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Effect of race/ethnicity on risk of complete and partial molar pregnancy after adjustment for age

Alexander Melamed MD MPH [a,b,c], Allison A. Gockley MD [a,b,c], Naima T. Joseph MD [a,b,c], Sue Yazaki Sun MD [d,e,f], Mark A. Clapp MD MPH [a,b,c], Donald P. Goldstein MD [a,c,f,g], Ross S. Berkowitz MD [a,c,f,g], Neil S. Horowitz MD [a,c,f,g,*]

[a] Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Boston, USA
[b] Vincent Department of Obstetrics, Gynecology and Reproductive Biology, Massachusetts General Hospital, Boston, USA
[c] Department of Obstetrics, Gynecology & Reproductive Biology, Harvard Medical School Boston, MA, USA
[d] Department of Obstetrics, Paulista School of Medicine, UNIFESP - São Paulo Federal University, São Paulo, SP, Brazil
[e] Trophoblastic Disease Center of São Paulo Hospital, Paulista School of Medicine, UNIFESP - São Paulo Federal University, São Paulo, SP, Brazil
[f] New England Trophoblastic Disease Center, Donald P. Goldstein, MD, Trophoblastic Tumor Registry, Boston, USA
[g] Gynecologic Oncology Program, Susan F. Smith Center for Women's Cancers, Dana Farber Cancer Institute/Harvard Cancer Center, Boston, USA

HIGHLIGHTS

- Race-Ethnicity is a risk factor for complete and partial molar pregnancy in the United States.
- Asian women are at increased risk of complete mole, and decreased risk of partial mole compared to whites

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ABSTRACT

Objective. To quantify the effect of race/ethnicity on risk of complete and partial molar pregnancy.

Methods. We conducted a cross-sectional study including women who were followed for complete or partial mole and those who had a live singleton birth in a teaching hospital in the northeastern United States between 2000 and 2013. We calculated race/ethnicity-specific risk of complete and partial mole per 10,000 live births, and used logistic regression to estimate crude and age-adjusted relative risks (RR) of complete and partial mole.

Results. We identified 140 cases of complete mole, 115 cases of partial mole, and 105,942 live births. The risk of complete mole was 13 cases per 10,000 live births (95% confidence interval [CI] 11–16) and that of partial mole was 11 cases per 10,000 live births (95% CI 9–13). After age-adjustment, Asians were more likely to develop complete mole (RR 2.3 95% CI 1.4–3.8, $p < 0.001$) but less likely to develop partial mole (RR 0.2; 95% CI 0.04–0.7, $p = 0.02$) than whites. Blacks were significantly less likely than whites to develop partial mole (RR 0.4; 95% CI 0.2–0.8, $p = 0.01$) but only marginally less likely to develop complete mole (RR 0.6; 95% CI 0.3–1.0, $p = 0.07$). Hispanics were less likely than whites to develop complete mole (RR 0.4; 95% CI 0.2–0.7, $p = 0.002$) and partial mole (RR 0.4; 95% CI 0.2–0.9, $p = 0.02$).

Conclusion. Race/ethnicity is a significant risk factor for both complete and partial molar pregnancy in the northeastern United States.

1. Introduction

Molar pregnancy represents two entities, complete and partial mole, which can be distinguished by gross morphology, histopathology and genetic analysis [1–4]. A complete mole results from monospermic or dispermic fertilization of an anuclear oocyte, and is characterized by absence of fetal tissue, diffuse swelling of the chorionic villi, and diffuse trophoblastic hyperplasia [5,6]. Partial mole results from dispermic fertilization of a normal ovum, and is characterized by focal trophoblastic hyperplasia and villous swelling, as well as presence of identifiable fetal tissue [1–4,7]. Significant geographic variation has been reported in the incidence of molar pregnancy, though whether these differences result from genetic, nutritional, or socioeconomic variation, or are artifacts of dissimilar study methodologies is unclear [8–10].

* Corresponding author at: Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA.
E-mail address: nhorowitz@partners.org (N.S. Horowitz).

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There are limited data addressing the association between a woman's race/ethnicity and her risk of molar pregnancy in the United States. While classic studies noted an elevated risk of molar pregnancy among Asian women residing in Hawaii, others have not found an association with race [11–14]. Data for blacks and Hispanic women are particularly sparse [15–18]. Furthermore, many of the previous studies were conducted prior to the routine availability of flow cytometery to establish ploidy, and immunohistochemical staining for p57, which enable more reliable diagnosis of complete and partial moles when histology is equivocal [19–21].

We conducted a hospital-based cross-sectional study with the aim of evaluating the potential relationship between race/ethnicity and risk of complete and partial mole within an academic medical center in the United States. Since age is associated with risk of molar pregnancy, we undertook an age-adjusted analysis to control for confounding introduced by difference in age distribution among pregnant women by race/ethnicity groups [22–24].

2. Methods

This cross-sectional study received approval form the Partners Human Research Committee. We identified all patients treated for complete and partial mole at Brigham and Women's Hospital from 2000 to 2013 using the Donald P. Goldstein, MD, Trophoblastic Tumor Registry of the New England Trophoblastic Disease Center. We included patients who underwent evacuation of complete and partial mole within our center, and those who were referred from other institutions for management of molar pregnancy. We excluded patients referred to the center for persistent elevation of human chorionic gonadotropin, or for the treatment of gestational trophoblastic neoplasia. Cases of molar pregnancy with concurrent twin were excluded. All cases of molar pregnancy were pathologically confirmed at Brigham and Women's Hospital by a specialist in gynecological pathology. Flow cytometry and immunostaining for p57 were utilized in cases where there was a question regarding the pathological diagnosis.

