



RESEARCH ARTICLE

ARE THERE ANY PREDICTIVE FACTORS IN MOLAR PREGNANCY FOR PERSISTENT GESTATIONAL TROPHOBLASTIC DISEASES?

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ABSTRACT

Objective: To evaluate the predictors of persistent trophoblastic disease which can lead to early diagnosis and increase the response rate to treatment. So we have studied numerous factors between two groups of molar pregnancy, those who progressed to GTT and those who were treated after evacuation.

Material and Methods: In this study, 227 patients with complete molar pregnancy, referred to our Gynecology Oncology center of Imam Hospital of Tehran University of Medical Science, Iran, were enrolled. Based on their progression to GTT, they were divided into two groups. Recorded information included the following: age, number of parity, fundal height, types of blood group, platelets count, prior history of infertility, existence of theca lutein cyst, and level of serum B hcg before evacuation, chemotherapy and level of serum B hcg within 1 and 2 weeks after evacuation. Two groups of patients were compared based on factors mentioned above.

Results: Among the investigated items, there was a significant difference between two groups in these factors: fundal height, frequency of complete molar pregnancy, serum B hcg level, platelet count and chemotherapy with methotrexate. ($P < 0.001$) Eventually we identified predictive factors for GTT.

Conclusion: We recommend that further evaluations are needed to confirm our results. With more documents it would be considered a scoring system to determine the risk of development of GTT and try to prevent it by early chemotherapy.

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INTRODUCTION

Well known that, complete molar pregnancies have the ability to invasion and distant metastases and after evacuation, the invasion and metastases are 15% and 4% respectively (Alessandro Cavaliere et al., 2009; Deng et al., 2009). Although they are detected earlier today, but the incidence of persistent trophoblastic tumor has not changed. The incidence of gestational trophoblastic tumors (GTT) after molar pregnancy was reported 18% and 8% in USA and Europe respectively (Wielsma et al., 2006). In previous studies, the role of several factors in progression to GTT has been investigated. In the event of early diagnosis and appropriate treatment of GTT, the potential for response to cure is high. Therefore, identifying the predictors of sustained disease, can lead to early treatment and increase the response rate to treatment. So we have also studied numerous factors between two groups of molar pregnancy, those who progressed to GTT and those who were treated after evacuation.

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MATERIALS AND METHODS

In this retrospective cohort study, 227 patients with complete molar pregnancy, referred to our Gynecology Oncology Center of Imam Hospital of Tehran, University of medical science, in Iran from 2011 to 2015, were enrolled. The inclusion criteria: patient with molar pregnancy and the exclusion criteria: incompleteness of the patient's files. If the file was incomplete, the patient would be excluded from this study. We used a questionnaire for collecting patient's information. To identifying GTT both clinical and histological materials were used. Based on their progression to GTT, they were divided into two groups. Recorded information included the following: age, number of parity, fundal height, blood group types, platelets count, prior history of infertility, existence of theca lutein cyst, and level of serum Beta human chorionic gonadotropin (B hcg) before evacuation, chemotherapy and level of serum B hcg within 1 and 2 weeks after evacuation. After collecting the required information, using the SPSS software version 13, the analysis of the collected data is paid. For qualitative variables, frequency and for quantitative variables, mean and standard deviations were calculated. Two groups of patients were compared based on factors mentioned above. We used Ki square, Fischer exact test and T test and the

significant level for the interpretation of relationships between variables was also considered 0.05. (P=0.05) At Imam Khomeini Hospital as a routine, at the onset of admission, patients fill the consent form in which the patient was allowed to use her file for future research. In this study patients name were not mentioned at any stage of the work and obviously there was no intervention because our study was a retrospective cohort. However, for this research, it was authorized by the Ethics Committee of the University. Actually the study has been reviewed by the appropriate ethics committee and had been performed in accordance with the ethical standards, and as mentioned ago all patients gave their informed consent prior to their inclusion in the study.

