Epidemiology of Epithelial Ovarian Cancer in Hispanic and Non-Hispanic White Women in Central California.

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Abstract

Objectives: Few epidemiologic studies have analyzed epithelial ovarian cancer (EOC) risk by race/ethnicity. This study evaluates factors associated with EOC risk in Hispanic and Non-Hispanic White (NHW) women.
Methods: We conducted a population-based epidemiologic case-control study to evaluate EOC risk in NHW and Hispanic women residing in the California's Central Valley. Telephone interviews were completed for 45 cases and 203 controls self-identified as Hispanic and 190 cases and 815 controls self-identified as NHW.
Results: Hispanic women with EOC were younger than NHW cases. Hispanic cases were more educated, less likely to be married and more likely to have been born in the U.S. than Hispanic controls. Hispanic women were more likely to be diagnosed with serous borderline tumors compared to NHW women.
Reproductive factors affect EOC risk similarly in Hispanic and NHW women. Heavier Hispanic women experienced a statistically significant 2.5 increase in EOC risk versus lighter women, a finding not observed in NHW women. Oral contraceptive use did not provide protection against EOC in Hispanic women.
Conclusions: California Hispanic women experience an excess of EOC serous borderline tumors compared to NHW. Acculturation may eventually lead to EOC rates that approximate that of NHW women in California and the U.S. ***Journal of Women's Cancer Volume 5 (1), Pg. 9-17, 2005.***

Ovarian cancer incidence varies by race/ethnicity in the U.S. such that non-Hispanic white women (NHW) carry the largest burden of this disease. In California the age adjusted incidence rate of this disease in 1999 was 17.3/100,000 in NHW, 11.9/100,000 in Hispanics, 11.7/100,000 in Blacks and Asian/Pacific Islanders (API). Nevertheless, each year almost 400 Hispanic women in California are diagnosed with the disease and 200 die from it (1). Although epidemiologic research has been conducted to identify risk factors for this deadly disease, few studies have analyzed risk by race/ethnicity. Previous studies suggest that differences in risk between race/ethnic groups may be attributed to reproductive, genetic or other nonhereditary factors and that these comparisons may provide clues as to the etiology of ovarian cancer (2-5). Previous studies of ovarian cancer risk by race/ ethnicity have been limited to NHW, Black and Asian women only.

Hispanics are the fastest growing ethnic minority the U.S., making up 13.7% of the population according to 2003 population estimates(6) an increase of 4.7% since 1990 (7). In California, 32% of the total population is Hispanic and Mexican Americans comprise 77% of the Hispanic population (8) 27% of California's female adult (over age 18) population is Hispanic and almost 400,000 of those women live in the Central Valley of California where the proportion of Hispanic women varies from a high of 42% to a low of 13% (9).

Therefore, in this population-based case-control study we evaluated menstrual and reproductive characteristics, exogenous hormones and lifestyle factors for newly diagnosed EOC in the Central Valley of California and evaluated these factors separately in NHW and Hispanic women.

Materials and Methods

A population-based epidemiologic case-control study of EOC was conducted in 22 counties of Central California that comprise the reporting area for two regional cancer registries. All newly diagnosed histologically confirmed EOC patients were available for inclusion in this study for the years 2000 and 2001.

Cases were women identified via a rapid case ascertainment (RCA) procedure as having been diagnosed with EOC, (malignant neoplasms of the ovary, ICD-O 3 = C56 (9) living in the Central Valley during a twenty-four month period from January 1, 2000 through December 31, 2001 and age 18 or older. Tumors were designated as borderline if the behavior code was designated as "1", or if the pathology report described the tumor as borderline, low malignant potential or atypically proliferating (10). All other tumors were classified as invasive. Histologic subtypes were identified by pathologic report or by ICD-O 3 morphology codes. The histologic subtypes included were serous, mucinous, endometrioid, clear cell, and other epithelial/unclassified. The other epithelial/unclassified category included unspecified adenocarcinomas as well as undifferentiated tumors in which a cell type could not be classified histologically. A board certified pathologist reviewed the pathology reports of a sample of cases. Physician consent was obtained by mailing the physician of record a letter and informing him/her that an interview with the patient was planned. If the physician did not respond within a three-week period, passive consent was assumed.

The control group consisted of women 18 years or older selected by random digit dialing (RDD) techniques who were residents of the area, who had not been diagnosed with EOC and who had at least one intact ovary at the time of the interview. Controls were frequency matched to cases on age and race/ethnicity.

