The prevalence of molar pregnancy among patients with incomplete miscarriage at a maternity teaching hospital

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Abstract

Background and objective: Gestational trophoblastic disease (GTD) involves a range of interrelated disorders that originate from the placenta; it can be benign or malignant. In the Kurdistan region of Iraq, data about GTD and its consequences is scarce. This study aims to identify the prevalence of GTD and its types among a cohort of Kurdish women.

Methods: A cross-sectional study was conducted for a one-year duration from April 1, 2020, to April 1, 2021, at the Emergency Department of Maternity Teaching Hospital, Erbil City. Pregnant women in their first trimester and early second trimester (4–14 weeks of gestation) with vaginal bleeding, pregnant women with vaginal bleeding due to incomplete miscarriage, and pregnant women with a history of missed miscarriage were included in the study. A specialized questionnaire was prepared for the purpose of data collection.

Results: Out of 380 incomplete miscarriage cases who were interviewed, fifty patients with gestational trophoblastic disease were included in the current study. The prevalence of GTD was 13.1%, and the majority of patients had a partial type of GTD. The current analysis indicated that there was a statistically significant association between the types of GTD, the personal history of molar pregnancy, and the age of participants. The analysis indicated that there is no statistical association between parity, blood group, and history of miscarriage and the type of GTD.

Conclusion: The prevalence of GTD was remarkably high, and the partial type of GTD was the most common form present among the participants. The majority of the cases were diagnosed during the first trimester of the pregnancy. Complete GTD was more common among patients of advanced age.

Keywords: Gestational trophoblastic disease; GTD; Miscarriage; Incomplete miscarriage.

Introduction

The term gestational trophoblastic disease (GTD) refers to abnormal cells or tumors that form in the uterus during pregnancy, deriving from the trophoblast, which is the first layer of cells that develops into the placenta. It is a rare condition, and it can be malignant or benign. GTD involves a range of interrelated disorders that originate from the placenta. 2

A group of genetic disorders called GTD includes molar pregnancy (full and partial hydatidiform mole), invasive mole, choriocarcinoma, placental site

trophoblastic tumor, and epithelioid trophoblastic tumor. The above conditions, except molar pregnancy, can metastasize and be fatal if left untreated; they are also known as gestational trophoblastic neoplasia (GTN).³⁻⁷

Worldwide, the incidence reported of GTD varies broadly, and similarly, there is a wide variation with regard to the incidence of molar pregnancy.⁵ For instance, in Paraguay, the incidence of GTD is reported to be low (23 per 100,000 pregnancies), whereas in Indonesia, it is reported to be high (1,299 per 100,000

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pregnancies). In the USA, the incidence is reported to be around 110 to 120 per 100,000 pregnancies.⁸

For the development of a complete hydatidiform mole, numerous potential risk factors have been assessed. There are two main risk factors that play an important role in developing a complete hydatidiform mole, namely extremes of maternal age and a history of molar pregnancy. Higher rates of complete hydatidiform mole were documented to be more commonly associated with advanced or very young maternal age. Prior hydatidiform mole predisposes to another molar pregnancy, as after one molar pregnancy, the risk of recurrent molar pregnancy is about 10 to 20 times the risk for the general population.7, 10

A uterus larger than the gestational age and second-trimester vaginal bleeding are the main clinical manifestations. Since early detection and diagnosis are usually made through ultrasound examination in the first trimester, complications like hyperemesis gravidarum, anemia, hyperthyroidism, respiratory distress, and preeclampsia are less common.^{6,7}

Due to the routine use of ultrasonography and beta human chorionic gonadotropin hormone (β -hCG) testing, women with complete hydatidiform moles are usually diagnosed early in gestation and thus often have no clinical manifestations at the time of diagnosis. 6

In the diagnosis of molar pregnancy (both complete and partial moles), ultrasonography plays a crucial role and has effectively substituted all other methods of diagnosis preoperatively.^{4, 6,12} Proper clinical management of the patient relies on an accurate diagnosis.^{13, 15}

