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Disparity in Metabolic Conditions among Hispanic/Latina Women with Breast Cancer

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Abstract

Background: Breast cancer is the most common cancer in Hispanic/Latina women. Common metabolic conditions prevalent in American Hispanics include diabetes mellitus, dyslipidemia, hypertension, and obesity and have been associated with poor overall survival. The association of such coexisting conditions with breast cancer risk, treatment and breast cancer characteristics in this population is largely understudied. In this study, we sought to explore the prevalence of one or combination of these comorbid conditions with breast cancer and possible association with breast cancer characteristics and subtypes in a predominantly Hispanic patient population.

Methods: After IRB approval, we conducted a retrospective cross-sectional study of consecutive breast cancer patients treated in a University based tertiary medical center in the large border city of El Paso, TX. We evaluated the prevalence of 4 common metabolic conditions in a Hispanic patient population using the breast cancer center database of patients treated between 2005 and 2014. Adjusted association analyses were carried out using multiple Poisson regression analyses and results were presented with prevalence ratio (PR) and p-value.

Results: 1,003 patients with breast cancer were included in the analysis. The majority of patients had at least one comorbid condition (72%) with a high prevalence obesity 49.8% (95% CI: 24.58%, 30.1%), followed by hypertension, diabetes mellitus and dyslipidemia. After adjusting for variable of interests, the presence of all four comorbidities combined was associated with Estrogen Receptor positive (ER+)/Progesterone Receptor positive (PgR+) breast cancer subtype and Human Epidermal Receptor 2 neu negative ER+/PgR+/HER2 - status Presence of at least one of the comorbidities appeared to show a positive association with HER2 – subtype (PR=1.16, p=0.10) and ER+/PgR+/disease (PR=1.08, p=0.09).

Conclusion: Our study suggests an increased prevalence of diabetes, hyperlipidemia, hypertension and obesity in Hispanic woman with breast cancer, particularly in the hormone receptor positive group. These findings have potential implications, not only on raising awareness to screen for these conditions but possibly on future cancer preventive strategies in this underserved population. Further research is needed to confirm the increased risk of breast cancer in patients with metabolic co-morbidities and to elucidate potential underlying etiologies.

Keywords: Breast cancer; Hypertension; Hyperlipidemia; Diabetes mellitus

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Introduction

Breast cancer is the most common invasive cancer in women worldwide and the second most common cause of cancer death in women in the United States [1]. Individuals with breast cancer who also have common metabolic conditions or diseases such as diabetes mellitus (DM), dyslipidemia, hypertension, and obesity have been shown to have inferior survival overall [2]. Among women with early stage breast cancer, cardio-metabolic risk factors have been associated with cardiovascular and other-cause mortality, but not breast cancer mortality [3]. It remains unclear whether the complex aetiology of these comorbidities can lead to increased risk for breast cancer and whether it affects the severity of disease presentation. The presence of these comorbidities, however, increases the complexity of the decision-making process due to their significant impact on treatment and outcome. In the era of personalized medicine, it would be important to understand how common these conditions are and whether they are associated with different breast cancer characteristics. The association between potential breast cancer risk factors and the mechanism of disease is an active area of research and a better understanding of these correlations would provide guidance for developing more preventive and treatment strategies. The prevalence of cardiovascular risk factors in American Hispanics and their associated morbidity and mortality have been reported [4-6]. However, there is a paucity of literature regarding the prevalence of these factors among Hispanic breast cancer patients, a growing minority population. We aimed in this study at exploring the prevalence of hypertension, Diabetes Mellitus, dyslipidaemia, and obesity in Hispanic women with breast cancer and assess the potential association of these factors, individually or in combination with any breast cancer subtype. The city of El Paso, TX at the US-Mexico border region has a majority Hispanic population and provided the ideal setting for this study.

