Research Article

Maternal age and parity as risk factors for prediction of GTN

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Abstract
Gestational trophoblastic neoplasia (GTN) represents a rare complication of pregnancy. It may occur after a full-term delivery and a spontaneous miscarriage however, the risk of occurrence is more common after molar pregnancy. in this study we try to evaluate the management strategies and outcome of cases of molar pregnancies at maternity hospital Minia university over one year from July 2019 up to July 2020. Our study include 94 patients having picture of molar pregnancy. The post molar rising B-hcg titter occur more commonly with patients more than 35 years old and with patients with high parity Para five or more. while spontaneous resolution common with young, low parity patients. In our study we try to find the prediction model for the patients at high risk for developing persistent GTD. Thus we find that persistent GTD is more common in women aged 35 years old or more and women having high parity. Based on the results of the present study we concluded that molar pregnancy in patients with old age , high parity at high risk to develop persistent GTD. The early prediction and recognition of persistent GTD allow early and better treatment for patients with high risk . which lead to the better prognosis for this patients.
Key words: Molar pregnancy, Risk factor, GTN.

Introduction
Hydatidiform mole or molar pregnancy is uncommon, genetically abnormal. Pregnancy that occurs in approximately one in 700 (PHM) to: one in 2000(CHM). Complete and partialmolar pregnancies are distinct pathologic entities with unique genetic and risk profiles. Both their patho-logies put the woman at the risk for developing gestational trophoblastic neoplasia, a form of locally invasive or metastatic malignancy arising from abnormal products of the conception (Albright et al., 2020).

The most common antecedent pregnancy is that of a hydatidiform mole, usually there is a genetic disorder of pregnancy in which placental-like tissue is present only. The patients may present with abnormal vaginal bleeding from the onset of pregnancy and their uterus which are much larger than expected. Gestational trophoblastic neoplasia most commonly follows a molar pregnancy but can follows a normal pregnancy, abortion, or ectopic pregnancy. It should be considered always when a patient has continued bleeding in the post delivery period. Other common signs include bizarre neurologic symptoms in a female within the reproductive age group and

asymp-tomatic lesions on routine chest x-ray (Soper, 2003).

The probability of cure depends on histological type (complete mole, partial mole , invasive mole, or choriocarcinoma), the extent of spread of the disease, the level of the human chorionic gonadotropin (HCG) titre, the duration of disease from the initial pregnancy event to start of treatment, the specific sites of metastases, the nature of antecedent pregnancy and the extent of prior treatment (Wagner et al., 1996).

The symptoms are vaginal bleeding, enlarged uterus, high hCG titer, ovarian masses and irregular basal body temperature (BBT). Choriocarcinoma is often diagnosed by the presence of metastasis. Multiple pulmonary foci show the progress of malignancy. The hCG titer should be checked even in non-gynecological cases when pulmonary round foci are found in the female patient (Jelly, 2016).

The symptoms resulting from distant metastasis suggest choriocarcinomae.g. abdominal pain and hemorrhage in hepatic lesion, persistent headache and vomiting followed by uncons-ciousness and apnea in brain metastasis (Jelly, 2016).

The recommended treatment of any suspected molar pregnancy is the uterine evacuation. Post procedural care includes monitoring the B-hcg level in the blood for early prediction of any residual or progressing disease (Albright et al., 2020).

It was estimated that after molar evacuation 6-36% of patients progress to GTN (Niemann, 2006). Current treatment of GTN is effective; however, occasionally, progression and death can occur in patients with metastatic disease Features of the high-risk population are still controversial, and literature reports discrepant results on the effectiveness of different prognostic factors (Berkowitz et al., 2009)

A hysterectomy may be necessary in case of uncontrolled vaginal bleeding. Hysterectomy may reduce the total number of chemotherapy cycles needed to achieve remission(Suzuka et al., 2001).

Patients and Methods

This study was conducted at the Obstetrics & Gynecology Department of Maternity hospital Minia University from the first of July 2019 to the first of July 2020 after being approved by the department ethical committee at 8th of June 2019 with serial number of (MUEOB00040). A total of 94 patients were included in this prospective study presenting with picture of molar pregnancy. These patients were recruited from the attendees of Gynecological outpatients clinic, two of them refused to be included in this study, two cases missed during follow-up. All patients with clinical picture and ultra-sonographic picture of molar pregnancy are included but patients who refuse to participate in the study from the admission consent are excluded. Full history (personal, Obstetric, menstrual, medical, surgical, family, drug history especially chemotherapy,.....) were taken from all patients. Clinical examination (general & local), laboratory investigations: including B-HCG, ultrasound examination, CBC, Blood group, coagulation profile, RBS, liver and kidney function tests and Chest X-rays were done. Suction evacuation was performed according to the protocol of the department of obstetrics and gynecology, Maternity hospital Minia university and the products were sent to histopathological examination .Follow up after treatment by B-HCG weekly and ultrasound every two weeks. Patients were instructed to postpone pregnancy for at least 6 months and patients with 3 successive negative samples of B-hcg were discharged from follow up .on the other hand, patients with persistent tropho-blastic disease identified by rise of B-hcg titter or failure of decline of the titter was managed by chemotherapy.

