

Factors Contributing to Molar Pregnancy Through a Study in Jiblah University Hospital, IBB: Study from 2017 to 2022

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Abstract

Background: The reported prevalence rates of hydatidiform mole (HM) vary greatly across geography and time, making worldwide comparisons challenging, especially in developing countries and resource-limited settings. To date, few studies have been reported in Yemen regarding the epidemiology, management, and outcome of patients with HM. The current study sought to investigate the prevalence of HM among women who visited a large tertiary center at Jiblah University Hospital in Yemen.

Method: A retrospective study was conducted between Jun 2017 and Sep 2022 at Jiblah University Hospital, Ibb, Yemen including all women with a diagnosis of HM. Complete medical histories for all HM patients were collected and analyzed.

Results: A total of 160 women diagnosed with HM at Jiblah University Hospital - Ibb study from 2017 to 2022 years were included in the study. The mean gestational age on admission was 25.2 years. Sixty-two patients (38.7%) have Hb less than normal range and 94 of patients (58.8 %) have Hb normal range 12- 15g/dl and 4 patients (2.5 %) have Hb more than normal range 15g/dl. However, the percentage blood types (A+, A-, B-, B+, O+, O- and AB+) were 40.6%, 0.6%, 5%, 0.6%, 41.9 %, 7.5% and 3.8%, respectively.

On the other hand, among the sample, 4 (2.5%) women were diagnosed histopathologically to have previous V.M and while 156 (97.5%) women were diagnosed histopathologically to have no previous V.M. A number of women who had previous abortion were recorded 46(28.7%) and while the women had not previous abortion was 114(41.4%). Among the women who had smoking and no smoking were recorded 2(1.3%) and 158(98.7%), respectively. Finally, unfortunately the researchers didn't find following risk factors in the register of patients, such as (Ovulation induction, genes mutation, infertility and birth control pills), by researching the record of patients with HM or registered as having HM. However, our study found the relationship between age groups and the previous abortion about associate risk factors of molar pregnancy. There is statistically significant difference between previous abortion and age, with P-value =0.007.

Conclusion: The present study showed that incident hydatidiform mole were higher in 20-29 years of maternal age, so we found that the incidence of HM in younger age patients is the most common. Also, we found that the significant positive correlation was found between age with previous abortions. Therefore, it is recommended that

women should undergo health care before pregnancy and further studies are required to provide solutions to reduce the cases of HM.

Keywords: Hydatidiform Mole, Molar Pregnancy, Prevalence, Clinical Presentation, Yemen, Jiblah University Hospital.

Introduction

Gestational trophoblastic disease (GTD) is a group of illnesses that begin with premalignant circumstances of hydatidiform mole (HM), which can develop as a complete hydatidiform mole (CHM) or a partial mole (PMH), to malignant conditions including invasive mole, choriocarcinoma, and placental site trophoblastic tumor (PSTT) [1,2]. Women diagnosed with gestational trophoblastic neoplasia (GTN) should be properly monitored and, if necessary, treated with chemotherapy to decrease the risk of complications and metastases [3]. The incidence varies by region, although CHM accounts for 90% of HMs [3]. GTD affects one in every 40,000 births and is particularly frequent in Asia [4]. The reported frequency in Yemen is 1 in 164 pregnancies, 1 in 386 births in Oman, and 1.26 in 1000 deliveries in western Saudi Arabia [1,3,5].

Factors associated with GTD developments were investigated in several previous reports. Factors such as maternal age (> 35 years and < 20 years), low parity, a history of previous molar pregnancy or miscarriage, and use of birth control pills. There is little evidence linking GTD development to smoking, alcohol intake, food, socioeconomic level, Husband's jobs and especially exposure to dust and soil, and pesticide exposure [4,6-8].