Methods

After obtaining Institutional Review Board (IRB) approval, we conducted a retrospective cross-sectional study utilizing the electronic medical database at a tertiary university based medical center. We identified all Hispanic women diagnosed with primary breast cancer consecutively between 2005 to 2014. We completed any missing diagnostic and comorbidities information of the target population using individual records from the cancer research core facility database housed at Texas Tech University Health Sciences Center in El Paso, TX. Age, Body mass index (BMI), ethnicity, breast cancer diagnosis, subtype, type of surgery and treatment, comorbidities including diabetes mellitus (DM), dyslipidemia, hypertension(HTN), obesity defined using Body Mass Index ≥ 30 kg/m^2, and coronary artery disease (CAD), as well as patient demographics and disease characteristics including menopausal status (by age older than 50 years), stage, estrogen receptor (ER), progesterone receptor (PgR) and Human epidermal receptor 2 neu (HER2) status were extracted from the database.

The primary exposure variable was defined in one of three ways:

- Presence of at least one comorbidity.
- Number of comorbidities.
- Individual comorbidities.

The primary outcome variables were considered as HER2+, ER+ or PgR+, Triple Negative Breast Cancer (TNBC if ER- and PR- and HER2-), Hormonal Positive (ER+ or PgR+), and ER+/PgR+ and HER2-. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Statistical considerations

The aim of this study was to determine the association of individual and combined comorbidities specifically DM, HTN, obesity and dyslipidemia with breast cancer and tumor characteristics. The quantitative variables were described using mean and standard deviation (SD) while categorical data were described using frequency and percentage. The prevalence of each comorbidity along with 95% confidence interval (CI) was estimated using binomial distribution. Clinical and tumor characteristics of the patients were compared based on DM status (yes *vs.* no), HTN status (yes *vs.* no), obesity status (yes *vs.* no), and dyslipidemia status (yes *vs.* no) using either unpaired t-test or Fisher's exact test. The adjusted effects of individual status of DM, HTN, obesity, and dyslipidemia on ER+, PgR+, HER2, HR, ER/PR+ and HER2-, and TNBC status were examined using multiple Poisson regression with robust variance analyses to obtain prevalence ratio (PR). Further, Poisson regression with robust variance analysis was carried out to determine adjusted effects of number of comorbidities and presence of any comorbidity on tumor characteristics. Variable were found to be statistically significant in the unadjusted analysis were considered in the multivariable models. The results of Poisson regression analysis were presented using Prevalence Ratio (PR) along with 95%CI and p-value. All statistical analyses were carried out using STATA 13.

Results

A total of 1,003 breast cancer patients were included in the analysis. Average age was 56 years (SD: 12) and average body mass index (BMI) was 30.7 Kg/m^2 (SD: 6.3) (**Table 1**). displays the patients' characteristics for the entire cohort and the presence of the metabolic cardiovascular risk factors of interest. Of total, 85% of the cohort were self-identified Hispanics. Pathological type and characteristics of breast cancer were distributed as follows: 86.7% invasive ductal carcinoma, 68% ER+ tumors, 57% PgR+, and 18.6% HER2+ tumors. One-third of the patients were pre-menopausal. Patients with presence of at least one metabolic condition were more likely to be older, post-menopausal, receive more lumpectomies compared to mastectomies, have more CAD, and have higher prevalence of ER+/PgR+ tumors. The highest prevalence was noted for obesity 49.75% (95% CI: 46.61%, 52.89%) followed by HTN at 37.59% (95% CI: 34.58%, 40.67%), DM at 27.31% (95% CI: 24.58%, 30.1%) and dyslipidemia at 24.23% (95% CI: 21.60%, 27.00%). The majority (more than two-third) of individuals had at least one comorbidity (71.98%, 95% CI: 69.09%-74.75%). The distribution

Table 1 Gene expression profiles, prognostics and treatment options.