RESULTS

The mean of age in persistent GTT was 25.6 and in another group was 25.4 years old and the difference was not significant (P>0.05). The number of parity in GTT group and molar pregnancy group were 1.35 and 1.34 respectively and 85% of first group and 87% of the second group were nullipar and there was no significant difference between two groups (P>0.05). There was a significant difference of the frequency of complete and partial molar pregnancy between two groups and the frequency of complete molar pregnancy in GTT group was higher than another one (67% >45%). (P=0.001) Table 1. In the ultrasound imaging of the GTT group, 24% of patients had theca lutein cyst in their ovaries and in another group, the frequency was 20% and the difference was not significant. (P>0.05) there was no meaningful difference between the frequency of blood types A, B, AB and O between two groups (p>0.05). There were significant differences between 2 groups in B hcg serum level before evacuation and 1 and 2 weeks after evacuation, in all of them mean of serum B hcg level was higher in GTT group than another group. (Before evacuation: 347025 mu/ml>202883mu/ml), (1 week after evacuation: 15938 mu/ml>5376 mu/ml) and (2 weeks after evacuation: 7816mu/ml>814mu/ml). P value was less than 0.001.

Table 1. There was a significant difference of the frequency of complete and partial molar pregnancy between two groups and the frequency of complete molar pregnancy in GTT group was higher than another one (67% >45%). (P=0.001) ■ GTT: gestational trophoblastic tumor

Groups	Complete molar pregnancy	Partial molar pregnancy	Total
GTT■	64 (67.4%)	31(32.6%)	95(100%)
Not persistent disease	59(44.7%)	73(55.3%)	132(100%)
total	123(54.2%)	104(45.8%)	227(100%)

Table 2. There were significant difference between 2 groups in B hcg serum level before evacuation and 1 and 2 weeks after evacuation, in all of them mean of serum B hcg level was higher in GTT group than another group. (before evacuation:347025 mu/ml>202883mu/ml), (1 week after evacuation:15938 mu/ml> 5376 mu/ml) and (2 weeks after evacuation: 7816mu/ml> 814mu/ml). P value was less than 0.001. ■GTT: gestational trophoblastic tumor

before evacuation	number	mean
GTT■	95	347025
Non persistent disease	132	202883
total	227	263206
1 week after evacuation	n	mean
GTT■	95	15938
Non persistent disease	132	5376
total	227	9796
2 weeks after evacuation	n	mean
GTT■	95	7816
Non persistent disease	132	814
total	227	3745

The gradient drop in serum level of B hcg was higher in GTT group than another group and the difference was significant too (P<0.05). Table 2 and Figure 1.

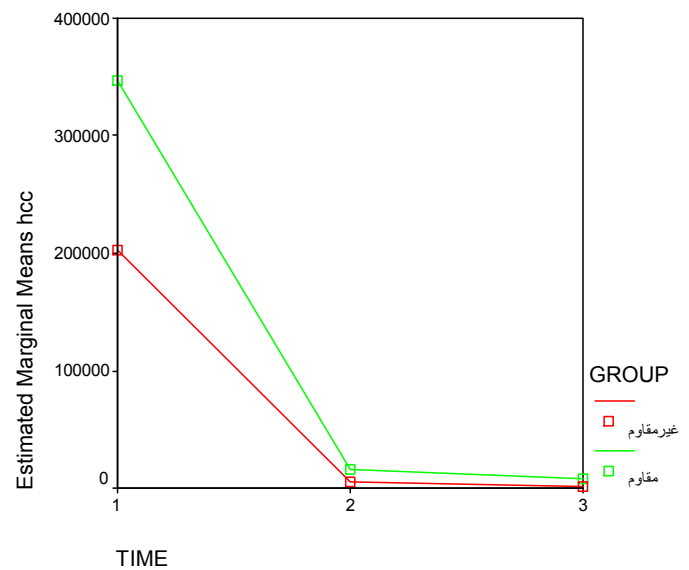


Figure 1. The gradient drop in serum level of B hcg was higher in GTT group than another group and the difference was significant too. (P<0.05)

