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Prevalence, Management, and Outcomes of Patients Diagnosed with Molar Pregnancy at the Georgetown Public Hospital Corporation (GPHC) between 2018 to 2022.

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KEYWORDS

Molar, Hydatidiform Mole, Abnormal, human chorionic

ABSTRACT:

Background

Hydatidiform mole, also known as molar pregnancy, is a type of gestational trophoblastic disease (GTD) caused by abnormal trophoblast cell growth inside the uterus after conception. This disease is rare and can lead to the development of a tumor in the uterus from tissue formed after conception. Treatment involves surgical removal of the molar pregnancy and monitoring of human chorionic gonadotropin levels to confirm the resolution of the disease or detect the development of gestational trophoblastic neoplasia, which is the malignant form of the disease. To ensure proper care and recovery, early diagnosis and treatment followed by reliable contraception use is recommended by international health organizations such as FIGO and NCCN.

Objectives:

To estimate the prevalence of Molar pregnancy at the GPHC.

To identify the clinical presentation of patients diagnosed with molar pregnancy at the GPHC.

To identify the management and follow-up of patients with molar pregnancy at the GPHC.

To evaluate the outcomes of patients managed for molar pregnancy at the GPHC.

Methods:

A retrospective cohort study of all patients diagnosed with molar pregnancy from 1st January 2018 to 31st December 2022, evaluating the prevalence, clinical presentation, management, and follow-up of patients diagnosed with molar pregnancy. All patients who were admitted to the gynecology ward with an ultrasound diagnosis of molar pregnancy and patients who presented at the Gynecology-outpatient department with a histopathological diagnosis of molar pregnancy during the study period were included in the study.

Results:

At GPHC, the prevalence of molar pregnancy is 0.85 per 1,000 live births. Of all the patients, 68% experienced bleeding per vagina, while 32% had incidental findings on ultrasound. All the patients underwent a dilation and suction evacuation procedure. 72% of patients did not follow up after their discharge. Among the patients who were treated for molar pregnancy, 36% opted for the barrier method of contraception, 28% used the sub-dermal implant, 12% chose Depo-Provera, 8% underwent bilateral tubal ligation, 8% used combined oral contraceptive, 4% selected the IUCD, and 4% went for the withdrawal method.

29% of the patients had complete molar pregnancies, 8% had partial moles, and 59% of the histopathology findings were unknown.

Recommendations:

Development of a national registry for all Molar pregnancies and a standardized protocol for management of Molar pregnancy.

Conduct histopathology for all patients who have undergone uterine evacuation for missed or incomplete abortion.

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Beta hCG testing should be made available consistently or sub-contract the test if not available to minimize the cost to patients, ensuring follow-up.

Introduction

Gestational trophoblastic disease is a series of interrelated tumors arising from the placenta, including benign molar pregnancies as well as malignant conditions, termed gestational trophoblastic neoplasia (GTN). [4]

Over the years, analysis of the global incidence of molar pregnancy has been a challenge to obtain due to variations in reported rates and the lack of updated studies. [1] In recent decades, with the aid of the first-trimester ultrasound and serum Beta hCG, the presentation of molar pregnancy has changed from a second trimester to a first-trimester disease which is the main cause for patients to have few to no symptoms at the time of diagnosis. However, accurate diagnosis relies on expert histopathology along with molecular and genetic techniques. [4]

Early diagnosis and close follow-up of patients with molar pregnancy are extremely important because they are at an increased risk of developing Gestational Trophoblastic Neoplasia (GTN). The International Federation of Gynecology and Obstetrics (FIGO) and the National Comprehensive Cancer Network (NCCN) recommend consecutive quantitative b-hCG levels until normalization. If b-hCG levels plateau or start to rise, further investigation and intervention are required since this signifies persistent GTD or a progression to the malignant form of the disease, also known as post-GTD malignancy.

In addition, a reliable contraceptive method during the entire interval of b-hCG monitoring is recommended since a new pregnancy during this period would make it impossible to interpret b-hCG results and would complicate management.

Literature Review

Gestational trophoblastic disease (GTD) describes a set of diseases originating in placental tissue, specifically the chorionic villi and extra-villous trophoblast. GTD is the benign, premalignant form of the disease and it includes hydatidiform molar pregnancy. If GTD is not adequately treated, it can develop malignant conditions known as Gestational Trophoblastic Neoplasia (GTN). [2,3]

Molar pregnancy is a genetically abnormal pregnancy that results from abnormalities in fertilization and that can be divided into complete hydatidiform mole (CHM) and partial hydatidiform mole (PHM).

Complete and partial molar pregnancies are distinct pathologic entities with unique genetic and risk profiles. Complete hydatidiform mole is associated with more generalized trophoblastic hyperplasia and hydropic swelling of the chorionic villi and is not comprised of fetal or embryonic tissues. A complete mole most commonly has a 46, XX karyotype, with all chromosomes of paternal origin. This results from the fertilization of an “empty” egg (i.e. absent or inactivated maternal chromosomes) by a haploid sperm that then duplicates. Rarely, in familial recurrent molar pregnancy, CHM has a biparental chromosomal pattern and is associated with a mutation in the genes *NLRP7* or *KHDC3L*. [2,4]

Partial hydatidiform moles are pathologically and karyotypically distinct from complete moles. They are associated with more focal trophoblastic hyperplasia and hydropic swelling of villi and are often associated with fetal or embryonic tissues. They are usually triploid (69, XXX; 69, XXY; rarely 69 XYY) due to the fertilization of an ovum by two sperm. [2,4]

Although it is difficult to establish a generalized global incidence of molar pregnancy due to several factors such as variation in reported rates, limited resources, and lack of updated studies; there is an estimated 66 to 121 molar pregnancies per 100, 000 pregnancies in North America and European countries, and 23 to 1299 per 100,000 pregnancies in Latin America, Asian and Middle Eastern Nations. [1]

Regionally, a study conducted at the University Hospital of the West Indies, Jamaica reported an incidence of 2.81 molar pregnancies per 1000 pregnancies [8]. There are no published studies regarding local statistics of molar pregnancy.

