Prevalence of hydatidiform moles in pathologic samples of Iranian women sent to pathology laboratory: A systematic review and meta-analysis

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Abstract

Introduction: Gestational trophoblastic disease (GTD) refers to a spectrum of diseases associated with placenta which varies from benign to malignant and very aggressive mode including hydatidiform mole, invasive mole and choriocarcinoma. the aim of present systematic review and meta-analysis is to evaluate the prevalence of hydatidiform moles in pathologic samples of Iranian women sent to pathology laboratory.
Methods: The methods used in this systematic review are developed based on the Checklist Guidelines (PRISMA). The searches were conducted by two independent researchers and the purpose of the search was to find published studies from 1/1/2000 to 5/30/2019.
Results : Based on the random effect model, the total Frequency of complete hydatidiform moles in 1589 patients was 56% (95% confidence interval and 99.5% ,54-59%).The total Frequency of partial moles in 1589 patients was 42% (95% confidence interval , 40% ,45%).
Conclusion: Our results showed a higher prevalence of complete mole in comparison to partial mole in patients suspected to molar pregnancy

Keywords: hydatidiform moles, moles, gestational trophoblastic disease, pathology.

Introduction

Gestational trophoblastic disease (GTD) refers to a spectrum of diseases associated with placenta which varies from benign to malignant and very aggressive mode including hydatidiform mole, invasive mole and choriocarcinoma (1-4).Hydatidiform moles, which account for 80% of GTD cases, are divided into complete and partial moles .Clinical presentations such asexcessive vomiting, having an uterus in biggerthan expected for pregnancy, continuous or intermittent spotting from week twelve of pregnancy, absence of fetal heart rate, and the incidence of eclampsia / preeclampsia before 24 weeks pregnancy are well-known characteristics of this disorder. However, the ultrasound examination in the first trimester is being performed in most of health centers now and this leads to early detection of the disease which may cause different

presentations and pathologies(5-7).Molar pregnancy is characterized histologically by disorders of chorionic villi including trophoblast proliferation and villus stromal edema.Moles usually occupy uterine cavity but sometimes fallopian tube and even the ovaries are involved. Gestational trophoblastic disease includes a group of tumors that depend on each other,(complete and incomplete hydatidiform mole, placental trophoblastic tumor and choriocarcinoma)which have different potential for localized invasion and metastases. (8-10).Several studies have suggested that the risk increases with increasing mother's age, while other studies have suggested that the incidence is higher in younger mothers or teenagers.The role of factors such as gravidity, estrogen status, oral contraceptives and nutritional factors in the incidence of trophoblastic disease has not been determined.The aim of present systematic review and meta-analysis is to evaluate the prevalence of hydatidiform moles in pathologic samples of Iranian women sent to pathology laboratory.

Methods

Inclusion criteria (eligibility criteria)

The methods used in this systematic review are developed based on the Checklist Guidelines (PRISMA). We included cross-sectional studies, case studies, and cohort studies, and excluded case studies, letters to editors, case reports, clinical trials, study protocols, systematic reviews, and reviews.

Participants: All studies on the Frequency of hydatidiform moles in Iranian womenwere studied.The main purpose of this study was to determine the Frequency of hydatidiform moles .

Sampling methods and sample size: All observational studies, regardless of their design, were included in the systematic review. The minimum sample size was 25 patients or more.

Search strategy

The searches were conducted by two independent researchers and the purpose of the search was to find published studies from 1/1/2009 to 5/30/2019. Studies published in MEDLINE were searched through PubMed, EMBASETM through Ovid, the Cochrane Library, and the English Trip database.Systematic review articles using MESH phrases and open phrases in accordance with print standards. After the MEDLINE strategy was finalized, the results were compared to search other databases, and PROSPERO was searched for recent or ongoing systematic reviews.The keywords used in the search strategy were: hydatidiform moles , moles , woman , pathology .