Variables	All Data N (%)	Any comorbidities		
		No N (%)	Yes N (%)	p value
BMI (Kg/m^2): mean, SD	30.72 (6.28)	--	--	--
Age (in years): mean, SD	56.36 (12.04)	52.72 (13)	57.78 (11.35)	<0.0001
Ethnicity				
Hispanics	849 (84.65)	237 (84.34)	612 (84.76)	0.8461
Non - Hispanics	154 (15.35)	44 (15.66)	110 (15.24)	
Diagnosis				
Ductal	867 (86.7)	235 (83.63)	632 (87.9)	0.1349
Lobular	61 (6.1)	18 (6.41)	43 (5.98)	
Ductal and Lobular	8 (0.8)	2 (0.71)	6 (0.83)	
Other	64 (6.4)	26 (9.25)	38 (5.29)	
Menopausal				
Pre - menopause	319 (31.8)	130 (46.43)	186 (25.83)	<0.0001
Post-Menopause	684 (68.2)	150 (53.57)	534 (74.17)	
Stage				
Unknown	239 (23.83)	74 (26.33)	165 (22.85)	0.0813
Stage I/II	485 (48.35)	120 (57.97)	365 (65.53)	
Stages III/IV	279 (27.82)	87 (42.03)	192 (34.47)	
Type of Surgery				
None	74 (7.46)	33 (12.04)	41 (5.71)	0.0001
Lumpectomy	527 (53.13)	120 (43.8)	407 (56.69)	
Mastectomy	385 (38.81)	118 (43.07)	267 (37.19)	
Unknown	6 (0.6)	3 (1.09)	3 (0.42)	
CAD				
No	962 (95.91)	281 (100)	681 (94.32)	<0.0001
Yes	41 (4.09)	0 (0)	41 (5.68)	
ER +				
No	310 (31.86)	94 (35.07)	216 (30.64)	0.191
Yes	663 (68.14)	174 (64.93)	489 (69.36)	
PgR +				
No	413 (42.53)	128 (47.76)	285 (40.54)	0.0498
Yes	558 (57.47)	140 (52.24)	418 (59.46)	
HER2 neu positive				
No	676 (81.45)	167 (76.61)	509 (83.17)	0.042
Yes	154 (18.55)	51 (23.39)	103 (16.83)	
ER+/PgR+ (HR+)				
No	297 (29.61)	91 (32.38)	206 (28.53)	0.0967
Yes	674 (67.20)	177 (62.99)	497 (68.84)	
unknown	32 (3.19)	13 (4.63)	19 (2.63)	
TNBC				
No	643 (64.11)	167 (59.43)	476 (65.93)	0.0343
Yes	185 (18.44)	51 (18.15)	134 (18.56)	
unknown	175 (17.45)	63 (22.42)	112 (15.51)	

SD: Standard Deviation; ER: Estrogen; PgR: Progesterone; HER2: Human Epidermal Receptor 2; HR: Hormonal Receptor; TNBC: Triple Negative Breast Cancer

of the 4 comorbidities was as follows: 1 comorbidity (32.4% of patients), 2 comorbidities (19%), 3 comorbidities (13.4%) and 4 comorbidities (7%). 28% of all patients had no identifiable comorbidity (28%) (**Tables 2 and 3).** provide distribution and association of considered clinical and tumor characteristics according to DM, HTN, Obesity, and dyslipidemia. Breast cancer patients with DM were more likely to have increased BMI, older age, dyslipidemia, CAD, HTN, post-menopausal status and ER+/PgR+ tumors. Presence of dyslipidemia was similarly found to be associated with increased BMI, older age, presence of DM, obesity, CAD and postmenopausal status but was associated with both ER+/PgR+ as well as TNBC. HTN and Obesity were associated with all considered comorbidities and did not associate with any tumor characteristics **Table 4** shows adjusted association of individual and combined comorbidities with ER, PgR and HER2 status. The presence of at least one comorbidity was associated with the prevalence of ER+/PgR+ breast cancer (PR=1.15, p=0.04) and expressed a trend association with HER2 negative status (PR=1.08, p=0.086) after adjusting for significant confounders. Among individual factor associations, hypertension was found to be more prevalent as an independent factor in HER2 negative tumors (PR=1.12, p=0.003). Patients with all four comorbidities were more likely to have ER+ tumors (PR=1.18, p=0.033) after adjusting for potential confounders. Presence of 3 comorbidities (PR=1.25 p=0.013) or 4 comorbidities (PR=1.34, p=0.003) was significantly prevalent among individuals with ER+/PgR+ tumors after controlling for significant variables. In the adjusted analysis, HER2 negative status was found to be associated with 2 or more comorbidities. **Table 5** shows the association of comorbidities with combination of ER, PgR and HER2 status. This table clearly shows that the presence of 4 comorbidities was associated with HR+ status (PR=1.16, p=0.048) in adjusted models. ER+/PgR+ and HER2- was highly associated with the presence of the 4 comorbidities (PR=1.35, p=0.018) and showed a trend association with 3 comorbidities (PR=1.23, p=0.078). TNBC status was not found to be associated with the number of comorbidities or presence of any individual comorbidity. It only showed a trend association with presence of DM (PR=1.07, p=0.11).

