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A Clinical Study of Hydatidiform Mole

Visenuo Ethel Solo[1], Akoijam Tamphasana[2], Gyaneshowri Laishram[3], Laiphrakpam Ranjit Singh[4], R.K. Praneshwari Devi[5], Nungsangtemjen[6]

[1,6]*(Post graduate, Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences, Imphal, Manipur, India)*

[2,3]*(Senior Resident, Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences, Imphal, Manipur, India)*

[4]*(Professor & Head of Department, Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences, Imphal, Manipur, India*

[5]*(Associate Professor Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences, Imphal, Manipur, India)*

Corresponding Author: Akoijam Tamphasana

Abstract: ***Introduction:*** *Hydatidiform mole is a spectrum of gestational trophoblastic disease resulting from abnormal gametogenesis and fertilization. It is a benign neoplasm of the chorion with malignant potential. The frequency of hydatidiform molein different countries varies and depends on multiple factors. The diagnosis and follow-up is based on ultrasound and serial β-hCG estimation in serum.*

Objective: *To find out the incidence of hydatidiform mole and evaluate the outcome of the disease following treatment.*

Materials and methods: *A cohort study was conducted for a year and a half, among patients with hydatidiform mole. Before and after suction & evacuation, β-hCG monitoring was done. If β-hCG was persistently high, rises again or maintains a plateau in the follow up period, the patient was designated as a case of persistent trophoblastic disease.*

Results: *Sixty cases of hydatidiform mole were studied out of 19,023 pregnancies. The incidence is increased with parity and 21-29 years was the most common age group affected. The most common complaint was vaginal bleeding. Hyperthyroidism was seen in 13.3% cases and bilateral theca luteal cysts were noted in 15% cases. During follow up, β-hCG levels decreased and remained undetectable for 83.3% of the patients while 13.3% and 3.4% had increasing and plateau of β-hCG levels, respectively.*

Conclusion: *In this study, the incidence of hydatidiform mole was 3.1 per 1000 pregnancies. Majority of the cases (83.3%) were successfully treated with suction & evacuation, while 16.7% developed persistent trophoblastic disease requiring chemotherapy.*

Keywords: *Hydatidiform mole, β-hCG*

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I. Introduction

Hydatidiform mole is a spectrum of Gestational Trophoblastic Disease (GTD) resulting from abnormal gametogenesis and fertilization and is characterised by trophoblastic proliferation with varying degree of hyperplasia and dysplasia. The complete mole has a karyotype of 46XX or XY without any fetal part with higher risk of developing persistent disease in as much as15-20%. On the other hand, partial mole has a karyotype of 69XXX or 69XXY with fetal elements and has 1-5% risk of developing persistent disease.The incidence of hydatidiform mole varies greatly in different parts of the world.[1]The important risk factors are age, parity, decreased consumption of carotene, fats, vitamins & protein and a history of previous hydatidiform mole. Clinically, hydatidiform mole presents with amenorrhea, painless vaginal bleeding, high serum and urinary β human chorionic gonadotrophin (β-hCG) levels and passage of grape-like vesicles. Other symptoms are anaemia, hyperemesis gravidarum, inappropriate uterine size, early onset pre-eclampsia, thyrotoxicosis, etc. Theca lutein cysts may be associated due to ovarian hyperstimulation as a result of high β-hCG. Haemorrhage, sepsis, perforation and choriocarcinoma are important complications. Sonographically, a complete mole appears as an echogenic uterine mass with numerous anaechoic cystic spaces but without a fetus or amniotic sac, called as 'snowstorm appearance'. The gold standard in treating hydatidiform mole is suction and evacuation. Histopathological examination should be done to confirm the diagnosis. Follow-up is usually done by serial β-hCG monitoring at regular intervals. The malignant forms of gestational trophoblastic disease are termed gestational trophoblastic neoplasia (GTN) which involves clinical conditions including invasive moles,

choriocarcinoma, placental site trophoblastic tumours and epitheloid trophoblastic tumours. GTN is typically sensitive to chemotherapy and the cure rate is 80-90%.[2]

