Original Article

Frequency of Molar Pregnancy in Patients Presenting With Miscarriage

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Abstract

Objective: The present study aimed to determine the frequency of molar pregnancy in patients presenting with miscarriage.
Methodology: A descriptive cross-sectional study was conducted at the Outpatients Department of Obstetrics & Gynaecology, Jinnah Postgraduate Medical Center (JPMC), Karachi, Pakistan, from September 25, 2020, to March 24, 2021. All eligible patients who sought medical attention at JPMC, Karachi, were included in the study after obtaining informed consent and explaining the study's procedure, risks, and benefits. Relevant data pertaining to patients' age, gestational age, and parity were collected and recorded. Transabdominal ultrasound scanning was performed to evaluate the presence of molar pregnancy. All collected data were entered into an attached proforma and stored electronically for research purposes.
Results: A total of 178 patients were included with a mean age of 28.7 ± 5.8 years. A mean parity of 2.4 ± 0.95 and a gestational age of 11.2 ± 3.5 weeks were observed. Previous molar pregnancy was found in 65 (36.5%) patients, and a positive family history of molar pregnancy was found in 33 (18.5%) patients. Molar pregnancy was found in only 01 (0.5%) patient. No significant association was found between age, BMI, parity, gestational age, previous molar pregnancy, and family history.
Conclusion: It is concluded that molar pregnancy is very unlikely to be prevalent in patients with miscarriage, but we cannot rule out residual confounders.
Keywords: Histopathology, Hydatidiform, Miscarriage, Mole, Placenta, Ultrasound.

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Introduction

A molar pregnancy, also known as a hydatidiform mole, is a rare pregnancy issue marked by the abnormal growth of placenta-forming trophoblasts.[1] Hydatidiform moles (HMs) are a kind of gestational trophoblastic disease (GTD) in which villus growth is evident. Histologically, these conditions are distinguished by anomalies in the placenta. Specifically, these placentas have chorionic villi with varying degrees of trophoblastic development and edema of the villous stroma. Complete hydatidiform moles (CHMs) and partial hydatidiform moles (PHMs) are two distinct types of hydatidiform moles that can be distinguished by their underlying biology and genetics.[1]

Partial hydatidiform moles have a much lower progression rate (5%), while 15-20% of complete moles progress to gestational trophoblastic neoplasia.[2] It is more common for a complete hydatidiform mole to be diploid; however, tetraploid and androgenic pregnancies do occur. In cases of paternal partial hydatidiform moles, the extra haploid set of chromosomes originates from the father. Serum hCG levels and clinical indications are commonly used to determine the mole's

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recurrence during therapy (for instance, vaginal bleeding and persistent or chronic pregnancy symptoms).[3] Molar pregnancies range in prevalence from one area to another.

It is commonly considered that the rate is higher in developing countries. Women under the age of 20 and beyond the age of 40 have the highest rates of occurrence, respectively. It is also more common among patients with a low socioeconomic status, infertile women, and women who do not get enough of the nutrients they need, including protein, folic acid, and beta-carotene.[4] The risk of GTD increases with both age and a history of failed or abortive pregnancies. Having an abortion or experiencing a miscarriage increases the risk of having a molar pregnancy.[1]

Abortive or unsuccessful pregnancy is a common result of molar pregnancies. The diagnostic gold standard is the histopathological evaluation of the fetus or embryo. The low prevalence of HM has led some authors to argue that a thorough histopathologic examination of tissue collected after an abortion is unnecessary.[5]

Standard abortion therapy is insufficient to detect all molar pregnancies since the tissue is not frequently sent for histological evaluation, particularly in locations with limited resources.[6] In 55% of cases, a normal-term pregnancy occurred first, whereas in 13% of cases, a miscarriage or an intentional abortion occurred first, and in 1% of cases, a molar pregnancy occurred.[7-10] The purpose of this study was to assess the prevalence of molar pregnancy in patients presenting with a miscarriage. This topic has been a little bit reported and studied in developed countries, but no information is available for women of developing countries. Generating data could be utilized in directing efforts in their control and thereby, especially in resource-poor countries where modalities of treatment may not be readily available.

The primary objective of this study is to investigate the occurrence of molar pregnancy among patients who have experienced miscarriage, with a particular focus on developing countries where awareness of this condition may be limited. By determining its prevalence, the study seeks to improve the diagnosis and management of molar pregnancy, particularly in regions with resource constraints.

Methodology

Between September 25, 2020, and March 24, 2021, a descriptive cross-sectional study was carried out at the Outpatients Department of Obstetrics & Gynaecology, Jinnah Postgraduate Medical Center (JPMC), Karachi,

For participant recruitment, a non-probability, consecutive sampling technique was utilized. The sample size was determined using OPENEpi software, considering the reported prevalence of molar pregnancy in patients with miscarriage as 13.3% [9], a margin of error of 5%, and a confidence interval of 95%. As a result, a minimum sample of 178 participants was required.