Discussion

This large study suggests a high prevalence of hypertension, DM, dyslipidemia and obesity in Hispanic women with breast cancer, especially postmenopausal women. The prevalence of obesity (BMI>30) was alarmingly high at around 50%, also DM in this study population (27.31%) was higher than the one reported for the general population both at the national level (10.9%) and at the U.S.-Mexico border in a similar population (15.7%) respectively [6,7]. Also, this study suggests that the combination of more than one of these metabolic conditions appear to be prevalent in our breast cancer study population, particularly in postmenopausal women. 72% of the individuals studied had at least one condition and over 20% had three or four comorbidities. In a National Center for Health Statistics (NCHS) study, about 13% of the U.S. population had two of the following chronic conditions: hyperlipidemia, HTN, or DM, and 3% of the population had all three conditions [4]. We found that the combined presence of more than one comorbidity was more prevalent in HR+ positive tumor in postmenopausal women but that could reflect the common presentation of this breast cancer

Table 2 Unadjusted associations of cofactors with diabetes and hypertension.

Variables	Diabetes			Hypertension		
	No N (%)	Yes N (%)	p value	No N (%)	Yes N (%)	p value
BMI (Kg/m^2): mean, SD	29.97 (5.85)	32.72 (6.9)	<.0001	29.88 (5.86)	32.12 (6.68)	<0.0001
Age (in years): mean, SD	54.92 (12.44)	60.19 (9.98)	<.0001	53.7 (11.82)	60.77 (11.09)	<0.0001
Ethnicity						
Hispanics	612 (83.95)	237 (86.5)	0.3763	529 (84.5)	320 (84.88)	0.928
Non - Hispanics	117 (16.05)	37 (13.5)		97 (15.5)	57 (15.12)	
Diagnosis						
Ductal	621 (85.3)	246 (90.44)	0.1971	538 (86.08)	329 (87.73)	0.481
Lobular	49 (6.73)	12 (4.41)		36 (5.76)	25 (6.67)	
Ductal and Lobular	6 (0.82)	2 (0.74)		6 (0.96)	2 (0.53)	
Other	52 (7.14)	12 (4.41)		45 (7.2)	19 (5.07)	
Menopausal						
Pre - menopause	278 (38.13)	41 (14.96)	<0.0001	254 (40.71)	62 (16.49)	<0.0001
Post-menopause	451 (61.87)	233 (85.04)		370 (59.29)	314 (83.51)	
Stage						
unknown	171 (23.46)	68 (24.82)	0.3463	149 (23.8)	90 (23.87)	0.0709
Stage I/II	346 (47.46)	139 (50.73)		288 (60.38)	197 (68.64)	
Stage III/IV	212 (29.08)	67 (24.45)		189 (39.62)	90 (31.36)	
Type of Surgery						
None	63 (8.76)	11 (4.03)	0.0054	55 (8.91)	19 (5.07)	0.0101
Lumpectomy	361 (50.21)	166 (60.81)		306 (49.59)	221 (58.93)	
Mastectomy	290 (40.33)	95 (34.8)		251 (40.68)	134 (35.73)	
Unknown	5 (0.7)	1 (0.37)		5 (0.81)	1 (0.27)	
Hypertension						
No	534 (73.25)	92 (33.58)	<0.0001	--	--	--
Yes	195 (26.75)	182 (66.42)				
Diabetes						
No	--	--	--	534 (85.3)	195 (51.72)	<0.0001
Yes				92 (14.7)	182 (48.28)	
Obesity						
No	404 (55.42)	100 (36.50)	<0.0001	345 (55.11)	159 (42.18)	<0.0001
Yes	325 (44.58)	174 (63.50)		281 (44.89)	218 (57.82)	
Dyslipidemia						
No	616 (84.5)	144 (52.55)	<0.0001	558 (89.14)	202 (53.58)	<0.0001
Yes	113 (15.5)	130 (47.45)		68 (10.86)	175 (46.42)	
Coronary artery disease						
No	713 (97.81)	249 (90.88)	<0.0001	619 (98.88)	343 (90.98)	<0.0001
Yes	16 (2.19)	25 (9.12)		7 (1.12)	34 (9.02)	
ER +						
No	239 (33.76)	71 (26.79)	0.0443	211 (34.99)	99 (26.76)	0.0087
Yes	469 (66.24)	194 (73.21)		392 (65.01)	271 (73.24)	
PgR +						
No	316 (44.7)	97 (36.74)	0.0286	276 (45.77)	137 (37.23)	--
Yes	391 (55.3)	167 (63.26)		327 (54.23)	231 (62.77)	
HER2-neu positive						
No	483 (80.9)	193 (82.83)	0.5523	384 (77.73)	292 (86.9)	0.0092
Yes	114 (19.1)	40 (17.17)		110 (22.27)	44 (13.1)	
HR+						
No	229 (31.41)	68 (24.82)	0.1452	205 (32.75)	92 (24.4)	0.0067
Yes	478 (65.57)	196 (71.53)		398 (63.58)	276 (73.21)	
unknown	22 (3.02)	10 (3.65)		23 (3.67)	9 (2.39)	
TNBC						
No	142 (19.48)	43 (15.69)	0.1119	119 (19.01)	66 (17.51)	0.0001
Yes	454 (62.28)	189 (68.98)		375 (59.9)	268 (71.09)	
unknown	133 (18.24)	42 (15.33)		132 (21.09)	43 (11.41)	