The mean of gestational age was 14.2 weeks and 15.6 weeks between two groups respectively and it was not meaningful but there was a significant difference between two groups in fundal height as it was higher in GTT patients. The mean of platelet count in GTT group was lower than non-persistent patients (182000 versus 217000) and it was significant also. (P<0.05) there were 4 infertile patients in GTT patients and only one patients in another group had prior infertility history. It was not significant (P>0.05). In Both groups, if the B hcg serum level was higher than 100.000 before evacuation, chemotherapy with methotrexate 50 mg/m² IM was prescribed. The frequency of receiving chemotherapy was compared between two groups and it was less in GTT group than other one. (59% and 65% respectively), (P<0.001) Table 3.

Table 3. Both of two groups had received methotrexate chemotherapy if the B hcg serum level was higher than 100.000 before evacuation. The frequency of receiving chemotherapy was compared between two groups and it was less in GTT group than another one. (59% and 65% respectively), P<0.001 • MTX: methotrexate

Serum level B hcg	MTX●-received	MTX●did not received
B hcg< 100.000	4 (803%)	44 (91.7%)
B hcg> 100.000	55 (65.5%)	29 (34.5%)
B hcg< 100.000	2(16.7%)	10(83.3%)
B hcg> 100.000	49(59.0%)	34(41.0%)

Eventually Among the investigated items, there was a significant difference between two groups in these factors: fundal height, frequency of complete molar pregnancy, serum B hcg level, platelet count and chemotherapy with methotrexate. (P<0.001) there was no significant difference between two studied group in patient's age, parity, gestational age, existence of theca lutein cyst in ultra sound imaging and history of prior infertility.

DISCUSSION

GTT is seen in about 7-20% of complete and in 2-4% of partial molar cases, and in the situation of correct diagnosis and proper treatment, the potential for response to treatment is high

(Monchek and Wiedaseck, 2012; Shaaban *et al.*, 2017). Many studies have tried to identify predictive factors and this identification of these factors can be used to detect patients at risk of GTT and provide early treatment of chemotherapy for them. Use of chemotherapy in the identified high risk group can reduce the distance between the diagnosis of molar pregnancy and beginning of treatment of the later GTT and thus, improve the final outcome. In one study was shown that higher age of patients was related to more frequency of arising GTT (Garner *et al.*, 2007). But in our study, two groups had no significant difference in age of patients. In the study in 2011, was shown that the platelet count in GTT group is lower than others (Verit, 2011). Also in our study, it was described that the lower platelet count can be a predictive factor for persistent disease. Another studies looked at the role of Bhcg serum level before evacuation and over the next 2 weeks later (azamosadat Mousavi *et al.*, 2014; Kang *et al.*, 2010; Khoo *et al.*, 2009). In these studies, the levels of Bhcg was a reliable predictive factor for arising GTT. In our study the result was the same. In one study, history of infertility and its treatment were investigated in the development of the next GTT and there was no role for infertility in final result (Rosenbusch, 2008). In our study the result was the same too. In one study the efficacy of the grading system to distinguish high risk molar pregnancy and early treatment with chemotherapy was measured. High risk patients were divided into two groups and none of 50 patients who received methotrexate, did not get GTT in the follow up period, while 50% of patients in the control groups, and progressed to GTT (Kim *et al.*, 1998). In our study also the frequency of methotrexate therapy in GTT groups was lower.

Study limitations: The only important limitation of our study was the small sample size.

Conclusion

Among the investigated items, there was a significant difference between two groups in these factors: fundal height, frequency of complete molar pregnancy, B hcg level, platelet count and methotrexate therapy. ($P < 0.001$) there was no significant difference in patient's age, parity, gestational age, existence of theca lutein cyst in ultra sound imaging and history of prior infertility. Therefore, in this study, we were able to introduce predictive factors for GTT. We recommend, further evaluations are needed to confirm our results. With more documents it would be considered a scoring system to determine the risk of development of GTT and try to prevent it by early chemotherapy.

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