The clinical presentation of CHM includes excessive uterine enlargement, theca lutein ovarian cysts, hyperemesis, preeclampsia, and hyperthyroidism. Whereby, theca lutein ovarian cysts, preeclampsia, and hyperthyroidism are primarily associated with marked

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trophoblastic proliferation, high human chorionic gonadotropin (hCG) levels, and excessive uterine size. In recent years, the majority of CHM is diagnosed earlier in the first trimester, where these signs and symptoms are less frequent. A chart review conducted by Soto-Write et al in New England reported a decline from 51% of cases of excessive uterine size to 28 %, from 27% of cases of preeclampsia to 1.3%, from 26 % to 8 % of cases of hyperemesis, and from 7% to 0% of cases of hyperthyroidism [13]

In contrast with CHM, PHM rarely presents with the classic signs and symptoms of CHM. Abnormal uterine bleeding is the most common symptom of presentation and is usually interpreted as a missed or incomplete abortion.

Berkowitz et al and company, in a series of 81 patients with PHM, found that 74 (91%) were thought to have a missed or incomplete abortion before uterine evacuation. In more recent years, similar to CHM, PHM is generally diagnosed in the first trimester. [14] Sun et al in a study at Brigham and Women's Hospital from 1994 through 2013, reported that the median gestational age at uterine evacuation for both CHM and PHM was 9 and 12 weeks, respectively. [4]

Given the very high curability rate of trophoblastic disease, the risk of further molar pregnancy after CHM or PHM as well as the risk of second primary tumors and fertility compromise after chemotherapy for GTN represent major concerns.[9] Both pathologies put the woman at risk of developing gestational trophoblastic neoplasia, a form of locally invasive or metastatic malignancy arising from the abnormal products of conception. [10] In other countries, these rates may be higher, possibly reflecting differences in hCG assays, hCG criteria for the diagnosis of GTN, lack of whole population demographics, or, less likely, a genuine difference in disease biology. [6]

For this reason, close follow-up of a patient with beta hCG is recommended to diagnose and treat any arising malignancy. In a study conducted in the UK, this occurs after 15-20% of CHM and 0.5 -5% of PHM. [5,6,7]

Several factors predispose a woman to a hydatidiform or molar pregnancy which includes extremes of maternal age, parity, and history of molar pregnancy.

With regards to outcome for molar pregnancies, a retrospective analysis of the Sheffield Trophoblastic Screening Service over 13 years found that 35 of 5030 women (0.7%) with the gestational trophoblastic disease had a recurrent molar pregnancy. The risk of a second molar event was highest in the second year after the initial diagnosis and reduced thereafter. There was a trend toward a slightly increased risk in Indian/Pakistani women when compared with Caucasian women. Patients who presented with a PHM tended to have a PHM as a second event, whereas patients who presented with a CHM were at risk of a subsequent CHM, PHM, or choriocarcinoma. 6% of patients required chemotherapy for the second molar event, thus suggesting no increase in aggressiveness in second moles.

A review of all cases of molar pregnancy registered between 1992 and 1998 at Charing Cross Hospital in England showed that 1417 of the 2578 women with CHM has a subsequent pregnancy that was affected by CHM in 22 cases (1.5%) and by PHM in 5 (0.3%).

Live birth rates and stillbirth rates were 75.9 and 0.4%, respectively. Overall, 1512 of the 2627 women with PHM had a further pregnancy that consisted of CHM in 8 (0.5%) cases and PHM in 17 (1.1%). Live birth rates and stillbirth rates were 78.4 and 0.4%, respectively.

The proportion of preterm live births before the 37th week or severely preterm live births in, the 32nd week following CHM were 4.0 and 0.7%, respectively, and following PHM were 5.5 and 0.8%, respectively, which were similar to those expected in London general population during the same period (6.2 and 1.1%). The frequency of preeclampsia after CHM and PHM was 1.5 and 1.9%, respectively.

The overall risk for recurrent molar pregnancy after CHM or PHM was 1.8%. Since the prevalence of HM in the British population was approximately 1:1000 pregnancies, the occurrence of a CHM or PHM was associated with a 20-fold increase in the risk of a molar event in subsequent gestation. Three of the 27 cases with a repeat mole following CHM had at least one further pregnancy complicated by CHM, suggesting that the recurrence risk following two previous CHM is approximately 10%.

The risk of malignant disease following surgical evacuation of a complete mole is 15%-20% and after an incomplete or partial mole, it is 0.5%-5%. Follow up care after uterine evacuation, requires patients to be enrolled in a serum hCG surveillance protocol. Serum hCG levels are a highly sensitive marker for trophoblastic proliferation.