Patients with GTD should regularly monitor their beta-human chorionic gonadotropin (β hCG) levels and avoid conception during the treatment time. Women with PHM or CHM are frequently treated by surgical surgery [9]. However, up to one in every five women with CHM will have persisting molar tissue, which can

grow into an invasive mole. In rare situations, it may progress to choriocarcinoma [6]. In both cases, more therapy is essential. Using sonography, CHM in the first trimester appears as a uterine cavity filled with multiple sonolucent areas of varying size and shape (known as a snowstorm appearance) without the presence of fetal structures, and it may be associated with ovarian theca lutein cysts. PHM presents as an enlarged placenta with multicystic avascular sonolucent spaces ('Swiss cheese' appearance), and a fetus can be demonstrated by ultrasound [9]. Histopathologically, CHM has a typical appearance of a voluminous mass of grape-like structures of chorionic villi, which are cystically dilated and swollen. For instance, CHM appears as circumferential trophoblast hyperplasia and swollen avascular villi. On the other hand, PHM, which is compatible with early embryogenesis with the formation of some triploid fetal parts, has some normal chorionic villi [8].

To date, few studies have been reported in Yemen regarding the epidemiology, management, and outcome of patients with HM [5]. Additionally, aside from the financial concerns for histological diagnosis of the products of conception, there is no scientific rationale for not undertaking routine histopathological diagnosis in our situations, as there are in many other resource-constrained contexts. In these circumstances, most abortion cases are empirically handled utilizing a comprehensive post-abortion care package, except for a few extremely questionable instances where atypical clinical symptoms may need histological examination of the products of conception. This approach has contributed to a lack of data on the underlying pathological reasons for early pregnancy losses in the nation, as well as the prevalence of GTDs because ultrasound's accuracy in diagnosing hydatidiform moles (HMs) during the first trimester is quite low.

The current study sought to investigate the prevalence of HM among women who visited a large tertiary center at Jiblah University Hospital in Yemen. This study intends to alert medical providers to HM clinical presentation, treatment, and

outcome. This might lead to earlier diagnoses and improved treatment results for HM-affected women.

Material and Method

1- Type of Study:

This study was conducted retrospectively with overall aim to identify and understand the factors contributing to development of molar pregnancy, on all women diagnosed with molar pregnancy at Jiblah University Hospital in Ibb city, From 2017 to 2022.

2- Place of Study:

This study was conducted at obstetric and gynecological department in Jiblah University Hospital, Ibb city, Yemen. One hundred sixty patients who were diagnosed and registered as molar pregnancy during the period of the study (2017 to 2022) were included in the study.

3- Period of Study:

The study was conducted during the period from 2023 /2/8 to 2023/5/25.

4- Study Population:

The study involved all women pregnancy who were admitted to gynecological wards which were diagnosed with Hydatidiform mole, women who had hydatidiform were selected as study population.

5- Data Collection:

For data collection, the maternity records available in the hospital archive were used. The sampling method in this study was based on complete enumeration and all the records in the hospital archive in 2017-2022 were evaluated.

Cases were excluded from analysis for women lost to follow-up or with missing data. The hospital database including the hospital information system (archive medical records), gynecology operating theater and histopathology laboratory registries were used to collect the following data: maternal demographics and risk factors for HM (age, previous abortion, previous Vesicular mole, Ovulation induction, smoking and genes mutation, Hemoglobin, Blood types, infertility, and use of birth control pills).

6- Ethical Approval:

The proposal of the study was approved, and ethical approval was obtained from the College of Medicine and Health Sciences, Dean of Midwifery Department, Jiblah University Hospital -Ibb.

7- Statistical Analysis:

Data entry was done using Microsoft Office Excel 2010 according to the pre codes and we used the SPSS) version 25) for data analysis. Descriptive statistics were used to describe the demographic characteristics, baseline clinical characteristics, and histopathological. To test the association between the HM and its risk factors, we used the chi-square test. A p-value ≤ 0.050 was considered statistically significant.