SD: Standard Deviation; ER: Estrogen; PgR: Progesterone; HER2: Human Epidermal Receptor 2; HR: Hormonal Receptor; TNBC: Triple Negative Breast Cancer

Table 3 Unadjusted associations of cofactors with lipids and obesity.

Variables	Dyslipidemia			Obesity		
	No N (%)	Yes N (%)	p value	No N (%)	Yes N (%)	p value
BMI (Kg/m²): mean, SD	30.32 (6.1)	31.95 (6.65)	0.0004	--	--	--
Age (in years): mean, SD	54.85 (11.89)	61.07 (11.31)	<.0001	56.14 (12.99)	56.58 (11.02)	0.566
Ethnicity						
Hispanics	638 (83.95)	211 (86.83)	0.3074	416 (82.54)	433 (86.77)	0.0662
Non - Hispanics	122 (16.05)	32 (13.17)		88 (17.46)	66 (13.23)	
Diagnosis						
Ductal	658 (86.69)	209 (86.72)	0.2525	432 (86.06)	435 (87.35)	0.86
Lobular	45 (5.93)	16 (6.64)		31 (6.18)	30 (6.02)	
Ductal and Lobular	4 (0.53)	4 (1.66)		5 (1)	3 (0.6)	
Other	52 (6.85)	12 (4.98)		34 (6.77)	30 (6.02)	
Menopausal						
Pre - menopause	278 (36.68)	38 (15.7)	<0.0001	175 (34.93)	141 (28.26)	0.0248
Post-menopause	480 (63.32)	204 (84.3)		326 (65.07)	358 (71.74)	
Stage						
unknown	177 (23.29)	62 (25.51)	0.4345	126 (25)	113 (22.65)	0.5718
Stage I/II	364 (62.44)	121 (66.85)		236 (62.43)	249 (64.51)	
Stage III/IV	219 (37.56)	60 (33.15)		142 (37.57)	137 (35.49)	
Type of Surgery						
None	65 (8.66)	9 (3.73)	0.013	46 (9.27)	28 (5.65)	0.0637
Lumpectomy	384 (51.13)	143 (59.34)		248 (50)	279 (56.25)	
Mastectomy	296 (39.41)	89 (36.93)		198 (39.92)	187 (37.7)	
Unknown	6 (0.8)	0 (0)		4 (0.81)	2 (0.4)	
Hypertension						
No	558 (73.42)	68 (27.98)	<0.0001	345 (68.45)	281 (56.31)	<0.0001
Yes	202 (26.58)	175 (72.02)		159 (31.55)	218 (43.69)	
Diabetes						
No	616 (81.05)	113 (46.5)	<0.0001	404 (80.16)	325 (65.13)	<0.0001
Yes	144 (18.95)	130 (53.5)		100 (19.84)	174 (34.87)	
Obesity						
No	397 (52.24)	107 (44.03)	0.0272	--	--	--
Yes	363 (47.76)	136 (55.97)				
Dyslipidemia						
No	--	--	--	397 (78.77)	363 (72.75)	0.0272
Yes				107 (21.23)	136 (27.25)	
Coronary artery disease						
