GYNECOLOGY

Effect of race/ethnicity on clinical presentation and risk of gestational trophoblastic neoplasia in patients with complete and partial molar pregnancy at a tertiary care referral center

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BACKGROUND: The reported incidence of molar pregnancy varies widely among different geographic locations. This variation has been attributed, at least in part, to racial/ethnic differences. While the incidence of molar pregnancies is decreasing, certain ethnic groups such as Hispanics, Asians, and American Indians continue to have an increased risk of developing gestational trophoblastic disease across the globe.

OBJECTIVE: We sought to describe the potential effect of ethnicity/race on the presentation and clinical course of complete mole and partial mole.

STUDY DESIGN: All patients followed up for complete mole and partial mole at a single institution referral center from 1994 through 2013 were identified. Variables including age, race, gravidity, parity, gestational age, presenting signs/symptoms, serum human chorionic gonadotropin values, and development of gestational trophoblastic neoplasia were extracted from medical records and patient surveys. Patients with complete mole and partial mole were categorized into race/ethnicity groups defined as white, black, Asian, or Hispanic. Due to low numbers of non-white patients with partial mole in each non-white category, patients with partial mole were grouped as white or non-white. Continuous variables were compared using the Kruskal-Wallis test and binary variables were compared using the Fisher exact test.

RESULTS: A total of 167 complete mole patients with known race/ethnicity status were included (57.48% white, 14.97% Asian, 14.37% black, 13.17% Hispanic). Hispanics presented at younger age (median 24.5 years) compared to whites (median 32.0 years, $P = .04$) and Asians (median 31.0 years, $P = .03$). Blacks had higher gravidity than whites ($P < .001$) and Hispanics ($P = .05$). There was no significant difference in presenting symptoms, gestational age at diagnosis, and preevacuation serum human chorionic gonadotropin level by race/ethnicity. Hispanics were significantly less likely than whites to develop gestational trophoblastic neoplasia (absolute risk difference, 28.6%; 95% confidence interval, 8.1−39.2%; $P = .02$). A total of 144 patients with partial mole were analyzed. There were 108 white and 36 non-white patients. Median age was 31 years for white and 29 years for non-white patients ($P = .006$). Median gravidity was 2 for white and 3 for non-white patients ($P < .001$), and median parity was 0 for white patients and 1 for non-white patients ($P = .003$). There were no significant differences with respect to presenting signs and symptoms, gestational age, preevacuation human chorionic gonadotropin level, or risk of progression to gestational trophoblastic neoplasia.

CONCLUSION: Hispanic patients with complete molar pregnancy had a significantly lower risk of developing gestational trophoblastic neoplasia than white patients. There were no significant differences among groups in terms of presenting symptoms, gestational age at diagnosis, or preevacuation human chorionic gonadotropin levels for either complete mole or partial mole patients.

Key words: ethnicity, gestational trophoblastic neoplasia, molar pregnancy, race

Introduction

"Gestational trophoblastic disease" (GTD) is a broad term for the group of pathologic lesions arising from abnormal proliferation of placental trophoblastic tissue, including complete mole (CM), partial mole (PM), and various forms of gestational trophoblastic neoplasia (GTN).[1-3] CM pregnancy occurs when an anuclear oocyte is fertilized by a single sperm or 2 spermatozoa resulting in diffuse trophoblastic hyperplasia, villous swelling, and absence of fetal tissue.[4,5] PM pregnancy occurs when dispermic fertilization results in focal hyperplasia of trophoblastic tissue, limited villous swelling, as well as fetal tissue.[1-3,6]

The reported incidence of molar pregnancy varies widely among different geographic locations. This variation has been attributed, at least in part, to racial/ethnic differences.[7,8] Literature suggests that the incidence of hydatidiform mole ranges from 0.73-1 per 1000 pregnancies and may be twice as common in Japan and among certain Middle-Eastern subgroups.[9-11] These differences have also been reported among women of different ethnicities living in the same geographic location. A study of women in Northern England and Wales described an increased incidence of molar pregnancy among Asian women as compared to their non-Asian counterparts.[12] In the United States, Asian women in Hawaii were also found to have an increased incidence of molar pregnancy as compared to non-Asian women in Hawaii.[13]

While the incidence of molar pregnancies is decreasing according to recent

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reports in Asia as well as the United States,[14-16] certain ethnic groups such as Hispanics, Asians, and American Indians continue to have an increased risk of developing GTD across the world.[13,17-21] These differences may have implications for treatment of GTD and its sequelae. For example, American Indian women have an increased risk of molar pregnancy as well as invasive mole and choriocarcinoma as compared to other ethnic groups.[19] Similarly, Asian women have recently been shown to have more aggressive disease more often requiring additional chemotherapy for low-risk GTN.[22]

To investigate the potential relationship between race/ethnicity and the natural history of CM and PM pregnancy, we conducted a retrospective cohort study of women treated for molar pregnancy at the New England Trophoblastic Disease Center (NETDC) over the last 2 decades (1994 through 2013). The current study describes associations between race/ethnicity and presentation as well as the clinical course of CM and PM pregnancy in a diverse population of women treated at a regional referral center in the United States.