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FIGO 2018 guidelines require patients diagnosed with CHM, the beta HCG should be repeated weekly until normal and then monthly for 6 months, after which patients can be discharged from follow up. For PHM the beta HCG is repeated weekly until normal and repeat 1 month after, once beta HCG remains normal patient can be discharged from follow up.

National Comprehensive Cancer Network (NCCN) guidelines also suggest following hCG levels every one to two weeks. When three consecutive hCG levels are normal, two additional hCG assays should be obtained every three months, with discontinuation of hCG monitoring if the hCG remains normal. [11]

Women becoming pregnant within 6 months after diagnosis of molar pregnancy (or 12 months after chemotherapy for malignant disease) have an increased risk of morbidity and mortality. For this reason, contraception is mandatory and should be started immediately because ovulation returns rapidly after uterine evacuation. Up to 12%-23% of women conceive before the scheduled end of the monitoring period, suggesting that the contraceptive method used should be highly effective.

Initial studies of hormonal contraception in women with a recent diagnosis of GTD suggested an increased risk of developing malignancy. Trophoblastic cells have sex steroid receptors, the proliferative activity of which can be modulated by reproductive hormones. [15]

A systematic review concluded a lack of causality between hormonal contraception and GTD and 2 large case series not included in the review failed to demonstrate any detrimental effect of hormonal contraception. [15]

To date, there is no evidence to contraindicate hormonal contraception during the clinical management of women with GTD. All hormonal contraceptives can be used without any restrictions after GTD, but, despite no evidence of any detrimental effect on disease outcome, intrauterine contraception is contraindicated until after human chorionic gonadotropin levels have returned to normal. Among clinicians, there appears to be a natural reluctance to insert a device into a uterus which may be more vulnerable to perforation and, perhaps, hemorrhage [7].

Methodology

Study design:

A retrospective cohort study of all patients diagnosed with molar pregnancy from 1st January 2018 to 31st December 2022, evaluating the prevalence, clinical presentation, management, and follow-up of patients diagnosed with molar pregnancy.

Procedure and Sampling Methodology

After obtaining approval from the GPHC research committee and the Ministry of Health institutional review board (IRB), a letter of request was sent to the head of GPHC's medical records for permission to access data from charts of patients admitted from 1 January 2018 to 31 December 2022.

All patients admitted and managed for Molar pregnancy and who met the inclusion criteria were included in this study. A structured data sheet was formulated in Microsoft Excel and relevant data were entered and stored in a password-protected personal computer. Data collected included patients' demographics, chief complaints on presentation to the hospital, ultrasound findings, laboratory results, procedure and complication, contact numbers, etc.

The data were then tallied and represented on tables, graphs, and charts and the same were analyzed. Some patients were interviewed via telephone to assist with follow-up information.

The prevalence of molar pregnancy at GPHC was calculated per 1000 live births and was done using the following formula:

$$\frac{\text{Total number of molar pregnancies during the study period}}{\text{Total number of births at GPHC during the study period}} \times 1000$$

Results/Analysis/Discussion

There was a total of 26 patients managed for molar pregnancy at the GPHC between 2018 to 2022. After applying the inclusion and exclusions criteria, one (1) patient was excluded from this study because of histopathological results confirming normal pregnancy.

The prevalence of molar pregnancy at the GPHC between 2018 and 2022 was calculated as 0.85 per 1,000 live births. This value falls within reported ranges in the USA, however, it is less than that reported regionally. [8]

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Age of Women Managed for Molar Pregnancy				
<15	**15-25**	**26-35**	**36-45**	**>45**
4%	44%	40%	4%	8%
Ethnicity of Women Managed for Molar Pregnancy				
African	**East Indian**	**Amerindian**	**Mixed**	**Latin-American**
32%	16%	20%	24%	8%
Parity				
Nulliparous	**Primiparous**	**Multipara**	**Gran Multipara**	
20%	28%	44%	8%	
Administrative Region				
1	**2**	**3**	**4**	**8**	**9**
20%	8%	8%	56%	4%	4%

Figure 1. Demographics of patients managed for molar pregnancy at GPHC, 2018-2022

In this study, 44% of patients diagnosed with molar pregnancy were between the ages of 15 and 25, while 40% were between the age of 26-35. The average age of presentation was 26 years. This aligns with existing literature which suggests that molar pregnancy is most common in women under 15 or over 35 years old.

In addition, it can be noted that women in the advanced maternal age groups represented 16% of the study population.

African-Guyanese patients were mostly affected, representing 32% of the cases, followed by patients of mixed ethnicity at 24%, Amerindians at 20%, Indo-Guyanese at 16%, and Latin-American migrants at 8%.

Out of all the patients, 20% (n=5) came from region one, 8% (n=2) from region two, 8% from region three, 56% (n=14) from region four, and 4% (n=1) came from regions eight and nine each.

Patients who had previously given birth (multiparous) represented the largest group at 44%, followed by first-time mothers (primiparas) at 28%, women who had never given birth (nulliparas) at 20%, and women who had given birth five or more times (gran multiparas) at 8%.