No	751 (98.82)	211 (86.83)	<0.0001	493 (97.82)	469 (93.99)	0.0023
Yes	9 (1.18)	32 (13.17)		11 (2.18)	30 (6.01)	
ER +						
No	239 (32.61)	71 (29.58)	0.4249	162 (33.33)	148 (30.39)	0.3359
Yes	494 (67.39)	169 (70.42)		324 (66.67)	339 (69.61)	
PgR +						
No	322 (44.05)	91 (37.92)	0.0984	217 (44.83)	196 (40.25)	0.1537
Yes	409 (55.95)	149 (62.08)		267 (55.17)	291 (59.75)	
HER2-neu positive						
No	497 (80.42)	179 (84.43)	0.2195	332 (79.81)	344 (83.09)	0.2459
Yes	121 (19.58)	33 (15.57)		84 (20.19)	70 (16.91)	

HR+						
No	229 (30.13)	68 (27.98)	0.0852	154 (30.56)	143 (28.66)	0.2673
Yes	502 (66.05)	172 (70.78)		330 (65.48)	344 (68.94)	
unknown	29 (3.82)	3 (1.23)		20 (3.97)	12 (2.4)	
TNBC						
No	137 (18.03)	48 (19.75)	0.0817	92 (18.25)	93 (18.64)	0.9361
Yes	479 (63.03)	164 (67.49)		322 (63.89)	321 (64.33)	
unknown	144 (18.95)	31 (12.76)		90 (17.86)	85 (17.03)	

SD: Standard Deviation; ER: Estrogen; PgR: Progesterone; HER2: Human Epidermal Receptor 2; HR: Hormonal Receptor; TNBC: Triple Negative Breast Cancer

Table 4 Adjusted association of commodities with tumor characteristics.

Model	ER+		PR+		HER 2 -	
	PR (95%CI)	p-value	PR (95%CI)	p-value	PR (95%CI)	p-value
Model 1						
1 comorbidity	1.02 (0.90, 1.14)	0.794	1.09 (0.94, 1.27)	0.240	1.04 (0.95, 1.15)	0.386
2 comorbidities	1.07 (0.94, 1.21)	0.334	1.11 (0.94, 1.32)	0.212	1.10 (0.99, 1.21)	0.067
3 comorbidities	1.10 (0.96, 1.25)	0.190	1.25 (1.05, 1.49)	0.013	1.14 (1.03, 1.27)	0.015
4 comorbidities	1.18 (1.01, 1.37)	0.033	1.34 (1.10, 1.63)	0.003	1.08 (0.95, 1.24)	0.251
Model 2						
Any comorbidities	1.06 (0.96, 1.17)	0.284	1.15 (1.01, 1.30)	0.041	1.08 (0.99, 1.17)	0.086
Model 3						
Diabetes	1.07 (0.97, 1.19)	0.175	1.10 (0.97, 1.25)	0.142	0.97 (0.90, 1.05)	0.434
Hypertension	1.08 (0.98, 1.19)	0.102	1.10 (0.97, 1.24)	0.129	1.12 (1.04, 1.20)	0.003
Obesity	1.03 (0.94, 1.12)	0.537	1.06 (0.95, 1.18)	0.285	1.03 (0.96, 1.10)	0.39
Dyslipidemia	0.96 (0.87, 1.07)	0.483	1.02 (0.90, 1.16)	0.749	1.00 (0.93, 1.08)	0.937