II. Materials and methods

A cohort study was conducted in the Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences, Imphal, Manipur, to find out the incidence of hydatidiform mole and evaluate the maternal outcome during follow-up. All cases of hydatidiform mole admitted in Obstetrics and Gynaecology department from September 2016 to February 2018 were included in the study. All pregnant women admitted in Obstetrics and Gynaecology department was considered for calculating the incidence. Taking prevalence of molar pregnancy as 4.17 from a study[3], calculated sample size was 77. Ethical approval was obtained from the Research Ethics Board, RIMS. Suction and evacuation was done for all the patients. The patients were followed up by weekly serum β-hCG measurements until β-hCG became undetectable. Then, 2 further specimens were obtained at weekly intervals. Subsequently, the patient was tested monthly for 6 months and then every 2 months for a further 6 months to ensure that β-hCG level remains undetectable. If β-hCG was persistently high or rises again or maintains a plateau in the follow up period, the patient was designated as a case of persistent trophoblastic disease or GTN. All statistical analysis was performed using IBM SPSS Version 21 for Window.

III. Results and observations

There were 19,023 antenatal patients admitted during the study period and 60 cases of hydatidiform mole, giving an incidence of 3.1/1,000 pregnancies.

Table 1. Clinico-epidemiological profile of patients with molar pregnancy

Variables	**Categories**	**N(%)**
Age group	<20	7 (11.7)
	20-29	30 (50)
	30-39	16 (26.6)
	≥40	7 (11.7)
Mean age ± SD	28.82±8.24	
Oral contraceptive pill (OCP) use	Yes	9 (15)
	No	51 (85)
Period of gestation (weeks)	**Mean±SD**	**Min-Max**
	10.75±3.78	5-22
Uterine Size (weeks)	13.43±5.53	6-28
Hb (gm%)	10.13±1.97	5-14
Duration of hospital stay (days)	6.20±3.98	1-19
Time to resolution (weeks)	5.92±1.66	3-9

Table 2. Age wise incidence of hydatidiform mole

Age (in years)	**No. of pregnancies**	**No. of hydatidiform mole**	**Incidence rate/1,000 pregnancies**
<20	2,233	7	3.1/1,000
20-29	9,960	30	3.0/1,000
30-39	5,755	16	2.7/1,000
≥40	1,075	7	6.6/1,000
Total	19,023	60	3.1/1,000

Table 2 shows that highest proportion of patients were in the age group of 20-29 years. But the incidence was highest in patients who were more than 40 years.

Table 3. Parity wise incidence of hydatidiform mole

Parity	**No. of pregnancies**	**No. of hydatidiform mole**	**Incidence rate/1,000 pregnancies**
P0	8,209	16	1.9/1,000
P1	6,406	21	3.2/1,000
P2	2,724	11	4.0/1,000
P3	921	5	5.4/1,000
≥P4	763	7	9.1/1,000
Total	19,023	60	3.1/1,000

Table 3 shows that highest proportion of hydatiform mole was seen in parity 1.

Most of the patients (63.3%) came with complaints of vaginal bleeding. Other complaints in decreasing order of frequency were pain abdomen, amenorrhea, nausea & vomiting and passage of grape-like vesicles in the vaginal bleeding. O+ve was the most common blood group encountered in the study. One patient was Rh-ve

(A-ve) for which anti-D was given after evacuation. Seventy percent of the patients required blood transfusion during hospital stay.Hyperthyroidism was seen in 13.3%. Ultrasonography findings showed 51 complete moles cases, 6 partial moles and 3 invasive moles. Theca-lutein cysts was seen in 15% cases. Before suction & evacuation, 36.7% of the cases required prior dilatation of the cervix. Histopathological examination of specimen from suction & evacuation showed complete mole in 90% and partial mole in 10% of the cases.β-hCG levels during follow up decreased and remained undetectable for 83.8% of the patients, while 13.3% and 3.4% had increasing or plateau of β-hCG level respectively.

