Differences in Breast Cancer Subtypes Among Racial/Ethnic Groups

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Abstract

Purpose

Differences in incidence of breast cancer subtypes among racial/ethnic groups have been evaluated as a contributing factor in the disparities seen in breast cancer prognosis. We evaluated new breast cancer cases in Hawaii to determine if there were subtype differences according to race/ethnicity that may contribute to known disparities.

Methods

We reviewed 4,318 cases of women diagnosed with breast cancer from two large tumor registries between 2013-2020. We evaluated the new breast cancer cases according to age at diagnosis, self-reported race, and breast cancer subtype (ER, PR, and HER2 receptor status).

Results

We found both premenopausal and postmenopausal Native Hawaiian women were less likely to be diagnosed with triple negative breast cancer (OR=0.33, P=0.009; OR=0.62, P=0.03 respectively). Premenopausal Japanese women were 71% less likely to be diagnosed with triple positive (ER+/PR+/HER2+) breast cancer (OR=0.29, P=0.0003). Postmenopausal Filipino women were 89% more likely to be diagnosed with ER-/PR-/HER2+ breast cancer (OR=1.89, P=0.02).

Conclusions

Results of our study support that there are racial/ethnic differences in breast cancer subtypes among our population which may contribute to the differences in outcome seen. Further evaluation of other clinical and pathological features in each breast cancer subtype may inform potential mechanisms for outcome disparities seen among different racial/ethnic groups.

Introduction

Extensive research has been done evaluating the heterogeneous nature of breast cancer according to subtypes and its variable impact among different populations. The prognostic importance of this heterogeneity is complicated by a wide array of underlying behavioral, environmental, social, economic, and biological factors. Race/ethnicity has been shown to be a correlative factor with differences in risk and clinical outcomes of certain breast cancer subtypes. The Carolina Breast Cancer study showed that the triple negative (TN) subtype (ER-/PR-/HER2-) was significantly more prevalent and luminal A subtype (ER+/PR+/HER2+ or ER+/PR-/HER2+ or ER-/PR+/HER2+) was significantly less prevalent, among premenopausal Black women compared to postmenopausal black and white women of all ages [1]. These findings suggested that a higher prevalence of triple-negative and lower prevalence of luminal A tumors among premenopausal Black women could explain poor prognosis and higher mortality rates seen [1-2].

The results of these studies highlight differences in tumor biology which may contribute to mortality disparities seen between Black and White women.

There are known racial/ethnic disparities between different groups in Hawaii's population. The ethnic population of Hawaii is diverse. Hawaii has no racial/ethnic majority group, based on population size. About half of the population is of Asian heritage (Japanese, Filipino, Korean, Chinese), about a quarter is of European ancestry (White), and about 20% is Native Hawaiian [3]. Loo et al. examined differences in incidence and mortality among women who were diagnosed with invasive breast cancer between 1984-2013 and are of the five major racial/ethnic populations in Hawai'i: Native Hawaiian, Non-Hispanic White, Japanese, Chinese, and Filipino. Mortality rates for most individual Asian subpopulations (i.e. Japanese, Chinese, Filipino) were lower compared to Non-Hispanic White women however Native Hawaiians had the highest mortality rates overall [4]. Native Hawaiians consistently had the highest incidence and mortality rates compared to all racial/ethnic groups in Hawaii and were disproportionately affected by poorer survival for both localized and advanced stages at time of diagnosis [4]. The most common breast cancer subtypes among all patients between 2010-2013 was hormone positive (ER+/PR+/HER2- or ER+/PR-/HER-), followed by TN and HER2+ (ER-/PR-/HER2+) subtypes [4]. Japanese and Native Hawaiians had higher incidence rates of HR+ (ER+/PR+/HER2- or ER+/PR-/HER2- or ER-/PR+/HER2-) breast cancer compared to Non-Hispanic Whites. Japanese women had higher incidence rates of triple negative compared to Non-Hispanic Whites.

To better understand these differences, we evaluated new breast cancer diagnosis from two major health systems in Hawaii from 2013-2020. We found differences in breast cancer subtypes among racial/ethnic groups in Hawai'i's uniquely diverse population.

Methods

Data was collected from the Hawai'i Pacific Health Tumor Registry of women who had a diagnosis of breast cancer between January 1, 2013-December 31, 2019, as well as the Queens Tumor Registry of women who had an initial date of diagnosis between January 1, 2015 and August 31, 2020. We evaluated patient age at diagnosis, race, and breast cancer subtype according to ER, PR, and HER2 receptor status.

Race was self-reported and categorized according to six racial/ethnic groups: Asian, Filipino, Native Hawaiian (NH), Japanese, Other, and White. The racial/ethnic category designated as 'Other' encompassed women who have racial/ethnic backgrounds including Samoan, Micronesian, Tongan, Chamorro, Black, American Indian/Aleutian/Eskimo, Asian Indian/Pakistani, and Kampuchean. Racial/ethnic groups were identified using the first race/ethnicity group listed. For women with multiple ethnicities, the first race/ethnicity was selected.