A disease-specific tumor marker, hCG, is easily measured quantitatively in both blood and urine, and the measures of hCG have been reported to be associated with the disease burden.^{4,16}

Giving either actinomycin D or methotrexate chemotherapy as a preventative measure during or right after

molar extraction can lower the risk of post-molar GTN.^{4, 17}

It is recommended that after uterine evacuation, all Rh-negative women be offered anti-D immune globulin to prevent alloimmunization.18 In addition. recommended that reliable contraception should be received by women undergoing after hydatidiform follow-up throughout the entire follow-up period.19 There is not enough study clear information about GTD and its consequences in Erbil, Kurdistan, Iraq. Therefore, this study aims to identify the prevalence of GTD and its types among the study group. It also aims to determine the factors that may affect the quality of life

Methods

status of women with GTD.

A cross-sectional study was conducted for a one-year duration and carried out from April 1st, 2021, to April 1st, 2022, at the Emergency Department of Erbil Maternity Teaching Hospital, during which a total of 380 patients with vaginal bleeding were managed.

The researchers interviewed a total of 380 cases of incomplete miscarriage and pregnant women with a history of missed miscarriage who agreed to participate in the study. Then, after the cases had been sorted out according to the exclusion and inclusion criteria, the remaining 50 patients who had gestational trophoblastic disease were enrolled in the current study.

Those pregnant women that were selected conveniently were suffering from vaginal bleeding due to incomplete miscarriage and undergoing uterine evacuation during the first trimester and early second trimester of pregnancy; similarly, we involved pregnant women with a history of missed miscarriage in our study. Physical and manual gynecological examinations were done for the pregnant women, and ultrasounds were performed for the pregnant women before diagnostic diagnosis. Moreover, blood samples were taken from all the pregnant women in the

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study sample and sent for beta human chorionic gonadotropin hormone level for confirmatory purposes. In addition to that, a complete blood count, liver and renal function tests, and serum electrolytes were done as part of the medical evaluation, but we did not include this information in the data analysis process.

Afterwards, diagnostic curettage pieces of the conception product were sent for histopathological examination. Other relevant information, such as sociofeatures demographic (age, race. educational level, occupation, and history of previous residency, parity, of previous abortions. and history hydatidiform moles), was taken included in the data collection, which was done by direct interview with the pregnant women using a special questionnaire that has been designed for this reason.

Inclusion criteria: first trimester and early second trimester pregnant (4–14 weeks) women with vaginal bleeding and pregnant women with a history of incomplete abortions or missed abortions.

Exclusion criteria: late second trimester and women who refused to participate in the study.

The data was collected by designing a specialized questionnaire prepared for this purpose by the researchers, and then the data was collected by the researchers through direct interviews with patients. The patients filled out the questionnaires through face-to-face interviews. It was clarified to the patients that they had the right to refuse to answer any question whenever they felt uncomfortable; other clinical data, apart from the questionnaires, was collected from the patients' medical questionnaire records. The included information about the following:

Socio-demographic characteristics include age, occupation, educational level, and residency.

Asking about obstetrical history, gestational age, parity, and history of previous abortions.

Previous history of GTD. Checking

maternal blood group or rhesus status.

Statistical analysis: The statistical package for social science (SPSS, version 25) was used to analyze the data, and the chi-square test of association was used to compare proportions. When the expected frequency (value) was less than five of more than 20% of the cells in the table, Fisher's exact test was used. To compare the means of the two samples, a student's t-test of two independent samples was used. A P-value of ≤ 0.05 was considered statistically significant.

Ethical approval: This study was approved by the Research Ethics Committee at Hawler Medical University/ College of Medicine (approval number 5, 23 of May 2021). Verbal informed consent to participate in the study was obtained from each woman. An official acceptance obtained from the letter was Directorate of Health, granting permission to conduct this research at the hospital. participants were assured confidentiality would be maintained and that their information would only be used for research purposes.