The overall data collection period covered a two-year period, with each respondent being interviewed only once during this period by telephone. Interviews were conducted with both cases and controls on a monthly basis throughout the two-year period.

All cases and controls were approached via an introductory letter that included a prompt list that described topics the interview questions would address. The Institutional Review Board at the Public Health Institute in Oakland, California approved the study protocol.

The telephone interview obtained information on demographic factors as well as information pertinent to the respondent's birthplace, menstrual and reproductive experience, family history of cancer, gynecologic surgical history and use of exogenous hormones. Each respondent was also asked to choose the one ethnicity she identified with most.

Crude odds ratios were initially calculated followed by age-adjusted odds ratios using the Mantel-Haenszel method (11). Multivariate adjusted odds ratios were calculated using unconditional logistic regression (12). Separate multivariate models were constructed for the NHW and Hispanic subgroups including age as a continuous variable, birthplace (in or outside the U.S.), education level, pregnancy history, number of live births, age at first birth, ever breastfed, body mass index, history of breast and/or ovarian cancer in a first degree family member, ever use of oral contraceptives or hormone replacements and gynecologic surgical history as categorical variables. Backward logistic regression analysis was conducted to confirm the statistical significance of variables remaining in the model. Non-significant variables were systematically removed from each race/ethnicity model to determine the most parsimonious design. We used the Hosmer and Lemeshow Goodness-of -Fit test statistic to verify that the model's estimates fit the data at an acceptable level. The covariates included in the final model for NHW included age as a continuous variable and body mass index, ever had a live birth, ever breastfed, ever use of oral contraceptives (OC) and ever use of hormone replacement therapy (HRT) as categorical variables. The covariates included in the final Hispanic model included age as a continuous variable and birthplace in or outside the U.S., body mass index and ever breastfed as categorical variables. Interaction was assessed by comparing stratum specific odds ratios. If the stratum specific odds ratios differed by more than 100%, interaction was also assessed by including first order cross product terms into the logistic model and examining the significance of the interaction coefficient. Tests for trend were conducted for variables that were ordinal in nature by recoding

the categories into continuous form and evaluating the Wald statistic associated with the resulting coefficient.

Results

The regional cancer registries initially identified a total of 652 cases of confirmed epithelial ovarian cases residing in the 22 county study area diagnosed between January 1, 2000 and December 31, 2001. Seventeen cases were excluded due to speaking a language other than English or Spanish or due to hearing/speech impairment resulting in 635 cases that met the study criteria. Of the 446 cases identified as NHW, 52 died prior to research contact. 190 of the remaining of the 394 cases were successfully interviewed for a response fraction of 48%. 77 cases were identified as Hispanic and 7 died prior to contact. 45 of the remaining 70 cases were interviewed for a response fraction of 64%.

Households with eligible women were identified through RDD methods resulting in 1964 controls that met the study criteria. 358 of the eligible women were lost to follow-up and 19 reported that they were too ill to participate. Of the remaining 1587 contacted controls, 465 refused to participate resulting in 1122 completed control interviews for a response fraction of 71% (1122/1587) for controls approached. 203 controls stated that their ethnicity was Hispanic, while 815 controls described themselves as NHW.

The demographic characteristics of all cases and controls and cases and controls stratified by race/ethnicity are shown in Table 1. Hispanic cases and controls were both younger and less likely to have completed high school than NHW cases and controls. Hispanic cases were also more likely to be single compared to both Hispanic controls and NHW cases and controls and the difference was statistically significant (p=<.0001) for the latter relationship. A larger proportion of Hispanic cases and controls were born outside the United States (p=<.0001) compared to NHW cases and controls however, when compared to Hispanic controls, Hispanic cases were more likely to have been born in the U.S. (p=.005). Most Hispanic women born outside of the U.S. were born in Mexico (88% of cases and 91% of controls). 97% of Hispanic cases and 95% of Hispanic controls born in the U.S. were born in one of four border states, California, Arizona, New Mexico or Texas (data not shown).

Table 2 describes the distribution of cases by level of invasiveness and histologic subtype for all cases, Hispanic cases and NHW cases. Hispanic cases were almost twice as likely to be diagnosed with a borderline tumor compared to NHW cases, the difference was statistically significant (p=.023) and attributable to the serous subtype only (p=.007). There was no statistical difference between Hispanics and NHW in the other histologic subgroups.

