Clinicopathological Factors Associated to HER-2 Status in a Hospital-based Sample of Breast Cancer Patients in Puerto Rico

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Breast cancer is the most common female malignancy in Puerto Rico. Cases with human epidermal growth factor receptor 2 (HER-2) oncoprotein overamplification are associated with aggressive clinical behavior. Given the limited availability of information for Puerto Rico, we aimed to evaluate the prevalence and clinical correlates of HER-2 gene overexpression among a hospital-based female population of breast cancer cases. We analyzed data from 1,049 female patients with invasive breast cancer (diagnosed 2000-2005) at the *I. González Martínez Oncologic Hospital* and the *Auxilio Mutuo Hospital*. HER-2 status and other clinical characteristics were retrieved from the hospitals' cancer registries, from the Puerto Rico Central Cancer Registry, and from a review of medical and pathological records. Prevalence odds ratios were estimated with 95% confidence intervals, using logistic regression models to quantify the association between HER-2 status and different clinicophatological factors. The overall prevalence of positive HER-2 expression was 22.5%. In the multivariate logistic regression model, factors significantly associated with HER-2 positivity included a diagnosis age of <50 years, having a tumor with negative progesterone receptor (PR) status, and having regional disease ($p < 0.05$). No significant differences in HER-2 positivity were observed by tumor histology or estrogen receptor (ER) status ($p > 0.05$). This is the most comprehensive epidemiological study to date on HER-2 status in Puerto Rico. The prevalence and correlates of HER-2 overexpression in this study are comparable to those observed in US populations. Study results will aid in the development of breast cancer control strategies in Puerto Rico. [*P R Health Sci J 2010;3:265-271*]

Key words: Breast cancer, HER-2, Puerto Rico

Breast cancer is the most common cancer diagnosed among females and represents the most common cause of cancer death among women worldwide (1). In Puerto Rico, breast cancer accounted for 34.3% of all incident cases in 2003 and 19.7% of all cancer related deaths in 2004 (2). Variations in disease occurrence and outcome according to geographic regions and ethnic background exist (3). In the United States (US), the rate by which breast cancer incidence is increasing differs among ethnic populations. For example, the risk of developing breast cancer is increasing at a faster rate among females residing in Puerto Rico than among non-Hispanic white (4) females residing in the US. Whereas although higher incidence rates exist for non-Hispanic white and Hispanic women in the US as compared to women in Puerto Rico, incidence rates are increasing for Puerto Ricans, even though they have remained stable for Hispanic and non-Hispanic whites in the US (5).

The c-erbB-2 proto-oncogene encodes for the human epidermal growth factor receptor 2 (HER-2/neu) oncoprotein, a receptor tyrosine kinase protein, and it is associated with certain tumors of the breast. While normal breast cells carry two copies of the c-erbB-2 gene on chromosome 17, certain

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breast tumors demonstrate amplification of this oncogene, thus exhibiting overexpression of the HER-2 oncoprotein (6). This can lead to excessive growth and invasion of mammary tissue, resulting in the development of malignant tumors. HER-2 overexpression has been inversely correlated with estrogen receptor (ER) and progesterone receptor (PR) status and positively correlated with stage and histological grade (7-8).

Patients with HER-2-positive tumors are subject to target therapies (9-10); thus, the American Society for Clinical Oncology recommends that HER-2 status be determined for each patient with invasive breast cancer (9). In fact, since 1996, the American Society of Clinical Oncology (ASCO) has published clinical practice guidelines that specify that newly diagnosed breast cancers be assayed for HER-2-positive oncogene expression (11). Trastuzumab (Herceptin; Genentech, South San Francisco, CA), a humanized monoclonal antibody against the HER-2 protein, improves response, time-to-progression, and breast cancer survival rates as well as reduces the risk of recurrence and mortality (9, 12). More recently, a dual HER-1/HER-2 tyrosine kinase inhibitor of HER-2 tyrosine kinase activity, lapatinib (Tykerb, GlaxoSmithKline, Philadelphia, PA), has also been shown to improve clinical outcomes in patients with advanced disease (13). Thus, HER-2 is a useful marker for therapeutic decision-making in patients with breast cancer, highlighting the importance of understanding its prevalence and correlates in the population.