Results

A total of 160 women diagnosed with HM at Jiblah University Hospital, Ibb study from 2017 to 2022 years were included in the study.

The mean gestational age on admission was 25.2 ± 6.1 years. Sixty-two patients (38.7%) have Hb less than normal range and 94 patients (58.8 %) have Hb normal range 12- 15g/dl and 4 patients (2.5 %) have Hb more than normal range 15g/dl. However, the percentage blood types (A+, A-, B-, B+, O+, O- and AB+) were 40.6%, 0.6%, 5%, 0.6%, 41.9 %, 7.5% and 3.8%, respectively.

On the other hand, among the sample, 4 (2.5%) women were diagnosed histopathologically to have previous V.M whereas 156 (97.5%) women were diagnosed histopathologically to have no previous V.M. A number of women who had previous abortion were recorded as 46(28.7%) where as the women who had not previous abortion were 114(41.4%). Among the women who were smoking and those with no smoking were recorded as 2(1.3%) and 158(98.7%), respectively. Finally, unfortunately the researchers didn't find the following risk factors in the register of patients, such as (Ovulation induction, genes mutation, infertility and birth control pills), through researching the record of patients with HM or registered as having HM, (Table 1 and figures; 1, 2, 3,4,5).

Table 1: Baseline Characteristics of patient HM

Characteristic	(N = 160)	Characteristic	(N = 160)
Age — year(no.)		Previous V.M — no. (%)	
Std. Deviation	6.5	YES	4 (2.5%)
Mean	25.3	NO	156(97.5%)
Range	15-50	Previous abortion— no. (%)	
Age category — no. (%)		Yes	46(28.7%)
< 20 years	35(21.9%)	No	114(71.3%)
From 20 to 29 years	85(53.1%)	Smoking — no. (%)	
From 30 to 39 years	36(22.5%)	Yes	2(1.3%)
>40 years	4(2.5%)	No	158(98.7%)
Hb— no. (%)		Contraceptive — no. (%)	
Range	12.7	No	160(100 %)
Mean	11.9	Infertility — no. (%)	
Std. Deviation	1.8	No	160(100 %)
Less than Normal 12g/dl	62(38.7%)	Gene's mutation— no. (%)	
Normal 12 -15 g/dl	94(58.8 %)	No	160(100 %)
More than normal	4(2.5%)	Ovulation induction — no. (%)	
Blood types — no. (%)		No	160(100 %)
A+	65(40.6 %)		
A-	1(0.6 %)		
B-	8(5 %)		
B+	1(0.6%)		
O+	67(41.9%)		
O-	12(7.5%)		
AB+	6(3.8 %)		

The results show in (table 2. Figure1) from the total (160) pregnant women who were admitted to Jiblah Hospital,if was found that 35 pregnant women (21.9%) were at the age group of less than 20 years, 85 pregnant women (53.1%) were at the age group of 20-29 years, 36 pregnant women (22.5%) of the age group of 30-39 years, and 4 pregnant women (2.5%) were above 40 years, The minimum age was 15 years,

while the maximum age was 50 years old. According to these results, the highest incidence rate was in the age group (20-29). In the current study, we found that the incidence of HM in younger age patients is the most common.

Table 2: Distribution of the hydatidiform mole patients according to age groups

Case (N=160) — no. (%)		
Age groups	Frequency	%
< 20 years	35	21.9
20 to 29 years	85	53.1
30 to 39 years	36	22.5
> 40 years	4	2.5