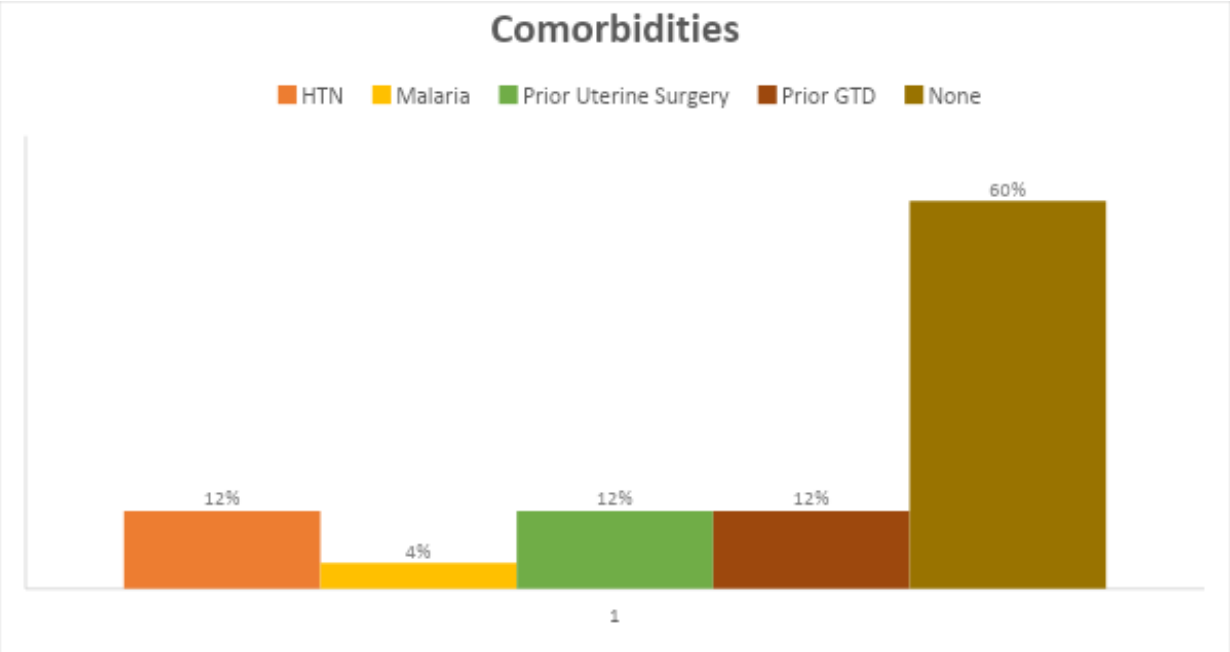

Figure 2. Significant medical history of patients managed for molar pregnancy at GPHC, 2018-2022

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Most patients in the study, 60%, did not have any significant past medical history, 12% had prior uterine surgery (LSCS), hypertensive disorders, and a history of a prior molar pregnancy. 4% (n=1) have a history of Malaria.

A history of GTD increases the risk for repeat molar pregnancy by 1 to 1.5 percent, which is 10 to 15 times the risk of the general population. A study published by Olivier Mulisya et al showed that women with a history of abortions (uterine evacuations) beyond the first trimester were at an increased risk of molar pregnancy. Of the study population, 8% of the patients had prior uterine evacuations.

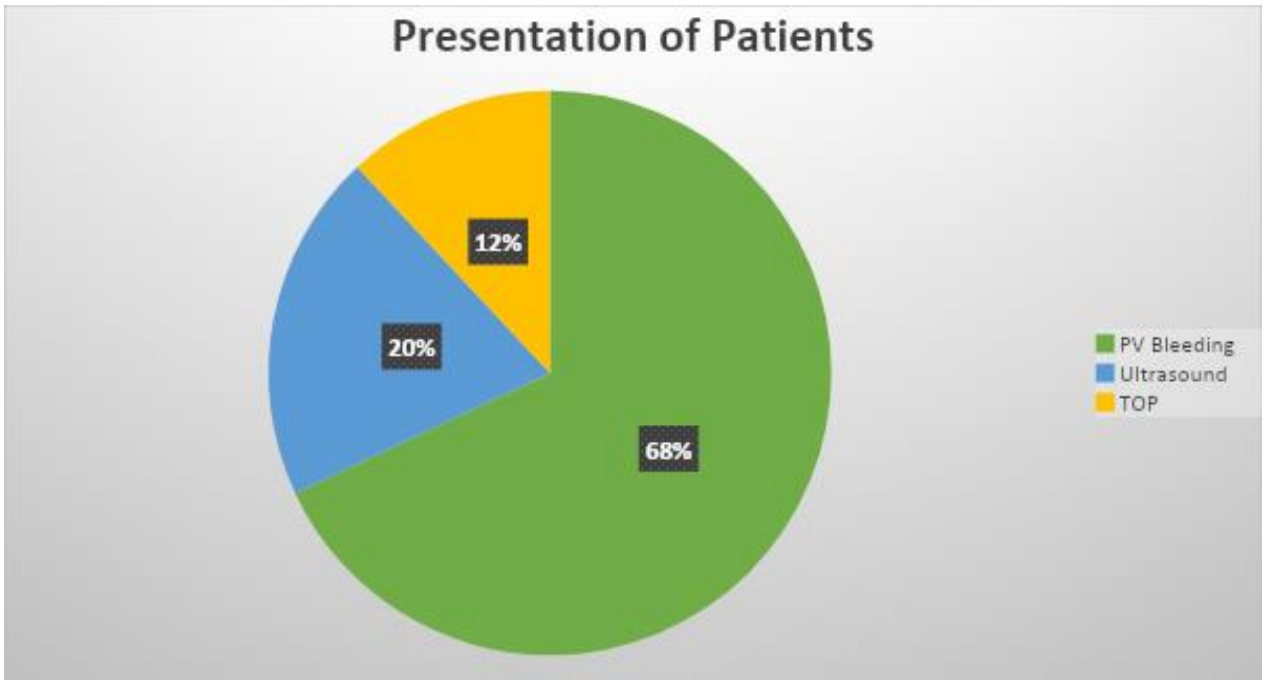

Figure 3. Clinical presentation of patients managed for molar pregnancy at GPHC, 2018-2022