ER: Estrogen; PgR: Progesterone; HER2: Human Epidermal Receptor 2; PR: Prevalence Ratio; CI: Confidence Interval; Model 1: Adjusted effect of number of commodities after adjusting for menopausal status, stage and diagnosis; Model 2: Adjusted effect of presence of any commodities after adjusting for menopausal status, stage and diagnosis; Model 3: Adjusted effect of DM, HTN, Obesity and Lipid after adjusting for menopausal status, stage and diagnosis.

Table 5 Adjusted association of commodities with combination of tumor characteristics.

Model	HR+		TNBC		ER+ and PR+ and HER2-	
	PR (95%CI)	p-value	PR (95%CI)	p-value	PR (95%CI)	p-value
Model 1						
1 comorbidity	1.02 (0.91, 1.14)	0.779	0.99 (0.90, 1.10)	0.915	1.09 (0.90, 1.33)	0.37
2 comorbidities	1.08 (0.96, 1.22)	0.217	1.01 (0.91, 1.13)	0.805	1.16 (0.93, 1.44)	0.19
3 comorbidities	1.10 (0.97, 1.26)	0.149	0.97 (0.86, 1.11)	0.674	1.23 (0.98, 1.56)	0.078
4 comorbidities	1.16 (1.00, 1.35)	0.048	1.08 (0.95, 1.22)	0.240	1.35 (1.05, 1.74)	0.018
Model 2						
Any comorbidities	1.06 (0.96, 1.17)	0.239	1.00 (0.92, 1.10)	0.912	1.16 (0.97, 1.38)	0.098
Model 3						
Diabetes	1.06 (0.97, 1.17)	0.208	1.07 (0.98, 1.17)	0.110	1.09 (0.92, 1.28)	0.326
Hypertension	1.10 (1.00, 1.21)	0.04	1.03 (0.95, 1.12)	0.473	1.14 (0.97, 1.33)	0.111
Obesity	1.02 (0.94, 1.11)	0.681	0.98 (0.91, 1.06)	0.588	1.09 (0.95, 1.26)	0.206
Dyslipidemia	0.96 (0.87, 1.06)	0.43	0.94 (0.86, 1.04)	0.227	0.97 (0.83, 1.15)	0.759

HR: Hormonal Receptor; TNBC: Triple Negative Breast Cancer; ER: Estrogen; PgR: Progesterone; HER2: Human Epidermal Receptor 2; PR: Prevalence Ratio; CI: Confidence Interval; Model 1: Adjusted effect of number of commodities after adjusting for menopausal status, stage and diagnosis; Model 2: Adjusted effect of presence of any commodities after adjusting for menopausal status, stage and diagnosis ; Model 3: Adjusted effect of DM, HTN, Obesity and Lipid after adjusting for menopausal status, stage and diagnosis

subtype. No individual condition was found to be associated with any particular breast tumor sub-type except for DM more likely to be seen in women with ER+/PgR+ tumors. Rather, the number of comorbidities (presence of two or more comorbidities) had a more increased association with ER+/PR+ and HER2 - tumors.

Given the significant prevalence of metabolic risk factors in Hispanic women with breast cancer, it would be desirable to further evaluate these conditions as underlying risk factors for this disease which, in turn, could be contributing to the increased cancer disparity previously noted in this patient population including a diagnosis at a younger age compared to non-Hispanic white women, a higher prevalence of TNBC and more advanced stages of disease [8].