Table 3 presents frequencies and multivariate-adjusted odds ratios for EOC risk modifiers by Hispanic and NHW ethnicities. Hispanic women with a birthplace outside of the U.S. were at a statistically significant lower risk of EOC than their U.S. born counterparts. There was no relationship between birthplace and EOC risk in NHW women. Education level was not associated with EOC risk.

Ever having been pregnant was protective for both Hispanic and NHW women but statistically significant only for NHW. Parity also reduced risk in both groups but was again statistically significant only in NHW women. Increasing number of live births was associated with increasing protection from EOC for Hispanic women up to 4 births but was not protective with greater than 4 births. Increasing parity did not provide statistically significant protection in NHW women.

There appeared to be a slight decrease in EOC risk with older age at first birth Hispanic and NHW women but it was not statistically significant. Breastfeeding offered statistically significant protection from EOC for both Hispanic and NHW women but was almost twice as protective for Hispanic women.

Hispanic women who were moderately overweight to obese (BMI≥ 25 kg/m2) had a statistically significant two and one-half increase in risk of EOC compared to lighter women. Risk was also increased to a lesser degree in NHW women and was not statistically significant. Neither family history of breast or ovarian cancer conferred a statistically significant risk for EOC in Hispanic or NHW women. It is noteworthy, however, that risk of EOC in Hispanic women with a family history of breast cancer (FHBC) was elevated while it was not in NHW. The opposite pattern occurred with family history of ovarian cancer (FHOC) as EOC risk was elevated in NHW women and not in Hispanic women.

Tubal ligation offered slight but not statistically significant protection from EOC for both Hispanic and NHW women. However, hysterectomy appeared to increase risk in

Table 1: Descriptive characteristics of EOC cases and controls in California's Central Valley by race/ethnicity, 2000-2001

Factor	Hispanic Women		Non-Hispanic White Women		All Women	
	Cases n (%) n=45	Controls n (%) n=203	Cases n (%) n=190	Controls n (%) n=815	Cases n (%) n=256	Controls n (%) n=1122
Mean age at Interview	47.0	49.5	59.4	56.9	56.6	55.0
Age Group						
<40	10 (22.2)	41 (20.2)	8 (4.3)	55 (6.7)	20 (7.8)	113 (10.0)
40-49	20 (44.4)	79 (38.9)	42 (22.1)	210 (25.8)	68 (26.6)	321 (28.6)
50-59	9 (20.0)	38 (18.7)	46 (24.2)	205 (25.2)	60 (23.4)	273 (24.3)
60-69	3 (6.7)	19 (9.4)	47 (24.7)	179 (22.0)	57 (22.3)	214 (19.1)
>70	3 (6.7)	26 (12.8)	47 (24.7)	166 (20.4)	51 (19.9)	201 (17.9)
Education						
<High School Graduate	18 (40.0)	120 (59.1)	14 (7.4)	77 (9.4)	34 (13.3)	209 (18.6)
High School Graduate	15 (33.3)	33 (16.3)	70 (36.8)	202 (24.8)	88 (34.4)	266 (23.7)
>High School Graduate	11 (24.4)	50 (24.7)	105 (55.3)	535 (65.6)	132 (51.6)	646 (57.6)
Don't know/Refused	1 (2.2)	0(0)	1 (0.5)	1 (0.1)	2 (0.8)	1 (0.1)
Marital Status						
Single	12 (26.7)	28 (13.8)	15 (7.9)	64 (7.9)	32 (12.5)	112 (10.0)
Married	23 (51.1)	130 (64.0)	109 (57.4)	492 (60.4)	139 (54.3)	679 (60.5)
Divorced/Separated	7 (15.6)	22 (10.8)	30 (15.8)	144 (17.7)	41 (16.0)	180 (16.0)
Widowed	3 (6.7)	22 (10.8)	36 (18.9)	113 (13.9)	44 (17.2)	147 (13.1)
Don't know/Refused	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.2)	0 (0.0)	4 (0.4)
Birthplace (%)						
In U.S.	29 (64.4)	81 (39.9)	182 (95.8)	771 (94.6)	223 (87.1)	934 (83.2)
Outside U.S.	16 (35.6)	122 (60.1)	8 (4.2)	44 (5.4)	33 (12.9)	188 (16.8)

Hispanic women, although the finding was not statistically significant, while there was no relationship between hysterectomy and EOC in NHW women.

Use of oral contraceptives did not appear to protect Hispanic women from EOC as it did for NHW women. Increased EOC risk with Hormone Replacement Therapy (HRT) was observed in both Hispanic and NHW women but was statistically significant only with the latter group.