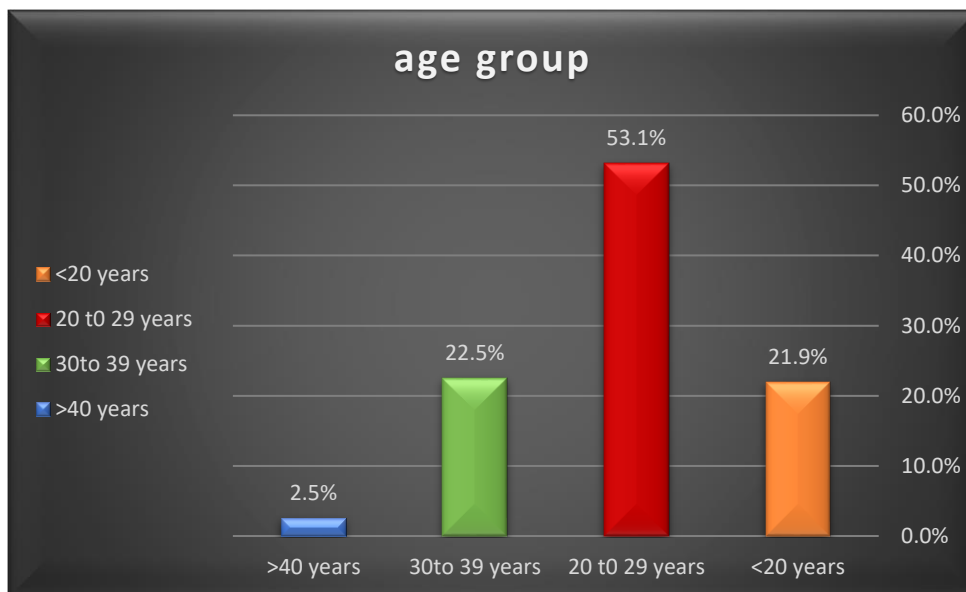


Figure 1: Distribution of the hydatidiform mole patients according to age groups

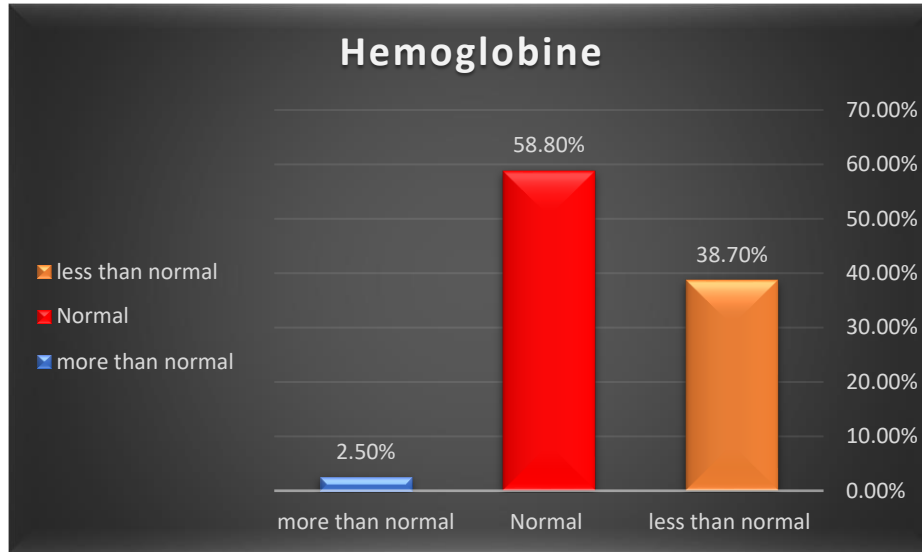


Figure 2: Distribution of the hydatidiform mole patients according to hemoglobin

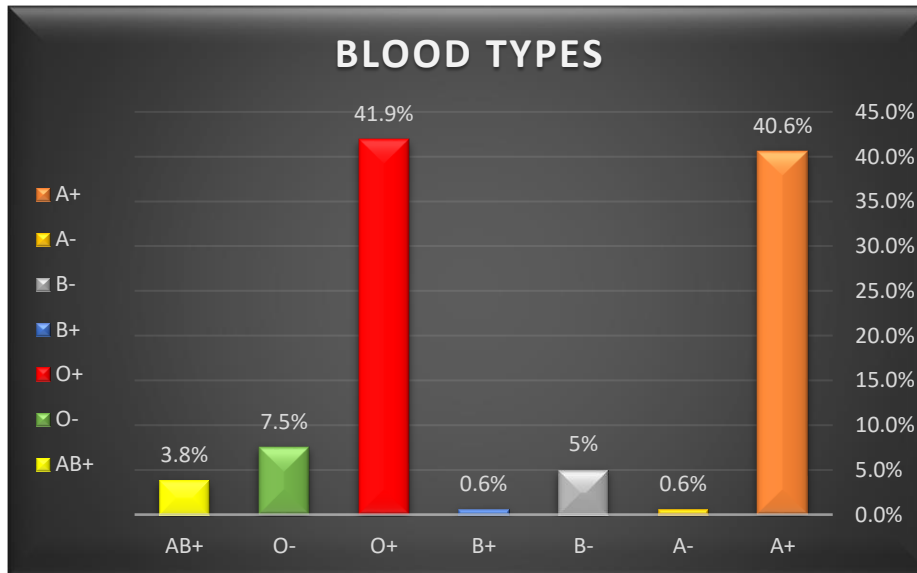


Figure 3: Distribution of the hydatidiform mole patients according to blood types

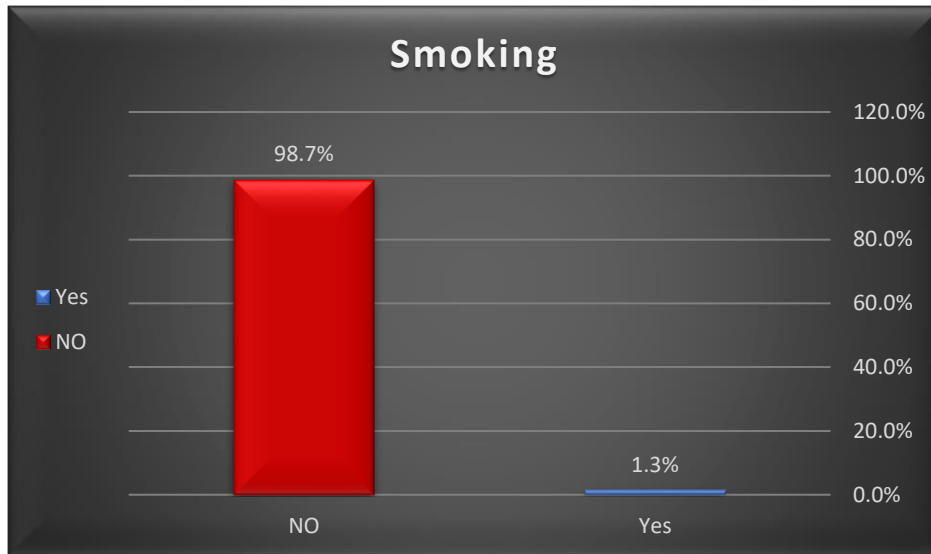


Figure 4: Distribution of the hydatidiform mole patients according to Smoking

Table 3: Distribution of the hydatidiform mole patients according to previous abortion and previous V.M.

Case (N=160) — no. (%)			
		Frequency	%
Previous Abortion	No	114	71.3
	Yes	46	28.7
Previous V.M	No	156	97.5
	Yes	4	2.5

The results That have been shown from (table 3 and figure 5), that forty-six patients (28.7%) were previous abortion and four patients (2.5%) were previous V.M, According to these results, the highest percentage incidence rate was previous abortion.

