Hydatidiform mole in Duhok, Iraq: Frequency, types and histopathological diagnostic features

Irak, Duhok'ta hidatidiform mol: Sıklığı, tipleri ve histopatolojik tanısal özellikler

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Abstract

Aim: There is a worldwide variation in the distribution of molar pregnancy with respect to its type. Difficulties in obtaining accurate data about miscarriage make the precise incidence uncertain. The aim of this study was to estimate the frequency of Hydatidiform mole among the miscarriages and deliveries in Duhok province, estimate their main types, partial or complete, and correlate them with histopathological diagnostic features.

Methods: This cross-sectional study was conducted between June 1, 2016 and September 1, 2019 and included Hydatidiform mole cases from the main histopathological centers in Duhok and Zakho. All childbirths and miscarriages were evaluated within the same areas and during the same period. Samples were examined histologically and divided into three groups as partial, complete, and indeterminate molar types, after which their correlation with the main histopathological features were examined. Additional efforts were made to identify the indeterminate cases, like the use of P57 marker.

Results: The frequency of Hydatidiform mole was less than 1%. Complete type represented 43% of the cases with a relatively high percentage of indeterminate molar pregnancies (26%). The highest percentage of women belonged to the 20-30 years-old group. The most common histological feature was circumferential trophoblastic proliferation.

Conclusion: The frequency of Hydatidiform mole in Duhok was within the world range, with a relatively high percentage of indeterminate types. More efforts should be made to establish an accurate diagnosis depending on histopathological features and additional markers like P57 should be used.

Keywords: Hydatidiform mole, Frequency, Types, Histopathology

Öz

Amaç: Molar gebeliğin türüne göre dağılımında dünya çapında bir farklılık vardır. Düşükle ilgili doğru veri elde etmedeki zorluklar, kesin insidansı belirsiz kılar. Bu çalışmanın amacı, Duhok eyaletindeki düşükler ve doğumlar arasındaki Hidatidiform mol sıklığını tahmin etmek, ana tiplerini, kısmi, tam veya belirsiz olarak sınıflamak ve histopatolojik tanı özellikleri ile ilişkilendirmekti.

Yöntemler: Bu kesitsel çalışma, 1 Haziran 2016 ile 1 Eylül 2019 tarihleri arasında Duhok ve Zakho'daki ana histopatolojik merkezlerden Hydatidiform mol vakalarında yapıldı. Tüm doğumlar ve düşükler aynı bölgelerde ve aynı dönemde değerlendirildi. Örnekler histolojik olarak incelendi ve kısmi, tam ve belirsiz molar tipler olarak üç gruba ayrıldı, daha sonra ana histopatolojik özelliklerle korelasyonları incelendi. Belirsiz vakaları tanımlamak için, P57 markörünün kullanımı gibi ek tetkikler uygulandı.

Bulgular: Hidatidiform mol sıklığı % 1'den azdı. Tam tip, nispeten yüksek oranda belirsiz molar gebeliklere (% 26) sahip olguların % 43'ünü temsil etmekteydi. Kadınların çoğunlukla 20-30 yaş grubundaydı. En sık görülen histolojik özellik çevresel trofoblastik proliferasyon idi.

Sonuç: Duhok'taki Hidatidiform mol sıklığı, belirsiz türlerin nispeten yüksek bir yüzdede görülmesiyle, dünya aralığındadır. Histopatolojik özelliklere bağlı olarak doğru tanı koymak için daha fazla çaba gösterilmeli ve P57 gibi ek belirteçler kullanılmalıdır.

Anahtar kelimeler: Hidatidiform mole, Frekans, Tipleri, Histopatoloji

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Introduction

There are broad variations in the distribution of Hydatidiform mole (HM) pregnancy worldwide, with higher incidences in certain parts of Asia, Africa and other developing countries. However, the methodological problems in obtaining curettage samples from all patients with miscarriage make the accuracy of the incidence and rates unclear [1]. In developed countries, the incidence of complete Hydatidiform mole (CM) is around 1–3/1000 pregnancies and those of partial Hydatidiform mole (PM) is approximately 3/1000 pregnancies [2]. The primary estimated frequency in developing countries 10 times less than some Asian or African countries [3,4].