Discussion

The younger age of both Hispanic cases and controls is explained by national, state, and local demography. A recent National Cancer Institute monograph (13) reported that Mexican American females are 8 years younger that all other U.S. females. Statistics from the California Health Interview Survey (14) indicate that the age distribution for NHW women in California is about 50% < 40 years of age and 50% ≥ 40 years of age. For Hispanic women the distribution is quite different with 78% < 40 years of age and 22% ≥ 40 years of age. The survey found a similar distribution for Central Valley women.

Hispanic women in California experience a higher proportion of borderline tumors in comparison to NHW women, especially papillary serous cystadenoma (16). This finding was confirmed by the present study. However, a recent descriptive study of the epidemiology of ovarian cancer in the United States, (17) although confirming papillary serous cystadenoma as the most common borderline tumor in Hispanic women, found that the age specific incidence rate for borderline ovarian tumors was higher in Hispanics versus NHWs only until ages 25-29. Thereafter the rates were similar. California and national incidence rate differences may be due to the proportion of Hispanic subgroups unique to each population. For example, 60% of the Hispanics in the United States are represented by Mexican Americans however in California they constitute 77% of the Hispanic population (9, 13).

In the present study, risk of EOC was decreased in Hispanic women born outside of the U.S. when compared to women born in the U.S. Women in more developed countries are at almost twice the risk for ovarian cancer as those women in less developed countries (18) and this difference is likely due to reproductive experiences. Previous

Table 2: Distribution of EOC cases by invasiveness/histology and race/ethnicity in the Central Valley of California, 2000-2001

Histology	Hispanic Women n=45	NHW Women n =190	All Women n=256
	n (%)	n (%)	n (%)
All Invasive	25 (55.6)	141 (74.2)	182 (71.1)
Serous Invasive	13 (28.9)	72 (37.9)	92 (35.9)
Mucinous Invasive	1 (2.2)	12 (6.3)	16 (6.3)
Endometrioid	6 (13.3)	25 (13.2)	35 (13.7)
Clear Cell	0 (0.0)	11 (5.8)	12 (4.7)
Other Epithelial	5 (11.1)	21 (11.1)	27 (10.5)
All Borderline	20 (44.4)	49 (25.8)	74 (28.9)
Serous Borderline	17 (37.8)	34 (17.9)	55 (21.5)
Mucinous Borderline	3 (6.7)	15 (7.9)	19 (7.4)

studies have clearly shown that breast cancer incidence in both Hispanics and Asians increases with U.S. acculturation, time since migration, U.S. birth versus birth in country of origin and number of generations since birth in the country or origin (19-22).

In a study of migration status and risk of EOC in Asian immigrants, younger women (<50 years) born in the U.S. had incidence rates similar to NHW while birthplace had no affect on incidence rates in older (50+years) women (4).

Level of education is one measure used in determining socioeconomic status (23-25) and socioeconomic status has been found to be positively associated with ovarian cancer risk, (23-26) that is consistent with our findings of higher risk associated with higher education among Hispanic cases.

Our findings concerning reproductive factors and EOC risk in Hispanic women generally confirm findings of a hospital based case-control study conducted in Mexico City (27). The Mexican study found that a larger proportion of controls had at least one pregnancy compared to cases and that risk was decreased in parous women.

However, a statistically significant trend for decreasing risk with increasing parity was found in that study, which we did not find. Another difference between the two studies was risk associated with age at first birth. The Mexico City study found a statistically significant increase in risk with age at first birth ≥ 26 years while the present study found a decrease risk with first birth ≥ 25 years that was not statistically significant. Both studies found a statistically significant decrease in EOC risk with a history of breastfeeding.

In general, the present study found that reproductive factors affected EOC risk similarly in Hispanic and NHW women. The protection offered by pregnancy and parity has been well documented in the literature (28) and was confirmed in both ethnic groups of this study. Age at first birth's effect on EOC risk is less clear, however, the differences may be due to selection of controls. Studies with hospital controls have generally found increased EOC risk with increased age at first birth while

Table 3: Frequencies[1], multivariate-adjusted odds ratios (OR) and 95% Confidence Intervals (95%CI) for EOC risk modifiers in Hispanic and NHW women in the Central Valley of California, 2000-2001