The study included all female patients aged between 18 to 45 years who experienced miscarriage, regardless of maternal parity, and provided informed consent. Participants with multiple pregnancies assessed through ultrasound were excluded from the study.

Enrollment of subjects or patients meeting the inclusion and exclusion criteria was done, and informed consent was obtained after explaining the study's objectives and methodology. Information on age, gestational age, and parity was collected using a pre-designed Performa. Transabdominal ultrasound scanning was performed by a consultant with at least five years of experience.

Molar pregnancy diagnosis was based on ultrasound findings, with complete moles exhibiting a classical "snowstorm" appearance, and partial moles showing an enlarged placenta with structural abnormalities or a deformed gestational sac. Miscarriage was defined as the sudden loss of pregnancy or conception within 24 weeks of gestation, confirmed through vaginal bleeding on clinical examination and visualization of the product of conception at the cervix on ultrasound. Molar pregnancy was recorded as positive according to the operational definition mentioned above and noted in the pre-designed Performa by the researcher herself.

Data was entered and analyzed using SPSS version 19. The mean and standard deviation were calculated for age, height, weight, BMI, parity, and gestational age. Frequency and percentage were computed for parity, previous molar pregnancy, family history of molar pregnancy, and the outcome variable, i.e., molar pregnancy. Effect modifiers such as age, BMI, previous molar pregnancy, family history of molar pregnancy, parity, and gestational age were controlled through stratification. A post-stratification Chi-square test or Fisher's Exact test was applied, with a significance level set at $P < 0.05$.

Results

A total of 178 patients were included with a mean age of 28.7 ± 5.8 C.I (27.84-29.55) years, mean height of 1.56 ± 1.2 C.I (1.3-1.73) meters, and weight of 68.2 ± 11.2 C.I (66.54-69.85) kg, and mean body mass index of 27.1 ± 5.1 C.I (26.34-27.85) kg/m2. A mean parity of 2.4 ± 0.95(2.25-2.54) and a gestational age of 11.2 ± 3.5 C.I (10.68-11.71) weeks were observed (Tabel I). Previous molar pregnancy was found in 65 (36.5%) patients and a positive family history of molar pregnancy was found in 33 (18.5%) patients (Table I). Molar pregnancy was found to be in only 01 (0.5%) patient (Table II).

Table I: Demographic information of study participants (n=178)

Parameter	Mean (SD)
Age in years	28.7 (5.8)
BMI in kg/m2	27.1 (5.1)
Parity	2.4 (0.95)
Gestational Age in weeks	11.2 (3.5)
Previous Molar Pregnancy	65 (36.5%)
Family History of Molar Pregnancy	33 (18.5%)

Table II: Frequency of Molar Pregnancy in the study

Molar Pregnancy	N (%)
Yes	01 (0.5%)
No	177 (99.5%)

Stratification of age group, body mass index, parity, gestational age, previous molar pregnancyand family history of molar pregnancy were done with respect to molar pregnancy in order to find statistical differences as shown from Table III. No significant association was found between age, BMI, parity, gestational age, previous molar pregnancy, and family history.

Table III: Stratification of Molar pregnancy with demographic and clinical history ofpatient

Parameters	Molar Pregnancy		p-value
Age Group	Yes	No	
18 – 30	1 (0.6%)	109 (61.2%)	0.618
> 30	0 (0.0%)	68 (38.2%)	
BMI			
18 – 24	0(0.0%)	91(51.1%)	0.489
> 24	1(0.6%)	86(48.3%)	
Parity			
0 – 2	0(0.0%)	84(47.2%)	0.528
> 2	1(0.6%)	93(52.2%)	
GestationalAge			
5 – 10	0(0.0%)	49(27.5%)	0.725
> 10	1(0.6%)	128(71.9%)	
Previous MolarPregnancy			
Yes	1(0.6%)	64(36.0%)	0.365
No	0(0.0%)	113(63.5%)	
Family History			
Positive	0(0.0%)	33(18.5%)	0.815
Negative	1(0.6%)	144(80.9%)	

Discussion

In our study, we reported a single case of molar pregnancy out of 178 participants. The mean age of the participants in our study was 28.7 ± 5.8 years. In comparison, Alsibiani A, et al. reported a mean age of 33.7 ± 7.5 years[3], and Riadh BT, et al. found a mean age of 32.21 years.[7] The mean parity in our study was 2.4±0.95, while Alsibiani A, et al. noted a parity of 3.1±2.2.[3]

The prevalence of molar pregnancy in our study was found to be 0.5% (01 patient). In contrast, another study reported a prevalence of 6.1%[1], and Alsibiani A, et al. noted a prevalence of 0.4% (02 patients).[3] Sebire NJ, et al. reported a prevalence of 13.3% in their study.[9]

When stratifying confounders/effect modifiers with respect to molar pregnancy, our study found insignificant differences in age group (P=0.618), body mass index (P=0.489), parity (P=0.528), gestational age (P=0.725), previous molar pregnancy (P=0.365), and family history of molar pregnancy (P=0.815).