The CM type is associated more with invasive subsequent complication compared to PM, which is probably correlated with the male origin of the DNA [5,6]. The complete type carries about 15% increased risk of developing malignancy, while the same risk for the partial type is considerably lower [7]. Management, including the use of chemoprophylaxis treatment after evacuation and follow-up, differ according to the subtype of molar pregnancy [8]. Therefore, distinguishing between these two types is significant to prevent the unnecessary use of chemotherapy or malignant changes.

This study aimed to estimate a primary frequency of HM among the miscarriage cases and labors in Duhok province and the surrounding districts including Zakho, detect the percentages of the subtypes and correlate them with age and important histopathological features.

Materials and methods

Ethical approval was obtained from the official Ethics Committee for Research in Duhok and scientific approval was obtained from the Scientific Committee for Research in College of Medicine/ University of Duhok.

HM cases from different histopathological centers in Duhok and the surrounding districts including Zakho were collected between June 01, 2016 and September 01, 2019 for retrospective evaluation. All diagnosed HM cases were included without any exclusion criteria. All recorded miscarriages and the number of childbirths were counted within the same areas during the same period, including alive and still births, based on the official center of health protection in Duhok to estimate the frequency of HM.

Samples were divided according to histological examination into partial, complete, and unclassified types, which were considered as indeterminate HM. The histopathological features present in the report and used for diagnosis included cistern formation, trophoblastic and circumferential proliferation, and presence of gross, grapelike vesicles. All these correlated with various subtypes of HM. Additional efforts were made to identify indeterminate cases, such as the use of P57 as a marker.

Statistical analysis

All obtained data were analyzed using the IBM SPSS software (Version 22). Descriptive data were presented as numbers and percentages. Cross table tests were performed with P-value at <0.05 indicating a significant difference.

Results

The total number of the HM diagnosed and confirmed by histopathology centers, collected from June 1,2016 until September 1, 2019 was 140. The number of miscarriages was 610, while there were 146,015 births recorded during the same period (Officially obtained from the Preventive Affairs Directorate in Duhok which included Duhok province and the surrounding villages and districts, including Zakho, and the refugee camps). Based on these numbers, the frequency of HM would approximately be 0.095%, which is less than 1%.

There were 43 partial HM and 61 CM cases, in addition to the 36 indeterminate HM cases. Figure 1 presents the percentages of these 3 diagnoses.

Types of Hydatidiform Mole

Indetermine (36) 26%
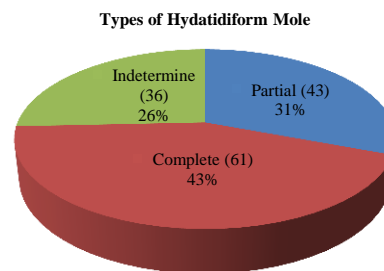Partial (43) 31%
Complete (61) 43%

Figure 1: The frequencies and percentages of the diagnosed types of hydatidiform mole

The mean age of all patients at time of diagnosis was 27.6 years. The mean age of PM at diagnosis was 25.1 years, while that of CM was 28.1 years. The highest percentages of HM, PM, and CM (53.6%, 62.8% and 50.8% respectively) were seen in the age group between 20 and 30 years, as seen in Table 1.

Table 1: The types of Hydatidiform mole in relation to the age of the patient

Age	Partial		Complete		Indeterminate		Total	
	n	%	n	%	n	%	n	%
>20	7	16.3	13	21.3	4	11.1	24	17.1
20-30	27	62.8	31	50.8	17	47.2	75	53.6
30-40	7	16.3	7	11.5	9	25	23	16.4
40-50	2	4.6	10	16.4	6	16.7	18	12.9
Total	43	100	61	100	36	100	140	100

The major features used in the histological reports for the diagnosis of HM and differentiation between PM and CM are listed in Table 2. Except for circumferential trophoblastic proliferation and gross vesicle formation, all other features were seen in relatively high percentages in all types of HM and no statistically significant difference was detected among distinct types. Vesicles were seen grossly in 46.5% and 68.9% of PM and CM cases respectively, while circumferential trophoblastic proliferation were encountered histologically in 2.3% and 55.7% of PM and CM cases, respectively. These values were statistically significant. Out of 140 cases, P57 was used only in 3 cases (2.1%) to confirm the type of HM.

