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ORIGINAL RESEARCH

Molar pregnancy: a 15-year experience in a single tertiary institution

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Background: Gestational trophoblastic disease (GTD) is a group of uncommon conditions associated with pregnancy that arise from abnormal trophoblastic tissue following abnormal fertilisation. There is minimal data from African countries. We studied the management outcomes of hydatidiform mole (HM) at a single tertiary institution in South Africa.

Methods: This was a retrospective descriptive study of HM from January 2004 to December 2019. We included all women with a confirmed histological diagnosis.

Results: There were 554 057 deliveries and 235 molar pregnancy cases, with an incidence of 0.42/1 000 deliveries. Suction evacuation was performed in 97.4% of patients. Patients between 20 and 40 years constituted 78.7% of cases, with most patients (51.3%) diagnosed in the second trimester. The most common presenting complaint was vaginal bleeding (37.4%). The most common complication was hyperthyroidism (16.6%). A blood transfusion was required by 26 patients (11.2%). Due to ongoing bleeding, 17 patients (7.2%) required a second evacuation, with four patients (1.7%) requiring a hysterectomy due to excessive haemorrhage. Patients with molar pregnancy normalised their human chorionic gonadotropin (hCG) at 12 weeks post-evacuation. There were 42 cases of persistent trophoblastic disease (PTD), expressing hCG levels above 6 000 mIU/ml and 4 000 mIU/ml at four and eight weeks, respectively. Almost 45% of patients never completed follow-up.

Conclusion: The incidence of GTD at our centre is declining but remains an important cause of morbidity. We recommend a revised follow-up protocol for patients with complex socio-economic backgrounds, as the current protocol is associated with an increased rate of follow-up loss.

Keywords: gestational trophoblastic disease, hydatidiform mole, hCG, persistent trophoblastic disease, lost to follow-up

Introduction

Gestational trophoblastic disease (GTD) is a group of rare conditions associated with pregnancy that arise from placental trophoblastic tissue following abnormal fertilisation.[1,2] The spectrum includes hydatidiform mole (HM), persistent trophoblastic disease (PTD), invasive mole, choriocarcinoma, and the rare placental site trophoblastic and epithelioid trophoblastic tumours. Despite its rarity, it is of clinical and epidemiological importance because it affects women in the reproductive age group, is associated with morbidities, and may be fatal.[3]

Most patients with GTD follow the benign course, presenting with either a complete hydatidiform mole (CHM) or a partial hydatidiform mole (PHM), which regresses spontaneously after evacuation of the uterus. Only a few patients develop PTD, often requiring additional treatment. The diagnosis can be made based on gross morphology, histopathology, and genetic analysis.[4] The incidence and aetiological factors contributing to the development of GTD have been difficult to characterise.[5] Problems accumulating reliable epidemiological data can be attributed to inconsistencies in case definitions, inability to adequately characterise the population at risk, no centralised databases, a lack of well-chosen control groups against which to compare possible risk factors, and disease rarity.[5]

Worldwide, there is marked temporal, regional, and ethnic variation in the prevalence of CHM.[6] Estimates range from 0.6 to 1.1/1 000 in Europe, Australia, New Zealand, and North America, while estimates range from 0.8 to 5.8/1 000 in South America, Southeast Asia, Japan, and the Middle East.[5,7] The highest prevalence is reported in East Asia, with rates approaching 1 in 120 pregnancies.[1] In Uganda, the prevalence is 1 in 294 deliveries, with Nigeria reporting a figure of 1 in 379.[3,8]

The incidence of PHM is about 3 per 1 000 pregnancies.[2] A South African review from a single referral institution estimated an incidence of 1 in 833 deliveries for HM.[9] The statistics highlight regional variation in the disease's prevalence. These could be influenced by genetic, environmental, and other health-related factors endemic in different communities.