Results

A total of 380 uterine bleeding and incomplete miscarriage cases were interviewed bγ the investigators for a duration of one year at the maternity hospital, and only 50 patients had gestational trophoblastic disease (GTD), making the prevalence of GTD 13.1%, as presented in Figure 1. Out of 50women (40%) of them were 25-34 years old and 32% of them were <25 years, also the majority (70%) of respondents were urban residential, (36%) of them were collage graduates by that remark 20% of them were illiterate, the majority (76%) were housewives while less than a quarter (24%) of subjects were employees, 72% of them were multiparous, less than half (48%) of them had A blood group, and (34%) of them had O blood type, followed by (84%) of them were not smokers while the rest (16%) were smoking cigarettes (Table 1).

Out of 50 participants, findings from Table 2 illustrate that (66%) of respondents were in their first trimester, more than half of them had a history of miscarriage, three-quarters (76%) of the subjects did not have a history of hydatidiform mole,

the majority (70%) of participants had a partial type of GTD, (80%) of their blood pressure was normal, while (20%) of them were suffering from hypertension, (44%) of pregnant women had regular antenatal care, and (40) of them had an irregular history of antenatal visits.

Table 1 Genera Characteristics of the Participants.

Variables	Categories	Frequency	Percent
Age categories (years)	< 25	16	32
	25-34	20	40
	≥ 35	14	28
Residence	Rural	15	30
	Urban	35	70
Educational level	Illiterate	10	20
	Primary	5	10
	Secondary	17	34
	Collage	18	36
Occupation	Housewife	38	76
	Employee	12	24
Parity	Primigravid	14	28
	Multigravid	36	72
Blood group	A	24	48
	B	1	2
	AB	8	16
	O	17	34
Cigarette smoking	Yes	8	16
	No	42	84
Total		50	100

Table 2 Gynecological History and Blood Pressure of the Participants.

Variables	Categories	Frequency	percent
Trimester	1st trimester	33	66
	2nd trimester	17	34
History of miscarriage	Yes	26	52
	No	24	48
History of hydatidiform mole	Yes	12	24
	No	38	76
Type of GTD	Complete	15	30
	Partial	35	70
Blood pressure	Normal	40	80
	Abnormal	10	20
Antenatal care visit	not present	8	16
	Regular	22	44
	Irregular	20	40
Total	•	50	100

Findings from Table 3 reveal that there was a significant statistical association between the age categories and the type of GTD. More than 51.4% of the participants of the partial type of GTD were young participants (25–34 years old), while more than half (53.4%) of the complete GTD type were older patients (\geq 35 years old). The chi square was significant, and the *P*-value was 0.001).

There was a significant association between educational level and type of GTD; most (33.3%) of complete-type GTD cases were illiterate women, whereas the majority of partial-type GTD cases were either college graduates or from secondary school (40% for each of them). It was significant, and the p-value was 0.008.

There was a significant statistical association between trimester and type of GTD; two-thirds (66.7%) of complete GTD were diagnosed during the first trimester of pregnancy, and in reverse, the most common diagnosis of partial GTD (77.2%) happened during the second trimester of gestation. It was significant, and the *P*-value was 0.001. Expectedly, about

three-quarters of them (73.3%) of complete GTD cases had a positive history of hydatidiform; on the other hand, the vast majority (94.3%) of partial GTD cases did not have such a history; the *P*-value was significant and was 0.001.

statistically There was а significant association between blood pressure and type of GTD; 46.7 percent of complete GTD cases had high blood pressure; in contrast, only 8.6% of the partial type had high blood pressure; it was significant, and the P-value was 0.001. There was statistically significant association between antenatal care visits and type of GTD; most (46.8%) of complete type GTD cases had irregular visits, and in reverse, half of them (51.4%) of partial type cases did regular antenatal care visits. It was significant, and the p-value was 0.030. was statistically significant There а association between cigarette smoking and type of GTD; the prevalence of smoking was much higher among complete GTD cases (33.3%) in comparison to only 8.6% among partial GTD cases; it was significant, and the *P*-value was 0.005.