Select study and extract data

The two researchers independently analyzed the titles and abstracts of the articles according to the eligibility criteria. After eliminating additional studies, the full text of the studies was collected based on the eligibility criteria and information about the authors if necessary. General information (relevant author, province and year of publication), information about the study (sampling technique, diagnostic criteria, data collection method, research conditions, sample size and risk of bias) and output scale were collected. .

Quality evaluation

The developed scale of Hoy et al. Was used to assess the quality of the method and the risk of bias in each observational study. This scale collected 10 items to evaluate the quality of studies according to their external validity (items 1 to 4 of the target population, sampling framework and minimum participation bias) and internal validity .

Results

Study selection

A total of 564 articles were extracted through initial searches in various databases. Out of 421 essential studies identified by analyzing titles and abstracts. 387 studies were omitted due to irrelevant titles. 37 articles were removed from 43 existing studies. Out of the remaining studies, 6 studies met the study criteria. (figure 1).
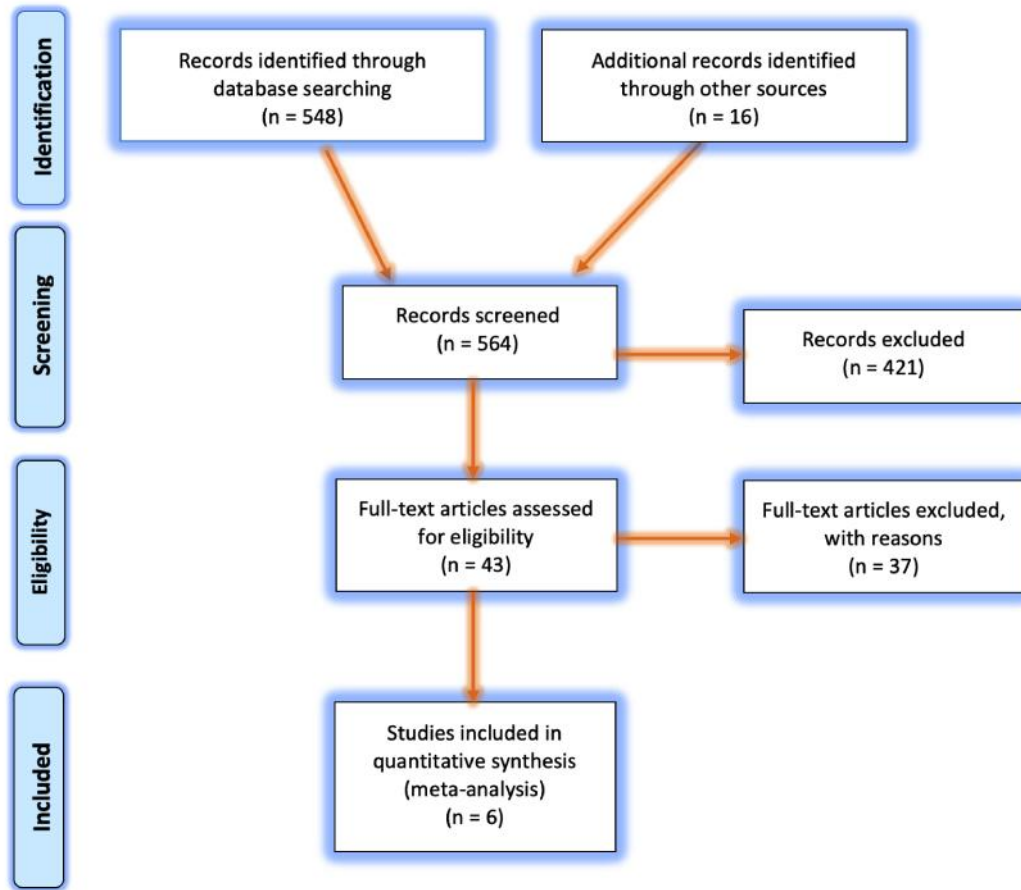
PRISMA 2009 Flow Diagram

Figure 1:PRISMA flow diagram

Research specifications

A total of 1589 patients were evaluated. All studies were retrospective studies. A total of 6 studies from 5 provinces that met the inclusion criteria were reviewed. Among these studies, 2 studies were from Tehran, 4 studies from Kermanshah ,Kashan,Babol and Hamadan were included in the study. The risk of bias was low in most studies. The main method of data collection was medical records. The main study siteswas hospital(Table 1).

