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ORIGINAL ARTICLE

Hormone receptor and HER2 status in patients with breast cancer by races in southeastern Turkey

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Summary

Purpose: *Hormone receptor (HR) status is a prognostic factor in women with breast cancer and differs among different ethnic groups. HR status among Turkish, Kurdish and Arabic women with breast cancer living in Turkey is unknown and in this study we investigated the relationship between HR and HER2 status and race.*

Methods: *FA total of 648 women with breast cancer (Turkish 438, Kurdish 174, Arabic 35 and Armenian 1) living in southeastern Turkey and referred to the Department of Radiation Oncology between July 2006-July 2012 were included in the study.*

Patients were categorized into 4 groups according to their HR status. Estrogen receptor (ER) and progesterone receptor (PR) positive (ER+/PR+), ER positive and PR negative (ER+/PR-), ER negative and PR positive (ER-/PR+) and ER and PR negative (ER-/PR-). Human epidermal growth factor receptor 2 (HER2) status was recorded immunohistochemically (IHC) as negative (0 and 1+), and positive (3+). Statistical analysis included ER, PR, HER2, triple subtypes (combination of ER, PR and HER2), and race.

Results: *The median age at diagnosis was 48 years (range 20-83). ER+, PR+ and HER2+ patients were 453 (70%), 470 (72.6%) and 206 (32.1%), respectively. ER+/PR+ rates among Turkish and Arabic patients were similar, but were higher than Kurdish patients ($p<0.002$). Triple-negative (ER-/PR-/HER2-) rates among Kurdish and Arabic patients were similar, but were higher than Turkish patients ($p=0.04$).*

Conclusion: *Turkish, Kurdish and Arabic women with breast cancer in southeastern Turkey differed by HR status. Compared to Turkish and Arabic patients, Kurdish patients had more unfavorable prognostic factors.*

Key words: *breast cancer, estrogen receptor, HER2, progesterone receptor, race*

Introduction

Breast cancer is the most common malignancy and the second most common cause of cancer deaths in women [1]. Several clinical and pathological factors including tumor size, lymph node status, histologic grade and mitotic count affect the prognosis of breast cancer. HR (ER and PR) status is one of these factors [2].

Treatment responses of patients with HR positive tumors are different from patients with HR negative tumors regardless of tumor stage. Patients with HR positive breast tumors have lower recurrence rates and better survival than those with HR negative tumors [3-5].

In many studies HR status has been reported to differ among races [6-11]. HR status among Turkish, Kurdish and Arabic women with breast cancer living in Turkey is unknown. In this study, we investigated the HR and HER2 status of women with breast cancer by races in southeastern Turkey referred to the Department of Radiation Oncology between July 2006-July 2012.

Methods

Approval of the institutional ethics board was obtained for this study. Patients were asked about their race during their consultation at the department or by telephone. Other medical data was obtained from the medical records.

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Table 1. Distribution of selected characteristics among Turkish, Kurdish and Arabic patients with breast cancer