While a constellation of symptoms and signs has historically been associated with HM, such events are less common due to routine ultrasonography in early pregnancy and the resulting early HM diagnosis.[1] Several potential risk factors for HM have been suggested, including paternal age, vitamin deficiencies, maternal genetic translocations, and environmental toxins; however, the only clear data relates to the impact of maternal age and the previous occurrence of a HM.[4,10,11] With minimal data from African countries about GTD, there remains a greater need for early recognition, timely referral, and prompt and proper treatment.[12]

GTD produces the pregnancy hormone human chorionic gonadotropin (hCG), which serves as an excellent biomarker

of disease progression and response to treatment and can be used as subsequent post-treatment surveillance.[2] Thus, a plateaued or rising hCG level enables the early detection of CHM progression and PHM to PTD that occurs in 15–20% and 0.5–5% of cases, respectively.[2] The use of this biomarker and the development of highly effective therapies have transformed survival outcomes so that today, nearly all women affected by gestational trophoblastic neoplasia (GTN) can expect to be cured if appropriately managed.[2]

Materials and methods

This was a retrospective descriptive study of all women with HM referred to our tertiary gynaecological oncology unit of the Department of Obstetrics and Gynaecology at Groote Schuur Hospital (GSH) in Cape Town, Western Cape Province, South Africa, from the referring hospitals in the Metro West from January 2004 to December 2019.

Inclusion criteria were patients registered and followed up at the molar clinic at GSH with a confirmed HM diagnosis on histology. We excluded all patients without histological confirmation of HM, missing patient notes, and non-molar histology.

Statistical analysis

A total of 292 case records were retrieved; 235 records were included in the study, and 57 were excluded (32 were unspecified moles, 18 had no histological diagnosis of molar pregnancy, six folders had missing clinical notes, and one had a histological diagnosis of choriocarcinoma).

Stata version 17 (StataCorp LLC, College Station, United States) software and WINPEPI (www.brixtonhealth.com/pepi4windows.html) were used for data analysis. Continuous variables were summarised using means (standard deviation, SD) or medians (interquartile range, IQR). Categorical variables were summarised using count (per cent). The t-test or Wilcoxon rank-sum test was used to compare the means between the two groups. Associations between categorical variables were tested using Pearson's chi-square or Fisher's exact test. Estimates were reported with the corresponding 95% confidence intervals. The significance level was set at $p < 0.05$.

Results

Initially, 292 records of patients with HM were retrieved, but 57 were excluded, resulting in a final sample of 235 medical records (Figure 1).

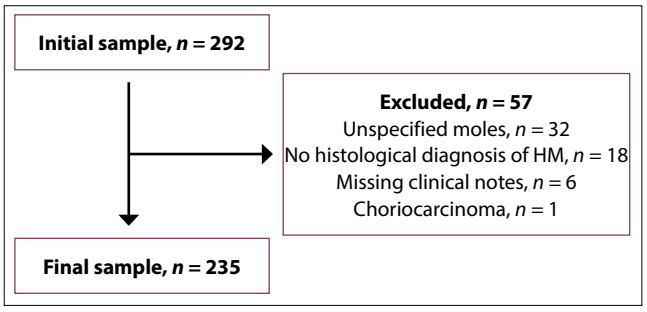

Figure 1: Selection of patients with hydatidiform mole.
HM – hydatidiform mole

The patients' mean age at diagnosis was 28 years (SD 8.67); 13% of the patients were adolescents, whereas 8% were older than 40 years. Antecedent pregnancy type was term in 90% of the women. The median time between antecedent pregnancy and HM diagnosis was 48 months. Nearly 60% of patients were multiparous. About 51% of HM were detected during the second trimester. A greater number of patients (70%) did not smoke. Human immunodeficiency virus (HIV)-positive individuals represented a smaller proportion (18%) of cases. The most common blood group was blood group O (Table I).