Several studies conducted in the late 1980s and early 1990s estimated that the prevalence of HER-2 overexpression in women with invasive breast cancer tumors was approximately 20-34% (7, 14-19), although a recent study suggests that the proportion (but not the incidence) of HER-2-positive tumors may be declining in the population (20). So far, two small-scale studies investigating the prevalence of HER-2 overexpression among females in Puerto Rico have been published (6, 21), the results of which estimate the prevalence of HER-2 overexpression among invasive breast cancer tumors in women living in Puerto Rico to be 20-28%. However, these studies have been limited both in sample size and in their ability to associate HER-2 overexpression with other relevant clinical outcomes. Even though differences in the prevalence of overexpression of HER-2 among ethnic groups have not been consistently found (8, 22-26), a recent study supports the theory that race modifies the association between pathologic prognostic indicators of breast carcinoma, such as stage and grade, and the likelihood of an individual having HER-2-positive carcinoma (8). More specifically, even though significant associations were seen between HER-2 positivity and more advanced stage and grade tumors in Caucasians, these associations were not seen for African Americans (8). In addition, biological factors associated with poor prognosis are found with a significantly higher frequency in breast tumors from Hispanic and black women in the US (25). This is of special relevance, as tumors with a more aggressive biology can lead to a higher stage at diagnosis, resulting in a poorer prognosis for survival (25).

The main objective of this study is to estimate the prevalence and clinicopathological correlates of HER-2 overexpression in female patients (from a hospital-based population in Puerto Rico) with invasive breast cancer. Even though the prevalence of HER-2 overexpression in breast cancer tumors has been well documented in the US, information on the prevalence of HER-2 status in Puerto Rican cancer patients and its association with disease outcomes is still limited. Given that breast cancer tumors overexpressing the HER-2 oncoprotein are associated with a more aggressive clinical behavior (27-30), information regarding the prevalence of this protein among females with breast cancer in Puerto Rico may be useful for the development of cancer control strategies in this area, including secondary and tertiary prevention strategies. For example, more precise estimates of HER-2 overexpression and its correlates in this population may help us to better understand the clinical necessities of that population regarding targeted breast cancer treatment, with the aim of increasing survival of and reducing mortality from the disease.

Methods

Study population

The study consisted of a retrospective review of breast cancer cases diagnosed in two major cancer care hospitals in Puerto Rico. More specifically, our study population consisted of newly diagnosed (2000-2005) cases of invasive breast cancer, categorized according to the International Classification of Disease (ICD-O-3, codes C50.0-C50.9) (31) and diagnosed at the *I. González Martínez Oncologic Hospital* and the *Auxilio Mutuo Hospital* in Puerto Rico. HER-2 overexpression began to be evaluated as a standard of care in the late 1990s. Thus, evaluation of this parameter after this period is more accurate and complete. This study was approved by the Institutional Review Board (IRB) committees of the Medical Sciences Campus, the *I. González Martínez Oncologic Hospital*, and the *Auxilio Mutuo Hospital*.

From 2000 to 2005, 2,047 incident cases of breast cancer were identified in the above hospitals. Of those cases, 455 were eliminated because the patients had in situ breast cancer, 6 were eliminated because there was no information on tumor behavior, and 537 were eliminated because there was no information on HER-2 status. The study population consisted of 1,049 invasive breast cancer cases diagnosed from 2000 to 2005 at the *I. González Martínez Oncologic Hospital* (n = 540 cases) and the *Auxilio Mutuo Hospital* (n = 509 cases); all cases included information on HER-2 status, corroborated by the presence of an immunohistochemistry (IHC) pathology report. Conclusive cases had HER-2 scores of 0, 1+, or 3+. From the inconclusive cases (n=134) (HER-2 score of 2+), 81 were re-evaluated using

available flouorescence in situ hybridization (FISH) reports, for a final study population with conclusive HER-2 status of 985 women.

