Original Article

Gestational trophoblastic diseases in North East of Iran: 10 years (2001-2010) prospective epidemiological and clinicopathological study

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Abstract

Background: Many aspects of epidemiological and clinicopathological features of gestational trophoblastic disease (GTD), one of the important subject in gynecology oncology, needs to be defined so as to recommend the best approach and management toward it. In the present study, we evaluated 10-years incidence of trophoblastic diseases in north east of Iran in prospective epidemiological and clinicopathological study.

Materials and Methods: We reviewed the registered histopathology database archive (120 records) related to trophoblastic diseases of the Ghaem Hospital, Mashhad University of Medical Sciences from 2001 to 2010.

Results: Evaluation of the pathological reports revealed 5 (4.2%) choriocarcinom and 115 (95.8%) of hydatidiform mole (HM), with complete and partial HM diagnosis in 29 (25.2%) and 86 (74.8%) patients, respectively. The pregnancy rate of HM patients (2.72 ± 1.86) and choriocarcinoma patients (3.56 ± 2.8) was not significantly different ($P = 0.61$). There was no statistical significant difference between the number of pregnancies in HM (2.90 ± 3.13) and choriocarcinoma (3.84 ± 3.80) patients ($P = 0.46$). The ratio of complete to partial mole increased with age, although this correlation was not significant. Most patients in both the groups had no history of abortion. O positive was the predominant blood group among the studied patients.

Conclusion: Trophoblastic diseases occur during the fertility age mostly, and there is an increased risk with more previous pregnancies; ultrasound sonography is a useful method for primary diagnosis of this disease. Further pathological studies are needed to define the mole type.

Key Words: Epidemiology, pathology, sonography, throphoblastic diseases

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INTRODUCTION

Hydatidiform mole (HM), described as a disorder of fertilization, is one of the several related disorders of fertilization considered as a gestational trophoblastic disease (GTD).

GTDs consist of five distinct clinicopathological entities: Complete HM (CHM), partial HM (PHM),

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invasive mole (IM), choriocarcinoma (CCA), and placental site trophoblastic tumors (PSTTs).[1-3] The reported incidence of HM varies widely geographically in different regions of the world. As incidence of molar pregnancy in southeast Asia (1-12 per 1000 pregnancies) is 7-10 times higher than that in Europe or North America (0.5-1 per 1000 pregnancies).[4-8] The reported incidence of CCA is different geographically, ranging between 2 and 7 per 100,000 pregnancies for Europe and North America.[9,10] Incidence of PSTT has been rarely reported (<250 cases) in papers. Previous case control studies have been reported by obtaining the increasing age, prior spontaneous abortion, infertility,[11] and dietary factors including decreasing intake of animal fat and dietary carotene, a vitamin A precursor as the risk factors for global differences of pregnancy.[4] It is suspected that some of this variation is in part from the discrepancies between population-based versus hospital-based pregnancy.[12-14]

Flam *et al*.,[15] showed that there are some non-registered statistics about GTD as 25% of HM patients were not included in the Swedish Cancer Registry. Furthermore, in Iran, there is no centralized registration of nationwide network that report this disease incidence.

The aim of the present study was to determine incidence rates of GTD in the Iranian population during 10 years by using records of hospital-based pregnancy of patient's referred to the Ghaem Hospital, Mashhad University of Medical Sciences between 2001 and 2010.

MATERIALS AND METHODS

In this descriptive, analytical cross-sectional study, we used the histopathology database archive of the Ghaem Hospital from 2001 to 2010 that contained the abstracts of all histopathology and cytopathology reports generated in northeast Iran. In this hospital, the abstracts of all pathology reports of the participating hospital laboratory is transferred to the central databank. We reviewed abstracts of patients' with throphoblastic diseases. These abstracts consist of encrypted patient identification data (including patient's family name, age, number of pregnancies or parities, abortion history, and blood group) and a summary of the pathology report. The pathology report consisted of diagnostic codes were made available. A selection of the central database was obtained containing records of patients diagnosed with GTD based on the following items: Complete mole, partial mole, and choriocarcinom. Finally, all identified patients in the database confirmed diagnosis of GTD with a histologically diagnosis. We reviewed 140 reports from 2001 to 2010, but our revisions excluded 20 records due to incomplete files. Therefore, 120 remaining reports were reviewed and categorized to complete mole, partial mole, and choriocarcinom.