Materials and Methods

This study was approved by the Partners Healthcare Institutional Review Board. All women diagnosed with CM or PM pregnancy were identified in the Donald P. Goldstein, MD, Trophoblastic Tumor Registry of the NETDC. Women diagnosed with CM or PM at an outside institution who were referred to the center for treatment of GTN were excluded to avoid referral bias. While our center often cares for patients diagnosed with GTN at an outside institution, we wanted to limit how a referral group of patients with complex, already malignant cases may alter the patient population demographics and therefore excluded these patients. If patients referred to our center after developing postmolar GTN were included, this study would substantially overestimate the risk of GTN after a CM pregnancy. We did however include patients diagnosed with molar pregnancy at an outside institution who obtained treatment and follow-up for their molar pregnancy at the NETDC. All cases were histopathologically confirmed by gynecologic pathologists at Brigham and Women's Hospital. Cytogenetic analysis and immunohistochemical staining for p57 were used in cases when the pathologic diagnosis was in question.

Patient age, gravidity, parity, gestational age (number of completed weeks estimated by last menstrual period), preevacuation ß-human chorionic gonadotropin (hCG) level, and self-reported race/ethnicity group were abstracted from medical records. Patients who identified as white, black, Asian, or Hispanic were included in this analysis. If race/ethnicity could not be obtained from clinical records, surveys were sent to patients requesting self-identified race/ethnicity information (white, black, Hispanic, or Asian). Due to the low prevalence of non-white women among subjects with PM, for the purpose of statistical analysis, all categories of non-white patients were collapsed into a single category.

Patient charts were further reviewed for the presence of anemia (hemoglobin <11 mg/dL), vaginal bleeding (per patient report or by examination), excessive uterine size (defined as 4 weeks larger than expected for gestational age), presence of theca lutein ovarian cysts (by sonogram or examination), preeclampsia (blood pressure $\geq 140/90$ mm Hg and proteinuria), biochemical hyperthyroidism (thyroid-stimulating hormone <0.5 mIU/L), clinical hyperthyroidism (symptoms requiring use of β-blockers), and hyperemesis (nausea and vomiting requiring administration of medications). After uterine evacuation, ß-hCG was measured weekly until it fell below assay (<5 mIU/mL) for 3 weeks, and then monthly for 6 months thereafter. GTN was defined as ß-hCG plateau or elevation using the International Federation of Gynecology and Obstetrics 2002 criteria.[23] In analysis of progression to GTN, 2 women who received prophylactic chemotherapy at the time of uterine evacuation for mole (both white with CM), 4 women with CM who were lost to follow-up (2 Asian and 2 black), and 3 women with PM also lost to follow-up (2 white and 1 non-white) were excluded.

Kruskal-Wallis and Fisher exact tests were used to compare differences in continuous and binary variables among ethnicity/race groups. Significance in comparisons was adjusted using the Holm-Bonferroni method, which was applied to all pairwise comparisons.[24] All statistical analysis utilized software (SAS 9.2; SAS Institute Inc, Cary, NC).

Results

A total of 311 patients with CM and PM with known race/ethnicity were treated at the NETDC from 1994 through 2013. In all, 167 (53%) patients had CM. The majority ($n = 96$, 57%) of these women were white, while 71 (43%) belonged to a non-white ethnicity. This included 25 (15%) Asian women, 22 (13%) Hispanic women, and 24 (14%) black women. Demographic characteristics and presenting features of patients with CM are presented in Table 1. There were significant differences in the distribution of gravidity by race/ethnicity group ($P = .004$) despite identical median values due to the proportion of women with gravidity that was either >2 or <2.

There were significant age differences by ethnicity/race group ($P = .025$). In pairwise comparisons, Hispanics were significantly younger than whites and Asians ($P = .04$ and .03, respectively). Age differences among other ethnicity/race groups did not reach statistical significance ($P > .09$ for all). Given the existing evidence that older women are more likely to progress to GTN from CM,[25] women were then stratified by age group (12-19, 20-39, and ≥ 40 years) (Table 2), however the small number of patients in each group made age-stratified race/ethnicity analysis infeasible.

Women with CM had similar clinical presentations irrespective of race/ethnicity group (Table 1). Race/ethnicity was not associated with any difference in frequency of vaginal bleeding ($P = .53$), hyperemesis ($P = .97$), biochemical hyperthyroidism