ORIGINAL ARTICLE

PROFILE OF GESTATIONAL TROPHOBLASTIC DISEASES IN TWO TEACHING HOSPITALS IN ADDIS-ABABA, ETHIOPIA

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ABSTRACT

BACKGROUND: *Gestational Trophoblastic Disease is one of the causes of maternal morbidity and mortality among women in the reproductive age group. However the magnitude, clinical features and risk factors are not well documented in Ethiopian setting. This study was conducted to describe these important aspects of the disease entity in two teaching hospitals in Addis-Ababa.*

Patients and Methods: Data of a five-year record from December 1, 1994-November 30, 1999 , of two teaching hospitals was abstracted and analyzed in April 2000 to determine the magnitude, the clinical pattern and associated factors of gestational trophoblastic disease. The data were cleaned, edited and entered in to a computer and analyzed using EPI-INFO version 6 statistical package. Statistical tests were employed where appropriate at the level of significance of 5%.

RESULTS: *The magnitude of gestational trophoblastic disease was found to be 2.8 per 1000 deliveries; patient's age ranged from 14 to 53 years with median age of 34.5 years and mean (±SD) age of 30.9(±6.5)years . Forty-seven (50.5%) have five or more pregnancies while 44 (47.3%) were grand multiparas. Parity, gravidity and age of the mother had a statistically significant association with gestational trophoblastic diseases (P<0.0001). Thirty-Five (37.6%) had experienced at least one abortion. Vaginal bleeding was the commonest presenting symptom in 84 (90.3%) of the patients. Hydatidiform mole was the commonest disease accounting for 67 (72.0%), followed by choriocarcinoma 14 (15.0%) and invasive mole 12 (12.9%). Various modalities of treatments, including evacuation using medical and surgical methods and chemotherapy were used. Forty-three (46.2%) of the patients had at least two or more follow-up and the final outcome of the disease was not known in 70 (75.3%) which is a limitation in his study.*

CONCLUSION: *The magnitude of gestational trophoblastic disease in this study, which is 2.8 per 1000 deliveries, is low. The disease was more commonly seen in those with history of two or more abortions, five or more pregnancies and in those who were 35 years and above. Compared to other studies, lower remission rate and follow up of cases were observed. Only small numbers of patients were managed with chemotherapy while it's the mainstay of treatment. We recommend use of chemotherapeutic agents and laarge scale health facility based study of this disease.*

KEY WORDS: *Gestational Trophoblastic diseases, risk factors, Outcome, Addis Ababa*

INTRODUCTION

Gestational trophoblastic diseases (GTD) refers to a wide spectrum of pregnancy related trophoblastic proliferative abnormalities ranging from a benign process, hydatidiformmole, invasive mole to the most metastatic and malignant tumor, choriocarcinoma. The disease encompasses a fascinating continuum of tumors that arise in the fetal chorion during pregnancy (1).

The clinical entity of hydatidiform-mole was recognized by Hippocrates and was carefully described in the sixth century by Actues of Amida, who was the first to use the term hydatid. However, it was not until 1903 that Marchand identified uterine choriocarcinoma as a chorionic malignancy rather than a uterine malignancy arising in the decidua (2). Though gestational trophoblastic disease has been known since the ancient Greeks, it remains as one of the causes of maternal mortality and morbidity (3). Clinical and pathological entities include benign partial and complete moles; persistent, invasive or metastatic moles; placental site trophoblastic tumors; and gestational choriocarcinoma. Complete and partial mole, invasive mole and choriocarcinoma all exhibit proliferation of both cytotrophoblastic and syncytotrophoblastic cells which maintain secretion of human chorionic gonadothropin (hCG). They have been always of interest to clinicians because of the diagnostic and management challenge they present (4, 5).

Incidence of the disease is believed to vary with racial and environmental factors from approximately 0.5-5 per 1000 deliveries or 0.23 - 12.9 per 1000 pregnancies. It showed a decreasing trend in the developed world, while it still remain to be a significant problem in developing countries like South-East Asia and the sub-Saharan Africa (2,3).

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Age of 35 or more, having history of five or more pregnancies and two or more abortions were identified as associated risk factors (3). The clinical symptoms and signs were reported to be, vaginal bleeding, abdominal or low back pain, anemia, intrauterine fetal death, small for date uterus, severe pre-eclampsia. The majority of the patients had blood groups A and B unlike the preponderance of blood group "O" which was reported in other studies (3,6).