Table 3 Association between the Type of GTD and Variables.

Variable	Categories	Туре с	<i>P</i> -value	
	· ·	Complete	Partial	
Age categories (years)	< 25	5 (33.3%)	11 (31.4%)	0.001
	25-34	2 (13.3%)	18 (51.4%)	
	≥ 35	8 (53.4%)	6 (17.2%)	
Educational level	illiterate	5 (33.3%)	4 (11.4%)	0.008
	primary	3 (20%)	3 (8.6%)	
	secondary	3 (20%)	14 (40%)	
	Collage	4 (26.7%)	14 (40%)	
Trimester	1 st trimester	5 (33.3%)	27 (77.2%)	0.001
	2 nd trimester	10 (66.7%)	8 (22.8%)	
History of hydatidiform mole	yes	11 (73.3%)	2 (5.7%)	0.001
	no	4 (26.7%)	33 (94.3%)	
Blood pressure	Normal	8 (53.3%)	32 (91.4%)	0.001
	high	7 (46.7%)	3 (8.6%)	
Antenatal care visit	not present	4 (26.6%)	4 (11.4%)	0.030
	regular	4 (26.6%)	18 (51.4%)	
	irregular	7 (46.8%)	13 (37.2%)	
Cigarette smoking	Yes	5 (33.3%)	3 (8.6%)	0.005
_	No	10 (66.7%)	32 (91.4%)	
Total		15 (100%)	35 (100%)	

Table 4 reveals that there was a non-significant statistical association between type of GTD and residence, occupation, parity, blood group, and history of miscarriage, and the *P*-value was >0.05.

Discussion

The incidence reported about GTD generally varies globally, and with regard to the KRI, there is no sufficient data about the incidence of GTD and its consequences. Therefore, this study aimed to identify the prevalence of GTD and its types among a cohort of Kurdish patients. It was found that the majority of the cases in the current study were multiparous and had no history of hydatidiform mole.

The current analysis indicated that the GTD was present among a considerable number of patients (i.e., patients with incomplete miscarriage), with the majority having a partial type of GTD. Similarly, another study also reported that the partial hydatidiform mole was the most common (around 43%) histopathological finding.²⁰ In addition, Riyamiet al. (2019) likewise found that around 55% of the sample was diagnosed with partial hydatidiform mole and approximately 44% of the sample was diagnosed with complete hydatidiform mole.²¹

A wide range of studies reported varied GTD incidence per pregnancy in different parts of the world.^{5,7-10,22} However, with regard to the incidence of GTD reported in patients with incomplete abortions, the data is scarce. Yet, the current finding is alarming, as the prevalence of GTD is substantially higher compared to other literature. For instance, in Tanzania (2019), it was found that the prevalence of molar pregnancy among patients with incomplete abortions was about 13%.¹¹

It is widely documented in the literature that molar pregnancies are commonly diagnosed during the first half of pregnancy, 18, 23 and the results of the current study reinforce that, as the majority of the cases were diagnosed during the first trimester of the pregnancy. More than half of the cases in the present study had a history of pregnancy loss; this is in contrast to what was found in another study conducted in Tanzania, in which most of the participants had no history of miscarriage. The most common blood group type among the participants was blood group A, and this is in agreement with the findings of another study. 11 On the contrary, blood group O was observed to be the most common blood group type among participants in another study.

Table 4 Association between Type of GTD and Variables.

