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Nipple aspirate fluid producer status among premenopausal women in Hawaii

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To the Editor:

Nipple aspirate fluid (NAF) collection is a simple, non-invasive method to obtain breast fluid and ductal epithelial cells, thus providing information on cellular and non-cellular markers of breast cancer risk (1). However, not all women produce NAF (1,2). Diverse factors have been linked with NAF producer status from reproductive characteristics to ethnicity and dietary intake (2,3) while NAF producer status is associated with higher breast cancer risk in premenopausal women (4). The current study assessed the baseline characteristics of NAF producers vs. non-producers among premenopausal women who participated in a randomized, crossover soy intervention study (5). We also examined the influence of lifetime soy intake on NAF production given the low NAF production rates among Asians in whom soy consumption, especially in early life, is associated with protection against breast cancer (6).

Non-lactating women aged 18–50 years were recruited and prescreened by telephone (5). Of the 825 women who responded, 310 (38%) were eligible and proceeded to a screening visit. All participants completed demographic and lifetime soy food frequency questionnaires, weight and height measurements, and a NAF collection procedure. A lifetime soy food frequency questionnaire estimated the frequency of intake of soy food products, such as tofu and soymilk, from infancy through adulthood as weighted average servings/week.

NAF was collected by a trained staff member using a FirstCyte© Aspirator (7,8). Women were categorized as producers if they yielded any amount (>0 μL) from at least one breast. However, only women who produced ≥10 μL were eligible for the intervention study because a minimum collection of 10 μL was needed for planned lab analyses. Accordingly, we compared non-producers vs producers at the 0 μL and 10 μL cut points.

Demographic comparisons of non-producers vs. producers at the 0 μL and 10 μL levels were conducted using χ^2 for categorical variables and Student's t test for continuous variables. Women were categorized into 93 Caucasian, 128 Asian American and 89 Other (55 Native Hawaiian and Pacific Islander, 5 African American, 2 American Indian, 24 Latina, and 3 Other). Stepwise logistic regression models with an α-level of 0.10 explored the independent predictors of NAF producer status at the 0 μL level (>0 vs. 0 μL) and higher NAF volume at the 10 μL level (≥10 vs. <10 μL); potential predictors included ethnicity (Asian and Other vs. Caucasian as reference), age at screening (year; continuous), age at menarche (<13 vs. ≥13 years), parity (yes vs. no), body mass index (BMI; kg/m^2; continuous), and lifetime soy intake (≥2 vs. <2 servings/week).

Of the 310 women screened, 148 (48%) produced NAF (Table 1); of these, 112 (76%) produced ≥10 μL. NAF producers were older by 3 years ($p<0.001$), slightly heavier ($p=0.07$), and more likely to be parous than non-producers (68% vs. 53%; $p<0.01$). Age at first live birth ($p=0.41$), age at menarche ($p=0.40$) and lifetime soy intake ($p=0.31$) did not

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differ between producers and non-producers. Across ethnic groups, 55% of Caucasians, 40% of Asian Americans, and 52% of Others produced NAF. Asian women who produced NAF were more likely to be low producers; the proportion who produced ≥10 μL was 47% in Caucasians, 39% in Others, and 26% in Asian Americans ($p<0.01$). In the final model, producing any NAF was associated positively with older age at screening (OR: 1.06; 95% CI: 1.03–1.10) and negatively with Asian ethnicity (OR: 0.59; 95% CI: 0.37–0.94) whereas parity, age at menarche, BMI, Other ethnicity, and lifetime soy intake were not associated. At the 10 μL level, parity (OR: 2.10; 95% CI: 1.25–3.52) and younger age at menarche (<13 vs. ≥13 years; OR: 1.61; 95% CI: 0.98–2.63) were predictors of higher NAF production, while Asian (OR: 0.33; 95% CI: 0.19–0.60) and Other (OR: 0.59; 95% CI: 0.32–1.10) ethnicities were negatively associated.

In the current study among non-lactating, premenopausal women, NAF producers were older, more likely to be parous, and slightly heavier than non-producers, whereas Asian ethnicity was associated with being a non-producer. Mean age at menarche did not differ by producer status while younger age at menarche was weakly associated with higher NAF volume. Unlike a recent study (3), age at first live birth showed no relation with NAF producer status. A borderline difference in BMI noted between producers and non-producers was likely due to the lower BMI of Asian women in the non-producer category. Lifetime soy intake did not explain the lower NAF producer rate in Asians, which suggest that genetic or other unknown factors likely contribute to the lower proportion of NAF producers in this ethnic group. Further comparison of NAF producer status and additional cytologic evaluation within and across ethnic categories and regions may provide an important clue to further understanding varying breast cancer risk.

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Table 1

Characteristics of participants by NAF producer status, N= 310

		Non-producer	Producer			
NAF volume at screening		**0 μL**	**Any NAF**	***p* value**	**≥10 μL NAF**	***p* value**
N (%)		162 (52.3)	148 (47.7)		112 (40.9)	
Age (years)		37.0±8.1	40.2±6.4	**<0.001**	39.9±6.6	**<0.01**
Age at menarche (years)		12.7±1.6	12.5±1.5	0.40	12.5±1.5	0.30
Parity, N (%)	Yes	85 (52.5)	100 (67.6)	**<0.01**	77 (68.7)	**<0.01**
	No	77 (47.5)	48 (32.4)	---	35 (31.3)	---
Age at first live birth (years)		26.7±5.3	27.4±6.6	0.41	27.2±6.8	0.54
Body mass index (kg/m^2)		25.2±5.7	26.4±6.2	0.07	26.3±5.9	0.13
Ethnicity, N (%)	Caucasian	42 (45.2)	51 (54.8)	0.06	44 (47.3)	**<0.01**
	Asian American	77 (60.2)	51 (39.8)	---	33 (25.8)	---
	Other	43 (48.3)	46 (51.7)	---	35 (39.3)	---
Soy intake (servings per week) *	Early life (<20 years)	1.4±2.3	1.5±3.1	0.88	1.3±3.0	0.71
	Adult life (≥20 years)	3.2±4.7	3.6±4.5	0.43	3.7±4.7	0.36
	Lifetime	2.1±2.5	2.4±3.2	0.31	2.4±3.2	0.42

* N=308 for adult life (2 women are <20 years old)