RESEARCH ARTICLE

Is Sunlight a Predisposing Factor for Triple Negative Breast Cancer in Turkey?

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Abstract

Intraduction: There is known to be a relationship between vitamin D level and more aggresive breast cancer subtypes, especially triple-negative breast cancer (TNBC). It was reported that sunlight exposure has an effect on the prognosis of patients with cancer, possibly related to the conversion of vitamin D to its active form with sunlight. We aimed to evaluate the effect of sunlight exposure on patients with TNBC. Materials-Methods: A total of 1,167 patients with breast cancer from two different regions of Turkey (Antalya and Kayseri, regions having different climate and sunlight exposure intensity over the year) were analysed retrospectively. The ratio of patients with TNBC was identified in those two regions. Results: The ratio of patients with TNBC was 8% and 12% for Kayseri and Antalya regions, respectively, and this difference between the two groups was statistically significant (p=0.021). Discussion: Sunlight exposure may be associated with more prevalent TNBC. This finding should be investigated with a prospective study.

Keywords: Breast cancer - sunlight exposure - season - triple negative

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Introduction

Breast cancer is the most common cancer type in women (Parkin et al., 1999). Triple-negative breast cancer (TNBC) is defined by absent expression of the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). Approximately, TNBC accounts for 20% of all breast cancers (Swain, 2008) and the prognosis of patients with TNBC is usually worse than other types of breast cancer. Some factors such as parity, obesity, age at first pregnancy, BRCA mutations were reported as risk factors for TNBC (Trivers et al., 2009; Gonzalez-Angulo et al., 2011).

It was previously reported that sufficient sunlight exposure and vitamin D levels may decrease the morbidity and mortality due to breast cancer (Freedman et al., 2002; Abbas et al., 2008). The incidence and mortality of breast cancer were found to be lower in the regions with higher sunlight exposure (Mohr et al.2008; Rhee et al., 2009).

The conversion of vitamin D to its active form was mediated via sunlight exposure in the skin. Vitamin D binds to and activates the vitamin D receptor (VDR). VDR acts as a transcription factor to modulate gene expression affecting cell cycle proliferation, cell cycle arrest, induction of differentiation, and activation of apoptosis (Peppone et al., 2012).

In this study, we aimed to evaluate whether more sunlight exposure has an effect on the ratio of patients with TNBC.

Materials and Methods

A total of 1167 patients with breast cancer from two different regions of Turkey (Antalya and Kayseri, those regions have different climate and sunlight exposure intensity for a year) were included in this study. The exposure hours to sunshine per day in those regions was given in Table 1. The patients were divided into two groups: Kayseri region which has a colder climate, and Antalya region with a warmer climate and more sunlight exposurethan Kayseri region. Of patients 743 were from the Akdeniz University located in Antalya region and 424 patients were from the Kayseri Training and Research Hospital located in Kayseri were analysed retrospectively, using hospital records. The ratio of patients with TNBC was calculated. The age, stage, menopausal status, histological and nuclear-grade were evaluated in patients with TNBC. Statistical analysis was done using SPSS version 16.0 (Statistical Product and Service Solutions, SPSS Inc, Chicago, IL, USA). Frequencies analysis was carried out and independent two samples t-test and chi square test were used.

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Table 1. Hours of Exposure to Sunshine Per Day in Kayseri and Antalya

Months	Hours of exposure to sunshine per day Kayseri	Antalya	P Value
January	3	5	
February	4	7	
March	5	7	
April	6	9	
May	8	11	
June	10	12	
July	12	13	
August	11	12	
September	9	11	
October	7	9	
November	5	7	
December	3	5	
Day/Hours (mean)	6.9/207	9/270	0.097