Study variables

Information from cases was collected from the cancer registries of each of the participating hospitals. In addition, information on relevant covariates not available in the registries was abstracted from pathology reports and medical records. Also, clinical characteristics of study participants were corroborated with information from the Puerto Rico Central Cancer Registry (PRCCR). Information on HER-2 protein expression for all cases was obtained from IHC pathological analyses. According to the staining intensity, the pathologist categorized HER-2 status as positive (IHC score = 3+), negative (IHC score = 0, 1+), or equivocal (inconclusive IHC score = 2+). In addition, we collected information on age at diagnosis, on ER and PR receptor status (positive, negative), and on tumor histology (lobular, ductal, other), size (<2cm, ≥2cm), and grade (I, well-differentiated; II, moderately well-differentiated; III, poorly differentiated; and IV, undifferentiated). Information on stage at diagnosis (localized, regional, distant, unknown) was defined according to Surveillance Epidemiology and End Results Staging (SEER Summary Staging) criteria. For cases diagnosed in the year 2000, the SEER Summary Staging 1977 (SSS1977) codes were used (32), while for cases diagnosed between 2001 and 2005, the SEER Summary Staging 2000 (SSS2000) codes were used (33). The use of both codes to track staging of breast cancer cases is supported by the fact that coding changes in SSS2000 had little effect on the classification of staging (Kappa = 0.84, $p < 0.001$) of breast cancer cases (34). For example, breast cancer cases with supraclavicular lymph node involvement were *distant* according to SSS1977 but are considered *regional* under SSS2000. Lymph node metastasis (yes, no) at time of diagnosis was also assessed. We did not compare statistics regarding race, as there is no clear demarcation of race in Puerto Rico.

Statistical analysis

Descriptive statistics such as frequency, mean, and standard deviation were used to describe the study population. For bivariate analysis, chi-square distribution was used to assess the comparison of the characteristics associated with HER-2 overexpression status among breast cancer patients. To determine the magnitude of these associations, the prevalence odds ratio (POR) was estimated (with a 95% confidence interval) using a simple logistic regression model. Multivariate logistic regression models were used to adjust the previous associations by potential confounder variables. Interaction terms formed by all pairs of the combinations of the predictor variables within the multivariate model were tested with the likelihood-ratio test (35). The hospital effect was considered as a random component, using a multilevel approach to estimate the parameters of the logistic regression model. Data analysis was done using the statistical software package Stata 10.

Results

Characteristics of the study population

Overall, 21.2% of the cases were HER-2-positive, 72.7% of the cases were HER-2-negative, and 6.1% had inconclusive results (Table 1). When inconclusive cases were eliminated, the prevalence of HER-2-positive tumors was 22.5%, whereas 16.6% had triple-negative status (Table 2). Even though the overall prevalence of HER-2 did not differ between the years studied ($p = 0.378$), we saw a higher prevalence of HER-2 positivity in the *I. González Martínez Oncologic Hospital* (26.8%) as compared to the *Auxilio Mutuo Hospital* (18.1%) ($p = 0.001$) (data not shown).

Table 1. HER-2 oncoprotein expression of study participants (n=1,049).

HER-2/neu expression	n	%
HER2 +	222	21.2
HER2 -	763	72.7
Inconclusive	64	6.1

Table 2. Clinical groupings in the study population according to receptors (n=974).

Clinical groupings	n	%
HER2 +	220	22.5
HER2 -/ER-/PR-	162	16.6
HER2 -/ER+ or PR+	592	60.9

The clinical and pathological characteristics of the study population with conclusive HER-2 status (n = 985) are summarized in Table 3. The average age at diagnosis was 58.3 ± 14 years, while 68.6% of the study population was 50 years or older at the time of diagnosis. Most of the cases had invasive ductal carcinoma (75.7%). Regarding hormone receptor status, 72.2% and 58.6% of the study population were ER positive and PR positive, respectively, whereas 55.2% had combined ER/PR positive status. Most patients (63.0%) had tumor grades ranging from well to moderately differentiated, 64.1% had localized disease at the time of diagnosis, 53.3% had a tumor size of ≥2 cm, and 38.5% had positive lymph nodes (Table 3).

Bivariate analysis

Table 3 also shows the association of HER-2 overexpression with common clinicopathological characteristics of the cases at the time of diagnosis. In our study population, HER-2 overexpression was significantly associated with a younger age at diagnosis (<50 years), invasive ductal cancer type,

negative PR and ER hormonal receptor status, a larger tumor size (≥2 cm), and positive lymph node metastasis ($p < 0.05$). In addition, the likelihood of HER-2 positivity increased by increasing grade and stage ($p\text{-value}_{trend} < 0.001$). When data were stratified by hospital of diagnosis, similar results were observed regarding clinicopathological factors associated with HER-2 status (data not shown).