Factor	Hispanic Women			Non-Hispanic White Women		
	Cases n (%) n=45	Controls n (%) n=203	MV-Adjusted OR[2] (95% CI)	Cases n (%) n=190	Controls n (%) n=815	MV-Adjusted OR[3] (95% CI)
Birthplace						
In the U.S.	29 (64.4)	81 (39.9)	1.0	182 (95.8)	771 (94.6)	1.0
Outside the U.S.	16 (35.6)	122 (60.1)	**.34 (.16-.73)**	8 (4.2)	44 (5.4)	.76 (.34-1.68)
Education Level						
< High School	18 (40.9)	120 (59.1)	1.0	14 (7.4)	77 (9.5)	1.0
≥ High School Graduation	26 (59.1)	83 (40.9)	1.07 (.44-2.57)	175 (92.6)	737 (90.5)	1.48 (.80-2.74)
Ever Pregnant[4]						
No	6 (13.3)	9 (4.5)	1.0	27 (14.2)	57 (7.0)	1.0
Yes	39 (86.7)	193 (95.5)	.49 (.14-1.71)	163 (85.8)	758 (93.0)	**.52 (.30-.91)**
Ever Parous[5]						
No	1 (2.6)	1 (0.5)	1.0	13 (8.0)	16 (2.1)	1.0
Yes	38 (97.4)	192 (99.5)	0.36 (.02-6.21)	150 (92.0)	742 (97.9)	**0.31 (.14-.69)**
Number of live births						
1-2	20 (52.6)	61 (31.8)	1.0	79 (52.7)	400 (53.9)	1.0
3-4	9 (23.7)	72 (37.5)	**0.34 (.13-.85)**	63 (42.0)	270 (36.4)	1.01 (.69-1.49)
>4	9 (23.7)	59 (30.7)	0.82 (.29-2.28)	8 (5.3)	72 (9.7)	0.49 (.22-1.08)
Age at First Birth						
< 25 years	32 (84.2)	144 (75.4)	1.0	112 (74.7)	489 (66.0)	1.0
≥ 25 years	6 (15.8)	47(24.6)	0.50 (.18-1.35)	38 (25.3)	252 (34.0)	0.77 (.51-1.16)
Ever Breastfed[6]						
No	20 (52.6)	45 (23.4)	1.0	66 (44.0)	235 (31.7)	1.0
Yes	18 (47.4)	147 (76.6)	**0.34 (.16-.72)**	84 (56.0)	506 (68.3)	**0.67 (.46-.96)**
Body Mass Index						
<25 kg/m^2	10 (22.7)	63 (35.6)	1.0	71 (37.8)	378 (46.6)	1.0
≥25 kg/m^2	34 (77.3)	114 (64.4)	**2.51 (1.08-5.82)**	117 (62.2)	433 (53.4)	1.38 (.99-1.93)
Family History of Breast Cancer						
No	41 (91.1)	194 (95.6)	1.0	162 (86.2)	696 (85.9)	1.0
Yes	4 (8.9)	9 (4.4)	2.11 (.54-8.30)	26 (13.8)	114 (14.1)	0.88 (.55-1.42
Family History of Ovarian Cancer						
No	43 (95.6)	192 (96.0)	1.0	168 (90.8)	748 (94.3)	1.0
Yes	2 (4.4)	8 (4.0)	1.08 (.21-5.58)	17 (9.2)	45 (5.7)	1.74 (.95-3.19
Tubal Ligation						
No	32 (71.1)	130 (65.0)	1.0	157 (83.1)	614 (75.5)	1.0
Yes	13 (28.9)	70 (35.0)	0.68 (.30-1.50)	32 (16.9)	199 (24.5)	0.78 (.51-1.21
Hysterectomy ≥ 2 yrs						
No	37 (82.2)	180 (89.1)	1.0	145 (76.3)	657 (80.7)	1.0
Yes	8 (17.8)	22 (10.9)	2.27 (.82-6.30)	45 (23.7)	157 (19.3)	1.06 (.70-1.61
Oral Contraceptive use						
No	16 (35.6)	82 (40.6)	1.0	82 (43.2)	259 (31.8)	1.0
Yes	29 (64.4)	120 (59.4)	0.95 (.41-2.17)	108 (56.8)	556 (68.2)	**0.68 (.46-.99)**
HRT						
Never to < 1 yr	37 (82.2)	172 (85.1)	1.0	95 (50.8)	496 (61.1)	1.0
≥ 1 year	8 (17.8)	30 (14.9)	1.49 (.54-4.09)	92 (49.2)	316 (38.9)	**1.50 (1.04-2.14**

[1] For some factors the sum does not add up to the total due to missing values
[2] Adjusted for age, birthplace (in or outside U.S.), ever breastfed and body mass index
[3] Adjusted for age, ever parous, ever breastfed, body mass index, ever oral contraceptive use and ever hormone replacement therapy
[4] Ever parous taken out of the model
[5] Gravid women only
[6] Parous women only

population-based studies and prospective studies have either found no relationship or a decreased risk with increase age at first birth (28). The stronger protective relationship for breastfeeding and EOC in Hispanic women found by the present study was not explained by either increased months of breastfeeding nor due to increased numbers of live births (data not shown).