Characteristics	*All patients 647 (100%) N (%)*	*Turkish 438 (68%) N (%)*	*Kurdish 174 (26.8%) N (%)*	*Arabic 35 (5.2%) N (%)*	*p-value*
Menopausal status					0.8
Pre	381 (59.4)	260 (59.6)	99 (58.2)	22 (62.8)	
Post	260 (40.5)	176 (40.3)	71 (41.7)	13 (37.2)	
Unknown	6 (0.1)	2 (0.1)	4 (0.1)	-	
Histopathology					0.6
Ductal carcinoma	584 (90.3)	392 (89.4)	158 (90.8)	34 (97.1)	
Lobular carcinoma	26 (4)	19 (4.3)	7 (4)	-	
Other	37 (5.7)	27 (96.1)	9 (5.2)	1 (2.9)	
TNM stage					0.07
I	20 (3)	15 (3.5)	4 (2.3)	1 (2.8)	
II	259 (40)	191 (43.7)	57 (32.7)	11 (31.6)	
III	305 (47.2)	193 (44)	91 (52.3)	21 (60)	
IV	50 (7.7)	30 (6.8)	19 (10.9)	1 (2.8)	
Carcinoma in situ	13 (2.1)	9 (2)	3 (1.8)	1 (2.8)	
Grade					0.2
1	29 (4.5)	25 (5.7)	4 (2.3)	-	
2	284 (43.9)	192 (43.8)	76 (43.7)	16 (45.7)	
3	291 (45)	191 (43.6)	84 (48.3)	16 (45.7)	
Unknown	43 (6.6)	30 (6.9)	10 (5.7)	3 (8.6)	
ER status					0.002
ER+	543 (70)	322 (73.5)	104 (59.7)	27 (77.1)	
ER-	194 (30)	116 (26.5)	70 (40.3)	8 (22.9)	
PR status					0.001
PR+	470 (72.6)	337 (77)	108 (62)	25 (71.4)	
PR-	177 (27.4)	101 (23)	66 (38)	10 (28.6)	
HER2 status					0.3
HER2+	206 (31.8)	132 (30.2)	63 (36.2)	11 (31.5)	
HER2-	434 (67.1)	302 (68.9)	109 (62.6)	23 (65.7)	
Unknown	7 (1.1)	4 (0.9)	2 (1.2)	1 (2.8)	
ER/PR status					
ER+/PR+	393 (60.8)	284 (64.9)	84 (48.3)	25 (71.5)	<0.0001
ER+/PR-	60 (9.3)	38 (8.6)	20 (11.5)	2 (5.7)	0.4
ER-/PR+	77 (11.9)	53 (12.1)	24 (13.8)	-	0.06
ER-/PR-	117 (18)	63 (14.4)	46 (26.4)	8 (22.8)	0.002
Triple subtypes					
ER+/PR+/HER2+	101 (15.8)	71 (16.3)	22 (12.7)	8 (23.5)	0.2
ER+/PR+/HER2-	287 (44.8)	210 (48.3)	61 (35.4)	16 (47)	0.01
ER-/PR-/HER2+	52 (8.1)	32 (7.3)	23 (13.3)	3 (8.9)	0.06
ER-/PR-/HER2-	65 (10)	35 (8)	25 (14.5)	5 (14.7)	0.04

A total of 648 breast cancer patients (Turkish 438, Kurdish 174, Arabic 35 and Armenian 1) who were living in southeastern Turkey and referred to the Department of Radiation Oncology for radiation therapy between July 2006-July 2012 were included in the study. Only one Armenian patient who had triple-negative tumor was excluded from statistical analysis.

Tumor stage at diagnosis was defined according to the American Joint Committee on Cancer [12]. Tumor grade was defined according to Bloom-Richardson criteria as I, II, III, and other/unknown [13]. Menopause was defined as the absence of menses for a minimum of 12 continuous months prior to the diagnosis of breast cancer.

According to their HR status, patients were categorized into 4 groups: ER+/PR+, ER+/PR-, ER-/PR+, and ER-/PR-. HER2 status was scored by IHC as negative for 0 and 1+, and positive for 3+. Specimens scored 2+ were further evaluated by fluorescence in situ hybridization (FISH) technique (copies ≤ 2: negative, copies > 2: positive).

Statistics

Analyses were conducted using the Statistical Package for Social Sciences (SPSS, version 18) software. The frequency of distribution was calculated for tumor characteristics, stage at diagnosis, menopausal status and race. Statistical analysis was done using chi square test with regard to patients' ER, PR, HER2 status, triple subtypes (combinations of ER,PR and HER2) and race. P values less than 0.05 were considered significant.

Results

The median patient age at diagnosis was 48

years (range 20-83) and 381 (59.4%) of the patients were premenopausal. Invasive ductal carcinoma was the most common histologic diagnosis in all races. Although Turkish patients had smaller tumor size (<5 cm;47.2%) compared to Kurdish (35%) and Arabic (34.4%) patients (p=0.008), stage was similar among races and stage II-III disease was more common among all races. Selected characteristics of Turkish, Kurdish and Arabic patients are shown in Table 1.