Hydatidiform mole should be suspected in any women with bleeding in the first half of pregnancy with or without passage of vesicles per vaginum. Any women presenting with bleeding or a tumor in any organ who has a recent history of molar pregnancy, abortion, or term pregnancy should at least have one hCG assay to be sure that metastatic neoplasm is not the cause. This is important, for the fact that the cure rate of early diagnosed and properly treated metastatic GTD is 90% (7).

Invasive mole is reported in 10-15% of patients who have had primary molar pregnancy. Although considered benign, it is locally invasive and may produce molar deportation as in the other forms of GTD. Choriocarcinoma is rare, reported in 2.5% of cases of all cases of GTD (8).

The incidence of GTD is higher in women under 20 years and above 40 years of age, in patients of low socio-economic status, in those whose diets are deficient in protein and folic acid and in those with carotene deficiencies (9). The incidence is believed to vary with racial and environmental factors (10, 11, 12).

There appear to be an increase in the far East and Sub-Saharan African countries, but still for many countries the incidence is unknown. The only available reports from Ethiopian settings were; a report on ten cases of GTD in 1980 from Tikur-Anbessa hospital, and a second retrospective hospital based study in North-Western Ethiopia on 41 cases of GTD from June 1985 to June 1995 which has documented an incidence of 1.9 per 1000 pregnancies (3, 13).

The magnitude and pattern of GTD is not well documented in Ethiopia. Therefore, this study was conducted to describe these important aspects of the disease entity in two teaching hospitals in Addis-Ababa.

PATIENTS AND METHODS

The study was conducted in the setting of two teaching hospitals, (Tikur-Anbessa and St. Paul's Hospitals), which are staffed with specialists, residents, interns, and midwives and registered nurses along the study years. Both hospitals serve as central referral hospitals for Gynecologic and Obstetric services. According to the hospital records the annual deliveries ranged from 6000-7000, while they handle about 600-800 abortion cases.

A cross-sectional study based on the review of health service records of all cases of GTD in the two teaching hospitals from December 1, 1994 to November 30, 1999 was made in April 2000. The diseases were diagnosed on clinical grounds and classified as complete mole, partial mole, invasive mole and choriocarcinoma together with histopathology reports and supported with urinary hCG measurement in titers. Charts of patients which did not have complete information or those who did not fulfill the inclusion criteria for GTD were excluded. The inclusion criteria were charts with clinical diagnosis with or without hCG and or histopathology record.

Data on different socio-demographic characteristics and past reproductive history, clinical presenting symptoms and signs, type of blood group, treatment modalities, follow-up pattern, and final disease outcome were abstracted from admission record books, patients' charts, discharge summaries and pathology report books using a format prepared for this purpose. Ethical clearance was obtained Department of Obstetric and Gynecology, Medical faculty, Addis Ababa University, and all the information from the charts of the patients was kept confidential.

The data were cleaned, edited and entered in to a computer and analyzed using EPI-INFO version 6 statistical package. Statistical tests were employed where appropriate at the level of significance of 5%. The data were summarized using tables and graphs.

RESULTS

There were 33, 438 deliveries conducted in both Tikur Anbessa and St. Paul's Hospitals during the study period. Gestational trophoblastic disease was diagnosed in 105 women of whom the complete medical records of 93 patients were obtained with a coverage rate of 88.6%. The median age and the mean (± SD) of patients was 34.5 years and 30.9(±6.5) years, respectively. The youngest and the oldest patient being 14 and 53 years, respectively. Sixty six (70.2%) were housewives, 70 (75.3%) married. The median gravidity was 4, the minimum and maximum being 1 and 12, respectively. Fifteen (16.1%) were primigravidas, 47 (50.5%) had five or more pregnancies, 9 (9.7%) were primiparas, 42 (45.2%) were grand multiparas and 35 (37.6%) had experienced at least one abortion (Table 1).

Table 1. Socio-demographic Characteristics of Patients with GTD.