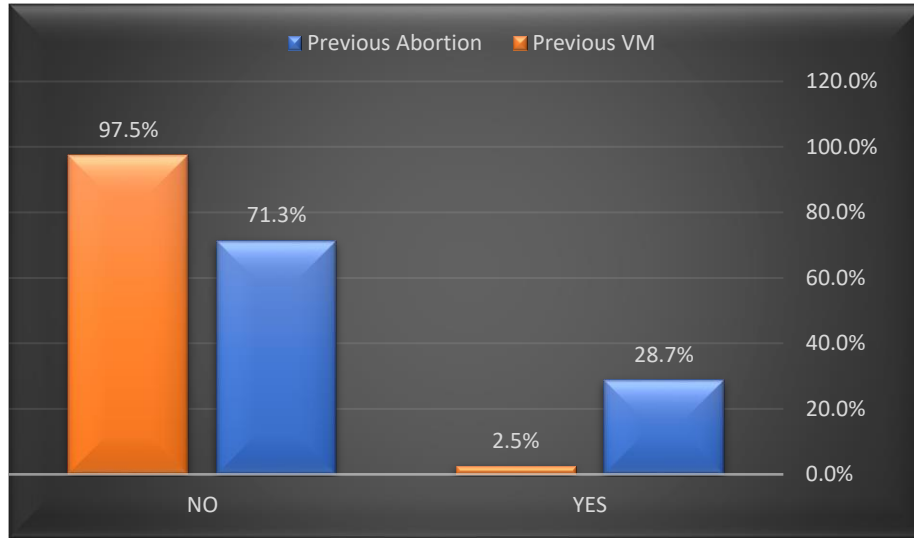


Fig 5: Distribution of the hydatidiform mole patients according to previous abortion and previous V.M.

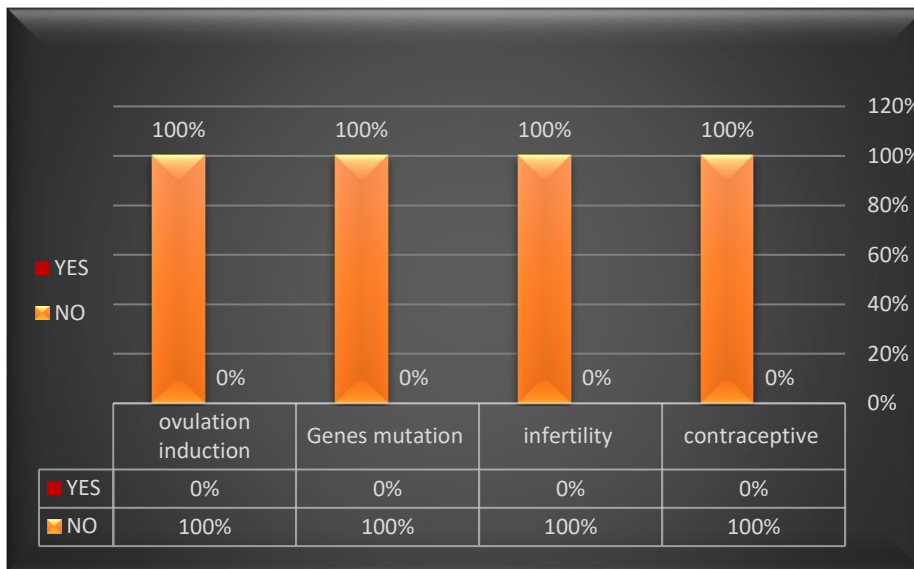


Fig 6: Distribution of the hydatidiform mole patients according to ovulation induction, genes mutation, infertility, contraceptive.

The results show in (figure 6), unfortunately the researchers found no the following risk factors in the register of patients, such as (Ovulation induction, genes mutation, infertility and birth control pills), Through researching the record of patients with HM or registered as having HM.

Table 4. The Relation between age groups and Previous abortion about Associate risk factors of molar pregnancy.

Variables	Abortion pervious (N=160) — no. (%)		Statistically	
	NO	YES	Chi-squar	P-value
Age (years)				
< 20 years	33 (28.9)	2 (4.3)	12.095	.007
20 to 29 years	55 (48.2)	30 (65.2)		
30 to 39 years	24 (21.1)	12 (26.1)		
>40 years	2 (1.8)	2 (4.3)		

*statistically significant (P -value<0.05).