METRIQ software was used for data collection and management. The SAS 9.4 (SAS Institute Inc., Cary, NC) software performed all analysis. The LOGISTIC procedure applied multinomial logistic regression analyses on the four-category subtype outcome variable with race as the predictor. Separate models were run for pre- (under or at age 50) and post-menopausal (over age 50) patients.

Results

A total of 4,318 cases were evaluated. Of those cases, 953 (22.1%) were age 50 or younger (premenopausal) and 3,365 (77.9%) were over the age of 50 (postmenopausal) (Table 1). The most commonly represented ethnicity was Japanese with a total of 1199 cases (27.8%), followed by White with 938 cases (21.7%), Filipino with 765 cases (17.7%), Native Hawaiian with 709 (16.4%), Asian with 468 cases (10.8%), and Other with 239 cases (5.5%) (Table 1). The most common subtype was hormone positive (ER+ or PR+/HER2-) with a total of 3333 cases (77.2%), followed by triple positive (ER+/PR+/HER2+) with 403 cases (9.3%), triple negative (ER-/PR-/HER2-) with 383 cases (8.87%), and HER2+ (ER-/PR-/HER2+) with 199 cases (4.6%) (Table 1).

Table 1 Patient age, ethnicity and breast cancer subtype

		N	%
Age	≤50	953	22.1
	>50	3365	77.9
Ethnicity	Asian	468	10.8
	Filipino	765	17.7
	Native Hawaiian	709	16.4
	Japanese	1199	27.8
	Other	239	5.5
	White	938	21.7
Subtype	ER-/PR-/HER2-	383	8.87
	ER+ or PR+/HER2-	3333	77.2
	ER-/PR-/HER2+	199	4.6
	ER+ or PR+/HER2+	403	9.3

For premenopausal women, we found differences in subtype for Native Hawaiian women, Japanese women, and women who identified as a racial/ethnic background represented in Other. Premenopausal Native Hawaiian women were 67% less likely to be diagnosed with TN breast cancer (OR=0.33, P=0.009) (Table 2). Premenopausal Japanese women were 71% less likely to be diagnosed with triple positive breast cancer (OR=0.29, P=0.0003) (Table 2). Premenopausal women of a racial background represented in Other were 3.74-fold more likely to be diagnosed with HER2+ breast cancer (OR=3.74, P=0.007) (Table 2).

Table 2 Breast cancer subtype according to race/ethnicity in premenopausal women

Age	Race	N	%	ER-/PR-/HER2-				ER+ or PR+/HER2-				ER-/PR-/HER2+				ER+ or PR+/HER2+			
				N	%	OR	P	N	%	OR	P	N	%	OR	P	N	%	OR	P
≤50	Asian	113	11.9	12	10.6	0.79	.54	77	68.1	1.00		7	6.2	1.15	.78	17	15.0	0.85	.62
	Filipino	207	21.7	14	6.8	0.51	.06	139	67.1	1.00		18	8.7	1.64	.23	36	17.4	1.00	.99
	Native Hawaiian	161	16.9	8	5.0	0.33	.009	124	77.0	1.00		4	2.5	0.41	.14	25	15.5	0.78	.39
	Japanese	223	23.4	22	9.9	0.64	.15	175	78.5	1.00		13	5.8	0.94	.89	13	5.8	0.29	.0003
	Other	54	5.7	4	7.4	0.60	.37	34	63.0	1.00		10	18.5	3.74	.007	6	11.1	0.68	.42
	White	195	20.5	25	12.8	1.00		127	65.1	1.00		10	5.1	1.00		33	16.9	1.00	

For postmenopausal women, Filipino women were 89% more likely to be diagnosed with HER2+ breast cancer (OR=1.89, P=0.02) compared to White women (Table 3). In addition, postmenopausal Native Hawaiian women were 38% less likely to be diagnosed with TN breast cancer (OR=0.62, P=0.3) (Table 3).

Table 3 Breast cancer subtype according to race/ethnicity in postmenopausal women

Age	Race	N		ER-/PR-/HER2-				ER+ or PR+/HER2-				ER-/PR-/HER2+				ER+ or PR+/HER2+			
				N	%	OR	P	N	%	OR	P	N	%	OR	P	N	%	OR	P
>50	Asian	355	10.5	32	9.0	0.97	.90	268	75.5	1.00		17	4.8	1.38	.31	38	10.7	1.46	.09
	Filipino	558	16.6	60	10.8	1.18	.38	415	74.4	1.00		36	6.5	1.89	.02	47	8.4	1.17	.46
	Native Hawaiian	548	16.3	34	6.2	0.62	.03	445	81.2	1.00		16	2.9	0.78	.44	53	9.7	1.23	.31
	Japanese	976	29.0	85	8.7	0.87	.41	797	81.7	1.00		34	3.5	0.93	.77	60	6.1	0.78	.19
	Other	185	5.5	15	8.1	0.84	.57	145	78.4	1.00		7	3.8	1.05	.91	18	9.7	1.28	.39
	White	743	22.1	72	9.7	1.00		587	79.0	1.00		27	3.6	1.00		57	7.7	1.00	