Hydatidiform moles (HMs), also known as gestational trophoblastic disease (GTD), are characterized by abnormal placental alterations, specifically the development of villi. HMs are histologically defined and categorized by varying degrees of trophoblastic development or growth and edema of the villous stroma. They are primarily classified into complete hydatidiform moles (CHMs) or partial hydatidiform moles (PHMs) based on biology and genetics.[11] The hydatidiform mole, as a premalignant type of gestational trophoblastic neoplasia, holds clinical and epidemiological significance due to its potential impact on women's health.[12]

Hydatidiform moles are abnormal pregnancies characterized by vesicular swelling of the placental villi and varying degrees of trophoblastic growth (including cytotrophoblast and syncytiotrophoblast) in the absence or malformation of the fetus or embryo. Based on morphological and cytogenetic criteria, two hydatidiform mole syndromes have been defined.[13-15] Complete hydatidiform moles are characterized by early and consistent hydatid growth of villi in the absence of a detectable foetus or embryo, persistently hyperplastic trophoblast with varying degrees of atypia, and the absence of villous capillaries.

A miscarriage is defined as the loss of a pregnancy within 20 weeks of gestation or the delivery of a fetus weighing less than 500 grams, according to the Centers

for Disease Control and Prevention (CDC) and the World Health Organization (WHO).[15] Miscarriages occurring in the first three months of pregnancy are common and frequently encountered by obstetricians and gynecologists. This period, known as the first trimester of a clinical pregnancy, extends up to the first 12–14 weeks of gestation.[17] Historically, uterine evacuation of retained fetuses was the standard treatment for women experiencing recurrent miscarriages. However, advances in diagnostic and treatment procedures have led to more outpatient management and improved outcomes in recent years.[17]

The vast majority of placental tumors or malignancies arise from molar pregnancies, which are characterized by excessive hydropic enlargement and varying degrees of trophoblastic hyperplasia. These molar pregnancies are categorized into partial and complete subtypes based on histopathological and genetic criteria. Suction curettage is the recommended approach for the evacuation of molar pregnancies. Strict adherence to post-molar pregnancy surveillance is crucial due to the risk of developing gestational trophoblastic tumors (GTT). Substantial advancements have been made in the diagnosis, treatment, and follow-up of patients with molar pregnancy and GTT.

Significant progress has been made in the diagnosis, treatment, and follow-up of molar pregnancy and GTT patients. pGTD, which includes choriocarcinoma, is a well-known but uncommon complication that can occur after a non-molar term pregnancy.[18– 21] In some cases, genetic polymorphism analysis has conclusively demonstrated that these tumors originate in the term placenta. In other instances, a concurrent de novo intraplacental choriocarcinoma can be identified.[22, 23]

In a retrospective cohort study of 26,101 consecutive miscarriages, researchers utilized 24-chromosome SNP microarray testing and found that molar pregnancy occurs more frequently than what would be predicted by ultrasonography and/or histology.[24]

However, establishing a consistent pathophysiological mechanism by which persistent gestational trophoblastic disease (pGTD) could occur in a non-molar first-trimester pregnancy remains challenging given our current knowledge.

Several limitations are evident in the current study. Firstly, the small sample size restricted the generalizability of our study findings, as only one case of molar pregnancy was reported. To enhance the reliability of the findings, a more appropriate approach would involve a multicenter study to gather larger data sets.

Conclusion

Molar pregnancy appears to be a rare occurrence in patients with miscarriage; however, we cannot completely eliminate the possibility of residual confounders. To validate the findings of the present study, further research is warranted, involving a larger and more diverse sample size, along with the inclusion of additional parameters, in multiple study locations across Pakistan.