The striking increase in risk of EOC for overweight or obese Hispanic women in comparison to NHW bears further study since it is a preventable risk factor. A study of Hispanic immigrants to Washington state (29) found that highly acculturated Hispanics had a higher fat intake and less fruit and vegetable intake than their less acculturated counterparts. Kuper et al. (30) reported a positive relationship between BMI and EOC risk only in premenopausal women, and specifically for serous borderline ovarian cancer, possibly due to an increase in circulating insulin and androgens. Both have been implicated in ovarian carcinogenesis (30, 31). This hypothesis may explain the younger age of Hispanic EOC cases compared to NHW EOC cases in California as well the increase proportion of serous borderline tumors reported in California Hispanic women16 as well as in the present study.

The literature is quite limited in addressing the relationship between family history of breast or ovarian cancer and EOC risk in Hispanic women. Studies have reported increased risk of breast cancer in Hispanic women with a first-degree relative with breast cancer (32) and that Hispanic women with a positive family history of breast cancer were at increased risk for breast cancer compared to NHW with a family history of breast cancer (33). A California population study (34) found that risk of breast and ovarian cancer in mothers of Hispanic ovarian and breast cancer probands was elevated and similar to rates in NHW. Specific rates for ovarian cancer probands were not calculated. The percentage of Hispanic ovarian probands with a first degree relative with breast or ovarian cancer was 11.5% (3 out of 23 cases) and 22.1% for NHW (40 out of 141 cases). The present study found that 11.1% (5 out of 17 cases) of Hispanic cases and 21.1% (40 out of 150 cases) of NHW cases reported a first degree relative with breast or ovarian cancer (data not shown). We have no explanation for why Hispanic women appear to be at increase EOC risk with a FHBC but not with a FHOC while NHW women appear to be at increase risk with a FHOC but not with a FHBC. Further multi-ethnic population studies with a larger population of woman with positive family histories of breast or ovarian cancer are needed to validate and explain this finding.

To our knowledge, the relationship between tubal ligation and/or hysterectomy and EOC risk has not been evaluated in Hispanic women. Ness et al (35) reported that African-American women experienced protection almost equal to that for White women from both tubal ligation and hysterectomy, although the protection from hysterectomy was slight and not statistically significant. Our lack of significant findings for tubal ligation and protection from EOC is due to the relatively small sample size and number of exposed women.

The large proportion of Hispanic cases reporting a history of hysterectomy and resulting over two-fold increase in risk for EOC, although not statistically significant, may be explained by the fact that our Hispanic cases series appear to more acculturated than the control series in terms of education and birth in the U.S. and thus may chose hysterectomy as a medical option more frequently than less acculturated Hispanic women. The California Health Interview Survey14 has calculated the estimated prevalence of hysterectomy as 21.7% in NHW women and 8.8% in Hispanic women. Similarly, in the Central Valley of California, 24.7% of NHW and 8.9% of Hispanics reported having a hysterectomy, similar to what was reported in the control series of the present study.

Oral contraceptive use did not appear to be protective for EOC in Hispanic women. Riman et al. (36) found that oral contraceptive use was not protective for borderline tumors, which may explain the lack of protection for EOC in Hispanic women. A hospital-based study in Mexico City (27) found a positive trend for increased protection with increased duration of use of oral contraceptives. However, the use patterns for oral contraceptives were quite different from use patterns noted in the present study in which use of OC was much higher for both cases and controls.

HRT use increased risk for EOC similarly for both Hispanic and NHW however was not statistically significant in the former group due to the small number of women ever using HRT. However, in a study of Mexico City women there appeared to be no relationship between HRT use and EOC risk although use was approximately 30-40% of that in the present study (27).

The strength of this study is that it is the first attempt, to our knowledge, to analyze established factors related to the risk of EOC in Hispanic women of the United States. The Central Valley

of California affords a unique setting for such a study due to the large concentration of Hispanic women, primarily of Mexican descent.