Statistical analyses

Statistical analysis was performed using SPSS software, version 16. Incidence rates of HM and CCA were calculated as the number of patients diagnosed in our hospital divided by the total number of deliveries. Data on the number of deliveries included live births and stillbirths from 24 weeks gestation and onwards. Patients' characteristics including the categorical data in different histopathology diagnosis were analyzed by χ^2, independent *t*-tests and analysis of variance. A $P < 0.05$ was considered significant. Numerical data are expressed as mean ± SD or as a ratio.

RESULTS

Patients

During 2001 to 2010, total 140 cases of GTD were registered in the Ghaem Hospital. We evaluated 120 records due to their competency about their files. The mean age of the women with GTD were 27.07 ± 9.2 years (range: 15-52 years). Majority of the patients, 70 (58.33%), were aged 20-30 years. The mean interpregnancy interval was 2.18 ± 2.94 years with a range of 1 month to 15 years. In addition, the number of pregnancies ranged from 1 to 13 pregnancies with mean 3.15 ± 2.93 in our patients with GTD. History of some diseases like diabetes, cardiovascular disease, ovarian cyst, hyperthyroidism, and hypertension were recorded. Also, 116 (96.7%) patients had no history of consumption drugs, but 4 (3.3%) had used insulin, nitrocontin, metimazol, and verapamil. Parity ranged from 1 to 11, with 1.90 ± 2.75 births in the studied patients. In addition, 94 (78.3%) patients had no history of abortion, 21 (17.5%) with one abortion history and 5 (4.2%) with 2 abortion history. Delivery was reported vaginal (50.8%) and cesarean (4.2%), and the kind of delivery was unknown for 54 (45%) patients. The frequency of ABO blood groups were O+ (36.7%), A+ (26.7%), B+ (21.7%), AB+ (6.7%), O– (2.5%), B– (2.5%), A– (2.5%), and AB– (0.8%). Result of 98 sonograms available for review was in HM appearance support for 70 (71.4%) cases and failed pregnancy for 28 (28.6%) cases.

HM and CCA patients

Evaluation of the pathological reports revealed 5 (4.2%) choriocarcinom and 115 (95.8%) HM. Our reports confirmed that 29 (25.2%) and 86 (74.8%) of HM patients had complete and partial diagnosis, respectively. Frequency of several studied variables is presented in Table 1. The mean ages in both groups

Table 1: Incidence of studied moles expressed into different variables

Variables	Throphoblastic diseases (*n*=120)			*P* value
	Complete mole (*n*=29)	Partial mole (*n*=86)	Choriocarcinoma (*n*=5)	
Age, year (Mean±SD)	28.58±9.85	25.79±7.7	27.40±11.06	0.95
Pregnancies (Mean±SD)	3.29±3.99	2.82±2.50	3.84±3.80	0.46
Live birth (Mean±SD)	2.01±2.93	1.64±2.68	3.56±2.8	0.61
Abortions (%)				
No Abor.	21 (72.4)	68 (79)	2 (40)	0.83
1 Abor.	6 (20.7)	15 (17.4)	2 (40)	
2 Abor.	2 (6.9)	3 (3.5)	1 (20)	
Blood group (%)				
O+	12 (41.4)	27 (31.4)	2 (40)	0.15
O−	1 (3.4)	2 (2.3)	1 (20)	
A+	5 (17.2)	27 (31.4)	1 (20)	
A−	2 (6.9)	1 (1.2)	1 (20)	
B+	5 (17.2)	21 (24.4)	-	
B−	2 (6.9)	1 (1.2)	-	
AB+	2 (6.9)	6 (7)	-	
AB−	-	1 (1.2)	-	

of HM patients were similar ($P = 0.93$). Parity ranged from 0 to 8, with 2.72 ± 1.86 births in HM patients, and from 0 to 11 with 3.56 ± 2.8 births in CCA patients. There was no statistical difference between the two groups (HM and CCA) ($P = 0.61$) with respect to parity. The number of pregnancies was 2.90 ± 3.13 (range: 1-10) and 3.84 ± 3.80 (range: 1-13) for HM and CCA patients, respectively ($P = 0.46$). The ratio of complete to partial mole increased with age, although the correlation between the groups respecting this variable was not significant [Table 1]. Most of the patients in both studied groups had no history of abortion. Also, O+ was commonly observed as ABO blood group. The parity rate was higher in complete mole group and CCA patients rather than in PHM; however, this difference was no significant [Table 1].