Our study is consistent with other studies suggesting a strong association between increased breast cancer risk with obesity, DM, hyperlipidemia, and HTN. Obesity has been associated with the development of cancer, particularly breast cancer and is likely one of the most known modifiable risk factors for the development of breast cancer to date [9]. Several epidemiologic studies have noted that obesity, causing the development of a chronic low-grade inflammatory environment, may be more strongly associated with ER + postmenopausal breast cancer as seen in our study [10-12]. However, in a combined analysis of data from the Women's Health Initiative observational cohort and randomized trial, obesity was shown to be similarly related to both ER+ (hazard ratio=1.35, 95% CI: 1.20, 1.51) and TNBC (hazard ratio=1.37, 95% CI: 0.98, 1.93) [13]. The association of other metabolic risk factors with breast cancer risk and its outcome have been also explored. Type 2 DM has been thought to increase the risk of developing breast cancer, although the underlying mechanism is still uncertain [14,15]. Other studies have suggested that hyperlipidemia [16] and hypertension [17] might increase also the risk of breast cancer. Hypertension was linked to a 15% increase risk of breast cancer in the postmenopausal population (combined RR: 1.13; 95% Cl, 1.01-1.26) [17]. The effects of hyperlipidemia are less clear. Touvier et al. reported results of a meta-analysis confirming the evidence of a modest but statistically significant inverse association between hyperlipidemia and the risk of breast cancer, supported by mechanistic plausibility from experimental studies [18]. More recently a large study based on the Women's Health Initiative [19] examined the association of metabolic phenotypes of obesity defined by presence of the metabolic syndrome using baseline measurements of blood glucose, triglycerides, high-density lipoprotein(HDL) -cholesterol, blood pressure, waist circumference, and BMI (normal, overweight, obese) with risk of postmenopausal breast cancer in a prospective analysis of a cohort of postmenopausal women (n ~ 21,000). Over 15 years of follow-up, 1,176 cases of invasive breast cancer were diagnosed. Obesity, regardless of metabolic health, was associated with increased risk of breast cancer. Being obese and metabolically unhealthy was associated with the highest risk (Hazard Ratio, 1.62; 95% CI, 1.33–1.96). The study concluded that beyond BMI, metabolic health should be considered a clinically relevant and modifiable risk factor for breast cancer. Some studies have explored the utilization of certain tools such as the Charlson Comorbidity Index (CCI) to determine the impact of comorbidities including cardiovascular risk factors on breast cancer risk but no substantial association between morbidity measured with the CCI and breast cancer risk could be definitively identified, and the utility of these tools remain unclear [20]. However, studies have consistently identified metabolic syndrome, defined as at least three among abdominal obesity, high blood triglycerides, low HDL cholesterol, high blood glucose, and high blood pressure, to be an important risk factor for breast cancer in postmenopausal women suggesting that screening for and prevention of metabolic syndrome through lifestyle changes could confer protection against breast cancer [21]. Metabolic syndrome is characterized by a state of insulin resistance/hyperinsulinemia and subacute chronic inflammation and both conditions offer a plausible mechanistic link towards breast cancer. Thus, in addition to their increased risk of cardiovascular morbidity and mortality, women with this syndrome represent a group at elevated risk of developing breast cancer and poorer prognosis [22].

Conclusion

The strengths of our study include the focus on Hispanic/Latina women with breast cancer and is to our knowledge, the first study to determine the correlation of the combined metabolic comorbidities with breast cancer in this unique population. Also, the study adds to the body of evidence linking the metabolic conditions evaluated with ER + breast cancer (p=0.048). The study had several limitations including not applying the specific metabolic syndrome criteria due to the retrospective nature of the analysis and the non-availability of the required measures in the archived data. We used BMI as our marker for obesity, which reflects general adiposity and might not correctly with fat distribution measurements for abdominal obesity, hip and waist circumference and waist-to-hip ratio. Also, we did not include detailed information about the subtypes of the dyslipidemia due to the limitation in the database.

This study, nevertheless, adds to the body of evidence supporting a more focused approach to address obesity through lifestyle changes and screen for other metabolic conditions in the underserved Hispanic minority and others as potential modifiable risk factors against breast cancer. These findings should be confirmed in future larger studies but increasing awareness regarding the prevalence of these common conditions in Hispanic/Latino patients with breast cancer would be a reasonable first step.

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