Discussion

Our findings show racial/ethnic differences in breast cancer subtype according to menopausal status. It is well established that there are racial/ethnic disparities in breast cancer prognosis in Hawai'i. Loo et al. showed that the Native Hawaiian (NH) population experiences the poorest survival for both localized and advanced stage breast cancer of all racial/ethnic groups in Hawai'i and suggested that these poor outcomes may be due to biological factors [3]. Given these findings, it was expected that NH women would be more likely to have more aggressive breast cancer subtypes such as TN breast cancer. However, our data reveals that both premenopausal and postmenopausal NH women are more likely to have the hormone positive (ER+/PR+/HER2-) subtype rather than TN. Loo et al. found that NH women had a significantly higher incidence of hormone positive (ER+/PR+/HER2-), triple positive, and HER2+ breast cancer subtypes, compared to White women, but a significantly lower risk for the TN subtype, which is consistent with the results of our study [3]. These findings suggest that the poor outcomes that Native Hawaiian women with breast cancer experience may be due to factors other than subtype.

Conroy et al. conducted a multiethnic cohort study to examine the differential impact of obesity as a comorbidity on breast cancer survival. They showed that NH women with invasive breast cancer were more likely to have comorbidities such as obesity and cardiovascular disease compared to White, Japanese American, and Latino women. Compared to all other ethnic groups studied, obese NH women had a higher risk for all-cause mortality but a lower risk for breast cancer-specific mortality [5]. Another study conducted by Maskarinec et al. showed an inverse relationship between breast cancer-specific mortality and type 2 diabetes mellitus among NH women with invasive breast cancer [6]. They suggest that this may be due to the fact that NH women are more likely to have regular health visits for comorbidities and thus more likely to have early screening for breast cancer [6]. Nevertheless, these collective findings and the results of our study suggest that outcomes of NH women with breast cancer are multifactorial in nature.

Our findings show that premenopausal Japanese women are less likely to have the triple positive breast cancer subtype, which is consistent with findings in California-based studies that Japanese women were found to have lower rates of triple positive and TN breast cancer [7, 8]. In Hawai'i, Japanese women were found to have higher incidence rates of HR+ breast cancer compared to Whites, but Japanese women have lower 5-year mortality rates than White and NH women [3]. Japanese women in Hawai'i were also found to have a sharp increase in incidence of breast cancer which exceeds that of Whites but Japanese women have maintained relatively low mortality rates [3]. Improved clinical outcomes within this population may be directly attributed to higher incidence of the molecular subtypes associated with better outcomes, which may also be associated with higher rates for localized stage at diagnosis and smaller mean tumor size compared to other racial ethnic groups [3, 5]. Diagnosis at less advanced stages of disease may be due to

non-biological factors including access to and frequency of screening, and lower prevalence of comorbidities may play a role in clinical outcomes within this patient population.

Postmenopausal Filipino women were significantly more likely to have HER2+ breast cancer compared to Whites. This finding is consistent with California-based studies [7, 8]. Loo et al. also found that Filipino women with HER2+ breast cancer have poor 5-year survival rates compared to other racial/ethnic groups in Hawai'i [3]. These collective findings suggest that subtype may be a driving factor for clinical outcomes among postmenopausal Filipino women as these patients tend to have a poor prognosis, as measured by five-year survival for invasive breast cancer, compared to Japanese and White women [3].

We evaluated a significant number of new breast cancer cases from two major health systems in Hawaii. We recognize this is not a complete representation of our state based on the Hawaii Tumor Registry which reports an annual average number of new breast cancer cases of ~1,200 (Hawaii Tumor Registry-HTR, 2012-2016). In addition, there are other pathologic features that may contribute to clinical outcomes beyond subtype including grade, stage and treatment, which were not captured in this data review. Future studies evaluating these additional risk factors are underway and may help to further illuminate our understanding of the disparities we see.

Conclusion

Results of our study support that there are racial/ethnic differences in breast cancer subtypes among Hawaii's population which may contribute to the outcome differences seen. We are currently evaluating other clinical and pathological features in each breast cancer subtype to further evaluate the potential mechanisms for outcome disparities seen among different racial/ethnic groups in Hawaii.

Abbreviations

HTR-Hawaii Tumor Registry

NHPI-Native Hawaiian/Pacific Islanders

TN-Triple Negative

Declarations

Author's contributions

All authors made substantial contribution to conception and design, analysis and interpretation of data, and critical review of the manuscript. JF conceived of the study, coordinated the data acquisition and analysis, generated table and figures and helped to draft the manuscript. IP contributed to the statistical methods, data analysis, generated table and figures and helped to draft the manuscript. SB and AS

contributed to the data analysis and helped to draft the manuscript. EH and CJ contributed to the data analysis and helped to draft the manuscript. All authors read and approved the final manuscript

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Conflicts of interest/Competing interest

The authors declare that they have no competing interests.

Ethics approval and Consent to participate

The Institutional Review Boards at the University of Hawaii and Queens Medical Center approved this study. All aspects of the investigation complied with current rules for research involving Human Subjects.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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