Pattern of Cases of Gestational Trophoblastic Diseases among Pregnant Women Admitted to Maternity Teaching Hospital in Erbil City

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Abstract: - Gestational Trophoblasic Diseases (GTDs) are uncommon chorionic tumor of the placenta. It includes a spectrum of diseases from the usually benign hydatidiform mole to the highly malignant choriocarcinoma.
A descriptive observational study carried out on 40 cases with GTDs to determine the rate, epidemiological correlates, clinical behavior, and common complications of the disease.
The study done on pregnant women admitted to Maternity teaching hospital, Erbil city, North of Iraq, Kurdistan region during the period from 1st October 2008 to the 1st of April 2009. Demographic data were collected from each patient, history of prior molar pregnancy, socioeconomic state, presenting symptoms, complete examination and investigation done for all of them.
The incidence of GTD was 1 in every 318 pregnant women. The highest incidence was in 40 years old women and more, the mean gestational age was 11± 3.7 weeks, 82.5% of cases were complete mole, 10% were partial mole, and 7.5% were gestational trophoblastic neoplasm. Majority of cases (87.5%) presented with vaginal bleeding, pregnancy induced hypertension and preeclmpsia in 15%of cases, 67.5% had abdominal cramps, 50% presented with hyperemesis gravidarum, 25% had hyperthyroidism. There was a statistically significant association between the Gestational Trophoblastc Neoplasia and the presence of theca lutein cysts and history of molar pregnancy in the antecedent pregnancy.
The incidence of GTDs in Maternity teaching hospital (1 in 318) is comparable to the incidence in some Middle East and Far Eastern countries.

Key-words: - Gestational trophoblastic diseases, Hydatidiform mole, Gestational trophoblasic neoplasia, Hyper emesis gravidarum, Invasive mole, Choriocarcinoma.

1 Introduction

Gestational trophoblastic diseases, characteristically secreting high levels of B-HCG, are a heterogeneous group of neoplastic conditions arising from the abnormal development of trophoblastic tissues. The spectrum of GTD includes hydatidiform molar pregnancies (partial and complete), choriocarcinoma, and placental site trophoblastic tumor. Occasionally, malignant growth may not become clinically evident until years after the last gestation [(1)]. For reasons not well understood, the incidence of hydatidiform mole (HM) varies greatly in different parts of the world. The highest rates are reported in the Far East where the disease is 7 to 8 times more common than the west [(2)]. Epidemiological investigation of the incidence and etiology of the Gestational Trophoblastic Diseases (GTD) is receiving increasing attention. The early stages of a pregnancy in which a GTD develops typically seem normal, then symptoms of the pregnancy are exaggerated for example the uterus may grow more rapidly

than usual. The first obvious symptom is vaginal bleeding and lower abdominal cramps. The blood may contain hydatid vesicles; hyperemesis is possible, and signs and symptoms of preeclampsia are also possible. Other complications of GTD may include anemia, infection, trophoblast embolism, uterine perforation, and choriocarcinoma [(3)].

In Erbil city, little is known about the pattern of the GTD as a whole or its relation to the age groups and other different variables. As a result this study was carried out to throw a light on the pattern of this group of diseases in a sample of pregnant women who were admitted to the Maternal Teaching Hospital in Erbil city. This study is going to be a base for further studies in a wider level covering the entire Kurdistan region.

2 Objectives:

The aims of the study were to identify:

(1) The rate of the disease among pregnant women admitted to the Maternity Teaching Hospital in Erbil city during the study period.

(2) The presenting signs and symptoms of the disease and common complications.

(3) The probable associated factors

3 Patients and Methods:

A descriptive observational study on cases of GTDs among pregnant women admitted to Maternity Teaching Hospital in Erbil city was conducted during the period from 1st Oct 2008 to the 1st of April 2009.

Erbil governorate is located in Kurdistan region in north part of Iraq; the population of Erbil governorate was estimated to be 1,438,482 in 2006.

Maternity Teaching Hospital (MTH) is the only maternity hospital in Erbil city.

All Patients referred to the MTH within the period of the study and diagnosed having GTDs was included in the study. All patients gave a verbal consent. A specially designed questionnaire form was filled for each patient by direct Interview. The data requested includes demographic character, obstetrics and gynaecological history, history of prior molar pregnancy, clinical features, complete systemic examination and investigation (mainly hormonal assays T3, T4, TSH, HCG), Ultrasound examination.

Statistical software was used for data entry and analysis, namely SPSS version 13, aided by Excel. Descriptive study such as frequencies, percents, mean, S.D was done for some variables, Chi-Square test was used for testing association between different variables. P value $\leq$ 0.05 regarded statistically significant.

4 Results:

During the period of the study (6 months), 12557 pregnant women were admitted to the Maternity Teaching Hospital. The total number of GTD cases were (40), frequency rate of the GTD was 1 in every 314 pregnant women admitted to Maternity Teaching Hospital.