References

1. Mulisya O, Roberts DJ, Sengupta ES, Agaba E, Laffita D, Tobias T, et al. Prevalence and factors associated with hydatidiform mole among patients undergoing uterine evacuation at mbarara regional referral hospital. Obstet Gynecol Int. 2018;2018.
2. Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. Am J Obstet Gynecol. 2010;203(6):531–39.
3. Alsibiani A. Value of histopathologic examination of uterine products after first- trimester miscarriage. Biomed Res Int. 2014;2014:99-104.
4. Banet N, DeScipio C, Murphy KM, Beierl K, Adams E, Vang R, et al. Characteristics of hydatidiform moles: analysis of a prospective series with p57 immunohistochemistry and molecular genotyping. Modern Pathology. 2014;27(2):238-54.
5. Savage PM, Sita-Lumsden A, Dickson S, Iyer R, Everard J, Coleman R, et al. The relationship of maternal age to molar pregnancy incidence, risks for chemotherapy and subsequent pregnancy outcome. J Obstet Gynaecol. 2013;33:406–11.
6. Bakhtiyari M, Mirzamoradi M, Kimyaiee P, Aghaie A, Mansournia MA, Ashrafi-Vand S, et al. Postmolar gestational trophoblastic neoplasia: beyond the traditional risk factors. Fertil Steril. 2015;104:649–54.
7. Riadh BT, Abdellatif C, Wissal H, Leila A, Taher M, Abdelhamid K. Clinical analysis and management of gestational trophoblastic diseases: a 90 cases study. Int J Biomed Sci. 2009;5(4):321-25.
8. Hancock BW, Tidy JA. Current management of molar pregnancy. J Reprod Med. 2002; 47:347– 54.
9. Sebire NJ, Rees H, Paradinas F, Seckl M. The diagnostic implications of routine ultrasound examination in histologically confirmed early molar pregnancies. Ultrasound Obstet. Gynecol. 2001;18:662–5.
10. American Society for Reproductive Medicine; American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice. Prepregnancy counseling: Committee Opinion No. 762. Fertil Steril. 2019;111(1):32-42.
11. Schorge JOW, Schorge JO, Bradshaw KD, Halvorson LM, Schaffer JI, Corton MM. Williams Gynecology, McGraw-Hill, New York City, NY, USA, 2008.

12. Fu J, Fang F, Xie L, Chen H, He F, Wu T, et al. Prophylactic chemotherapy for hydatidiform mole to prevent gestational trophoblastic neoplasia. Cochrane Database Syst Rev. 2012;11(9): CD007289.
13. Szulman AE, Surti U. The syndromes of hydatidiform mole, I: cytogenetic and morphologic correlations. Am J Obstet Gynecol 1978;131:665-71.
14. Szulman AE, Surti U. The syndromes of hydatidiform mole, II: morphologic evolution of the complete and partial mole. Am J Obstet Gynecol 1978;132:20-7.
15. Schorge JO, Schaffer J, Halvorson LM, Hoffman BL, Bradshaw KD, Cunningham FG. "First trimester abortion," in Williams Gynecology, McGraw-Hill, New York, NY, USA, 1st edition, 2008.
16. Hinshaw K, Fayyad A, Munjuluri P. The Management of Early Pregnancy Loss, RCOG Revised Guideline, 2006.
17. Safe abortion: technical and policy guidance for health systems, World Health Organization, Geneva, Switzerland, 2nd edition, 2012
18. Cormio G, Greco P, Di Vagno G, Loverro G, Vimercati A, Selvaggi L. Choriocarcinoma following term pregnancy by transvaginal color Doppler ultrasound. A two case report. Eur J Gynaecol Oncol 1996;17:151–3.
19. Sood M, Sangwaan K, Sherwaal V, Marwah S, Sen R. An unusual case of choriocarcinoma following live term pregnancy. Aust N Z J Obstet Gynaecol 2000;40:101–3.
20. Hou HC, Chen CJ, Chang TC, Hsieh TT. Metastatic choriocarcinoma with spontaneous splenic rupture following term pregnancy: a case report. Changgeng Yi Xue Za Zhi 1996; 19:166–70.
21. Balat O, Verschraegen CF, Edwards CL, Silva E, Kudelka AP, Kavanagh JJ. Unusual presentation of a metastatic choriocarcinoma following a full term pregnancy: a case report. Eur J Gynaecol Oncol 1996;17:271–3.
22. Seckl MJ, Dhillon T, Dancey G, Foskett M, Paradinas FJ, Rees HC, et al. Increased gestational age at evacuation of a complete hydatidiform mole: does it correlate with increased risk of requiring chemotherapy? J Reprod Med 2004;49:527–30.
23. Sebire NJ, Foskett M, Paradinas FJ, Fisher RA, Francis RJ, Short D, et al. Outcome of twin pregnancies with complete hydatidiform mole and healthy co-twin. Lancet 2002;359: 2165–6.
24. Maisenbacher MK, Merrion K, Kutteh WH. Single-nucleotide polymorphism microarray detects molar pregnancies in 3% of miscarriages. Fertility and Sterility. 2019;112(4):700-6.