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Retrospective Evaluation of Patients Diagnosed with Gestational Trophoblastic Disease in Our Clinic

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Abstract

Inroduction: In this study, we were aimed to determine the clinical-pathological features by retrospectively evaluating the patients diagnosed with benign Gestational Trophoblastic Disease (GTD) in our clinic.

Materials and Methods: This study retrospectively analyzed 11,319 pregnant patients who were admitted to our hospital between 2015 and 2019. 61 patients who were diagnosed with benign GTD, treated and followed up were included in the study. The patient's ages, hospital admission complaints, ultrasound findings, serum B-HCG values, blood groups, gravidity, parity, number of miscarriages, histological GTD type and treatments were analyzed.

Results: In GTD cases, 11.5% were aged below 21 years, while 23% were above 35 years. 68.9% of the patients applied to our clinic with the complaint of vaginal bleeding, and 26% of the patient's received diagnosis during follow-up visits. The blood group distribution of GTD patients did not significantly differ from that of the general population, indicating that blood group A may not be an independent risk factor.

Conclusion: Although there are many studies in the literature on the etiology and incidence of GTD, differences are observed in the data obtained since most of the studies are clinic-based. There is a need to increase community-based studies on this issue. Upon initial admission, 78.7% of patients were clinically suspected of having GTD. Thanks to advances in diagnostic methods, earlier diagnosis of the disease has become possible, contributing to a reduction in complications arising from the disease. Raising public awareness about the importance of earlier medical consultations during pregnancy or in cases of pregnancy suspicion is crucial.

Key words: Gestational trophoblastic diseases; hydatiform mole; trophoblastic neoplasms; pregnancy

Inroduction

Gestational trophoblastic diseases (GTD) are a group of diseases that develop with abnormal proliferation of trophoblastic tissue, which originates from the placenta. Histologically, partial hydatiform mole (PHM), complete hydatiform mole (CHM) is classified as benign, while placental site trophoblastic tumor (PSTT), invasive mole and choriocarcinoma are classified as malignant. Today, GTD can be diagnosed at an early stage through ultrasonography (USG) and treated effectively (1,2). Vaginal bleeding is the main cause for hospital admission in patients diagnosed with CHM. BHCG values are higher than expected and the uterus may be large for gestational age (3). Patients with PHM, missed abortion or incomplete abortion findings may be observed. β-hCG value may be detected lower than CHM. For this reason, PHM cannot be defined without histological examination(4). The incidence of hydatiform mole varies between 0.57 and 2 per 1000 pregnancies (5). We aimed to determine the clinical-pathological features by retrospectively evaluating the patients with benign GTD in our clinic.

Materials and Methods

In this study, 11,319 pregnant patients who were admitted to our hospital between 2015 and 2019 were evaluated, and the medical records and electronic files of those diagnosed with GTD were retrospectively reviewed. 61 female patients over the age of 16 who had been diagnosed with benign GTD and were included in study. In addition to 3 patients diagnosed with Gestational trophoblastic Neoplasia (GTN), patients with missing medical and electronic records were excluded from the statistical analysis. Our study aimed to define the clinical-pathological features related to the clinical presentation and diagnosis of the disease by evaluating the patient's gravidity / parity / abortion numbers, B-HCG levels when the time

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Table 1: Demographic Data

		n	%
Age	21>	7	11.5
	21-35	40	65.6
	35<	14	23.0
Histological Type	Complete	35	57.4
	Partial	26	42.6
Operation	C	54	88.5
	TAH	2	3.3
	TAH BSO	5	8.2
Complaint	Vaginal Bleeding	42	68.9
	Follow-Up	16	26.2
	Vomiting	2	3.3
	Pain	1	1.6
Gravidity	≤2	29	47.5
	3	12	19.7
	4	20	32.8
Parity	≤2	48	78.7
	3	10	16.4
	≥4	3	4.9
Abortion	0	43	70.5
	1	12	19.7
	2	5	8.2
	6	1	1.6
Blood Group	0+	18	29.5
	0-	3	4.9
	A+	20	32.8
	A-	4	6.6
	B+	8	13.1
	AB+	7	11.5
	AB-	1	1.6
USG Findings	MA	8	13.1
	AA	6	9.8
	HM	40	65.6
	IA	7	11.5
Clinical Suspicious	No	13	21.3
	Yes	48	78.7