Multivariate analysis

Despite their statistical significance in bivariate analysis, the variables *tumor size* and *lymph node metastasis* were excluded from the multivariate logistic regression model in order to reduce the potential problems of collinearity, as these are already contemplated in the variable *stage at diagnosis*. We also excluded *tumor grade*, given its strong correlation with *tumor stage* ($p = 0.001$) (data not shown). Results of the multivariate analysis are shown in Table 4. In the multivariate logistic model, women with an age at diagnosis of <50 years were 55% (95% CI: 1.09-2.21) more likely to be HER-2-positive as compared to those with an age at diagnosis of ≥ 50 years, after adjusting for ER status, PR status, tumor histology, tumor staging, and hospital of diagnosis. Regarding hormone receptors, women with PR-negative status were two times more likely to be HER-2-positive compared to those with PR-positive tumors, when adjusting for age at diagnosis, ER status, tumor histology, tumor staging, and hospital of diagnosis. However, no significant differences ($p = 0.218$) were observed in HER-2 positivity when compared to ER status. Those with invasive ductal tumor histology were 64% more likely to be HER-2-positive compared to those with invasive lobular histology, when adjusting for the same covariates, although this result was marginally significant ($p = 0.087$). Women with regional disease were significantly more likely to be HER-2-positive compared to those with localized disease (POR 1.71; 95% CI: 1.20-2.43), when adjusting for age at diagnosis, ER and PR status, tumor histology, and hospital of diagnosis. In addition, the likelihood of HER-2 positivity increased when tumor stage increased ($p\text{-value}_{trend} < 0.001$). No significant interaction terms were detected in the model (LR Test: $X^2 = 32.34$, $p = 0.1822$).

Table 3. Clinicophatological factors associated to HER-2 status in a hospital-based sample of breast cancer patients in Puerto Rico (n=985).

Characteristics	Total n (%)	HER2 + n (%)	HER2 - n (%)	POR (95% CI)†
Age at diagnosis (n=985)				
<50	309 (31.4)	93 (41.9)	216 (28.3)	1.87 (1.37-2.56)
≥50	676 (68.6)	129 (58.1)	547 (71.7)	1.00
ER Status (n=978)				
Negative	272 (27.8)	85 (38.5)	187 (24.7)	1.91 (1.39-2.62)
Positive	706 (72.2)	136 (61.5)	570 (25.3)	1.00
PR Status (n=976)				
Negative	404 (41.4)	121 (55.0)	283 (37.4)	2.04 (1.51-2.77)
Positive	572 (58.6)	99 (45.0)	473 (62.6)	1.00
ER/PR Status (n=974)				
ER- / PR-	239 (24.5)	77 (35.0)	162 (21.5)	1.00
ER- / PR+	33 (3.4)	8 (3.6)	25 (3.3)	1.80 (1.19-2.72)
ER+ / PR-	164 (16.8)	44 (20.0)	120 (15.9)	1.57 (0.69-3.60)
ER+ / PR+	538 (55.2)	91 (41.4)	447 (59.3)	2.33 (1.64-3.32)
Tumor histology (n=971)				
Invasive lobular	163 (16.8)	21 (9.7)	142 (18.8)	1.00
Invasive ductal	735 (75.7)	183 (84.7)	552 (73.1)	2.24 (1.38-3.65)
Other	73 (7.5)	12 (5.6)	61 (8.1)	1.33 (0.62-2.87)
Tumor grade (n=841)				
Well differentiated	133 (15.8)	7 (3.5)	126 (19.6)	1.00*
Moderately differentiated	397 (47.2)	93 (47.0)	304 (47.3)	5.51 (2.48-12.20)
Poorly differentiated	269 (32.0)	82 (41.4)	187 (29.1)	7.89 (3.53-17.64)
Undifferentiated aggressive	42 (5.0)	16 (8.1)	26 (4.0)	11.08 (4.14-29.61)
Tumor size (n=835)				
< 2 cm	390 (46.7)	66 (37.9)	324 (49.0)	1.00
≥ 2 cm	45 (53.3)	108 (62.1)	337 (51.0)	1.57 (1.12-2.21)
Lymph nodes metastasis (n=842)				
Negative	518 (61.5)	92 (48.4)	426 (65.3)	1.00
Positive	324 (38.5)	98 (51.6)	226 (34.7)	2.01 (1.45-2.78)
Tumor staging (n=867)				
Localized	555 (64.1)	102 (53.1)	453 (67.1)	1.00*
Regional	293 (33.8)	83 (43.2)	210 (31.1)	1.76 (1.26-2.45)
Distant	19 (2.2)	7 (3.6)	12 (1.8)	2.59 (1.00-6.74)

†Using a simple logistic regression model; POR= prevalence odds ratio
* P-value trend <0.001.