The most common presenting symptom was vaginal bleeding (37%). The most common complication was hyperthyroidism (17%), which was more common in CHM (18% vs. 13%). Blood transfusion was required by 26 patients (11.2%). Importantly, 81% of patients experienced no complications. A second evacuation was required by 10 patients (4.2%), and four patients (1.7%)

Table I: Demographic characteristics of 235 HM patients

Variable	CHM		PHM		HM	
	n	%	*n*	%	*n*	%
Age (years)						
< 20	23	15	7	8	30	13
20–40	112	74	73	87	185	79
> 40	16	11	4	5	20	8
Antecedent pregnancy						
Term pregnancy	74	90	45	90	119	90
Spontaneous abortion	6	7	5	10	11	8
HM	2	2	0	0	2	1
Interval between antecedent pregnancy and diagnosis of molar pregnancy (months)						
Median (IQR)	48	24–72	48	30–96	-	
7–12	4	10	3	12	7	11
> 12	34	89	22	88	56	89
Parity						
Nulliparous	61	40	30	36	91	39
Multiparous	88	58	52	63	140	60
Gestational age at admission (weeks)						
< 13	28	44	25	53	53	48
13–26	36	56	21	45	57	51
> 27	0	0	1	2	1	1
Smoking						
Yes	25	30	14	30	39	30
No	59	70	33	70	92	70
HIV						
Positive	16	19	8	16	24	18
Negative	70	81	41	84	111	82
Blood group						
A	33	32	15	26	48	30
B	21	20	10	17	31	19
AB	4	4	5	9	9	6
O	46	44	27	47	73	45

CHM – complete hydatidiform mole, HIV – human immunodeficiency virus, HM – hydatidiform mole, IQR – interquartile range, PHM – partial hydatidiform mole

Table II: Average frequency and incidence of HM and persistent mole, 2004–2019

GTD diagnosis	*n*	%	Incidence†
HM	235	100	0.42
CHM	151	64	0.27
PHM	84	36	0.15
PTD	42	18	0.07

CHM – complete hydatidiform mole, GTD – gestational trophoblastic disease, HM – hydatidiform mole, PHM – partial hydatidiform mole, PTD – persistent trophoblastic disease
† Incidence per 1 000 deliveries.

Table III: Local protocol for HM (complete or partial)

1. Investigations
• Pelvic ultrasound, chest X-ray, serum β-hCG, Rhesus factor, thyroid function, full blood count, renal function, liver function, HIV testing, blood group, and screen to blood bank.
2. Management
• Suction curettage of the uterus under ultrasound guidance. Procedure should be performed before 22:00 to allow for available senior assistance if required.
• Cervical priming immediately before the curettage is safe.
• Medical induction is not recommended unless the fetus in a partial mole is too big for surgical removal.
• Oxytocin infusion before completion of the curettage is not recommended but may be used for heavy bleeding post-evacuation.
• Send tissue for histological evaluation.
• Anti-D prophylaxis is indicated if Rhesus is negative.
• Contraception for at least six months.
• IUCD/Mirena is not recommended because of possible perforation until β-hCG is undetectable.
• Follow-up is crucial and should be done by a specialised GTD clinic (two-week follow-up until β-hCG is negative, then monthly for six months).
• No role for routine second evacuation.
• It is recommended that the β-hCG quantified result is plotted on a graph.
• Follow-up for partial molar pregnancy is concluded once the β-hCG has returned to normal on two samples at least four weeks apart.
• Women with a normal pregnancy following a previous molar pregnancy do not need histology of the placenta nor a post-pregnancy β-hCG.

β-hCG – beta-human chorionic gonadotropin, GTD – gestational trophoblastic disease, HIV – human immunodeficiency virus, HM – hydatidiform mole, IUCD – intrauterine contraceptive device

required a hysterectomy. The indications for the hysterectomies were massive haemorrhage at initial evacuation and invasive molar pregnancy. The other two patients who had a rising hCG opted for a hysterectomy instead of chemotherapy, as they also had no further fertility desires. Almost all patients (80.8%) agreed to use a contraceptive method after their suction evacuation, with injectable contraception being the most common choice.