Results
Table (1): Demographic data of all patients (n=90)

Variables		Frequency	Percent %
Maternal age in years	**24 or less**	43	47.8%
	(25 ys to 34 ys)	24	26.7%
	35 ys or more	23	25.6 %
Mean ±SD	**27.28±8.79**	Range	17-51
Parity	**P 0**	25	27.8 %
	P1 : P4	41	45.6 %
	P5 or more	24	26.7 %
Mean ±SD	**2.24±2.25**	Range	0-8
Blood group	**(A)**	38	42.2 %
	(B)	13	14.4 %
	(AB)	9	10 %
	(O)	30	33.3 %
RH	**Positive**	83	92.2 %
	Negative	7	7.8 %
Previous history of VM	**Yes**	2	2.2 %
	No	88	97.8 %
History of abortion	**Yes**	41	45.6 %
	No	49	54.4 %

This table shows the demographic data of the patients included in this study , including Maternal age in years, Parity, Blood group, RH, Previous history of VM or abortion of the patients included in our study . it was observed that vesicular mole was more common with maternal age less than 24 ys., patients with low parity and patients with blood groups (A) & (O).
Quantitative data displayed as range, mean and standard deviation
Qualitative data as frequency and percentage

Table (2): correlation between maternal age and follow up of B-hcg titer :

	Plateau N=3	Post molar rising titer N=18	Spontaneous resolution N=69	p-value
24 or less	1(33.3%)	6(33.3%)	36(52.2%)	
25-34	1(33.3%)	4(22.2%)	19(27.5%)	0.309
35 or more	1(33.3%)	8(44.4%)	14(20.3%)	
Mean ±SD	27.33±8.02	30.39±9.52	26.46±8.57	0.244

It was observed that most of patients with spontaneous resolution had 24 years old or less and most of patients with post molar rising titer had 35 years old or more .
Quantitative data displayed as range, mean and standard deviation, analyzed by ANOVA test
Qualitative data as frequency and percentage, analyzed by chi-squared test
p-value is considered significant at <0.05.

Table (3) correlation between maternal parity and B-hcg :

	Plateau N=3	Post molar rising titer N=18	Spontaneous resolution N=69	p-value
P0	1(33.3%)	4(22.2%)	20(29%)	0.318
P1-4	1(33.3%)	6(33.3%)	34(49.3%)	
P5 or more	1(33.3%)	8(44.4%)	15(21.7%)	

This table shows that the difference of parity between patients with spontaneous resolution and patient with post molar rising titer.It was observed that post molar rising titer was more common in patients with high parity (P5 or more) 44.4%.

Qualitative data as frequency and percentage, analyzed by chi-squared test.p-value is considered significant at <0.05.

Discussion

Gestational trophoblastic neoplasia (GTN) repre-sents a rare complication of pregnancy. It can develop after a full-term delivery, a spontaneous miscarriage, or a termination of pregnancy; however, the risk of occurrence is more common after hydatidiform mole (Ngan, 2006).

The present study included 90 patients with molar pregnancy of whom (18/90) women (20%) expe-rienced persistent GTD and required chemo-therapy and three women of them required hysterectomy (3/90) 3%. Spontaneous resolution was occurred in (69/90) (77%), (3/90) patients plateau titer 3%. This incidence is in agreement with Tsukamoto, 1985 who reported an incidence of GTN 6 - 36 % & agreed with him.

Regarding the maternal age, we found that persistent trophoblastic results was more common in patients more than 35 years old than other patients but the difference was not statistically significant in contrast. Spontaneous resolution was more common in patients less than 35 years old. This is in agreement with Felmate, 2006 who reported that maternal age was not confirmed as a prognostic factor, probably because of the limited number of patients but they noticed that GTN was more common if the age is more than 35years also Garavaglia, 2009 agreed with him.

Regarding the parity we found that persistent GTD was more common in those with high parity more than five (8/18) (45%) than those with low parity (6/18) (33%) but the difference

was not statistically significant. This is in agreement with Ayhan, 1996 who found that patients with high parity are more liable to develop GTN and Seckl, 2010 agreed with him.

Conclusion

Based on the results of the present study we concluded that molar pregnancy in patients with old age and high parity at high risk to develop persistent GTD.

The early prediction and recognition of persistent GTD allow early and better treatment for patients with high risk by stratifying them in 2 risk group:

- High risk group who must be monitored closely with serum B-hcg titer and ultrasonic examination.
- Low risk group who may be reassured at time only of counseling and may be observed for a short period of time.

Recommendations:

According to the results of this study we recommend that:

All patients diagnosed as molar pregnancies require close follow up with B-hcg weekly and ultrasound examination every two weeks.

Patients with molar pregnancy at high risk group require closed follow up for early detection and proper treatment for persistent GTD.

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