Table 4. Distribution of time to resolution during follow-up

β-hCG level	**Time after evacuation**	**N(%)**
Decreased & remained undetectable	1-3 weeks	1(2.0)
	4-6 weeks	32(64.0)
	7-9 weeks	17(34.0)
Total		**50(100)**

Table 4 shows time to resolution (in weeks) for the patients in whom β-hCG level decreased and remained undetectable during follow-up. Plateau of β-hCG level was seen in 2 patients during the 4th week and 5th week following evacuation. Most of the patients (83.3%) were successfully treated by suction & evacuation and remaining 16.7% developed GTN.

Table 5. Relation of β-hCG level and GTN

Initial β-hCG (mIU/mL)	**Complete mole**	**Partial mole**	**GTN**	**N (%)**
<1Lakh	1	0	1	2 (3.3)
1-3Lakhs	17	1	1	19 (31.7)
>3Lakhs	26	5	8	39 (65)

From table 17, majority of the patients (65%) had initial β-hCG>3 Lakhs mIU/mL.Only 3.3% had β-hCG value <1 lakh mIU/mL.

Table 6. Association between parity and prognosis

Parity	**Prognosis**		**p-Value**
	GTN N (%)	**GTD N (%)**	
Nulli	3 (18.8)	13 (81.2)	0.914*
Primi	4 (18.2)	18 (81.8)	
Multi	2 (13.3)	13 (86.7)	
Grand	1 (14.3)	6 (85.7)	

*Fisher's Exact test, not significant

Table 6 shows the comparison between parity and outcome. Fisher's Exact test was not significant.

Table 7. Association between age and outcome

Age (in years)	**Outcome**		**p-Value**
	GTN N(%)	**GTD N(%)**	
<20	0 (0)	7(100)	0.074*
20-29	9(30)	21(70)	
30-39	1(6.3)	15 (93.8)	
≥40	0 (0)	7(100)	

*Fisher's Exact test, not significant

Table 7 shows the comparison between age and outcome. Fisher's Exact test was not significant.

IV. Discussion

During the study period, 60 patients (0.3%) were diagnosed with hydatidiform mole from a total of 19,023 antenatal patients admitted to our institution. This gave an incidence of 3.1 per 1,000 pregnancies. Hydatidiform mole is common among Asians especially Mongoloids and; since majority of the population in Manipur are Mongoloids, hence the high incidence. Incidence of hydatidiform mole in studies conducted by Dineshkumar et al[4], Agarwal N et al[3]and Teoh ES et al[5]were 4.56 per 1,000 deliveries in India, 4.17 per 1,000 live births in Nepal,and 1 per 823 live births in Singapore, respectively.

Mean age of the patients was 28.82±8.24 years. The extent of risk was much greater with older rather than younger maternal ages. It was only at the extremes of age that the increase in risk sharply rose. Incidence of hydatidiform mole increased with parity. In our study, 35% of the patients were para 1 and 26.6% were primigravida. Although highest association of risk of hydatidiform mole was associated with parity 4 or more,

majority of hydatidiform cases occurred in nulliparous women in similar studies.[6,7]The period of gestation (POG) at diagnosis in the study ranged from 5-22weeks (Mean±SD was 10.75±3.78) and the average uterine size at evaluation was 13.43±5.53 weeks. A study by Riadh BT et al[8] reported the mean gestational age at diagnosis was 13 weeks.In our study, uterine size was greater than the period of gestation in 48.3% of the patients.

Vaginal bleeding was the most common symptom (63.3%) of the patients in our study. The other presenting symptoms were pain abdomen (15%), amenorrhea (10%), hyperemesis gravidarum (6.7%) and passage of grape like vesicles (5%). In a study by Al-Talib AA[6], the commonest symptom was vaginal bleeding (86.4%) followed by hyperemesis gravidarum (41.0%).

All 60 subjects in our study had positive urine pregnancy test making diagnosis of molar pregnancy easier. Diagnosis may be delayed by a negative urine pregnancy test due to "hook effect" where falsely low or negative results occur from oversaturation of the signaling antibodies employed to detect β-hCG by the testing equipment. Nodler JL et al[9] reports a case of complete hydatidiform mole where the hook effect was noted.

