.6
Pain in lower abdomen	7	12.1
Hyperemesis gravidarum	9	15.5
Expulsion of mole	10	17.2
Pallor	47	81
Anemia requiring blood transfusion	8	13.8
Hyperthyroidism	1	1.7
Preeclampsia and eclampsia	0	0
Enlarged uterine size	53	91.3

54 cases (93%) showed snow storm appearances on ultrasonography (Table-VII). Bilateral cystic ovaries were present in 7 cases (12.1%) and unilateral cystic ovaries in 5 cases (8.6%). Invasive mole was found in only 1 case. In 3 patients (5.2%), the pre-evacuation serum β-hCG was less than 1,000 mIU/ ml, in 20 patients (34.5%) it was within 1,000 to 10,000 mIU/ ml, in 17 patients (29.3%) it was within 10,000 to 100,000 mIU/ ml, in rest 18 patients (31%) it was more than 100,000 mIU/ml (Table-VIII). On FIGO scoring, 12 patients belonged to high risk group (20.7%) and 46 patients belonged to low risk group (79.3%)(Table-IX).

Table 7: Uitrasonography And Chest X-Ray P- A View In Diagnosis

Features	No. of cases	Percentage
Snow storm appearance	54	93
Bilateral cystic ovaries	7	12.1
Unilateral cystic ovaries	5	8.6
Invasive mole	1	1.7
Mass lesion in uterus with metastasis	0	0
Metastatic lung lesions	0	0

Table 8: Baseline Serum B-Hcg Level (Miu /Ml)

Serum β-HCG estimation in mIU/ml	No. of cases	Percentage
<1000	3	5.2
1000- 10,000	20	34.5
10,000-100,000	17	29.3
>100,000	18	31

Table 9: Risk Groups

FIGO scoring	No. of patients	Percentage
Low risk group (score 0-6)	46	79.3
High risk group (score 7 or higher)	12	20.7

Table 10: Method Of Treatment

Treatment	No. of cases	Percentage
Suction & evacuation	57	98
Hysterectomy	1	1.7
Chemotherapy	23	39.6

Suction and evacuation was done in all cases of hydatidiform mole (Table-X). In one case (1.7%) hysterectomy was done for invasive mole. In 23 cases (39.6%), single agent chemotherapy (MTX-FA) was given. The failure rate was 21.7% and they are treated with EMA-CO (Table-XI). All patients were counseled regarding contraception in the follow up period. 27 patients (46.6%) used combined oral contraceptive and 31 patients (53.4%) used barrier method during follow up period.

Table 11: Choice Of Chemotherapy

Agent	Regimen	Indication	Route	Side effects	No. of cases	Failure Rate
Single agent chemotherapy	MTX-FA	RTD, Invasive mole	IV/IM	Nausea, vomiting	23	21.7%
Multiagent chemotherapy	EMA-CO	Failure of MTX-FA regimen	IV	Nausea Vomiting Diarrhea Fever, UTI Angular stomatitis granulocytopenia	5	0%

Table 12: Follow –Up (Serum B-Hcg Normalization Time)

Number of weeks	No. of cases	Percentage
Within 4 weeks	9	15.5
5-8 weeks	30	51.7
9-12 weeks	15	25.9
13-20 weeks	4	6.9
>20 weeks	0	0

No patient was lost during the follow up period of 6 month. Serum β-hCG was found to be negative within 4 weeks of treatment in 9 cases (15.5%) and in 30 patients (51.7%) it was negative within 8 weeks of treatment, in rest 15 patients (25.9%) it was negative in 13-20 weeks (Table-XII). Average time of remission was 7.4±3 weeks.

Discussion

There is a wide variation in incidence of molar pregnancies reported worldwide. The incidence in this study was 2.85 per 1000 deliveries. According to Tham B.W. et al. incidence of GTD in the Asian population was 1.95 times higher than in the non-Asian population (1/387 live births versus 1/752 live births) [4]. The 5- year prevalence of molar pregnancy at tertiary care centre at Nepal conducted by Agrawal et al. is 4.17 per 1000 live birth [5]. Lakra et al. in a study in Haryana reported incidence of 2.3 in 1000 deliveries [6]. Dinesh Kumar et al. from Imphal reported incidence of 4.5 per 1000 deliveries [7]. In this study, the cases of complete mole were found to be 53 (91.4%) which was much higher than the incidence of partial mole. There were only 4 (6.9%) cases of partial mole and one case of invasive mole (1.7%). Singh J et al. reported 76% cases of complete mole, 22% cases of partial mole and one case of complete mole with atypical proliferation (2%) [8]. Jethwani et al. also reported incidence of complete mole was 76% as which was higher as compared to partial mole which was 11% [9]. In the present study, highest incidence was in the age group of 21-30 years. Similarly, Dinesh Kumar et al. and Jathwani et al. reported highest incidence in the