A total of 554 057 deliveries were recorded from 1 January 2004 to 31 December 2019, with 42 PTD cases diagnosed within the same period. The incidence of PTD at the institution was 0.08 per

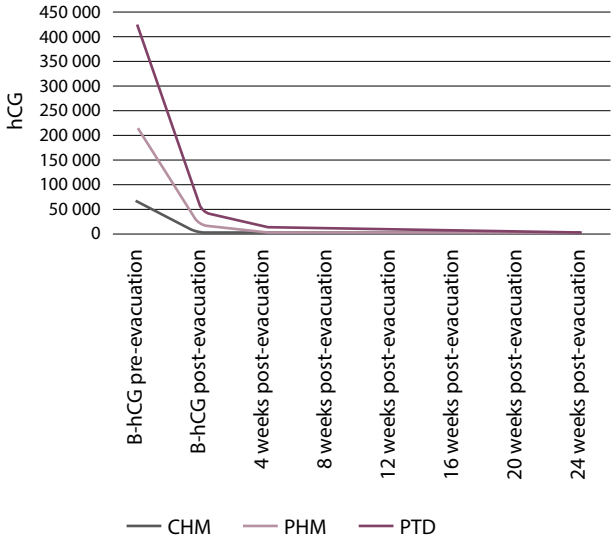

Figure 2: β-hCG trends for HM and persistent mole
β-hCG – beta-human chorionic gonadotropin, CHM – complete hydatidiform mole, HM – hydatidiform mole, PHM – partial hydatidiform mole, PTD – persistent trophoblastic disease

1 000 deliveries. Of these, 31 cases (74%) were CHM, and 11 cases (26%) were PHM (Table II).

The median initial hCG was 210 131 (IQR 88 452–545 240) in CHM and 60 880 (IQR 13 772–267 485) in PHM ($p < 0.001$). The post-evacuation median hCG was 18 498 (IQR 1 132–77 610) in CHM and significantly lower at 3 081 (IQR 538–34 530) in PHM ($p = 0.006$). There was a day 1 post-evacuation drop of 90% and 94% in hCG levels in CHM and PHM, respectively (median 428 247 IU/L vs. 42 247 IU/L) (Figure 2).

Patients with PTD spent an average of eight weeks after evacuation at the molar clinic before being referred for chemotherapy. Their last median hCG on referral was 6 308 and 4 650 at four and six weeks, respectively. A greater proportion of PHM (45.8%) completed their follow-up within the molar clinic than CHM (37.4%), a concerning observation given a higher likelihood of persistent disease associated with CHM. Not all patients in this study adhered to follow-up rules, as 44.3% were lost to follow-up and never returned. The final recorded hCG measurements before patients stopped attending follow-up care were 10 IU/L in the CHM group and 1 IU/L in the PHM group.

Discussion

This study shows that the incidence of HM in South Africa is low, but HM is mostly diagnosed in the second trimester. This data differs from studies in India and other documentation in the literature where most patients were diagnosed during the first trimester.[12,13] This is because dating scans are underutilised in the Metro West, especially among patients unaware of their last menstrual period.

Clinical hyperthyroidism was the most common complication. This result was much higher than previously reported by other investigators but similar to a study by Sinawat et al.[14] in Thailand and Pundir et al.[11] in India. This difference may be attributed to the fact that thyroid function assessment is performed routinely at our institution, probably explaining the high incidence of biochemical hyperthyroidism detected in our study. Early

detection and appropriate management of thyroid dysfunction can significantly improve outcomes and reduce the risk of complications in molar pregnancy cases. This underscores the importance of a multidisciplinary approach to managing molar pregnancies.

The low complication rate in this study can be attributed to the management policy of molar pregnancy in the Metro West as a well-designed and written policy (Table III). Every patient suspected of a HM diagnosis will have the following investigations performed immediately: pelvic ultrasound, chest X-ray, serum hCG, Rhesus factor, thyroid function, full blood count, renal function, liver function, HIV testing, blood group, and screen to blood bank. Once all investigations are reviewed by a consultant, a suction curettage of the uterus under ultrasound guidance will be booked on the emergency theatre slate. The procedure is only performed before 22:00 to allow for available senior assistance if required. Medical induction is not allowed, but an oxytocin infusion before completion of the curettage is highly recommended to minimise blood loss and decrease the chances of uterine perforation. The products are sent for histological evaluation, and a 48-hour post-evacuation hCG level is performed.

Upon discharging the patient, all results are checked and conveyed to the patient. A suitable contraception is administered, and a two-week follow-up date at the molar clinic is given to the patient before discharge. At the molar clinic, patients are seen every two weeks, and the hCG quantified result is plotted on a graph to facilitate early PTD detection. At every visit, patients are examined to exclude PTD. Once the hCG level has normalised, patients are seen monthly for six months for CHM, or two months for PHM, after which they are discharged from the molar clinic.