Table 2: The main gross and histological features used for the diagnosis and the differentiation of Hydatidiform mole types

Gross and histological features	Partial		Complete		P-value[1]	Indeterminate	
	n	%*	n	%**		n	%***
Gross Vesicles	20	46.5	42	68.9	0.01 Significant	20	55.6%
Cistern formation	41	95.3	54	88.5	0.20 Not significant	20	55.6%
Trophoblastic proliferation	43	100	56	91.8	0.10 Not significant	36	100%
Circumferential trophoblastic proliferation	1	2.3	34	55.7	0.05 Significant	14	38.9%

*Frequency of encounter among partial Hydatidiform moles (43), ** Frequency of encounter among complete Hydatidiform moles (61), *** Frequency of encounter among indeterminate moles (36), [1] P-value: between partial and omplete types

Discussion

This study examined the diagnosis and registration of HM cases in Duhok province including Zakho, and the refugee camps, to establish a primary frequency of HM, its types, and the accuracy of diagnosis. The strength of this study lied in the collaboration from different official registration centers.

The main limitation to this study was the probable shortage of obtaining data from all miscarriages. Although there are strict orders from the directory of health to send the products of conception of all miscarriages to histopathology laboratories, the private clinics do not usually comply. However, the same problem is encountered throughout many areas all over the world [1-4,9-12]. The incidence of HM in this study was approximately 0.095%, which is less than 1%. Some authors reported a wide range of incidence of HM, from 23 to 1299 cases per 100,000 pregnancies [13], while others found a significantly lower incidence in Europe and the United States than that from Asia, Africa and South America [2,3-14].

Joneborg et al. [9] stated the following: [We found evidence of a significant temporal increase in the incidence rate of HM, which could not fully be explained by an increase in maternal age over time. Changes in diagnostic methods probably contributed to the increased incidence rate of PM]. Even if the causes of varying incidences have not been clear, there were different explanations. Brown et al. [10] suggested that dietary and nutritional causes may affect the etiology. It is hard to compare the incidences of molar pregnancy from different types of studies, which is why several studies proposed diverse reasons: the inadequate description of the population at risk, the differences in the definition of the disease, the frequent changes in the diagnostic tools over time and the variation in the methodological designs [9-12].

CM was the commonest type in this study (43%) followed by PM (31%). HM was mostly seen in the age group of 20-30 years, with a mean age of 27.6 years. The fact that HM is more common at the extremes of reproductive age and that women under 20 or over 40 years of age have a higher risk [15] may change. Recently, and in agreement with our result, a Swedish study conducted in Stockholm found a significant increase in the age of HM diagnosis [9]. Similarly, another study determined the median maternal age of molar pregnancy as about 27 years and nearly 91% of cases occurred in females aged 18 to 40 years [16].

In the current study more than quarter of the cases (26%) were diagnosed as HM without determining the type. The diagnosis and sub-classification of HM is becoming more difficult due to the early pregnancy ultrasound examinations, which leads to the early evacuation of HM before the development of trophoblast proliferation [17]. Several authors have concluded that the diagnosis of HM depending on morphological features alone is defective and personally variable [18,19].

The histological features of circumferential trophoblastic proliferation and gross vesicle formation were seen more in CM, as well as in other types. No other features were significantly different among subtypes. Despite the relatively high percentage of indeterminate HM, p57 test was performed to only 3 out of 140 HM cases (2.1%).

The risk of gestational trophoblastic neoplasms, including choriocarcinoma, is much higher after the CM (reaching to 30%) than PM (about 0.5–5%), which renders accurate diagnosis important [18-20].

Limitations

People who live in Duhok belong to different castes. Plenty refugees from other parts of Iraq and Syria who escaped adjacent war-torn areas live in Duhok as well, but samples were collected from different Histopathology centers in Duhok and Zakho centers only. Refugees in different camps with complaints of bleeding were referred to specialized private Obstetrics and Gynecology Centers to undergo curettage. Unfortunately, there is no specialized hospital inside the camps for refugees. In this study, we were unable to address patients directly. Most cases weren't included in this study due to the need of obtaining a special and formal permit to research or enter refugee camps, which is difficult.

Conclusions

The correct diagnosis may strongly require additional immunohistochemical techniques to perform the p57 marker [20] test or molecular analysis including flow-cytometry, hybridization, or polymerase chain reaction (PCR) [17]. For all these reasons, it is highly recommended to use more of these above-mentioned techniques, especially the PCR, to establish diagnosis in problematic cases.

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