Table 1, reveals the characteristics of the sample size, the mean age was 27±8.66 years, more than half of cases (62.5%) were age group of 25-39 years. (Figure 1, shows the distribution of cases according to age groups), the mean parity of the sample size was 2.8±2.9, there was a highly significant association between parity and GTD (P value =0.005).

Twenty six cases (65%) were of low socioeconomic status, while 14 cases (35%) of high socioeconomic state.

The mean gestational age was 11±3.7 weeks, the GTD was most commonly (65% of cases) diagnosed at the first trimester. Uterine size was larger than the gestational age in 45% of cases, the same size in 40% of cases and smaller than the gestational age in 15% of cases. The frequency rate of GTD for each age group admitted to the hospital at the time of the study was illustrated in the Table 2, the highest frequency rate was at the age group of 40 years and above (1 / 122 women), while the lowest frequency rate was at age group of 20-39 years (1 case/ 413 pregnant women).

Figure 2, shows the distribution of cases according to the type of GTD, 82.5% of cases were confirmed to be complete molar pregnancy, 10% of cases were partial mole, while 7.5 % were diagnosed to be Gestational Trophoblastic Neoplasia (GTN).

Table 1: Characteristics of Sample Size

Parameter	groups	No(%)	mean	range
Age (year)	< 20	8(20)	27.97 ± 8.66	16-50
	20-39	25(62.5)		
	≥ 40	7(17.5)		
Parity *	Primigravida	9 (22.5)	2-8 ± 2.9	0–10
	P 1-4	21(52.5)		
	P ≥ 5	10 (25)		
Socio-economic status	High	(26)35		
	Low	(14) 65		
Gestational age (week)	1st trimester	26(65)	11 ± 3.7	6- 23
	2nd trimester	14(35)		
Fundal level	Larger EGA	18(45)		
	Same EGA	16(40)		
	Smaller EGA	6(15)		

EGA= Expected Gestational Age
* P value = 0.005 (significant)

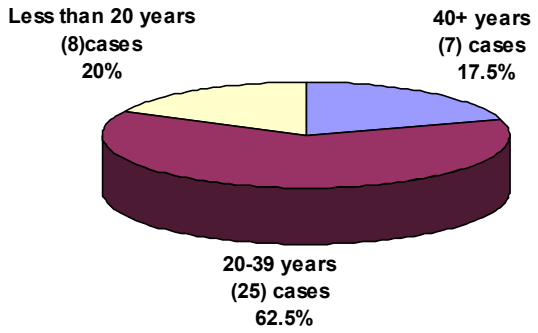

Fig1: Distribution of the cases according to the age groups

Table 2: The incidence of GTD according to age group

Age groups (Years)	No. of cases of GTD (numerator)	No. of pregnant women (denominator)	Frequency rate
Less than 20	8	1382	1/173
20-39	25	10321	1/413
40 +	7	854	1/122
Total	40	12557	1/314

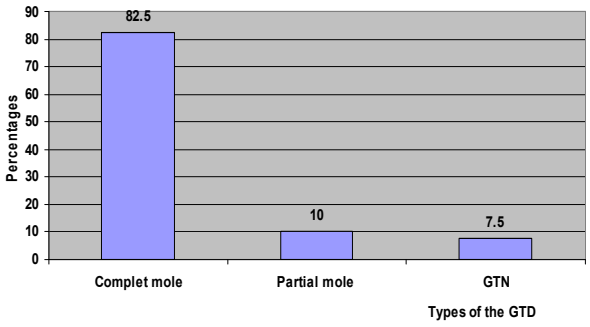

Fig 2: Distribution of the cases according to the types of GTD

Majority 35 (87.5%) of the cases presented with vaginal bleeding, Pregnancy induced hypertension (PIH) occurred in 5 cases (12.5%), with one case of pre- eclampsia (2.5%). Passages of villi vaginally by the patients were seen in only 3 cases (7.5%). Twenty seven (67.5%) of them had abdominal cramps at time of presentation, while 20 cases (50%) had hyper emesis gravidrum. Ten cases (25%) had hyperthyroidism with marked elevated T3, T4 (Table 3).

Table 3: Distribution of cases according to the clinical features

Symptoms	No. of cases	%
Vaginal bleeding	35	87.5
Anemia	27	67.5
Abdominal cramps	27	67.5
Hyper emesis	20	50
Hyperthyroidism	10	25
Passage of villi	3	7.5
PIH + Pre-eclampsia	6	15

There was a statistically significant association between hyperthyroidism and hyper emesis gravidorum as illustrated in Table 4.

Table 4: Association between hyperthyroidism and hyperemesis

		Hyperthyroidism		Total
		Yes	No	
Hyperemesis	Yes	10	10	20
	No	0	20	20
Total		10	30	40

P value = 0.003 (significant)

Three cases (7.5%) out of 40 had GTN, two cases were diagnosed as choriocarcinoma, and another one was diagnosed as invasive mole. All these patients had a history of intermittent vaginal bleeding; the diagnosis was confirmed by histopathology (Figure 3).