Differentiating between CHM and PHM is crucial for appropriate management and patient counselling, as the risk of complications and outcomes vary between the two types of HM. Nearly 50% of patients with CHM have pre-evacuation hCG levels > 100 000 mIU/ml. [5] In contrast, PHM is not distinguished by such elevated levels.[5] In our study, the statistically significant difference in the initial and post-evacuation hCG levels between CHM and PHM could serve as a marker to indicate to the clinician that the patient might be at an increased risk of PTD, especially in a low-resource setting where patient follow-up with HM is poor.

PTD diagnosis is mainly derived from hCG follow-up. After primary surgical treatment, weekly serum hCG assays should be obtained until three consecutive weekly assays are normal.[1] This usually occurs within eight weeks, but 20% of patients have elevated levels for 14–16 weeks post-evacuation.[1] In this study, hCG normalisation was achieved at 12 weeks for both CHM and PHM. PTD hCG at four and eight weeks was significantly higher than CHM and PHM. This study suggested that if the hCG at four and eight weeks is more or equal to 6 300 and 4 600, the chances of developing PTD are higher. Another important finding in the PTD group was that the post-evacuation hCG was twice as high as CHM's. A post-evacuation cut-off value of > 42 000 mIU/ml for CHM and > 31 000 mIU/ml for PHM could indicate persistent disease.

PTD rarely occurs after the spontaneous return of hCG levels to normal.[9] The hCG values fall spontaneously within the normal range, and patients can be safely discharged from follow-up.[15] The hCG data in this study agrees with the literature in that the hCG remained normal for the subsequent three months in both CHM and PHM. Bagshawe et al.[15] also found that none of the patients with hCG levels falling to the normal range within two months after evacuation developed sequelae requiring treatment. When hCG levels fell to normal two months after evacuation, the risk of recurrence was 1 in 96.[15] In our study, CHM and PHM showed a spontaneous normalisation of hCG levels by three months and two months, respectively. No patient developed any further sequelae requiring treatment once they showed normalisation of their hCG during the study period.

Of the 235 patients registered at the molar clinic, 44.3% of patients were lost to follow-up. These findings are comparable to those in Nigerian studies, where the follow-up rate was as low as 32–38.2%.[3] The poor follow-up rate among Metro West patients treated at the GSH molar clinic is attributed to their inability to afford transportation costs to attend the clinic.

A recommendation that patients are followed up until normal hCG levels are achieved would have resulted in 83% of patients being discharged from follow-up within three months. We further recommend that once a normal hCG level is achieved, telemedicine is employed to follow uncomplicated molar pregnancy patients for three more months. We believe this approach is a safe and reasonable compromise, as this study proves that malignant sequelae following a molar pregnancy diagnosis are low. Overall, the recommendation advocates for a patient-centred approach to molar pregnancy follow-up, balancing the need for effective monitoring with the practical considerations and challenges faced by patients, particularly those with complex socio-economic backgrounds. This approach underscores the importance of adaptability and innovation in healthcare delivery to ensure optimal patient outcomes.

Study strengths and limitations

This study was the first analysis of molar pregnancy at our institution and highlighted gaps in care for improvement in our treatment protocols and surveillance tools. The study was conducted over an extended period. Other strengths include a central pathology review and the use of a single, well-characterised hCG assay.

The retrospective nature of this study makes it susceptible to bias. The sample size was small, impacting statistical significance analysis. In addition, as with any retrospective study, we were limited in obtaining certain necessary detailed information due to not having a structured referral template. The other limitation is that the incidence of subsequent pregnancies after the complete treatment of molar pregnancy was not studied. A prospective study is recommended in the future.

Conclusion

In South Africa, the incidence of molar pregnancy is low and on a declining trend, witnessed globally. An early molar pregnancy diagnosis can change the clinical presentation and treatment

of the disease. Most of our patients have uncomplicated molar pregnancies. Early dating scans are crucial for accurate pregnancy dating and detecting abnormalities like HM. Given the poor follow-up rate within our population, we recommend using telemedicine/early down-referral once hCG normalises. Further surveillance should include three more normal hCG values for CHM and one more for PHM.

