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CONTRIBUTING FACTORS FOR MOLAR PREGNANCY AMONG SAMPLE OF IRAQI LADIES

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ABSTRACT

Background: Gestational trophoblastic disease (GTD) starts with a premalignant hydatidiform mole (HM) and progresses to malignant conditions such as invasive mole, choriocarcinoma, and placental site trophoblastic tumor. Several earlier publications looked into factors related to GTD developments. Anyhow; there is insufficient evidence about the contributing factors for molar pregnancy. **Objectives:** Is to determine the contributing factors for molar pregnancy among sample of Iraci women. Methods: This case series retrospective study included one hundred-fifty ladies, of them 50 ladies with molar pregnancy (cases), matched according to the age with 100 ladies (controls). From June 1, 2021, to May 1, 2024, the study was conducted at the Department of gynecology and obstetrics at Al Hamdanyia General Hospital in Nineveh Province/ Iraq. The questionnaire includes three parts. Part one for maternal demographic information. Part two for risk factors for molar pregnancy such as advancing maternal age, history of previous abortion, previous molar pregnancy, smoking, genetic mutations, blood group and Rh type, and usage of birth control pills. Part three for clinical presentation of patients. Results: The mean age \pm standard deviation of the study participants was 28.23 ± 7.27 years. It's evident that the most prevalent variables linked to patients with molar pregnancy are: age group of 20-30 years among 24 (48%) patients, gestational age of 8-12 weeks among 34 (68%) patients, multigravidity among 29 (58%) patients, blood group of A+ among 19 (38%) patients. Moreover; only 5 (10%) patients reported positive history of molar pregnancy and only 6 (12%) patients had previous history of abortion, 3 (6%) patients are active smokers, 11 (22%) patients are use oral contraceptive pills and only 3 (6%) had positive family history of molar pregnancy. The mean age \pm standard deviation of the study participants was 28.23 ± 7.27 years. It's evident that the most prevalent variables with patients with molar pregnancy are: age group of 20-30 years among 24 (48%) patients, gestational age of 8-12 weeks among 34 (68%) patients, multigravidity among 29 (58%) patients, blood group of A+ among 19 (38%) patients. Furthermore; only 5 (10%) patients reported positive history of molar pregnancy and only 6 (12%) patients had previous history of abortion, 3 (6%) patients are active smokers, 11 (22%) patients are use oral contraceptive pills and only 3 (6%) had positive family history of molar pregnancy. Statistically significant difference found between the two groups regarding the presence of previous molar pregnancy (P value <0.001). Lastly: cases with molar pregnancy found to had statistically significant vaginal bleeding (P value <0.001), hyperemesis (P value = 0.012), Theca lutein cyst (P value = 0.016) and hyperthyroidism (P value = 0.012). Conclusion: Patients aged more than 20 years, gestational age of 8-12 weeks, having multigravidity, blood group of A+, having positive previous history of molar pregnancy or previous history of abortion and those with chronic use of oral contraceptive pills were more commonly linked to molar pregnancy. Patients with molar pregnancy commonly presented with vaginal bleeding, hyperemesis, theca lutein cyst and had already diagnosed hyperthyroidism.

KEYWORDS: Gestational trophoblastic disease, Miscarriage, Nineveh, Iraq.

1- INTRODUCTION

Gestational trophoblastic disease (GTD) starts with a premalignant hydatidiform mole (HM) and progresses to

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malignant conditions such as invasive mole, choriocarcinoma, and placental site trophoblastic tumor.^[1] To reduce the risk of complications and

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metastases, women with gestational trophoblastic neoplasia (GTN) should get appropriate monitoring and, if required, chemotherapy treatment.^[2] The incidence varies by region, although CHM account for 90% of HMs. GTD affects one out of every 40,000 births and it is more prevalent in Asia.^[3-4] Several earlier publications looked into factors related to GTD developments.^[5-6] factors such low parity, a history of molar pregnancy or miscarriage, use of birth control pills, and mother's age (> 35 years and < 20 years). There is insufficient evidence that smoking, drinking, particular food intake, socioeconomic status, husband's jobs, and particularly exposure to dust, soil, and pesticides all contribute to the development of GTD.^[7-8]

Patients with GTD should stay away from getting pregnant while undergoing treatment and keep a close watch on their beta-human chorionic gonadotropin (β hCG) levels.^[9] Surgery is a common treatment for women with complete hydatidiform mole (CHM) or partial hydatidiform mole (PHM). Nonetheless, persistent molar tissue, which has the potential to develop into an invasive mole, may be present in up to one out of five women with CHM. Rarely, it could develop into choriocarcinoma.^[10]

Complete hydatidiform mole in the first trimester appears in ultrasound as a uterine cavity filled with many sonolucent regions of different size and form (known as а snowstorm appearance) which have no fetal structures and may be related with ovarian theca lutein cysts. While, partial hydatidiform mole is characterized by an enlarged placenta with a 'Swiss cheese' look and the presence of a fetus on ultrasound.[11-12] Regarding histopathological appearance; CHM typically manifests as a large mass of chorionic villi that resemble grapes and are swollen and cystically dilated, so, CHM manifests as enlarged avascular villi and circumferential trophoblast hyperplasia. While, PHM possesses some normal chorionic villi and is compatible with early embryogenesis with the production of some triploid fetal parts.^[13-14] Up to date, few studies have been reported in Iraq regarding the contributing factors of HM. Furthermore, most abortion cases are empirically managed using a comprehensive post-abortion care package, with the exception of a few exceedingly problematic situations where atypical clinical signs need histological investigation of the products of conception.