Note: C: Curettage, **TAH:** Total Abdominal Hysterectomy, **TAHBSO:** Total Abdominal Hysterectomy and Bilateral Salpingo-Oophorectomy, **MA:** Missed Abortion, **AA:** Anembryomic Abortion, **HM:** Hydatiform Mole, **IA:** Incomplete Abortion

of diagnosis, blood groups, complaints at hospital admission, USG findings, surgical intervention and pathology results. The data obtained from the study were analyzed with SPSS 22.0. First of all, the mean, standard deviation and frequency distributions of the demographic and clinical data obtained were calculated. For hypothesis tests, independent sample t test was used for comparison of two groups in normally distributed data, and Mann-Whitney U analysis was used in non-normally distributed data. In comparisons of more than two groups, the Kruskal-Wallis test was applied for normally distributed data and the Mann-Whitney U test was used for the Pos-Hoc test. Chi-Square analysis (with Bonferroni correction) was used to meet categorical data. The confidence interval in the analysis was determined as 95% ($p = 0.05$). Ethics committee approval dated 27.03.2024 and numbered 2024/010.99/2/24 was obtained from Kartal Dr Lutfi Kirdar City Hospital Ethics Committee for Scientific Research.

Results

Of the 61 patients included in the study, PHM was detected in twenty-six and CHM in thirty-five. A diagnosis of invasive mole was made in 1 patient, PSST in 1 patient, and choriocarcinoma in 1 patient. Patients with GTN were not included in the statistical studies because their number was low and statistically significant data could not be obtained. Among the patients, 57.3% were diagnosed with CHM, while 42.7% were diagnosed with PHM. It was observed that 11.5% of the

patients diagnosed with GTD were younger than 21 years of age, and 23% were older than 35 years of age. (Table 1). 68.9% of the presented with vaginal bleeding as their primary complaint and 26% of the patients received this diagnosis during follow-up. Of the patients observed, 29.5% were found to have the 0Rh+ blood group, whereas 32.8% were identified as having the Arh+ blood group. When evaluated in terms of Rh antibodies, it were present (+) in 86.9% of the patients and 13.1% had RH antibodies (-). Based on the ultrasonographic evaluation, GTD was initially considered in 65.6% of the patients, and was suspected in 78.7% of the patients overall. (Table 2)

Table 2: Comparison of Clinical and Demographic Data

	Type	N	Mean	SD	p
Age	CM	35	29,742	9.381	0.840
	PM	26	30,230	9.183	
Gravidity	CM	35	2,800	1.659	0.715
	PM	26	2,961	1.754	
Parity	CM	35	1,314	1.078	0.476
	PM	26	1,538	1.363	
Abortion	CM	35	0,485	1.094	0.803
	PM	26	0,423	0.757	
β-hCG	CM	35	208367,114	168248.367	0.010*
	PM	26	115023,269	65527.770	

Note. CM: Complete Mole, **PM:** Partial Mole, **N:** Number, **SD:** Standard Deviation, **p:** Independent Sample t-Test, ***:** Mann-Whitney U Test

Patients diagnosed with PHM had an average age of 29.7 years, whereas those diagnosed with CHM had an average age of 30.2 years. In the comparison made between PHM and CHM patients according to pathological type, no significant difference were detected in terms of Gravide, Parity and Abortion numbers. The average serum β-hCG levels at the time of admission were 208367 mIU/mL for patients diagnosed with CHM and 115023 mIU/mL for those with PHM. β-hCG levels were significantly higher in patients with CHM compared to those with PHM at the time of admission. (Table 3)

Table 3: Age-Operation Comparison

	N	Mean	SD	p	Diff
C	54	27.685	7.041	0.001	1<2 1<3 2<3
TAH	2	44.500	2.121		
TAHBSO	5	48.600	2.880		
Total	61	29.950	9.223		

Note: C: Curettage, **TAH:** Total Abdominal Hysterectomy, **TAHBSO:** Total Abdominal Hysterectomy and Bilateral Salpingo-Oophorectomy **N:** Number, **SD:** Standard Deviation, **p:** Kruskal-Wallis Test, **Diff:** Mann-Whitney U Test

Suction curettage was performed on 54 patients, total abdominal hysterectomy (TAH) was performed on 2 patients, and TAH + Bilateral Salpingo-oophorectomy (BSO) was performed on 5 patients. The mean age for patients who underwent TAH without Salpingo-oopherectomy operation was calculated as 44.5 years, for TAH + BSO procedure was calculated as 48.6 years and for Suction Curettage was calculated as 27.6 years. Patients who underwent hysterectomy (with or without BSO) were compared to those who had suction curettage. (Table 4)