The most common symptom reported by patients was vaginal bleeding, which was seen in 68% of the population. Within this group, 44% experienced spotting, 20% had heavy bleeding accompanied by weakness and passing of clots, and 4% reported grape-like bleeding. These results are consistent with previous studies.

Nausea and vomiting were not common complaints made by patients in the study. Approximately 20% of patients sought medical attention after undergoing an ultrasound to join an antenatal clinic, which suggested a molar pregnancy. Another 12% came for termination of an unwanted pregnancy.

At the time of diagnosis, most patients were unsure of their gestational age, as their last menstrual period was unknown. Of those with known gestational age, 32% presented in the second trimester, 28% in the first trimester, and 4% in the third trimester (n=1). Sun et al in a study at Brigham and Women's Hospital from 1994 through 2013, reported that the median gestational age at uterine evacuation for both complete hydatidiform moles and partial hydatidiform moles was 9 and 12 weeks, respectively[4].

It is possible that this difference is due to limited access to ultrasound in rural areas, as 36% of the patients in this study were from such regions (specifically, regions 1, 2, 8, and 9).

Management

All patients underwent a dilation, and suction evacuation procedure under anesthesia in the operating theater. Of these, 52% experienced less than 500mls of blood loss, 36% had 500mls to 1 liter of blood loss, and 12% had more than 1 liter of blood loss. One patient required emergency uterine evacuation due to active vaginal bleeding on the ward, while the rest had elective procedures.

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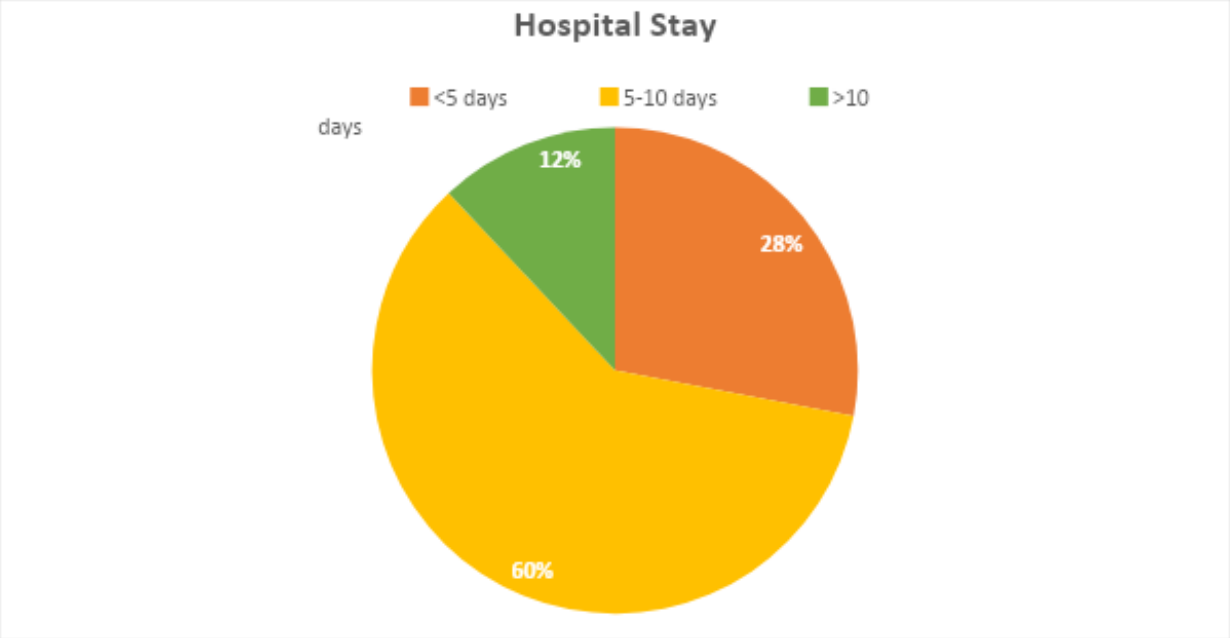

Figure 4. Duration of hospital stay for patients admitted for molar pregnancy at GPHC, 2018-2022

The majority of patients stayed in the hospital for a duration of 5 to 10 days, which accounted for 60% of all admissions. 28% of patients had a longer stay of more than 10 days, while 12% of patients had a shorter duration of stay of less than 5 days. Before undergoing a uterine evacuation, most patients spent their time in the ward awaiting optimization and surgical date for uterine evacuation.