This strategy has resulted to a lack of evidence on the histopathological causes of early pregnancy loss.

The aim of the study is to determine the contributing factors for molar pregnancy among sample of Iraqi women.

2- Patient and Methods

This case series retrospective study included one hundred-fifty ladies, of them 50 ladies with molar pregnancy (cases), matched according to the age with 100 ladies (controls). From June 1, 2021, to May 1, 2024, the study was conducted at the Department of gynecology and obstetrics at Al Hamdanyia General Hospital in Nineveh Province/ Iraq.

Nineveh Health Directorate's responsible committee for continuing medical education accepted the study's protocol, which complied with the Declaration of Helsinki's principles.

The questionnaire includes; maternal demographic information, and risk factors for HM include advancing maternal age, history of previous abortion, vesicular mole, previous molar pregnancy, smoking, genetic mutations, blood group and Rh type, and usage of birth control pills.

Version 30 of the SPSS (Statistical Package for Social Sciences) program (IBM Corporation, USA) was used to analyze the data. Frequency data were evaluated using the chi-square test. Statistical significance was defined as p-values less than 0.05.

3- RESULTS

The mean age \pm standard deviation of the study participants was 28.23 ± 7.27 years. It's evident that the most prevalent variables linked to patients with molar pregnancy are: age group of 20-30 years among 24 (48%) patients, gestational age of 8-12 weeks among 34 (68%) patients, multigravidity among 29 (58%) patients, blood group of A+ among 19 (38%) patients. Moreover; only 5 (10%) patients reported positive history of molar pregnancy and only 6 (12%) patients had previous history of abortion, 3 (6%) patients are active smokers, 11 (22%) patients are chronically use oral contraceptive pills and only 3 (6%) had positive family history of molar pregnancy. As shown in figure 3.1.

 Table 3.1: Patients' basic information (Number = 50 patients).

Variables	Number = 50	Percent
Maternal age (years):		
- Less than 20	9	18%
- 20-30	24	48%
- 30-40	15	30%
- More than 40	2	4%
Gestational Age (weeks):		
- 8-12	34	68%
- 13-16	16	32%
Gravidity:		

-	Primigravida	21	42%
	Multigravida	20	58%
- DL		29	3870
BI	ood groups:	10	
-	A+	19	38%
-	A-	1	2%
-	B+	5	10%
-	B-	4	8%
-	O+	13	26%
-	O-	3	6%
-	AB+	5	10%
-	AB-	0	0%
Pr	evious molar pregnancy:		
-Ye	es c	5	10%
-N	0	45	90%
Pr	evious abortion:		
-Ye	es	6	12%
-N	C	38	76%
Sn	oking:		
-Ye	es	3	6%
-N	0	47	94%
Ch	ronic use of oral contraceptive pills:		
-Ye	es	11	22%
-N	C	39	78%
Fa	mily history of molar pregnancy:		
-Ye	es i i i i i i i i i i i i i i i i i i i	3	6%
-N	C	47	94%

Table 3.2 shows patients with molar clinical manifestations. The mean age \pm standard deviation of the study participants was 28.23 ± 7.27 years. It's evident that the most prevalent variables with patients with molar pregnancy are: age group of 20-30 years among 24 (48%) patients, gestational age of 8-12 weeks among 34 (68%) patients, multigravidity among 29 (58%) patients,

blood group of A+ among 19 (38%) patients. Moreover; only 5 (10%) patients reported positive history of molar pregnancy and only 6 (12%) patients had previous history of abortion, 3 (6%) patients are active smokers, 11 (22%) patients are use oral contraceptive pills and only 3 (6%) had positive family history of molar pregnancy.

Table 3.2: Patients	' clinical m	anifestations	(Number	= 50 patients).
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Va	riable	Number	Percent
-	Vaginal bleeding	26	52%
-	Hyperemesis	10	20%
-	Preeclampsia	3	6%
-	Hyperthyroidism	9	18%
-	Lower abdominal pain	9	18%
-	Theca lutein cyst	8	16%
-	Per vaginal expulsion of grape like vesicles	6	12%

Table 3.3 illustrate comparison between cases with molar pregnancy and with no molar pregnancy regarding certain risk factors. Statistically significant difference found between the two groups regarding the presence of previous molar pregnancy (P value <0.001). On the other hand; no statistically significant difference between them regarding gestational age, parity, smoking and chronic use of oral contraceptive pills (P value >0.05) for all.