Table 4: β-hCG -Complaint Comparison

	N	Mean	SD	p	Diff
Vaginal Bleeding	42	199239.609	155835.689		
Follow-up	16	106504.375	81877.496		
Vomiting	2	117487.000	94801.806	0.138	-
Pain	1	74024.000	-		
Total	61	169698.200	142330.371		

Note. N: Number, **SD:** Standard Deviation, **p:** Kruskal-Wallis Test

68% (42) of the patients presented with bleeding complaints, 26% (16) with purpose ith pain. No significant correlation was of control, 3.2% (2) with vomiting and 1.6% (1) wfound between the presenting complaints and the β-hCG values of the patients (Table 5). Furthermore, an evaluation of patients based on their presenting complaints did not reveal any remarkable differences in parameters between those diagnosed with CHM and PHM. Similarly, no significant differences were observed among blood groups in patients diagnosed with either PHM or CHM. Additionally, there were no significant disparities found between blood groups regarding the detection of Gestational Trophoblastic Disease (GTD). No notable differences were identified in the surgical treatment methods applied to patients with CHM or PHM, irrespective of the disease type No significant difference were found between the histological types of patients diagnosed with CHM or PHM according to the USG findings at their first visit.

Discussion

GTD is characterized by abnormal proliferation of trophoblastic tissue, and its etiology is still not completely understood. Incidence of GTD; although it varies regionally due to reasons such as the level of development of countries, nutritional habits and ethnic differences, it is seen at a rate of 0.57-2 per thousand pregnancies (5,6).

Table 5: Type - Clinical Data Comparison

			Type		Total	p
			CM	PM		
Complaint	Bleeding	N	25	17	42	0.748
		%	59.5%	40.5%	100.0%	
	Follow-up	N	8	8	16	
		%	50.0%	50.0%	100.0%	
	Vomit	N	1	1	2	
		%	50.0%	50.0%	100.0%	
	Pain	N	1	0	1	
		%	100.0%	0.0%	100.0%	
Blood Group	0+	N	11	7	18	0.681
		%	61.1%	38.9%	100.0%	
	0-	N	2	1	3	
		%	66.7%	33.3%	100.0%	
	A+	N	11	9	20	
		%	55.0%	45.0%	100.0%	
	A-	N	1	3	4	
		%	25.0%	75.0%	100.0%	
	B+	N	5	3	8	
		%	62.5%	37.5%	100.0%	
	AB+	N	5_a	2	7	
		%	71.4%	28.6%	100.0%	
	AB-	N	0	1	1	
		%	0,0%	100.0%	100.0%	
USG	MA	N	3	5	8	0.603
		%	37.5%	62.5%	100.0%	
	AA	N	3	3	6	
		%	50.0%	50.0%	100.0%	
	HM	N	25	15	40	
		%	62.5%	37.5%	100.0%	
	IA	N	4	3	7	
		%	57.1%	42.9%	100.0%	
Suspicious	No	N	8	5	13	0.493
		%	61.5%	38.5%	100.0%	
	Yes	N	27	21	48	
		%	56.3%	43.8%	100.0%	

Note: CM: Complete Mole, **PM:** Partial Mole, **MA:** Missed Abortion, **AA:** Anembryomic Abortion**, HM:** Hydatiform Mole, **IA:** Incomplete Abortion, **N:** Number

In Alemdar et al.'s study conducted at a tertiary center in Tokat, the incidence was determined as 11/1000 (7). In Barut et al.'s study in a tertiary center in Southeastern Anatolia, the incidence was 22.6/1000 (8). Tosun et al. found this rate to be 2.4/1000 in another tertiary center in Istanbul (9). Among 11319 cases examined in our study, 61 patients were diagnosed with benign GTD and its incidence was determined as 5.4 per thousand pregnancies. We believe that the hospital where our study was conducted is a tertiary center and the referral chain system is effective in this rate being higher than the study conducted in our clinic. According to the literature, clinic-based studies are conducted rather than community-based studies on GTD, and the results detected in the studies vary depending on the clinical characteristics and regional factors where the study is conducted. For example, the high incidence in clinics that are the only tertiary center in their city may be related to the referral chain system. Therefore, population-based studies on incidence are needed. Advanced age, increased gravidity-parity number, and low socio-economic level are among the known risk factors of GTD. Literature reports indicate that GTD can occur both in the early stages of reproductive age and in older age groups. Lurain et al. reported in their study that the risk of GTD increased by 1.5-fold in individuals under the age of 20 and by 5.2-fold in those over the age of 40 (5). We think that this situation is due to low socio-economic levels and unplanned pregnancies in these age ranges. Alemdar et al. (7) found the average age of 134