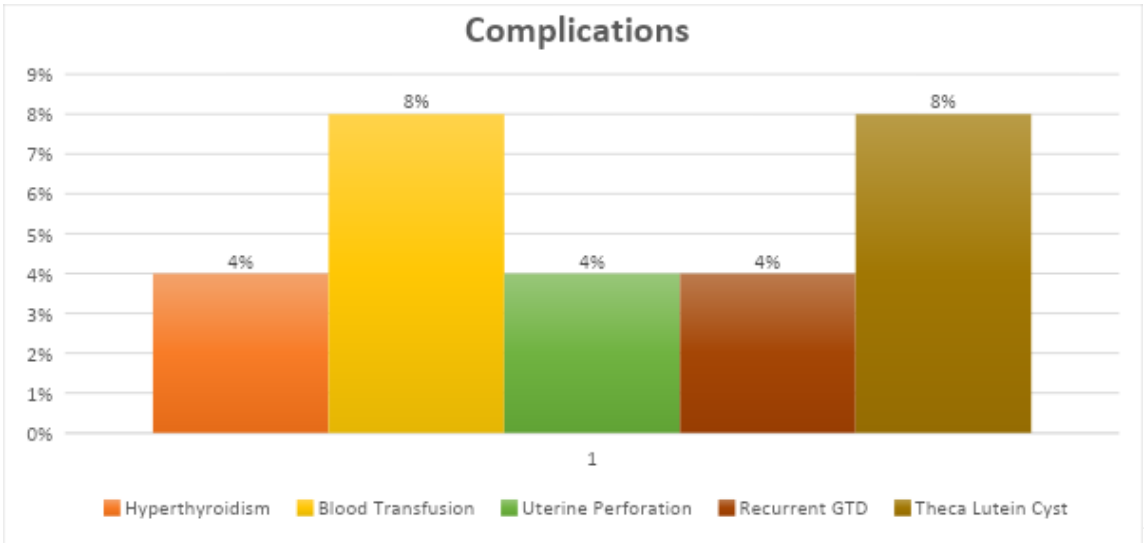

Figure 5. Complications of patients managed for molar pregnancy at GPHC, 2018-2022

Among the complications observed in molar pregnancy, the most frequent were pain associated with theca lutein cysts and anemia requiring blood transfusion, each accounting for 8% (n=2). Additionally, hyperthyroidism, uterine perforation, and recurrent mole were observed in 4% (n=1) of cases each. These complications are well-documented in existing literature. None of the patients required a hysterectomy, nor were they treated for gestational trophoblastic neoplasia.

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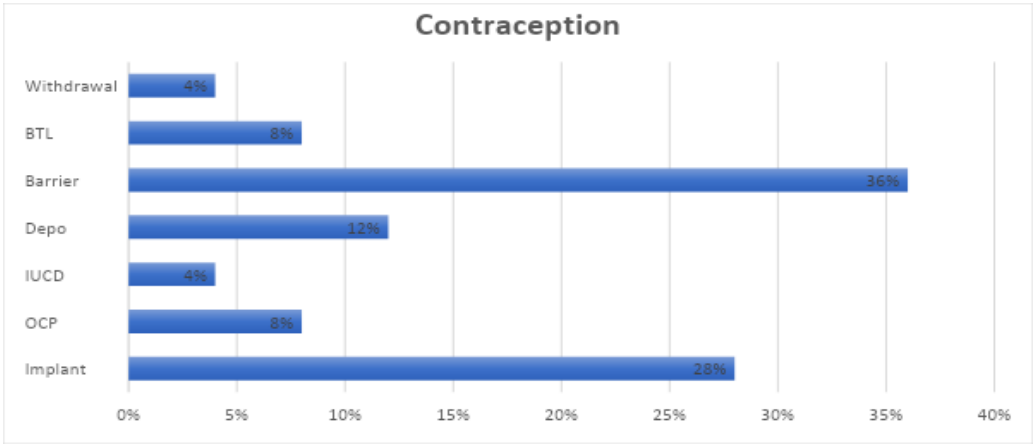

Figure 6: Method of contraception after uterine evacuation for molar pregnancy at GPHC, 2018-2022

After undergoing uterine evacuation for molar pregnancy, 36% of patients chose the barrier method of contraception. 28% had a sub-dermal implant inserted, 12% used Depo-Provera, 8% underwent bilateral tubal ligation, 8% used combined oral contraceptive pills, and 4% chose the withdrawal method.