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Table 3.3: Com	parison between	cases and controls	regarding ce	rtain risk factors.

Variable	Cases, number (%)	Controls, number (%)	P value
Gestational Age (weeks):			
- 8-12	16 (32%)	21 (21%)	0.690
- 13-16	34 (68%)	79 (79%)	0.089
Parity:			
- Primigravida	21 (42%)	19 (19%)	0.000
- Multigravida	29 (58%)	81 (81%)	0.892
Smoking:			

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-Yes	3 (6%)	2 (2%)	0.910
-No	47 (94%)	98 (98%)	
Chronic use of oral contraceptive pills:			
-Yes	11 (22%)	26 (26%)	0.621
-No	39 (78%)	74 (74%)	0.021
History of molar pregnancy:			
-Yes	5 (10%)	0 (0%)	-0.001
-No	45 (90%)	100 (100%)	<0.001

Table 3.4 shows compares between cases and controls regarding certain clinical manifestations. Cases group found to had statistically significant vaginal bleeding (P

value <0.001), hyperemesis (P value = 0.012), Theca lutein cyst (P value = 0.016) and hyperthyroidism (P value = 0.012).

Table 3.3: Com	parison between cases an	d controls regarding	ng certain clinical manifestations.

Variable	Cases, number (%)	Controls, number (%)	P value
Vaginal Bleeding	26 (54%)	2 (2%)	<0.001
Hyperemesis	10 (20%)	3 (3%)	0.012
Theca lutein cyst	8 (16%)	1 (1%)	0.016
Hyperthyroidism	9 (18%)	1 (1%)	0.012

4- DISCUSSION

Molar pregnancy is found in this study to be more prevalent among the age group of 20-30 years, which is runs with a study conducted in Iran at 2021.^[15] Moreover; about two thirds of the study patients had gestational age of 8-12 weeks which is going with what was published by the National Institutes of Health (NIH).^[16] Furthermore; regarding gravidity, most of molar pregnancy in this study were multigravida, which is in the same way Shaher Bano Iftikhar et al.^[17]

The study found that blood group of A+ was more prevalent than other blood groups. While no particular blood group is certainly the most common in molar pregnancies, studies show a greater incidence of molar pregnancies in people with blood groups A and O.^[18] Additionally; the study found only 10% of patients had previous history of molar pregnancy, this is means the risk of recurrence is low, but it's not uncommon for a woman to experience a second molar pregnancy after having a first one. Anyhow; Mehmet Ozer et al had found 17% of the patients with molar pregnancy had recurrent history.^[19] In the same way; about 12% of the study patients had previous history of abortion, which is confirm the idea of molar pregnancy is linked with previous bad obstetric history for uncertain causes, history of abortion might be associated with specific genetic or biological factors that increase the likelihood of molar pregnancy, which is agreed with Geetha Dharmesh Balsarkar et al. study results.^[20]

Active smoking is reported among 6% of the study patients, Shaina Bruce et al had comparable findings.^[21] While chronic using of oral contraceptive pills was reported among considerable portion (22%) of the study patients. Barun Kumar Das had reported lesser portion (9%).^[22] Anyhow; small sample size can lead to these results. With regard to family history of molar pregnancy; only 6 % report positive family history. Multiple moles within the same family are a

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characteristic of familial recurrent molar pregnancies, although this is uncommon. Mutations in particular genes, such as NLRP7, KHDC3L, and PADI6, have been connected to familial recurrence, supporting the theory that these family cases have a genetic basis.^[23]

On the other hand; the study found that vaginal bleeding was the commonest presenting complaint of molar pregnancy, which is parallel to Nahid Mirza et al study finding.^[24]

The study compares between patients with molar and normal pregnancy. Statistically significant difference found regarding the presence of previous molar pregnancy, Debra S. Heller et al had comparable results. ⁽²⁵⁾ Moreover; regarding the clinical manifestation of the study patients, the study found that the presence of vaginal bleeding, hyperemesis, theca lutein cyst and hyperthyroidism were significantly greater among patients with molar pregnancy, these results were consistent to Alimohammadi Niloufar et al study results.^[15]

The study's limitations are; it was conducted retrospectively which make it vulnerable to recall or selection bias. Other limitations of the current study include a failure to collect detailed information about all past pregnancy problems. Another limitation was that some women were unable to recall their entire medical history, therefore some histories were missed.

5. CONCLUSION AND RECOMMENDATION

Patients aged more than 20 years, gestational age of 8-12 weeks, having multigravidity, blood group of A+, having positive previous history of molar pregnancy or previous history of abortion and those with chronic use of oral contraceptive pills were more commonly linked to molar pregnancy. Patients with molar pregnancy commonly presented with vaginal bleeding, hyperemesis, theca lutein cyst and had already diagnosed hyperthyroidism.

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Conflict of Intertest

The authors of this study report no conflicts of interest.

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