Discussion

This is one of the first epidemiological studies to assess HER-2 expression, an important tumor marker that has proven effective for the clinical management of breast cancer patients, among Puerto Rican females with invasive breast cancer (6, 21). Our estimate of the prevalence of HER-2-positive breast cancer (23%) is closer to estimates by Peredo and colleagues (20%), although lower than those from Colon and colleagues (28%). This difference could be explained by the fact that, similar to our study, Peredo's study was based on newly diagnosed breast cancer cases, while Colon's included both new and recurrent cases. Nonetheless, our and previous estimates for Puerto Rico fall within the range of HER-2 positivity established by studies in the US and other populations (20-34%) (7, 14-19, 36).

Correlates of HER-2 positivity in this hospital-based sample of women in Puerto Rico show that hormone receptors and other important prognostic factors of breast cancer were significantly associated with

HER-2 overexpression status. Consistent with previous studies in other populations (37-40), a positive ER or PR status were negatively associated with HER-2 status, although results for ER were not statistically significant in multivariate analysis. When we considered the combination of ER/PR status, women positive for any of the hormone receptors were more likely to be HER-2-positive compared to those with ER-negative/PR-negative status, although the results was not statistically significant for those with ER-positive/PR-negative status. This is of relevance, as combined ER-positive/PR-positive tumors are associated with improved survival when compared to those with combined ER-negative/PR-negative tumors (41); in addition, such tumors respond to hormone inhibition treatment.

Table 4. Magnitude of the association between HER-2-positive status and clinical characteristics of the study population (n=844).

Characteristics	Adjusted POR† (95% CI)
Age at Diagnosis	
<50 yrs	1.55 (1.09-2.21)
≥50 yrs	1.00
ER Status	
ER+	1.00
ER-	1.32 (0.85-2.05)
PR Status	
PR+	1.00
PR-	2.01 (1.32-3.06)
Tumor histology	
Invasive lobular	1.00
Invasive ductal	1.64 (0.93-2.88)
Other	1.31 (0.56-3.08)
Tumor staging	
Localized	1.00*
Regional	1.71 (1.20-2.43)
Distant	1.98 (0.64-6.10)

†Hospital effect was considered as random effects using a multilevel approach to estimate the parameters of the logistic regression model.
*P-value trend <0.001.

Among other correlates of HER-2 status, our results showed that HER-2 positivity was also strongly associated with a younger age at diagnosis (< 50 years), ductal tumor histology, moderately to poorly differentiated tumor grade, tumor size greater than 2 cm, and advanced stage at diagnosis. The previous study in Puerto Rico by Peredo and colleagues found a significant association only between HER-2 positivity and nodal involvement, while the study by Colon found an association only for PR status. The smaller sample sizes included for analysis in these studies may have limited their statistical power for detecting these associations. Nonetheless, our results are consistent with previous reports that showed that HER-2 overexpression is associated with earlier age at diagnosis, nodal involvement, and a larger tumor size and is positively correlated with stage and histological grade (7-8, 26, 36, 38-40, 42). Results for tumor grade and stage are of particular interest, as recent data suggest that HER-2 positivity is associated with tumors of more advanced stages and grades in Caucasians, but not in African Americans, making disease behaviors in Puerto Rico similar to those of Caucasians, but not to those of African Americans (8). Also, although results were marginally significant, consistent with previous studies (39, 43), our results also support the notion that invasive lobular cancers infrequently overexpress HER-2 oncoprotein. Thus, as expected, the etiology and clinical characteristics of HER-2-positive tumors in Puerto Rico show similar behaviors to those of other populations.

Of interest is the fact that we saw a higher prevalence of HER-2 positivity in the *I. González Martínez Oncologic Hospital* compared to the *Auxilio Mutuo Hospital*, even after adjusting for clinicopathological characteristics of patients. This difference could be due to methodological differences in the laboratories that performed the analyses or to socioeconomic differences between the populations served at these hospitals (those from the *Auxilio Mutuo* tend to belong to higher socioeconomic classes). Given that HER-2 positivity is not a germline mutation, but one that is acquired over the course of the bearer's life, differences in environmental risk factors between these groups could account for some of the observed differences in HER-2 positivity between these populations. This theory is supported by a recent study that showed that vegetable consumption has a protective effect against HER-2-positive cancers (much stronger than the affect against HER-2-negative cancers), supporting the theory that this type of diet protects mainly against a specific breast cancer subtype (44). Further research is warranted to elucidate this finding.