Characteristics		Hydatidiform-mole (n=67)N°(%)	Invasive Mole (n=12)N°(%)	Choriocarcinoma(n=14)N°(%)	Total (n=93) (N°(%)
Age in Years	<15	3(3.2)	2(2.2)	1(1.2)	6(6. 5)
	15-19	10(10.8)	0(0)	2(2.2)	12(12.9)
	20-24	11(11.8)	2(2.2)	3(3.2)	15(17.2)
	25-29	10(10.8)	1(1.1)	2(2.2)	13(14.0)
	30-34	17(18.3)	3(3.2)	3(3.2)	23(24.7)
	35-39	10(10.8)	1(1.1)	2(2.2)	14(15.1)
	40-44	4(4.3)	3(3.2)	1(1.1)	8(8.6)
	45-49	1(1.1)	0(0)	0(0)	1(1.1)
	≥50	1(1.1)	0(0)	0(0)	1(1.1)
Occupation	House-wife	50(53.8)	6(6.5)	10(10.8)	66(70.2)
	Gov. Employee	4(4.3)	2(2.2)	0(0)	6(6.5)
	Students	6(6.5)	1(1.1)	1(1.1)	8(8.6)
	Private employee	3(3.2)	1(1.1)	0(0)	4(4.3)
	No Record	4(4.3)	2(2.2)	3(3.2)	9(9. 7)
Marital Status	Married	51(54.8)	9(9.7)	10(10.8)	70(75.3)
	Widowed	3(3.2)	1(1.1)	0(0)	4(4.3)
	Single	8(8.6)	1(1.1)	1(1.1)	10(10.8)
	No Record	5(5.4)	1(1.1)	3(3.2)	9(9. 7)
Gravidity	I	13(14.0)	2(2.15)	0(0)	15(16.1)
	II-IV	24(25.8)	1(1.1)	6(6. 5)	31(33.3)
	≥ V	30(32.3)	9(9. 7)	8(8.6)	47(50.5)
Parity	O	13(14.0)	2(2.2)	0(0)	15(16.1)
	I	7(7.5)	0(0)	2(2.2)	9(9.7)
	II-IV	20(21.5)	2(2.2)	5(5.4)	27(29.0)
	≥ V	27(29.0)	8(8.6)	7(7.5)	42(45.2)
Abortion	O	38(40.9)	9(9.7)	11(11.8)	58(62.4)
	I	18(19.4)	1(1.1)	3(3.2)	22(23.7)
	≥ II	11(11.8)	2(2.2)	0(0)	13(14.0)

Histopathologic result was available in 72 (77.4%) of the patients. Accordingly, the magnitude of GTD was 2.8 per 1000 deliveries. Magnitude of GTD in the two hospitals varied from 1.8 per 1000 deliveries between December 1, 1997 to November 30, 1998 to 3.8 per 1000 deliveries between December 1, 1998 to November 30, 1999. There was a decreasing trend in the magnitude in the first four years and about two-fold increase in the last year in comparison with the immediate preceding year (Fig.1).