A hospital obstetrical database was used to identify all singleton live births that occurred between 2000 and 2013 within the same institution. We abstracted maternal age, gravidity, parity, and self-reported race/ethnicity from electronic medical records and paper charts of women treated for molar pregnancy, and from the hospital obstetrical database for women who had live births during the study period. Race/ethnicity was defined as Asian, black, Hispanic, white or other/unknown.

Race/ethnicity-specific risk of complete and partial molar pregnancy per 10,000 live births, and corresponding 95% Poisson confidence intervals (CI) were calculated. Distribution of age group (<20 years, 20–24 years, 25–29 years, 30–34 years, 35–39 years, and 40 years and over), gravidity, parity, and race/ethnicity were compared between patients who had complete mole, partial mole, and live birth. Categorical and ordinal variables were compared with the χ^2 test while discrete variables were compared with the Kruskal-Wallis test. Crude and age-adjusted relative risks of complete mole and partial mole were estimated using univariate logistic regression, and multivariate logistic regression with age group included as a covariate, respectively. Patients with unknown/other race were included in the models, but results are not reported given the small numbers and heterogeneity of this category. We assumed that odds ratios were a good approximation of the relative risk for these rare outcomes. White race was used as the referent group for all calculations of relative risk because it was the largest group. All statistical analyses were carried out using SAS 9.3 (Cary, NC).

3. Results

We identified 263 women followed for molar pregnancy during the study period. Eight women were excluded because they were referral cases of twin pregnancy with mole and concurrent normal twin. Of the remaining cases, there were 140 patients with complete mole, 115 patients with partial mole. Flow cytometery and P57 immunostating were utilized for diagnostic confirmation in 42% of cases (35% among complete and 50% among partial moles). The majority of cases of molar pregnancy underwent molar evacuation and surveillance at Brigham and Women's Hospital (62%), while the remainder were referred to our institution after undergoing molar evacuation at another institution, with no suspicion of gestational trophoblastic neoplasia, and then had their post molar surveillance at our center.

We identified 105,942 patients who had singleton live birth during the same period. Characteristics of subjects who had molar pregnancies and live births are compared in Table 1. The age distributions differed significantly between the groups ($p < 0.001$). Subjects with complete mole were more frequently younger than 20 years or older than 40 years than those with partial mole or live birth. The distribution of gravidity varied significantly among patients with complete and partial mole, and live birth ($p = 0.004$); the proportion of women with a history of three or more pregnancies was highest among women with partial mole (47.8%), followed by women with complete mole (42.9%) and lowest among women who had a live birth (33.9%). The distribution of parity did not differ among the groups ($p = 0.8$).

The risk of any molar pregnancy (complete and partial) was 24 cases per 10,000 live births (95% CI 21–27). The risk of complete mole was 13 cases per 10,000 live births (95% CI 11–16) and that of partial mole was 11 cases per 10,000 live births (95% CI 9–13). Unadjusted risks of complete and partial mole per 10,000 live births, stratified by race/ethnicity group, are displayed in Fig. 1. Asian women had the highest risk of complete mole (25 cases per 10,000 live births; 95% CI 15–38) and the lowest risk of partial mole (2 cases per 10,000 live births; 95% CI 0.3–9). The risk of partial mole was highest among white women (12 cases per 10,000 live births, 95% 10–16).

Race/ethnicity was significantly associated with risk of complete molar pregnancy in both crude and age-adjusted analysis ($p < 0.001$ for both). Crude and age-adjusted relative risks for complete mole (using white women as the referent group) are tabulated in Table 2. Compared to white women, Asian women were more than twice as likely to have a complete mole (RR = 2.2; $p = 0.002$), and this association remained significant after adjustment for age (RR 2.3; $p < 0.001$). Compared to white women, black and Hispanic subjects had similar risk of complete mole in unadjusted analysis ($p = 0.54$ and 0.74 respectively). After adjustment for age, however, Hispanic women were 60% less likely to develop complete mole than their white counterparts ($p = 0.002$). A decreased risk of complete mole was also noted among black women after age-adjustment (RR = 0.6), though this association only reached marginal significance ($p = 0.07$).

Table 1
Characteristics of patients with complete molar pregnancy, partial molar pregnancy, and singleton live birth.

Characteristic	Complete mole n = 140	Partial mole n = 115	Live birth n = 105,942	p value[a]
Age group, n (%)				
<20 years	18 (12.9)	1 (0.9)	2396 (2.3)	<0.001
20–24 years	25 (17.9)	9 (7.8)	9640 (9.1)	
25–30 years	15 (10.7)	29 (25.2)	16,892 (15.9)	
30–34 years	39 (27.9)	44 (38.3)	37,070 (35.0)	
35–39 years	22 (15.7)	21 (28.3)	29,912 (28.2)	
40 years and older	21 (15.0)	11 (9.6)	10,032 (9.5)	
Median gravidity (IQR)	2 (1–3)	2 (1–3)	2 (1–3)	0.004
Median parity (IQR)	1 (0–1)	1 (0–1)	1 (0–1)	0.8
Race/ethnicity, n (%)				
Asian	21 (15)	2 (1.7)	8471 (8.0)	<0.001
Black	20 (14.3)	9 (7.8)	15,019 (14.2)	
Hispanic	15 (10.7)	9 (7.8)	14,434 (13.6)	
White	70 (50.0)	76 (66.1)	61,353 (57.9)	
Other/Unknown	14 (10.0)	19 (16.5)	6665 (6.3)	

IQR: Intraquartile range.
[a] Based of χ^2 test for categorical variables and Kruskal–Wallis test discrete variables.