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Conflict of interest

The authors declare no conflict of interest.

Disclosure statement

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Ethical approval

Ethical approval was obtained from the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee (HREC REF: 067/2021).

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References

1. Brown J, Naumann RW, Seckl MJ, Schink J. 15 years of progress in gestational trophoblastic disease: Scoring, standardization, and salvage. Gynecologic Oncology. 2017;177:200-7. https://doi.org/10.1016/j.ygyno.2016.08.330.
2. Makhathini BS, Dreyer G, Buchmann EJ. Gestational trophoblastic disease managed at Grey's Tertiary Hospital: a five-year descriptive study. Southern Afr J Gynaecol Oncol 2019;11(2):15-9. https://doi.org/10.1080/20742835.2019.1667627.
3. Igwegbe A, Eleje G. Hydatidiform mole: A review of management outcomes in a tertiary hospital in south-east Nigeria. Ann Med Health Sci Res. 2013;3(2):210.
4. Melamed A, Gockley AA, Joseph NT, et al. Effect of race/ethnicity on risk of complete and partial molar pregnancy after adjustment for age. Gynecol Oncol. 2016;143(1):73-6. https://doi.org/10.1016/j.ygyno.2016.07.117.
5. Lurain JR. Gestational trophoblastic disease I: Epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. Am J Obstetr Gynecol. 2010;203:531-9. https://doi.org/10.1016/j.ajog.2010.06.073.
6. Adewole IF, Olakokun A, Fawole O, Olawuyi JF, Adeleye JA. Fertility regulatory methods and development of complications after evacuation of complete hydatidiform mole. J Obstet Gynaecol (Lahore). 2000;20(1):68-9. https://doi.org/10.1080/01443610063516.
7. Kaye DK. Gestational trophoblastic disease following complete hydatidi-form mole in Mulago Hospital, Kampala, Uganda. Afr Health Sci. 2002;2(2):47-51.
8. Moodley M, Tunkyi K, Moodley J. Gestational trophoblastic syndrome: An audit of 112 patients. A South African experience. International Journal of Gynecologic Cancer. 2003;13(2):234-9. https://doi.org/10.1136/ijgc-00009577-200303000-00023.
9. Steigrad SJ. Epidemiology of gestational trophoblastic diseases. Bailliere's Best Practice and Research in Clinical Obstetrics and Gynaecology. 2003;17:837-47. https://doi.org/10.1016/S1521-6934(03)00049-X.
10. Soares RR, Maestá I, Colón J, et al. Complete molar pregnancy in adolescents from North and South America: Clinical presentation and risk of gestational trophoblastic neoplasia. Gynecol Oncol. 2016;142(3):496-500. https://doi.org/10.1016/j.ygyno.2016.07.002.
11. Pundir S, Gupta V, Prasad S. Scenario of molar pregnancy in a tertiary care centre in Delhi, India. Int J Reprod Contracept Obstet Gynecol. 2019;8:3981. https://doi.org/10.18203/2320-1770.ijrcog20194366.
12. Savage PM, Sita-Lumsden A, Dickson S, al. The relationship of maternal age to molar pregnancy incidence, risks for chemotherapy and subsequent pregnancy outcome. J Obstet Gynaecol (Lahore). 2013;33(4):406-11. https://doi.org/10.3109/01443615.2013.771159.
13. Ibrahim Abdullahi H. Hydratidiform mole: Incidence and management outcomes in a tertiary hospital in Abuja. European Journal Pharmaceutical and Medical Research. 2019. Available from: www.ejpmr.com.
14. Sinawat S, Srisuporngornkul A. Molar pregnancy in Srinagarind Hospital. Srinagarind Medical Journal. 2004;19(3):136-40.
15. Bagshawe KD, Dent J, Webb J. Hydatidiform mole in England and Wales 1973-83. Lancet. 1986;328(8508):673-7. https://doi.org/10.1016/S0140-6736(86)90179-0.