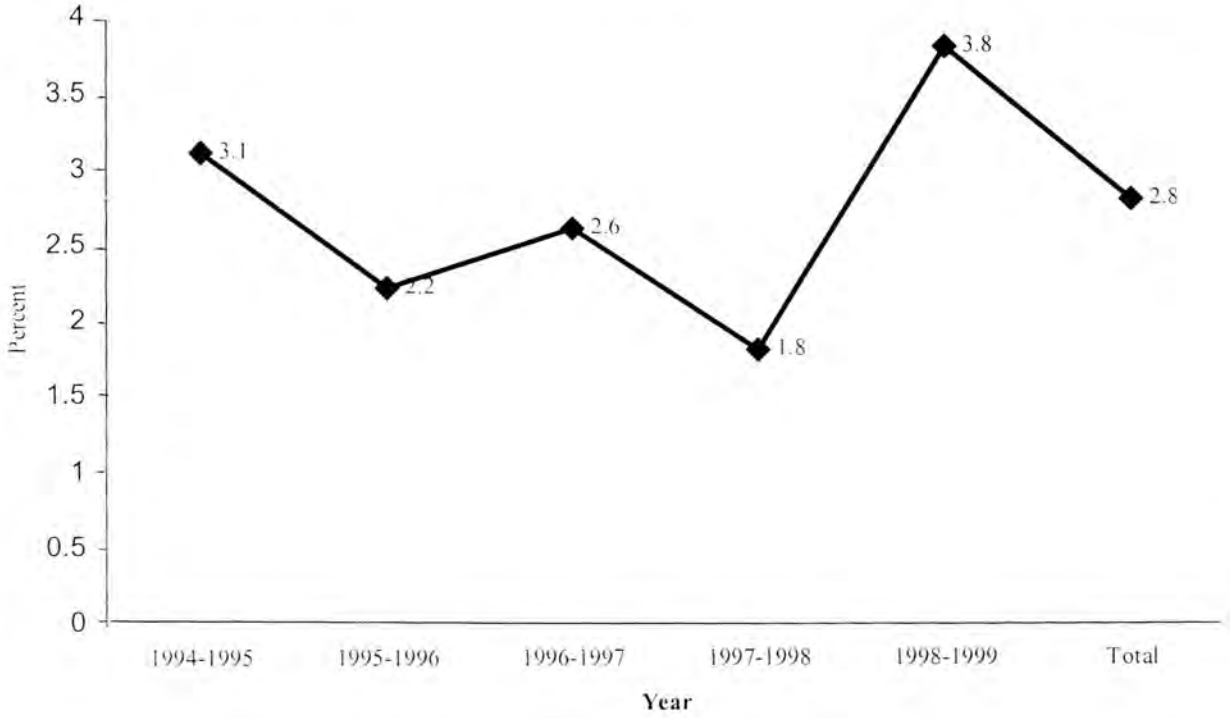

Figure 1. Trend of gestational trophoblastic diseases among 33.438 deliveries in Black lion and St.Paul's Hospitals by years.

Regarding past history of patients, those with five or more pregnancies and patients with history of two or more abortions tend to have a significant increase in the disease prevalence (P<0.0001). Bleeding was the commonest presenting symptom in 84 (90.3%) of the patients and 4 (4.3%) had more than one presenting symptoms. The majority (43.0%) had blood group "O", followed by those who had group "A", 26 (27.9%).

Sixty seven (72.0%) were diagnosed to have hydatidiform mole, 14 (15.1%) choriocarcinoma and 12 (12.9%) invasive mole. There was no patient with a diagnosis of partial mole or placental site trophoblastic tumor. Twenty one (22.6%) of the patients had metastatic or molar deportation evidence..

The most commonly offered treatment was evacuation of uterus after oxytocin administration. Surgical modalities, such as manual vacuum aspiration (MVA), dilatation and curettage (D and C), and evacuation and curettage (E and C) were done for 51(70.8%) of patients with hydatidiform mole. Chemotherapy was the most commonly used modality to treat cases of choriocarcinoma, accounting for 8(66.1%) of the cases and hysterectomy was the largely used surgical treatment to manage 9(64.3%) of the cases with invasive mole.

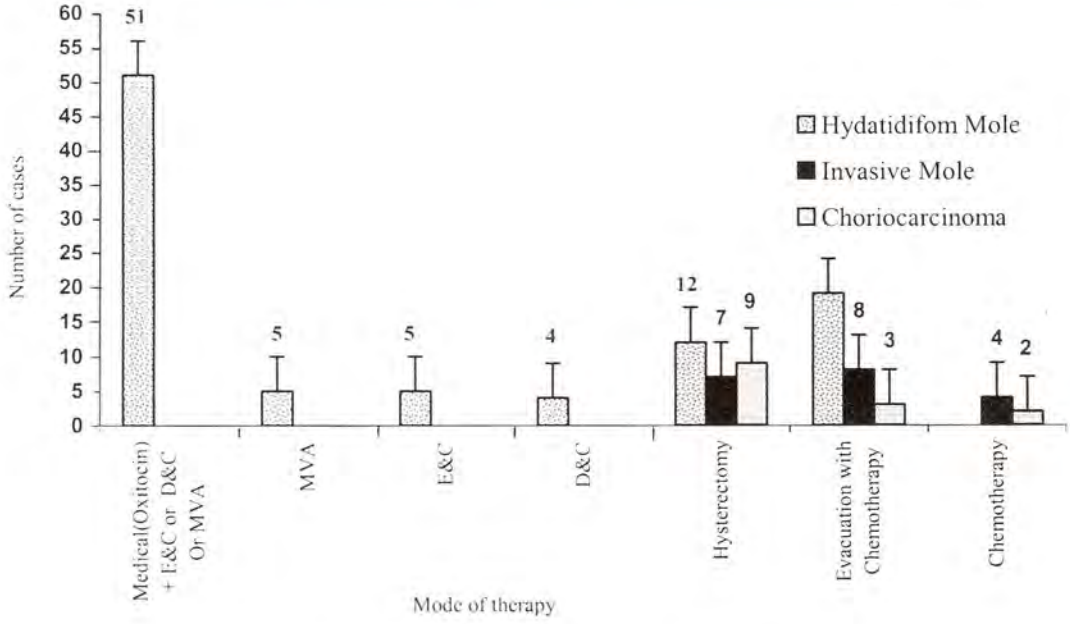

Figure 2. Mode of therapy among cases of GTD(n=93)

Table 2. Comparison of age and reproductive history of patients and the mothers who delivered in the two teaching hospitals during the study period.