DISCUSSION

Trophoblastic disease is defined as an excessive and inappropriate proliferation of the trophoblast with different biological properties throughout the world. The present study provides long-term data on the incidence of GTD (HM and CCA) in Mashhad, northeast Iran. Differences in reported incidence rates can also be considered by different denominators, which represent the population at risk, inaccurate ascertainment of the number of patients as a function of the number of gestational events.[7,14] Benson *et al.,*[16] revealed the rate of complete mole and partial mole were 82% and 5%, respectively, from 22 patients with sonograms available for review. Survey from 263 cases with HM incidence from 2000 to 2010 in Turkey found complete mole in 175 (66.5%) patients and partial mole in 86 (32.6%) patients.[17] While we found 86 (74.8%) and 29 (25.2%) cases had partial and complete mole, respectively. Incidence of malignant trophoblastic disease in Paraguay during the 10 years revealed 227 cases of HM and 21 cases of CCA.[18] Our results were in accordance to Rolon *et al.,*[18] as incidence of CCA and HM were 5 (4.2%) and 115 (95.8%), respectively during 10 years from the 120 registered records. Lazović *et al*.,[19] in a retrospective descriptive study about the presence of metastases, epidemiological characteristics, and 104 patients with GTD found that IM was more frequent than CCA (63.6%).

In our study, most patients were in their 30s. The previous reports confirmed that increasing age is the crucial risk factor for complete molar pregnancy and maternal age has not been associated with the risk of partial molar pregnancy.[20-22] We found increased proportion of complete mole to partial mole with age, while Tham *et al.,*[20] reported that the proportion of partial mole to complete mole in Asian women increased with age. Moreover, Nowak-Markwitz *et al*.,[23] in their epidemiological study about GTDs on 342 cases revealed that the risk of trophoblastic disease increased with the increase in maternal age and after third pregnancy. However, Mohammadjafari *et al.,* in a 10-year study about GTD in our country confirmed our study results[24] as they found the most common age range for hydatiform mole was 18-35 years. Women aged >40 years a complete hydatiform mole, which is similar to that in other countries. We found that most of the patients with HM or CCA had experienced more than three pregnancies. Garner *et al*.,[4] reported that the histories abortion or infertility is a risk factor for both complete and partial molar pregnancy. Although we did not find any significant difference between patients with HM and CCA about the history of abortion, low percentages of the studied patients (21.7%) had experienced abortion.

Jain[25] found that the sonographic appearance is correlated with the clinical presentation; accurate diagnosis is possible in most cases of GTD. We found 71.4% of sonograms available appearances support the HM. Also, Benson *et al*.,[16] found that sonography was in support of trophoblastic disease diagnosis in 79% patients.

Grimes[26] found that in spite of age, ethnicity, and a history of HM, ABO blood group interactions appear to be important risk factors for choriocarcinom. Parazzini *et al.,*[27] found that ABO blood groups were associated with the risk of GTD. They concluded that

when mating combinations of maternal/paternal blood groups were considered, women of group (A) married to males of group (O) had a risk estimate not substantially different than those married togroup A males. However, we did not consider the maternal ABO group, but we found that O+ was the most common blood group in both HM and choriocarcinom patients. Mohammadjafari *et al.*,[24] was found that there was a significant relationship between blood groups (O+ and A+) and complete mole and concluded that blood group are two risk factors for hydatiform mole. Also, we found that choriocarcinom occurred more in patients with negative Rh than positive Rh. However, we must conclude this result in larger sample size.

CONCLUSION

We concluded that GTDs including HM and CCA increased in maternal age according to increased number of pregnancies. Also, sonography is a useful method in the initial diagnosis of trophoblastic diseases, but pathology evaluation is needed for diagnosis of mole type.