The cumulative body of literatures states blood group A+ve as the most commonly associated with the disease.[10,11] However in our study, blood group O+ve was the most frequent blood group among study sujbects. A study from Singapore by Dawood MY et al[12] showed no significant shift in the ABO blood group distribution. A large proportion (70%) of the patients in our study required blood transfusion due to hemorrhage. Because of the thyrotropin-like effects of β-hCG, which cause serum free thyroxine levels to be elevated and TSH levels to be decreased, hyperthyroidism was encountered in 13.3% of the patients in the study. In similar study by Al-Talib AA[6], hyperthyroidism was seen in 4.5% of molar pregnancies.

Ultrasound reports in our study showed 51 cases of complete mole, 6 cases of partial mole and 3 cases of invasive mole. Ultrasound findings were associated with theca-lutein cysts in 15% of the cases in the study. This is comparable to findings of Al-Talib AA[6] and Hou JL et al[13] who reported 13.6% and 16.8% theca-lutein cysts among their cases. These findings are due to overstimulation of lutein elements by massive β-hCG.

Suction evacuation was done for all the patients. For 36.7% of the patients, prior dilatation with misoprostol tablet was done as the cervical os was closed. Histopathological examination of specimen of showed complete molar pregnancy as the most commonly encountered (90%) and followed by partial mole (10%). Riadh BT et al[8]also reported histological findings of complete mole in 66.66% of the cases and partial mole in 33.33% of the cases.

Most of the patients (65%) had initial β-hCG >3 Lakhs mIU/mL. Very few of them (3.3%) had β-hCG value <1 lakh mIU/mL. Jagtap SV et al[11] reported that majority of the cases in their study had β-hCG level 50,000-1,00,000 mIU/mL.

During follow up, β-hCG levels gradually decreased after suction & evacuation and remained undetectable in 83.3% of the patients. Time to resolution in our study was 3-9 weeks (mean±SD is 5.92±3.98) which can be compared with a study by Al-Talib AA[6], where majority of patients (63.6%) had normal β-hCG within 9 weeks (63 days) after suction curettage. In our study, 13.3% of the cases showed rise of β-hCG>10 percent during 3 weekly measurement while 3.4% of the cases showed plateau of β-hCG levels for four weekly measurements. GueyeM et al[14] reported that some cases of GTD developed GTN even after normalization of β-hCG.

In our study, 83.3% of molar pregnancies were successfully treated after suction & evacuation, while 16.7% were diagnosed as GTN and had to be referred to radiotherapy department. These findings are similar to a study by Riadh BT et al[8] where 90% of the molar pregnancies achieved remission without chemotherapy. Houet al[14] reported that incidence of post-molar trophoblastic neoplasia was 21%.

The present study showed no significant relationship in terms of parity and outcome of hydatidiform mole. Similarly, there was also no significant relationship between age and outcome of hydatiform mole. Sekchin KD et al[15] also reported in his study that patient's age, gravidity, parity, smoking, initial β-hCG and ultrasonographic mean lesion did not predict adjuvant chemotherapy requirement.

Gemer O et al[16] stated in his study that currently with routine first trimester ultrasonography, a significant proportion of patients with molar pregnancy were asymptomatic at the time of diagnosis. The widespread availability of ultrasound scans and estimation of serum β-hCG contributed to early diagnosis and management of the patients with better outcome.

V. Conclusion

The frequency of hydatidiform mole varies in different countries. There is an ethnic predisposition to hydatidiform mole which has increased prevalence in Asians, Hispanics and Americans. It depends on multiple factors which should be locally evaluated. When a patient presents with symptoms of pregnancy in an exaggerated form like hyperemesis gravidarum and disproportionate uterine size, the clinician should be alerted of the presence of gestational trophoblastic disease. If hydatidiform mole is suspected on clinical grounds, ultrasound scanning and quantitative estimation of serum β-hCG should be carried out to confirm the diagnosis.

The incidence in the US and Europe has been relatively constant at 1.2 per 1,000 deliveries. Early diagnosis, treatment and follow up are important to prevent morbidity and mortality. Multi-centered studies are required to determine the incidence and overall outcome of hydatidiform mole that will help in understanding the burden of the disease and also plan for optimal treatment.

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