The results show in (table 4), that there is relationship between age groups and the previous abortion about associate risk factors of molar pregnancy. This table showed that there is statistically significant difference between previous abortion and age , with P -value =0.007.

Discussion

Hydatidiform mole (HM) is a spectrum of abnormal gestations arising from villous trophoblast associated with pregnancy. HM has two histological types, including partial hydatidiform mole (PHM) and complete hydatidiform mole (CHM). HM is among gestational trophoblastic disease (GTD) and others include choriocarcinoma and placenta site trophoblastic tumors that arise from villous trophoblast and interstitial trophoblast respectively [1].

The reported incidence in Yemen is 1 in 164 pregnancies,[4] 1 in 318 in Iraq,[5] and 1 in 314 pregnancies in Iran.[6] The prevalence of hydatidiform mole in Brazil is 2.2%, South Africa 1.2 per 1000 deliveries and Nnewi, Southeast Nigeria is 0.3 per 1000 deliveries.[7] However, Incidence of GTD has decreased over time in Asia [8,9], whereas some European countries have reported steady or increased rates [10]. Thus, more recent and accurate data are necessary to evaluate actual incidence rates of GTD.

In the current study, we sought to assess the prevalence of molar pregnancy diseases among pregnant women at Jiblah University Hospital, Ibb study from 2017 to 2022. We also sought to determine the risk factors.

The age categories have been proposed in previous studies too. A study conducted in Iraq General Hospital represented that four groups as 14-21 years, 22-29 years, 30- 37 years and 38-45 years of maternal age, results showed prevalence of hydatidiform molar pregnancy as 38%, 31%, 14% and 17% respectively. These results are comparatively disagreement to our study as our data indicated prevalence within age categories of < 20 years, 20 – 29 years, 30- 39 years, >40 years with 21.2%), 55.3 %, 20.6 % and 2.4% respectively [47].

However, our result concords with the result of [48] when he found that the prevalence of HM was observed to be high (27.5%) in the age group below 20-29 years. Whereas it is concluded that the age between 15-25 years was the only risk factor associated with the development of hydatidiform mole.

Also, our results were similar to the results of [49], they clarified that the incidence in women under the age of 20 was higher and compared with them in that the incidence in women over the age of 40 is. Nevertheless, contrary to these findings, which also showed the risk of rising at age above 40 years, this trend was not observed in this sample, where it was found that the incidence rate in age groups 3

and 4 was small, likely due to early marriage in our community and by the age of 40 years, the majority of women completed their family. Such conflicting results underline the need for further studies involving a broader patient population to create an absolute correlation between HM and advanced maternal age. The above findings also showed that the prevalence of the disease is also high in the age group 2 [22-29], which indicates that this disease was more severe in reproductive age. [50], in his study, it is stated that in all regions and ethnic groups, the motherhood reproductive age is the risk factor most associated with hydatidiform mole [51]. It is also concluded that the molar pregnancies are more common at the extremes of reproductive age.

However, the activity of sex hormone and maturation of ovum in the period between 14- 29 years may lead to the hydatidiform mole. There are two main risk factors that increase the probability of molar pregnancy: Either the female is too young or too old to be pregnant (under 20 years, or over 35 years), and with past molar pregnancy history [52].

Unlike other published studies that demonstrated a significant association between several associated risk factors and the tendency to develop GTDs as prior miscarriage or GTD, family history of GTD, and use of oral contraceptives, our study was not able to show such an association. [53,54] These variations could be attributed to the small sample size and that the study is retrospective in nature with the possibility of missing some information.

In the present study, there was no significant difference in factors including blood groups, Rhesus (Rh) and contraceptive methods. Different studies all around the world have shown many variations and different environmental risk factors in the incidence of HM: vitamin A deficiency and lack of carotene, history of previous moles, blood type A and history of OCP intake [56,57]. Frequency of blood type A

in our case group was lower than blood type O and there was no significant difference between two groups in blood groups risk factor. In the similar study in Tehran, there was a significant increased risk of molar pregnancy in patients with OCP use, history of molar pregnancy and history of abortion.