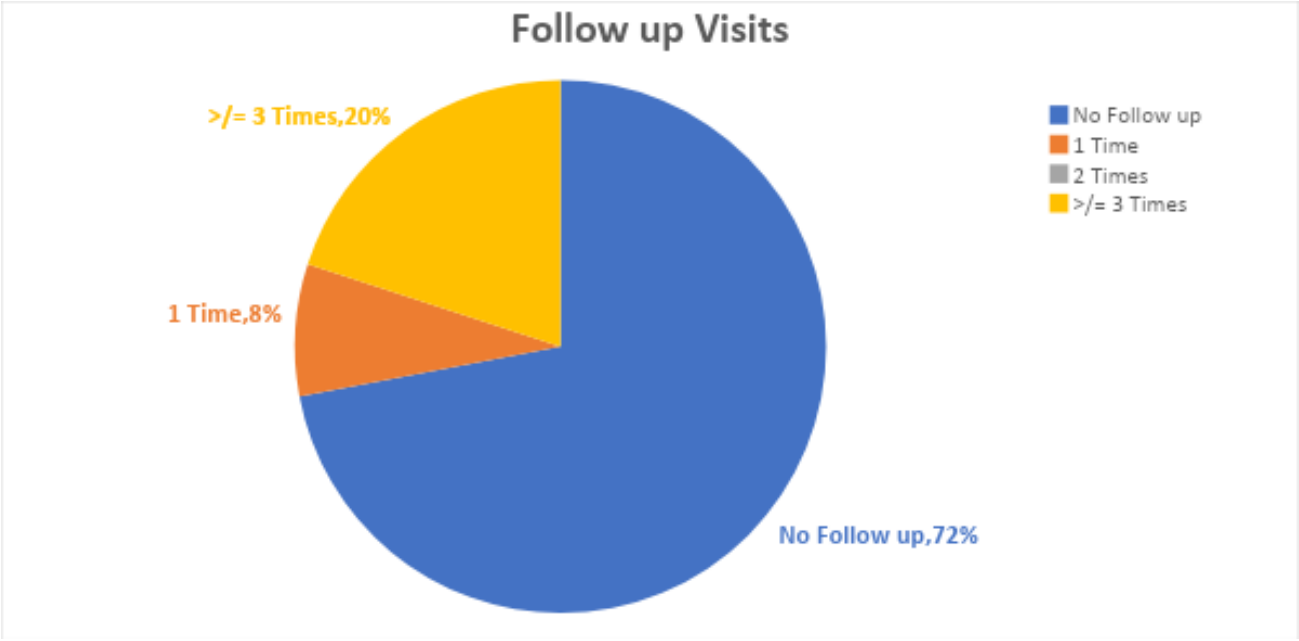

Figure 7. Number of follow-up visits of patients managed for molar pregnancy at GPHC, 2018-2022

Even though it was recommended that patients with molar pregnancy have a follow-up visit within a week of being discharged, 72% of these patients did not have any records of follow-up. 8% had only one follow-up visit and only 20% of patients had at least three follow-up visits.

Only 4% of patients (n=1) continued follow-up as recommended until they were discharged, while the other 96% of patients did not have an appropriate follow-up. The risk of malignant disease following surgical evacuation of a complete mole is 15%-20% and after an incomplete or partial mole, it is 0.5%-5%.

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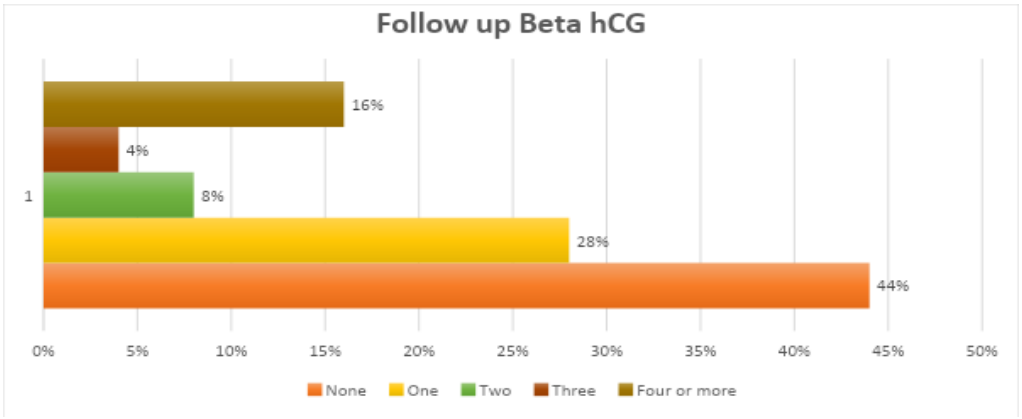

Figure 8: Beta hCG levels after uterine evacuation of molar pregnancy at GPHC, 2018-2022

It was found that 44% of patients diagnosed with molar pregnancy did not receive any follow-up beta hCG testing after uterine evacuation. Only 28% had one test, while 16% had at least four, 8% had two, and 4% had three. The main reason for the lack of follow-up with beta hCG was due to patients being unable to afford the cost of the test. FIGO 2018 guidelines require patients diagnosed with complete hydatidiform mole, the beta HCG should be repeated weekly until normal and then monthly for 6 months, after which patients can be discharged from follow-up. It is important to note that gestation trophoblastic neoplasia may occur many years after a molar pregnancy, inclusive during menopause [2], hence complete resolution is crucial.

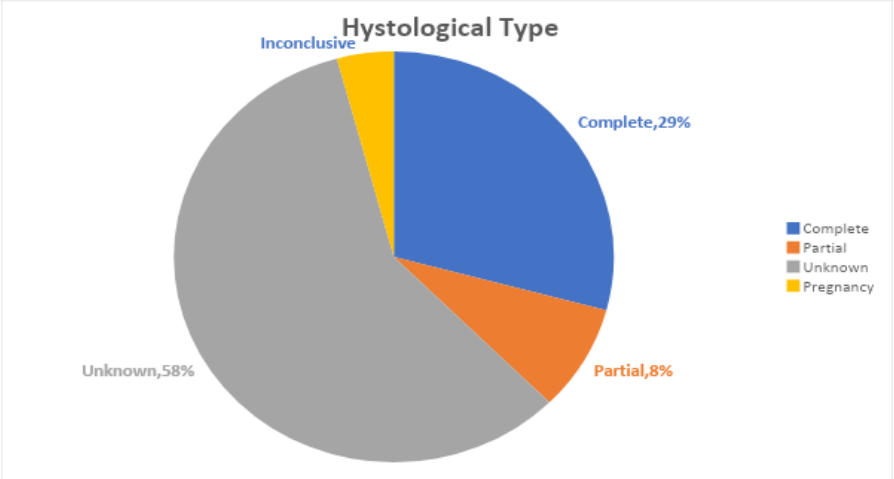

Figure 8. Histological results for patients managed as molar pregnancy at GPHC, 2018-2022