Table 1.characteristics of included studies

Author	Year	Participant	Province	Age	Bias	Complete mole	Partial mole
Rezavand[17]	2009	238	Kermanshah	---	Low	66%-0.307	33%-0.0304
Izadi[18]	2013	200	Tehran	27.9±8.3	Low	50%-0.0353	42%-0.0348
Ashrafi[19]	2015	16	Tehran	29.6	Low	75%-0.1082	19%-0.0980
Vakili[20]	2009	85	Kashan	---	Low	79%-0.0441	21%-0.0441
Ranaei[21]	2020	70	Babol	23.9	Low	40%-0.0585	58.6%-0.0587
Aghababaii1[22]	2016	980	Hamadan	26	Low	53%-0.0159	47%-0.0159

Study ID		ES (95% CI)	% Weight
Rezavand (2009)		0.66 (0.60, 0.72)	15.81
Izadi (2013)		0.50 (0.43, 0.57)	11.96
Ashrafi (2015)		0.75 (0.54, 0.96)	1.27
Vakili (2009)		0.79 (0.70, 0.88)	7.66
Ranaei (2020)		0.40 (0.29, 0.51)	4.35
Aghababaii (2016)		0.53 (0.50, 0.56)	58.94
Overall (I-squared = 90.9%, p = 0.000)		0.56 (0.54, 0.59)	100.00

-.962   0   .962

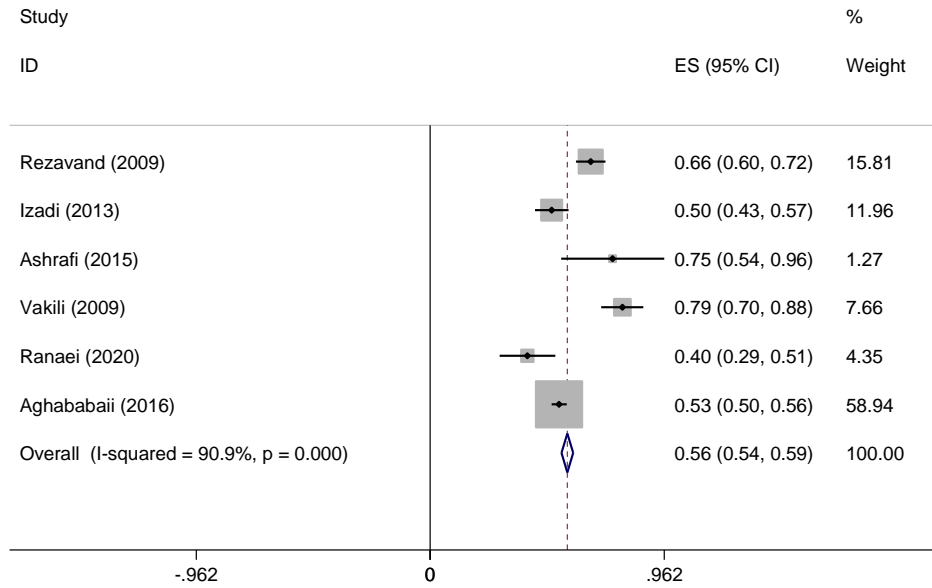**Figure 2:Meta-analysis of the frequency of complete moles in Iranian woman samples sent to pathology laboratory**