age group of 20-30 years [7,9]. However, Gockley found a positive correlation between the risk of molar pregnancy and extremes of maternal age (>45 years and <15 years) [10]. But none of our patients belonged to these ages, as most of the patients in rural India conceive between 18 to 35 years because of early age of marriage. Majority of the patients were from low socioeconomic status (70.7%) in present study, which was similar to study done by Seema Dayal who reported 74% cases with low socioeconomic status [11]. Jathwani et al. reported 54% cases with lower socioeconomic status [9]. 39.7% were primigravida in present study whereas Jathwani et al. and Fatima et al. reported highest incidence among nulliparous women [9,12]. In this study, 32.8% had molar pregnancies following term pregnancy and 27.5% had molar pregnancies following non- molar abortion. No patient with history of molar pregnancies was documented. In present study most of the women (66%) with molar pregnancies are presented in their second trimester with a mean gestational age of 12.8±2 weeks. It is comparable to the study by Lakra et al. [6], who reported 13.8±3 weeks as the mean age of gestation. Increase in diagnostic services over the years, have led to early recognition of the disease. Koirala et al. also reported second trimester as the most common period of presentation [13]. Jathwani et al. reported 98% cases presenting in between 8 to 20 weeks [9]. In our study, majority patients (56.9%) had blood group O positive. This was comparable to the studies by Jethwani et al. and Chandran JR et al. [9, 14]. However, literature showed increase incidence of the disease among women with blood group A positive [15]. Koirala and Lakra also reported increased incidence of molar pregnancies among women with blood group A positive (13, 6). However modified WHO scoring of FIGO 2002 has eliminated this as a risk factor. Most common presenting symptom was amenorrhea (100%) followed by vaginal bleeding (77.6%) in our study. Other less common complaints were pain abdomen (12.1%), excessive vomiting (15.5%), passage of grape like vesicles (17.2%). Koirala et al. reported in their study that abnormal uterine bleeding as the most frequent (86.3 %) complaint apart from amenorrhea with other presenting symptoms like pain abdomen (33.8 %), hyperemesis (26.5 %) and passage of grape like cysts (11.8 %) [13]. Jethwani et al. also reported similar results [9]. No case of eclampsia and haemoptysis was recorded in our study. Hyperthyroidism was reported only in one case. Dinesh Kumar et al. and Dayal et al. observed 3% and 5% of molar pregnancies with hyperthyroidism [7,11]. 91.3% cases had enlarged uterus on examination in the present study. Jethwani showed 42% of patients presented with uterine size more than period of gestation [9]. The clinical presentation of partial moles was those of incomplete abortion or missed abortion.

Anemia was the most common complication in present study. 81% had pallor but 13.8% required blood transfusion. Lakra et al. reported that 76.3% patients had pallor and 57.9% received blood transfusion [6].There were no ICU admissions or mortality in our study. 93% of complete mole showed typical snow storm appearances on ultrasonography in the present study. In 4 cases of partial mole, concurrent presence of fetus was found. Invasive mole was found in only 1 case which had echogenic vascular mass invading myometrium with high velocity flow in Doppler. Dinesh kumar et al. reported 31 cases of complete mole with typical snow storm appearances, 3 cases of partial mole and 3 cases of invasive mole out of 37 women with molar pregnancies with USG being as an important diagnostic tool in their study [7]. Bilateral cystic ovaries were present in 12.1% In present study, β HCG was elevated in all cases. In 31% cases, it was more than 100,000 mIU/ml. Serum β hCG of 18.4% patients was more than 1,00,000 mIU/ml in a study by Lakra et al. [6]. Jethwani et al. reported 40% cases with β hCG more than 1,00,000 mIU/ml[9]. As risk grouping was done in present study by FIGO 2002, 20.7% belonged to high risk group and 79.3% patients belonged to low risk group. Similar results were found by Chandran JR, in their study 93.6% of patients were low risk and 6.4% were high risk cases [14]. Fatima et al. reported 82% in high risk group and 18.6% in the low risk group [12].

Conclusion

Incidence of molar pregnancies in present study is much higher as this hospital is the there is a strong need to set up a system in India, so that the patients can be managed and followed properly to avoid complications and better guidelines can be formulated by studying their response to the various chemotherapy agents. Still molar pregnancies can be prevented by health education among people, preventing early marriage and early child bearing and taking balanced diet.

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