However, there was no significant difference between blood groups and molar pregnancy as well as this study [56]. The reason of no relationship between blood groups and RH in Qazvin and Tehran populations can be attributed to the same environmental and genetics factors in these cities. No significant difference between OCP use and HM in our study and this can be the result of less use of OCP in Qazvin because of cultural differences between two cities (18.2% in molar group, 9.1% in non-molar).

In the current study, 51 patients had a history of previous abortion among (30%) who had HM, while 118 patients had no history of previous abortion. These findings are similar to those by [57] which showed that the risk of HM increases with history of previous abortion [57]. Spontaneous type of abortion has been found to be more associated with HM than induced abortion as was seen in a study done in Italy [57]. This was also reflected in this study in which 15.5% of participants with spontaneous abortion were diagnosed to have HM while none of the participants with induced abortion had HM.

In contrast, other studies are contrary to our study, which is as follows; In this study, of all participants with blood group 'A+' 42.4 % were found to have HM. This was the highest percentage of HM as per blood groups. These findings are contrary to the study done by [58] which showed blood group 'B' to be predominant in cases with HM. However, it is inconclusive to say that participants with blood group 'A' are at an increased risk of HM partly because both the study population and other risk factors for HM were not evenly distributed based on blood group.

Strengths and Limitations

Our current study have many strengths and some limitations. Our study is the first in Ibb to study the risk factors that lead to molar pregnancy. Our study also provides more information about the risk factors that contribute to molar pregnancy. Our study findings will also help predict the rate of risk reduction in molar pregnancy, thus helping us to improve management in molar pregnancy patients in order to reduce evolutionary events.

Limitations

However, our study had a number of possible limitations particularly our use of a single center, small sample size, and the retrospective nature of the study, which may have contributed to missing data. First, this study was conducted on a small sample size and missing variables, so this may affect the result negatively. Second, this study was uncompleted data based on the records in the hospital archive. Third, this study was the present study include failure to record history of using drugs, maternal education and precise details of all pregnancy complications in previous pregnancies. Four, data on symptoms related to HM, such as pelvic pain or discomfort, fatigue and shortness of breath, preeclampsia, irregular, non-menstrual vaginal bleeding and infection, were unavailable, as was information on relevant therapies, such as lithotripsy, and medications used during treatment. These factors may have potentially affected the analysis in the current study. Another limitation is that some women could not recall all of their past medical history so some histories were missed.

Conclusions and Recommendations

Conclusion:

Our study demonstrated that incident hydatidiform mole were higher in 20-29 years of maternal age, so we found that the incidence of HM in these of the age patients is the most common. we also found that the significant positive correlation was found between age, and Smoking with previous abortions. Therefore, it is recommended that women should undergo health care before pregnancy and further studies are required to provide solutions to reduce the cases of HM.

Furthermore, our results can be used as guidance for establishing programs to detect risk factors. Further prospective studies in Ibb including multiple centers are recommended and establishing a local database for GTD and GTN is needed.

Recommendations:

In the light of the results reached to our study represented in the factors contributing to molar pregnancy through a study at Jiblah University Hospital, we were able to make a set of the following recommendations:

1. We recommend that the hospital should improve the patients, records and registration in the hospital.
2. We recommend that the hospital should establish a center for registration, management and follow up the patients with molar pregnancy.
3. We recommend that the hospital record patients' date should be in an integrated manner.
4. We recommend that the hospital should determine the type of Vesicular mole, is it partial mole or complete mole.
5. We recommend that the hospital should perform laboratory tests and diagnosis of histological features and outcomes in women with molar pregnancy.

6. We recommend that women should undergo health care before pregnancy.

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