IHC studies were performed on 647 (100%) patients, and the number of ER+, PR+ and HER2+ patients were 453 (70%), 470 (72.6%) and 206 (32.1%), respectively. ER+/PR+ rates between Turkish and Arabic patients were similar and were higher compared with Kurdish patients (p<0.002). HER2+ rates were similar among the three races (p>0.2). The most frequent triple subtype was ER+/PR+/HER2- (44.9%), followed by ER+/PR+/HER2+ (15.8%). Triple-negative rates between Kurdish and Arabic patients were similar (p>0.9) but were higher compared to Turkish patients (p=0.04). There was no relationship between triple subtypes and age or tumor stage at diagnosis, but pathologic grades I or II of ER+/PR+/HER2- patients predominated (66%; p<0.0001), while grade III predominated in ER-/PR-/HER2+ patients (71%; p=0.001).

Discussion

In this study, we investigated HR and HER2 status of Turkish, Kurdish and Arabic women with breast cancer living in southeastern Turkey and found that HR status vary among the 3 ethnic groups. It is known, however, that HR status differs among different ethnic groups. Several studies from different countries have demonstrated variations in hormone receptors of women with breast cancer. Vona Davis et al [14]. analyzed 6 studies and found that African-American women had higher ER- rates than Hispanics and White Americans. Melinda et al. [15] reported higher rates of ER-/PR- in Asian Filipino breast cancer patients compared to other Asian-American women. Bhoo-Pathy et al. [16] reported that ER status of Malay, Chinese and Indian women with breast cancer living in Singapore and Malaysia was different among 3 ethnic groups.

To our knowledge, this is the first study from Turkey evaluating the HR status in patients with breast cancer in terms of races. This is also the first study that presents age and stage at diagnosis, subtype incidence, characteristics of tumor, and menopausal status with respect to races. Runnak et al. [17] investigated a total of 814 Kurdish and Arabic women with breast cancer living in Northern Iraq and in 432 of these patients HR status was determined. They found no difference in ER, PR and HER2 status between Kurdish and Arabic breast cancer patients. Both the Runnak et al. study and the current study showed no difference in PR and HER2 status between Kurdish and Arabic patients. However, compared to Runnak et al. study, in our study that also included Turkish patients, ER+ rates of Arabic patients (77.1%) were higher than Kurdish patients (59.7%).

The variation of HR status among breast cancer patients with different races is explained by genetic disparities and socioeconomic status (SES) which is related to non-genetic factors [18]. Tumor biology may be affected by races. Unfavorable cancer types such as HR- tumors, HER2 overexpression, basal-like breast tumors or high grade tumors are seen more frequent in certain races [15-21]. ER- tumors are more frequent in some hereditary breast cancers which bear BRCA1 mutations [18]. There is no study evaluating genetic mutations in breast cancer patients by ethnicity in Turkey. Beside genetic variations, non-genetic socioeconomic factors such as environment and lifestyle may cause differences in HR status. It has been reported that low SES may be related to HR- breast cancer [19,20,22]. Reasons causing the difference in HR status of races in our study are also unknown. Further studies are needed to clarify the effects of genetics and socioeconomic factors on HR status in different ethnic groups.

HR status is a prognostic factor in breast cancer [2]. Survival of HR+ women with breast cancer is better than HR- women after adding hormonotherapy to the treatment [23-25]. The results of our study show that, compared to Arabic and Kurdish patients, Turkish patients have more favorable prognostic HR status and this may result in longer survival in Turkish breast cancer patients. However, long-term follow-up is needed to draw firm conclusions on this topic.

In conclusion, HR status is different between Turkish, Kurdish and Arabic women with breast cancer living in southeastern Turkey. Compared to Kurdish and Arabic patients, Turkish patients have more favorable prognostic factors. Further studies are needed to explain the cause and the results of these differences.