Table 2. Characteristics of Patients with TNBC in Two Region

Variables		Kayseri (n:33)	Antalya (n:90)	P value
Age (mean)		55.7±9.8	49.0±10.1	0.001
Menopausal Status	Premenopausal	8 (24%)	46 (51%)	0.028
	Perimenopausal	0 (0%)	1 (1%)	
	Postmenopausal	25 (76%)	43 (48%)	
Stage	1	4 (12%)	23 (26%)	0.054
	2	17 (52%)	48 (53%)	
	3	10 (30%)	12 (13%)	
	4	0 (0%)	0 (0%)	
	Unkonwn	2 (6%)	7 (8%)	
Histological Grade	1	1 (3%)	0 (0%)	0.155
	2	8 (24%)	33 (36%)	
	3	9 (27%)	32 (36%)	
	Unknown	15 (46%)	25 (28%)	
Nuclear Grade	1	1 (3%)	10 (11%)	0.569
	2	11 (33%)	38 (42%)	
	3	6 (18%)	19 (21%)	
	Unknown	15 (46%)	23 (26%)	

Results

The patients characteristics are given in Table 2. The mean age of patients with TNBC in Kayseri and Antalya regions were 55,7±9,8 and 49,0±10,1 year, respectively (p=0.001). There was a significant difference in menopausal status between two regions (p=0.028). While the majority of patients were postmenopausal in Kayseri region, the premenopausal patients were more common in Antalya region. We did not find a difference in stage, histologic and nuclear grades (p=0.054, p=0.155, p=0.569, respectively) between two groups. The ratios of patients with TNBC in Kayseri and Antalya regions were 8% and 12% for, respectively and there was a statistically significant difference between two groups (p=0.021).

Discussion

In present study, we evaulated whether sunlight exposure has an impact on the ratio of TNBC. We find that the ratio of patients with TNBC was higher in the region with a more sunlight exposure. The effect of sunlight exposure on the prognosis of patients with cancer is related to the conversion of vitamin D. Many studies reported that the adequate vitamin D level and more sunlight exposure decreased the incidence and mortality of breast cancer. In additon, it was reported that there was a relationship between low level of vitamin D and more aggresive breast cancer subtypes, especially TNBC (Rainville et al., 2009; Peppone et al., 2012; Yao et al., 2012). It was alsoreported that patients with TNBC had lower vitamin D level, and probably low level of vitamin D may be a characteristic of TBNC. The sunlight exposure is an important factor for the conversion of vitamin D to its active form, and in turn, the sufficient level of vitamin D have a positive effect on the prognosis of patients with cancer. Our results showed that the ratio with patients with TNBC were significantly higher in Antalya region with more sunlight exposure. However, in vitro studies showed that vitamin D decreases the estrogen and progesteron receptor expression on the breast cancer cells (Swami et al., 2000; 2003; Peng et al., 2007). Also, it was thouht that the anti-proliferative effects of the vitamin D analogue, EB1089 on breast cancer cell line was through the down regulation of estrogen receptor (James et al., 1994; Davoodi et al., 1995). The potential activities of vitamin D on ErbB2 overexpressing have not been detailed in literature but it was previously reported that vitamin D analogue, BXL0124 inhibited the growth of ErbB2 overexpressing mammary tumors through regulating the ErbB2/AKT/ERK signaling pathways (Lee et al., 2010). We previously reported that the positivity of progesteron receptor was significantly lower among patients with breast cancer in Antalya region with more sunlight exposure than Kayseri region and there was a trend for the higher positivity of estrogen receptor (Mutlu et al., 2011). Due to the effect of vitamin D on estrogen and progestreon receptor during cancer development, the ratio of patients with TNBC might be higher in the region with more sunlight exposure despite the decrease of incidence and mortality of all patients with breast cancer. According to our results, while the patients with TNBC were mostly premenopausal status in Antalya with more sunlight exposure, the majority of patients with TNBC were postmenopausal in Kayseri. In previous studies, it was reported that the TNBC subtype was more prevalent among premenopausal (Carey et al., 2006; Lin et al., 2012). The more sunlight exposure via vitamin d decreased ER and PR expression may be contribute that TNBC is more commonly at young age.

It is not fully understood that the function of sunlight and vitamin D on the development of cancer. The further studies are warranted to evaluate the effect of sunlight and vitamin D on the development of cancer.

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