Out of the histopathological results received, 29% indicated complete molar pregnancies, 8% were partial moles, 4% were inconclusive or insufficient, and 59% were unknown. The most common histological type found in this study was complete hydatidiform moles, which differs from a previous study at the University of the West Indies, conducted by D. Simms-Stewart et al, where partial moles were more common. This could be because partial moles were often incidental findings for patients with missed or incomplete abortions. At GPHC, products of conception for incomplete or missed abortions are not routinely sent for histopathology. Unfortunately, many cases remain without a histological diagnosis because samples never reached the pathology lab for analysis, despite clear documentation that they were sent. This highlights a deficiency in the transport of samples from the operating room to the pathology lab.

Limitations

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1. Misplaced medical records with poor storage and data retrieval of information at the medical records department.
2. No prior research on the pathology in Guyana.
3. Some patients were managed privately; therefore, their data are not included in the study.
4. Illegibility of medical records and poor documentation.

Conclusions

At the Georgetown Public Hospital Corporation, the prevalence of Molar pregnancy is 0.85 per 1000 live births.

The main clinical presentation of patients was per-vaginal bleeding (68%), ranging from spotting to heavy bleeding, with or without symptoms of anemia, while 20% were diagnosed during antenatal ultrasound, and the other 12% were diagnosed when presenting for pregnancy termination.

All patients with a diagnosis of molar pregnancy were managed by dilation, suction evacuation in the operating theater, and a follow-up plan to return to the gynecology outpatient department within one (1) week with repeated beta hCG. However, 72% of patients did not return to the clinic for follow-up after discharge.

Regarding outcomes, there were no fatalities reported and no patient underwent a hysterectomy. 8% of patients required blood transfusion due to excessive blood loss during uterine evacuation, while 4% of patients required treatment for hyperthyroidism. Additionally, 4% (n=1) had uterine perforation during evacuation and 4% experienced recurrent molar pregnancy.

Among women managed for molar pregnancy at GPHC, the most popular contraceptive method is the barrier method (36%), followed by the subdermal implant (28%), Depo-Provera (12%), bilateral tubal ligation (8%), combined oral contraceptive pills (8%), and the withdrawal method (4%).

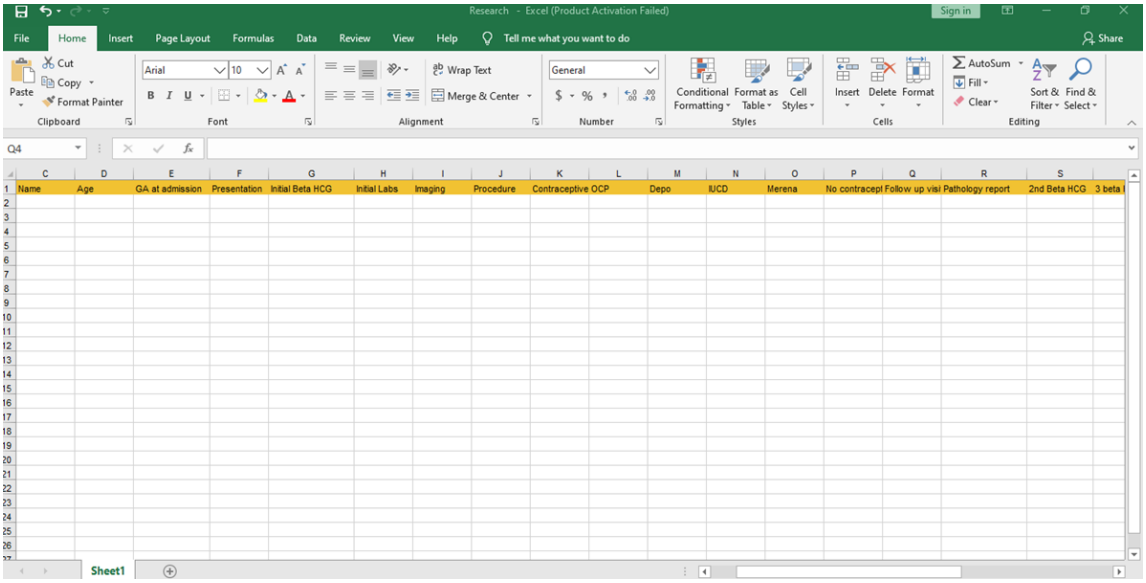
Recommendations

It is recommended to create a national registry, preferably digital, for all patients who have been treated for molar pregnancy. Additionally, it is important to conduct histopathology for all patients who have undergone uterine evacuation for missed or incomplete or at minimum a urine pregnancy test 3 weeks post evacuation.

Beta hCG testing should be made available consistently or sub-contract the test if not available to minimize the cost to patients, ensuring follow-up.

Lastly, it is crucial to establish a protocol for managing Gestational Trophoblastic Disease at both the GPHC and regional hospitals.

Appendix



Data sheet that was used to store and analyze data.

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