References

1. Jemal A, Siegel R, Xu J, Ward E. Cancer Statistics 2010. CA Cancer J Clin 2010;60:277–300.
2. Fitzgibbons PL, Page DL, Weaver D et al. Prognostic factors in breast cancer. College of American Pathologists Consensus Statement 1999. Arch Pathol Lab Med 2000;124:966–978.
3. Osborne CK, Yochmowitz MG, Knight WA 3rd, McGuire WL. The value of estrogen and progesterone receptors in the treatment of breast cancer. Cancer 1980; 46:2884–2888.
4. Rastelli F, Crispino S. Factors predictive of response to hormone therapy in breast cancer. Tumori 2008;94:370–383.
5. Dunnwald LK, Rossing MA, Li CI. Hormone receptor status, tumor characteristics, and prognosis: a prospective cohort of breast cancer patients. Breast Cancer Res 2007; 9:R6.
6. Chelebowski RT, Chen Z, Anderson GL et al. Ethnicity and breast cancer: Factors influencing differences in incidence and outcome. J Natl Cancer Inst 2005;97:439–448.
7. Elledge RM, Clark GM, Chamness GC, Osborne CK. Tumor biologic factors and breast cancer prognosis among White, Hispanic, and Black women in the United States. J Natl Cancer Inst 1994;86:705–712.
8. Chu KC, Anderson WF, Fritz A, Ries LA, Brawley OW. Frequency distributions of breast cancer characteristics classified by estrogen and progesterone receptor status for eight racial/ethnical groups. Cancer 2001;92:37–45.
9. Li CI, Malone KE, Daling JR. Differences in breast cancer hormone receptor status and histology by races and ethnicity among women 50 years of age and older. Cancer Epidemiol Biomarkers Prev 2002;11:601–607.
10. Hausauner AK, Keagen TH, Chang ET, Clarke CA. Recent breast cancer trends among Asian/Pacific Islander, Hispanic, and African-American women in the U.S.: Changes tumor subtype. Breast Cancer Res 2007;9:R90.
11. Gapstur SM, Dupuis J, Gann P, Collila S, Winchester DP. Hormone receptor status of breast cancer in Black, Hispanic, and non-Hispanic white women. An analysis of 13,239 cases. Cancer 1996;77:1465–1471.
12. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. American Joint Committee on Cancer Staging Manual (7th Edn). New York: Springer, 2010, pp 345–376.
13. Harris L, Fritsche H, Mennel R et al. American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer. J Clin Oncol 2007;25:5287–5317.
14. Vona-Davis L, Rose DP. The Influence of Socioeconomic Disparities on Breast Cancer Tumor Biology and Prognosis: A Review. J Womens Health (Larchmt) 2009;18:883–893.
15. Telli ML, Chang ET, Kurian AW et al. Asian ethnicity and breast cancer subtypes: a study from the California Cancer Registry. Breast Cancer Res Treat 2011;127:471–478.
16. Bhoo-Pathy N, Hartman M, Yip CH et al. Ethnic differences in survival after breast cancer in South East Asia. PLoS One 2012;7:e30995.
17. Runnak MA, Hazha MA, Hemin HA, Wasan AA, Rekawt RM, Michael HD. A population-based study of Kurdish breast cancer in northern Iraq: Hormone receptor and HER2 status. A Comparison with Arabic women and United States SEER data. BMC Womens Health 2012;12–16. Available from URL: http://www.biomedcentral.com/1472-6874/12/16.
18. King MC, Wieand S, Hale K et al. Tamoxifen and breast cancer incidence among women with inherited mutations in BRCA1 and BRCA2: National Surgical Adjuvant Breast and Bowel Project (NSABP-P1) Breast Cancer Prevention Trial. JAMA 2001;286:2251–2256.
19. Gordon NH. Socioeconomic factors and breast cancer in black and white Americans. Cancer Metastasis Rev 2003;22:55–65.
20. Gordon NH. Association of education and income with estrogen receptor status in primary breast cancer. Am J Epidemiol 1995;142:796–803.
21. Amend K, Hicks D, Ambrosone CB. Breast Cancer in African-American Women: Differences in tumor biology from Europan-American Women. Cancer Res 2006;66:8327–8330.
22. Andaya AA, Enewold L, Horner MJ, Jatoi I, Shriver CD, Zhu K. Socioeconomic disparities and breast cancer hormone receptor status. Cancer Causes Control 2012;23:951–958.
23. Smith RE, Good BC. Chemoprevention of breast cancer and the trials of the National Surgical Adjuvant Breast and Bowel Project and others. Endocr Relat Cancer 2003;10:347–357.
24. Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thürlimann B, Senn HJ. Meeting highlights: updated international expert consensus on the primary therapy of early breast cancer. J Clin Oncol 2003;21:3357–3365.
25. Fisher B, Jeong JH, Bryant J et al. Treatment of lymph-node-negative, oestrogen receptor-positive breast cancer: long-term findings from National Surgical Adjuvant Breast and Bowel Project randomised clinical trials. Lancet 2004;364:858–868.