Characteristics	Number of Deliveries	Cases of GTD	X^2	*P.Value*
Gravidity				
I	12706	15		
II-IV	12372	31	32.2	<0.0001
≥ V	8360	47		
Abortion				
O	31097	58		
I	1672	22	68.0	<0.0001
≥ II	667	13		
Age				
<15	44	6		
15-19	3512	12		
20-24	9640	16		
25-29	10994	13	288.0	<0.0001
30-34	5552	23		
≥ 35	3696	23		

Table 3. Distribution of cases of GTD by final disease outcome.

Final Disease outcome	Disease entity			
	Hydatidiform mole	Invasive mole	Chorio carcinoma	Total
Remission	9	2	1	12
Persistence	2	1	1	4
Recurrence	0	2	0	2
Death	1	0	4	5
Unknown	55	9	6	70
Total	67	14	12	93

Remission was recorded in 9, 2, and 1 of the cases of hydatidiform mole, invasive mole and choriocarcinoma cases while disease persistence was seen in 2, 1 and 1 cases, respectively. Recurrence was documented only in two cases of invasive mole and death was recorded in four of the choriocarcinoma and one of hydatidiform mole cases.

Final disease outcome was not known for 55(82.0%) of the cases of hydatidiform mole, 9 (12.9%) of invasive mole and 6(8.6%) of the cases of choriocarcinoma (Table 3).

DISCUSSION

The magnitude of GTD in this study was 2.8 per 1000 deliveries, that is 2.0 per 1000 deliveries for the complete mole, 0.4 per 1000 deliveries each for the choriocarcinoma and invasive mole, respectively. There was no patient with a diagnosis of partial mole and placental site trophoblastic tumor (PSTT) contrary to other studies where 61% partial mole and 1.1% of PSTT was found (6). This could be due to presentation of cases of partial mole as incomplete or missed abortion for which reason histopathologic diagnosis is a requirement. The failure to submit all aborted and curettage specimen was a limitation in this study and PSTT is a rare disease entity to be found in small scale studies like ours.

The GTD magnitude figure in our study was comparable with that of Northern Ireland and the hospital based study in Turkey, which were 2.2 and 2.5 per 1000 deliveries, respectively. But it is higher than the 1.9 per 1000 pregnancies of a hospital based study in Gondar and that of Britain and Western Europe, 1.46-1.56 per 1000 deliveries. On the other hand, Southeast Asian countries like Indonesia and the Philippines had higher figures, 12.9 per 1000 pregnancies and 7.0 per 1000 deliveries respectively (3, 6, 11). The possible explanation for this difference might be the fact that the studies in South east Asian countries were community and large scale facility based studiers unlike our study which is a small scale facility based. In addition high prevalence of protein and carotene efficiency in south east Asian countries could be another possible explanation for the differences (3,6,11)

There was a relative decrease in the magnitude in the first four years with a sharp rise in the last years, which could be explained by a decrease in the number of patients coming to the two hospitals because of the possible availability of health service at regional and zonal hospitals than before. This might have progressively decreased the patients referred both as a case of GTD and for delivery service. A statistical significant increase in the magnitude was seen in those aged 35 years or more; in patients who had 2 or more abortions; and in those who had 5 or more pregnancies, which was in agreement with reports from other studies (3).

Unlike the other studies, which reported predilection of the disease in patients with blood groups A and B (6, 14), there was no difference among cases with different blood groups in this study.

The most commonly offered treatment modality was evaluation using both medical and surgical methods followed by hysterectomy. But according to report in the 1960's and 1970's hysterectomy was done for approximately 50% of patients which is even higher than our finding (36.6%). On the other hand, our hysterectomy rate is still higher than the rate in 1990's from the same study (15). This could be because of unavailability of the drugs together with the higher cost needed to buy and use them.

While chemotherapy is the mainstay of treatment, it was given alone for only 5(5.4%) of patients and for 17 (18.3%) cases in combination with other treatment modalities. This could also explain the higher hysterectomy rate which might have been done often due to the lack of the chemotherapeutic agents.

In conclusion, the magnitude of gestational trophoblastic disease in this study, which is 2.8 per 1000 deliveries, is low. The disease was more commonly seen in those with history of two or more abortions, five or more pregnancies and in those who were 35 years and above. Compared to other studies, lower remission rate and follow up of cases were observed. Only small numbers of patients were managed with chemotherapy while it's the mainstay of treatment. We recommend use of chemotherapeutic agents and large scale health facility based study of this disease. A large-scale prospective

health facility based study together with strengthened follow-up schedules to know the exact rates of remission, persistence, recurrence, death and cure rates of the diagnosed cases is recommended.

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