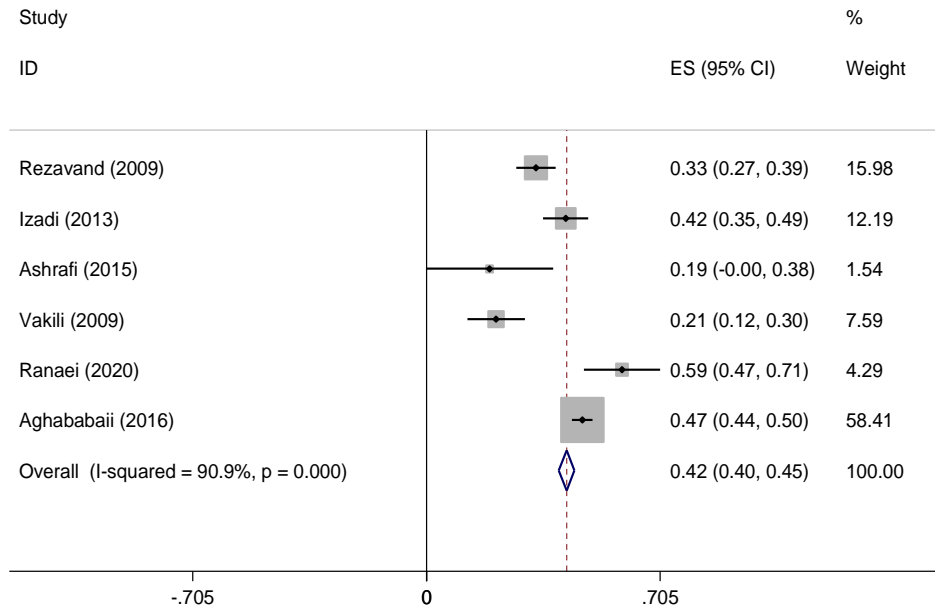| Study ID		ES (95% CI)	% Weight
Rezavand (2009)		0.33 (0.27, 0.39)	15.98
Izadi (2013)		0.42 (0.35, 0.49)	12.19
Ashrafi (2015)		0.19 (-0.00, 0.38)	1.54
Vakili (2009)		0.21 (0.12, 0.30)	7.59
Ranaei (2020)		0.59 (0.47, 0.71)	4.29
Aghababaii (2016)		0.47 (0.44, 0.50)	58.41
Overall (I-squared = 90.9%, p = 0.000)		0.42 (0.40, 0.45)	100.00

-.705   0   .705

Figure 3:Meta-analysis of the frequency of partial moles in Iranian woman samples sent to pathology laboratory
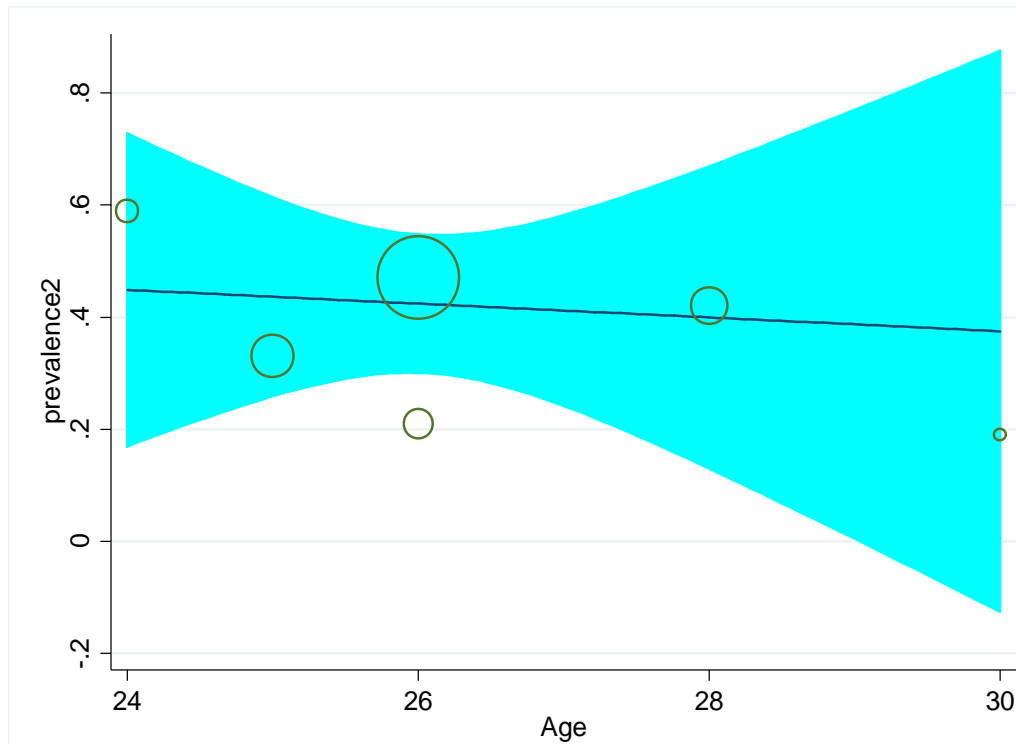
Figure 4:Meta-regression between age and Frequency of hydatidiform moles in Iranian woman samples sent to pathology laboratory