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REFERENCES

1. Goldstein DP, Berkowitz RS. Gestational trophoblastic neoplasms: Clinical principles of diagnosis and management. Major Probl Obstet Gynecol 1982;14:1-301.
2. Goldstein DP, Berkowitz RS. Gestational trophoblastic diseases. In: DeVita, Vincent T, Lawrence A, Theodore S. Rosenberg S, Steven DA, editors. Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology. 9th ed. Lippincott: Williams and Wilkins; 2011. p. 1363.
3. Shih LeM, Mazur MT, Kurman RJ. Gestational trophoblastic disease and related lesions. In: Kurman Robert J, editor. Blaustein's pathology of the female genital tract. New York: Springer: 5th ed., 2002. p. 1193-247.
4. Garner EI, Goldstein DP, Feltmate CM, Berkowitz RS. Gestational trophoblastic disease. Clin Obstet Gynecol 2007;50:112-22.
5. Garner EI, Lipson E, Bernstein MR, Goldstein DP, Berkowitz RS. Subsequent pregnancy experience in patients with molar pregnancy and gestational trophoblastic tumor. J Reprod Med 2002;47:380-6.
6. Altieri A, Franceschi S, Ferlay J, Smith J, La Vecchia C. Epidemiology and aetiology of gestational trophoblastic diseases. Lancet Oncol 2003;4:670-8.
7. Steigrad SJ. Epidemiology of gestational trophoblastic diseases. Best Pract Res Clin Obstet Gynaecol 2003;17:837-47.
8. Smith HO. Gestational trophoblastic disease epidemiology and trends. Clin Obstet Gynecol 2003;46:541-56.
9. Bracken MB, Brinton LA, Hayashi K. Epidemiology of hydatidiform mole and choriocarcinoma. Epidemiol Rev 1984;6:52-75.
10. Berkowitz RS, Cramer DW, Bernstein MR, Cassells S, Driscoll SG, Goldstein DP. Risk factors for complete molar pregnancy from a case-control study. Am J Obstet Gynecol 1985;152:1016-20.
11. Mosher R, Goldstein DP, Berkowitz R, Bernstein M, Genest DR. Complete hydatidiform mole. Comparison of clinicopathologic features, current and past. J Reprod Med 1998;43:21-7.
12. Bracken MB. Incidence and aetiology of hydatidiform mole: An epidemiological review. Br J Obstet Gynaecol 1987;94:1123-35.
13. Semer DA, Macfee MS. Gestational trophoblastic disease: Epidemiology. Semin Oncol 1995;22:109-12.
14. Gestational trophoblastic diseases. Report of a WHO scientific group. World Health Organ Tech Rep Ser 1983;692:7-81.
15. Flam F, Rutqvist LE. Under-registration of gestational trophoblastic disease in the Swedish Cancer Registry. Eur J Epidemiol 1992;8:683-6.
16. Benson CB, Genest DR, Bernstein MR, Soto-Wright V, Goldstein DP, Berkowitz RS. Sonographic appearance of first trimester complete hydatidiform moles. Ultrasound Obstet Gynecol 2000;16:188-91.
17. Oge T, Ozalp SS, Güngör T, Yildirim Y, Sanci M, Dogan A, *et al.* Hydatidiform mole in Turkey: Results from six centers. J Reprod Med 2012;57:259-61.
18. Rolon PA, Hochsztajn de Lopez B. Malignant trophoblastic disease in paraguay. J Reprod Med 1979;23:94-6.
19. Lazović B, Milenković V, Dordević S. Treatment of gestational trophoblastic disease-a 10-year experience. Med Pregl 2012;65:244-6.
20. Tham BW, Everard JE, Tidy JA, Drew D, Hancock BW. Gestational trophoblastic disease in the Asian population of Northern England and North Wales. BJOG 2003;110:555-9.
21. Altman AD, Bentley B, Murray S, Bentley JR. Maternal age-related rates of gestational trophoblastic disease. Obstet Gynecol 2008;112:244-50.
22. Bagshawe KD, Dent J, Webb J. Hydatidiform mole in England and Wales 1973-83. Lancet 1986;2:673-7.
23. Nowak-Markwitz E, Drews K, Spaczyński M. Gestational trophoblastic disease: The epidemiological analysis of 342 cases. Ginekol Pol 2000;71:767-72.
24. Mohammadjafari R, Abedi P, Tadayon M. The Gestational Trophoblastic Diseases: A Ten Year Retrospective Study. IJFS 2010;4:1-4.
25. Jain KA. Gestational trophoblastic disease: Pictorial review. Ultrasound Q 2005;21:245-53.
26. Grimes DA. Epidemiology of gestational trophoblastic disease. Am J Obstet Gynecol 1984;150:309-18.
27. Parazzini F, La Vecchia C, Franceschi S, Pampallona S, Decarli A, Mangili G, *et al.* ABO blood-groups and the risk of gestational trophoblastic disease. Tumori 1985;71:123-6.

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