patients diagnosed with GTD as 29.9 years in their study. No significant differences were detected between CHM and PHM patients in terms of age, number of gravidity/parity/abortions in our study and the average age for GTD was 29.9 years and the average gravity was 2.86 years, which is compatible with the data in the literature. The serum β-hCG value is a critical parameter in both the diagnosis and monitoring of treatment for GTD. In CHM, the β-hCG value is generally above 100,000 mIU/mL and is higher than the partial mole (5). Özgen et al. found the average β-hCG value of patients diagnosed with PHM to be 46014.66 mIU/mL, and this value to be 76292.26 mIU/mL in patients diagnosed with CHM (10). Barut et al. found the average β-hCG value to be 229082±354929.69 mIU/ml in patients diagnosed with PHM and 258017.47±379942 mIU/ml in patients diagnosed with CHM (8). The mean β-hCG value at the time of admission for patients diagnosed with CHM in our clinic (208,367.114 ± 168,248.367) was found to be significantly higher compared to that of patients diagnosed with PHM (115,023.269 ± 65,527.770). We hypothesize that the higher mean β-hCG value observed in patients diagnosed with PHM in the study by Barut et al. compared to our study may be attributable to the fact that their research was conducted in Southeastern Anatolia region and hospital admissions due to pregnancy are made later in the region. We think that the lower average β-hCG value of Özgen et al. is related to the ease of diagnosis with the development of ultrasonography devices in making preliminary diagnoses. Kurdoğlu et al. found that vaginal bleeding was the most common complaint with a rate of 77.6%. (11). The most common presenting complaint of the patients was vaginal bleeding in our study and no significant difference was found between the patients' serum β-hCG values at the time of admission and their complaints. The literature indicates a higher prevalence of maternal blood group A in Gestational Trophoblastic Diseases (GTDs). Barut et al. reported that 40.5% of their study population had blood group O, while 39.3% had blood group A. In Gülten et al.'s study, blood group A was observed in 38.3% of the patients, and blood group O in 29.4%. Eren's ABO blood group distribution data for Istanbul indicated that 43.81% of individuals had blood group A and 33.79% had blood group O (12). In our study, 39.4% of patients had blood group A and 34.4% had blood group O. These findings align with the existing literature. When comparing the ABO blood group distributions, the proportions of blood groups among patients diagnosed with GTD are similar to those observed in the general population. Given these observations, we suggest that further, more comprehensive studies are warranted to determine whether blood type A constitutes a significant risk factor for GTD.In the study by Budak et al., 61% of the patients were pre-diagnosed with GTD by USG, and missed abortion was found to be the second most common pre-diagnosis (13). In our study, it was determined that GTD was suspected in 78.7% of the patients and 65.6% of the patients were diagnosed with GTD, based on USG performed at their first admission. Other diagnoses considered in the preliminary diagnosis, respectively; Missed abortion, incomplete abortion and anembryonic pregnancy were determined. The findings from our study are consistent with those reported in the existing literature.

Study limitations: This study has several limitations. As a single-center retrospective analysis, the data were derived from patient records, which may contain incomplete or consistent information. The retrospective design also restricts the ability to establish causal relationships between variables. In addition, the findings reflect the experience of a single institution and therefore may not be fully generalizable to other clinical setting or populations.

Conclusion

Although there are numerous studies in literature regarding the etiology and incidence of gestational trophoblastic disease (GTD), differences in the obtained data are observed due to most studies being clinic-based. The fact that follow-up and treatments related to GTD are generally conducted in tertiary centers prevents the determination of incidence with clarity. Consequently, population-based studies are required. When comparing β-HCG levels at the time of patient admission with other studies, it is observed that regional and cultural practices play a role in whether the diagnosis is made early or late. In our study, 26% of patients diagnosed with GTD were diagnosed during hospital visits for control purposes. Therefore, raising public awareness about the importance of earlier medical consultations during pregnancy or in cases of pregnancy suspicion is crucial. Although blood group A is shown as a risk factor for GTD in the literature, when the population-based blood group distribution and the data from our study are examined, it is observed that blood group A might not be an additional risk factor for the disease.

Upon initial admission, 78.7% of patients were clinically suspected of having GTD. Thanks to advances in diagnostic methods, earlier diagnosis of the disease has become possible, contributing to a reduction in complications arising from the disease.

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