In terms of study limitations, our results might be affected by selection bias, as 34% of the eligible individuals were excluded because they were missing information on HER-2 status. Nonetheless, a comparison of study individuals (n = 1,049), with those excluded because they were missing information on HER-2 status (n = 537), showed that except for differences in the proportion of cases with "other" tumor histology (not lobular or ductal), these groups did not differ in any of the clinical characteristics under study, suggesting that selection bias was not an issue in the study. No differences were neither observed in the clinical characteristics of patients with conclusive or inconclusive HER-2 status (data not shown). Given that studies in the US have shown that demographic and clinical variations exist regarding which breast cancer patients received HER-2 testing (45), future studies should assess whether similar discrepancies exist in Puerto Rico, particularly as current guidelines call for all tumors to be assessed in order to adequately characterize prognosis and determine eligibility for HER-2-targeted therapy (45). The large amount of missing information on HER-2 status in medical records (34% of women with invasive breast cancer) is of relevance given that official recommendations for routine screening of breast cancer patients to determine their HER-2 status (in order to determine treatment options) preceded the study period (9, 11). Among other study limitations, caution must be used regarding the generalization of our results to the entire population of invasive breast cancer cases in Puerto Rico,

as our results are only directly generalizable to the population of patients diagnosed in these local hospitals between 2000 and 2005. In fact, according to data from the PRCCR, our study population (n = 1,049) represents approximately 12% of all invasive breast cancer cases diagnosed in Puerto Rico during the years of 2000 to 2005. Finally, even though IHC techniques were used to access HER-2 status, a disadvantage of this method is that laboratories may use different antibodies for their analyses, resulting in differences in HER-2 expression results (21).

Despite the previous limitations, this is the most comprehensive epidemiological study to date on HER-2 expression in Puerto Rico, and our results provided prevalence estimates similar to those in other populations; approximately one-fifth of all invasive breast cancer cases in this population of women in Puerto Rico were positive for HER-2 overexpression. In addition, as in other populations, overexpression of this marker was strongly correlated with unfavorable clinicopathological characteristics of the tumor, such as negative PR status and advanced tumor stage. Our results underscore the relevance of testing all breast cancer cases for HER-2 positivity in Puerto Rico, as these women may benefit from targeted therapies. Future analysis of this data will help us to understand the associations of disease markers with disease relapse and mortality. This and other comparative studies will be of relevance to the enhanced understanding of the differences in breast cancer mortality, survival, prognosis, and clinical characteristics associated with ethnicity/race distinctions between breast cancer patients in Puerto Rico and those in the US. Moreover, given that studies have determined that some breast cancer risk factors, such as parity, menopausal status, alcohol consumption, and diet, differ by HER-2 status (36, 44, 46), future studies in Puerto Rico should further assess the potential associations and interactions between HER-2-positive tumors and established or suspected risk factors for breast cancer in order to increase our understanding of the etiology of breast cancer in this population.

Resumen

El cáncer de mama es el más común entre las mujeres en Puerto Rico. Casos con sobreexpresión de la proteína tumoral conocida como HER-2 (por sus siglas en inglés) se asocian con un comportamiento clínico más agresivo. Dado que los datos para Puerto Rico son limitados, nuestro objetivo fue evaluar la prevalencia y los factores clínicos asociados a sobreexpresión del gen HER-2 en una población hospitalaria de mujeres pacientes de cáncer de mama. Analizamos los datos de mujeres pacientes de cáncer invasivo de mama diagnosticadas entre 2000-2005 en el *Hospital I. González Martínez* y el *Hospital Auxilio Mutuo* (n=1,049). Información sobre HER-2 y otras características clínicas fue extraída de los registros de cáncer hospitalarios, del Registro Central de Cáncer de Puerto Rico, y de revisión de expedientes médicos y patológicos. La prevalencia de sobreexpresión de HER-2 fue de 22.5%. A base del modelo de regresión logística multivariado, los factores significativamente asociados a tener un tumor positivo para HER-2 incluyeron edad al diagnostico <50 años, tener un tumor negativo a receptores de progesterona, y tener enfermedad regional ($p<0.05$). No se demostraron diferencias significativas por la histología y los receptores de estrógeno del tumor ($p>0.05$). La prevalencia y factores asociados a la sobreexpresión de HER-2 en este estudio es comparable a resultados de poblaciones en Estados Unidos de América; estos son de importancia para el desarrollo de estrategias de control de cáncer en Puerto Rico.

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