Variable	Categories	Туре	Type of GTD	
		Complete	Partial	
Residence	Rural	6 (40%)	9 (25.7%)	
	urban	9 (60%)	26 (74.3%)	0.081
Occupation	housewife	12 (80%)	25 (71.4%)	0.261
	Employee	3 (20%)	10 (28.6%)	
Parity	Primigravid	4 (26.6%)	10 (28.6%)	0.846
	Multigravida	11 (73.4%)	25 (71.4%)	
Blood group	Α	7 (46.6%)	16 (45.8%)	0.207
	В	1 (6.8%)	0 (0%)	
	AB	3(20%)	6 (17.1%)	
	0	4 (26.6%)	13 (37.1%)	
History of miscarriage	Yes	8 (53.3%)	19 (54.2%)	0.965
	No	7 (46.7%)	16 (45.8%)	

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The current study findings showed no statistical association between parity, blood group, history of miscarriage, or type of GTD. This fits with what other studies in Oman, Tanzania, and Egypt found: there was no link between the number of pregnancies, having had a miscarriage before, or blood group and the number of GTDs and their types. ^{20–22} Al Riyami et al. (2019) also reported no statistical association between GTD and multiparous women, although GTD was observed more in multiparous women. ²¹

In contrast, Lurain (2010) reported that a history of spontaneous abortion is a reported risk factor for molar pregnancies (both complete and partial). The risk of a molar pregnancy in those women who have a history of miscarriage increases by 2-3-fold compared to those who have no history of spontaneous abortion. ¹⁰

The current analysis indicated that there is a statistically significant association between the types of GTD and the personal history of molar pregnancy. Parazzini et al. (1991) reported that having a history of GTD increases the risk of both complete and partial hydatidiform moles.²⁴ Ngan et al. (2019)documented that for sporadic moles, having a history of a previous hydatidiform mole increases the risk 10 times. In Lurain reports (2019) that previous hydatidiform mole predisposes to another molar pregnancy. For instance, after one molar pregnancy, the risk of repeated molar pregnancy is about 10 to 20 times (or about 1%) the risk for the general population. 10

The analysis exhibited a statistically significant association between the types of GTD and the age of participants. Complete GTD was more common among patients with advanced age (i.e., ≥35 years), whereas partial GTD was common among patients aged between 25 and 34 years. Previous studies reported that both younger maternal age and advanced maternal age are considered risk factors for molar pregnancy. After age 35, the risk

increases, and after 45 years, there is a 5–10 times increased risk. Simultaneously, there is a two-fold risk of having a molar pregnancy in teenagers. The risk of is increased complete moles advancing maternal age. Sebire et al. (2002) also found a positive relationship between the risk of hydatidiform mole and both extremes of maternal age (i.e., ≥45 years and ≤15 years). 25 In addition, they also reported that the degree of risk is quite higher with older maternal age (≥45 years) than younger maternal age (≤15 years). This is further reinforced by other findings, such as Soper (2021), who reports that women older than 45 years old are in particular at increased risk for various GTDs.¹⁸

The current analysis revealed that there is an association between cigarette smoking and GTD types. An earlier study conducted in Italy also reported that cigarette smoking was associated with GTD, and the risk was higher for those women who smoked more cigarettes and for an extended period of time. Regarding the use of contraception, its route of administration, and their association with the GTD, current findings suggest no association. Earlier literature indicates that previous use of contraception was not associated with the risk of GTD; nonetheless, among the cases, intrauterine device usage was significantly more common.²⁶

Conclusion

GTD was present in all the participants and partial type of GTD was the most common form present among the participants. The majority of the cases were diagnosed during the first trimester of the pregnancy. There was a statistically significant association between the types of GTD and the age of participants. Complete GTD was more common among patients who aged ≥35 years and partial GTD was common among patients who aged between 25 to 34 years. There was also an association between the types of GTD and personal history of hydatidiform mole. There were

no statistical associations between parity, blood group, and history of miscarriage with the types of GTD.

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Competing interests

The authors declare that they have no competing interests.

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