Meta-analysis of the prevalence of complete and partial moles in Iranian woman samples:

Based on the random effect model, the total Frequency of complete hydatidiform moles in 1589 patients was 56% (95% confidence interval and 99.5% ,54-59%) (Figure 2).Based on the random effect model, the total Frequency of partial moles in 1589 patients was 42% (95% confidence interval , 40% ,45%)(Figure 3).

Subgroup analysis:

Meta-regression results:

Results of meta-regression between participants' age and Frequency of hydatidiform moles:

The meta-regression was evaluated according to the relationship between the Frequency of hydatidiform moles and participants' age.There was no significant linear trend in univariate meta-regression to explain the change in the effect of age of participants. (Figure 4).

Discussion

The description and classification of moles into complete and incomplete types is based on the presence or absence of embryos or embryonic elements, and in many cases this classification is difficult (11).Molecular hydatidiformity is diagnosed in approximately one in every 2,500-1500 pregnancies in the United States (12). They originate from the placental trophoblastic epithelium and are characterized by high blood levels of HCG.Its prevalence in North America and Europe is 57.0 per 1000 pregnancies and its prevalence is 7-10 times higher in Southeast Asian countries (13).Based on clinical, cytogenic and histopathological findings, trophoblastic diseases due to pregnancy include: complete mole, incomplete mole, invasive mole and choriocarcinoma.These diseases have different potentials for local invasion and metastasis (14).GTD diseases include hydatid mole, which is divided into complete and incomplete moles. Complete mole often presents during 11-25 weeks of pregnancy with vaginal bleeding or uterine enlargement depending on gestational age (15).

The clinical manifestations of complete molar pregnancy have changed dramatically in the last two decades. Vaginal bleeding was observed in 97% of patients studied during the 1960s to 1970s, and about half of the patients developed anemia due to prolonged bleeding (16).HCG levels were high and nausea and preeclampsia were seen in 26% and 27% of patients, respectively. During that decade, molar pregnancies were usually diagnosed in the second trimester of pregnancy, but today, early diagnosis (first trimester) is possible due to the widespread use of ultrasound during the first trimester and the early stages of pregnancy. Changes in the incidence of clinical manifestations and pathological findings of the disease (17).Patients with partial molar pregnancy usually do not have the classic clinical manifestations of complete molar and show signs and symptoms of incomplete miscarriage (18).Detection of incomplete moles is usually possible after histological examination of specimens obtained from curettage. There is a risk of developing stable trophoblastic and choriocarcinoma diseases for both complete and incomplete moles, with an incidence of usually 15% following complete moles and 0.5% following incomplete moles (19).Ultrasonography is a sensitive, reliable and selective method for diagnosing complete molar pregnancy. Over the past two decades, due to extensive ultrasound studies in the first trimester of pregnancy and the increase in the power of ultrasound resolution, molar pregnancies are detected earlier than the onset of pregnancy and as a result its clinical manifestations have changed and patients have fewer or fewer patients (20).Due to the obvious swelling, the complete mole in the ultrasound creates a special vesicular pattern, the typical image of which can be seen during the second trimester of pregnancy. Differential diagnosis of missed or incomplete abortion through ultrasound is difficult, especially in the first months of pregnancy.

Conclusion

Our results showed a higher prevalence of complete mole in comparison to partial mole in patients suspected to molar pregnancy.

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