Misclassification of race/ethnicity was minimized by using self-identification rather than third party classification.

There are several limitations to this study. We did not ask a question to clarify what Hispanic subgroup the participant identified. Since we did not frequency match on age within ethnic groups, there appears to be a selection bias towards younger Hispanic women for both cases and controls. The sample size available for analysis was based upon only a 24- month period of accrual and this limits our statistical power in many instances especially where exposure prevalence was low. Additionally, the low incidence of the disease in Hispanic women resulted in a relatively small number of Hispanic cases limiting the interpretation of findings due to lack of statistical significance. Although the response fraction was somewhat low for the entire cases series, the response fraction for identified Hispanic women was 64%. The histologic distribution of Hispanic women with EOC was not statistically different between interviewed and non-interviewed (p=.81).

In conclusion it may be that as Hispanic women of California become more acculturated their risk of EOC may approximate that of California NHW women. California Hispanic women experience a higher risk of borderline tumors, which may be related to body size. In general, reproductive factors affect EOC risk similarly in Hispanic and NHW women. Further study of ovarian cancer in Hispanic women and in specific Hispanic subgroups is indicated.

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References

1. Kwong SL, Perkins C, Morris CR, Cohen R, Allen M, Wright W. Cancer in California, 1988-1999. Sacramento CA: California Dept. of Health Services, Cancer Surveillance Section, 2001.
2. Mori M, Harabuchi I, Miyake H, Casagrande JT, Henderson BE, Ross RK. Reproductive, genetic and dietary risk factors for ovarian cancer. Am J Epidemiol 128(4): 771-777, 1988.
3. John EM, Whittemore AS, Harris R, Itnyre J. Characteristics relating to ovarian cancer risk: collaborative analysis of seven U.S. case-control studies. Epithelial ovarian cancer in black women. Collaborative Ovarian Cancer Group. J Natl Cancer Inst 85(2): 142-147, 1993.
4. Herrinton LJ, Stanford JL, Schwartz SM, Weiss NS. Ovarian cancer incidence among Asian migrants to the United States and their descendants. J Natl Cancer Inst 86(17):1336-1339, 1994.
5. Ness RB, Grisso JA, Klapper J, Vergona R. Racial differences in ovarian cancer risk. J Natl Med Assoc 92:176-182, 2000.
6. Population Division, U.S. Census Bureau. Table 4: Annual estimates of the population by sex and age of Hispanic or Latino origin for the United States: April 1, 2000 to July 1, 2003. Release date June 14, 2004
7. U.S. Census Bureau. 1990 Census Summary Tape File 3. Retrieved from http://homer.ssd.census.gov/cdrom/lookup on June 15, 2004.
8. California Department of Finance Demographic Research Unit. Census 2000, SF1: Selected racial groups and specific origins of Hispanic or Latino Profiles. Available at: http://www.dof.ca.gov . Retrieved April 28, 2004.
9. California State Census Data Center. U.S. Census Bureau, Census 2000 of population and housing, Summary File 1. Available at: http://www.dof.ca.gov . Retrieved April 28, 2004.
10. Ferrier A. Mullerian epithelial and mesenchymal tumors – introduction, clinical perspective, and principles of management. In: Surgical Pathology of the Ovary, 2nd ed (Farnsworth RP, ed). Churchill Livingstone, New York, 1997, pp 229-238.

11. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Ins 22:719-748, 1959.
12. Breslow NE, Day NE. Statistical Methods in Cancer Research. Volume1-The Analysis of Case-Control Studies. International Agency for Research on Cancer, Lyon, France, 1980.
13. Ramirez AG, Suarez LC. Cancer in Mexican American Women. In: Cancer in Women of Color Monograph (Glanz K, ed). Department of Health and Human Services, National Cancer Institute, Bethesda, MD, 2003.
14. California Health Interview Survey. CHIS 2001 Adult Public use File, Release 2 [computer file]. UCLA Center for Health Policy Research, Los Angeles, 2002.
15. SEER Program (www.seer.cancer.gov) SEER*Stat Database: California incidence 1988-2000, February 2003 Submission, 3/19/2003, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch.
16. Perkins CI, Cohen R, Young JL, Schlag R, Wright WE. Cancer in California: Detailed Site and Histology, 1990-1994. California Dept. of Health Services, Cancer Surveillance Section, Sacramento, CA, 1997.
17. Goodman MT, Howe HL, Tung KH, Hotes J, Miller BA, Coughlin SS, Chen VW. Incidence of ovarian cancer by race and ethnicity in the United States, 1992-1997. Cancer 97(10 Suppl): 2676-2685, 2003.
18. GLOBOCAN 2000. Cancer incidence, mortality and prevalence worldwide, Version 1.0. IARC Cancer Base No. 5. IARC Press, Lyon, 2001.
19. Ziegler RG, Hoover RN, Pike MC, Hildesheim A, Nomura AMY, West DW, Wu-Williams AH, Kolonel LN, Horn-Ross PL, Rosenthal JF, Hyer MB. Migration patterns and breast cancer risk in Asian-American women. J Natl Cancer Inst 85(22):1819-1827, 1993.
20. Stanford JL, Herrinton LJ, Schwartz SM, Weiss NS. Breast cancer incidence in Asian migrants to the United States and their descendants. Epidemiology 6(2): 181-183, 1995.
21. Deapen D, Lui L, Perkins C, Bernstein L, Ross RK. Rapidly rising breast cancer incidence rates among Asian-American women. Int J Cancer 99(5):747-750, 2002.
22. Pike MC, Kolonel LN, Henderson BE, Wilkens LR, Hankin JH, Feigelson HS, Wan PC, Stram DO, Nomura AMY. Breast cancer in a multiethnic cohort in Hawaii and Los Angeles: risk factor-adjusted incidence in Japanese equals and in Hawaiians exceeds that in whites. Cancer Epidemiol Biomarkers Prev 11(9):795-800, 2002.
23. Lui L, Deapen D, Bernstein L. Socioeconomic status and cancers of the female breast and reproductive organs: a comparison across racial/ethnic populations in Los Angeles County, California (United States). Cancer Causes Control 9(4):369-380, 1998.
24. La Vecchia C, Negri E, Franceschi S. Education and cancer risk. Cancer 70(12):2935-2941, 1992.
25. World Health Organization. Quantifying Selected Major Risks to Health. In: The World Health Report 2002. France:World Health Organization, pp. 47-97, 2002.
26. Faggiano F, Partanen T, Kogevinas M, Boffetta P. Socioeconomic differences in cancer incidence and mortality. IARC Sci Publ 138:65-176, 1997.
27. Salazar-Martinez E, Lazcano-Ponce EC, Lira-Lira GG, Escudero-De los Rios P, Salmeron-Castron J, Hernandez-Avila M. Reproductive factors of ovarian and endometrial cancer risk in a high fertility population in Mexico. Cancer Res 59:3658-3662, 1999.
28. Riman T, Persson I, Nilsson S. Hormonal aspects of epithelial ovarian cancer: review of epidemiological evidence. Clin Endocrinol (Oxf) 49:695-707, 1998.
29. Neuhouser ML, Thompson B, Coronado GD, Solomon CC. Higher fat intake and lower fruit and vegetables intakes are associated with greater acculturation among Mexicans living in Washington state. J Am Diet Assoc 104(1):51-57, 2004.
30. Kuper H, Cramer DW, Titus-Ernstoff L. Risk of ovarian cancer in the United States in relation to anthropometric measures: does the association depend on menopausal status. Cancer Causes Control 13:455-463, 2002.
31. Risch HA. Hormonal etiology of epithelial ovarian cancer, with a hypothesis concerning the role of androgens and progesterones. J Natl Cancer Inst 90:1774-1786, 1998.
32. Mayberry RM, Branch PT. Breast cancer risk factors among Hispanic women. Ethn Dis 4(1):41-46, 1994.
33. Li R, Gilliland FD, Baumgartner KB, Samet J. Family history and risk of breast cancer in Hispanic and non-Hispanic women: the New Mexico Women's Health Study. Cancer Causes Control 12(8):747-753, 2001.
34. Ziogas A, Gildea M, Cohen P, Bringman D, Taylor TH, Seminara D, Barker D, Casey G, Haile R, Liao S-Y, Thomas D, Noble B, Kurosaki T, Anton-Culver H. Cancer risk estimates for family member of a population-based family registry for breast and ovarian

cancer. Cancer Epidemiol Biomarkers Prev 9:103-111, 2000.

- Ness RB, Grisso JA, Klapper J, Vergona R. Racial differences in ovarian cancer risk. J Natl Med Assoc 92:176-182, 2000.
- Riman T, Dickman PW, Nilsson S, Correia N, Nordlinder H, Magnusson CM, Persson IR. Risk factors for epithelial borderline ovarian tumors: results of a Swedish case-control study. Gynecol Oncol 83:575-585, 2001.