Regarding the antecedent pregnancy; only 4 cases (10%) of them have had prior molar pregnancy; from these 4 cases of prior molar pregnancy two of them had recurrent HM, other two cases developed GTN, with a highly significant association between them ($x^2 = 11.7$, P = 0.001), as shown in Table 5. There was no significant association between the GTN and age group (P value =0.620)(Table 6), but there was a statistically significant association between the GTN and presence of Theica Lutein cyst (Table 7). Ultrasound was diagnostic in 95% of cases, while histopathological examination was diagnostic in 100% of cases. There was no any twin gestation, and no family history of GTD in the study sample.

Table 5: Association between GTN and prior molar pregnancy

		GTN		Total
		Yes	No	
prior molar pregnancy	Yes	2	2	4
	No	1	35	36
Total		3	37	40

P value = 0.001 (Highly significant)

Table 6: Association between GTN and age groups

		Age groups (years)		40 and over
		10-19	20-39	
GTN	Yes	0	1	2
	No	8	24	5
Total	40	8	25	7

P value = 0.620 (Non Significant)

Table 7: Association between GTN and Theca Lutein cyst

		Theca Lutein cyst		Total
		Yes	No	
GTN	Yes	3	0	3
	No	7	30	37
Total		10	30	40

P value = 0.002 (Significant)

5 Discussions:

The incidence of GTDs had two extremities**;** the highest one reported in Indonesia 1in 100 pregnancies and 1in 200 in Mexico, the lowest one in North America and Europe 1:2000 to 1:5000 in Paraguay [(4), (5)]. In the current study the incidence was similar to the incidence in the near by countries, 1in 318 in Iran [(6)] and 1/452 in Saudi Arabia [(7)].

More than half of our cases were in the age group 20-39 years , this result coincide with a study done in Egypt, center of clinical oncology by Kaser EL Ain[(8)]. Regarding the frequency rate in each age group the incidence of GTDs was highest in the age group 40 and more (1/122), women in their early teenage or peimenopausl years are most at risk, women older than 35 years have a 2-fold increase in risk, women older than 40 years experience a 5- to 10- fold increase in risk compared to younger women [(9)]. The rate of GTDs was low in nulliparous ladies in the current study, it is differ from some

Studies done a broad, a study done in Mexico by Moore (2008) revealed that parity dose not affect the risk of GTDs [(9)]. GTDs was diagnosed in 65% of cases in the 1st trimester , while in a study done in Malaysia by Aye and Karali (2009) , 75% of the cases were diagnosed at 1st trimester [(10)], this difference may be due to their facilities for early detection and diagnosis were better than our locality.

Abnormal vaginal bleeding remains the most common presentation in the GTDs, 87.5% of current study presented with vaginal bleeding, and this was in agreement with studies done by Soto Wrigh et al in USA [(11)], and by Chong and Koh in Singapore [(12)].

Twenty five percent of the current study cases presented with hyperthyroidism,
which was against the result reported by American Cancer Society (2009) where less than 10% of

women with GTDs presented with hyperthyroidism [13], this could be explained by the unknown aetiology of the GTDs and variability of some of the findings in different localities.

Theca Lutein cyst was present in 25% of the cases of current study, this rate was in agreement to the results done by Aye S and Karali HF [10], who reported that ovarian enlargement occurred in 20% of cases.

There was 3 cases out of 40(7.5%) diagnosed to be GTN, two cases were choricarcinoma (5%) and one case diagnosed as invasive mole (2.5), these findings was close to the result of a study done in Saudi Arabia by Al-Mulhim who reported 10% of their cases were GTN, invasive mole being (6.7%) and (3.3%) being choriocarcinoma[7]. Two third of cases with GTN were above the age of 40 years , Chattopadhyay et al in Saudi Arabia reported in their study also that the malignant GTD was higher than expected frequency for the older age group only (more than 40 years)[14]. In a study done in Finland by Loukovarra et al (2001), revealed that 49% of Choriocarcinomas identified during the study period were preceded by hydatidiform mole[4], this was in agreement with the current study findings (66.3 of cases had prior molar pregnancy).

6 Conclusions:

(1) The incidence of GTDs in Maternity teaching hospital is 1/318 pregnancies.
(2) Highest incidence rate was at the age group 40 and above and age group less than 20 years.
(3) The most common presentation was abnormal vaginal bleeding.
(4) 7.5% of cases were malignant gestational trophoblastic condition.
(5) Complications of GTDs such as infections, trophoblastic invasion and uterine Perforation were not found in current study.

7 Recommendations:

(1) Education of pregnant women in Antenatal care units about early signs and symptoms of GTDs and the hazards that maybe faced in the future.
(2) Establishment of a specialized center in the maternity Teaching Hospital for diagnosis, management and follow up of GTDs cases.
(3) Create initiative to stimulate research and further studies on GTDs in Erbil governorate and Kurdistan region; regarding incidence of GTNs, detecting risk factors, proper management, and complications.

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