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ORIGINAL ARTICLE

Association between Osteopontin and Hormone Receptor Status among Breast Cancer Patients

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ABSTRACT

Background: Breast cancer (BC) is problem in developed and developing nations and is linked to a high mortality rate.
Objective: In this study, we determined the relationships between osteopontin level, hormonal status, stage, BMI, and age in BC patients.
Materials and Methods: In a cross-sectional 178 BC patients, ages ranged from 28 to 95 were randomly enrolled. Body mass index were estimated. Plasma osteopontin were measured.
Results: From total of 178 BC patients, 54 (30.3 %) were trilpe negative, 124 (69.7%.) were hormone receptor positive. 86 (48.3%) had high plasma OPN level and 92 (51.7%) with OPN ≤ 55. Chi-square analyses show that osteopontin was significantly associated with triple negative breast cancer and tumor stage with (*P* = 0.002 and 0.011), and (odd ratio 1.653,1.604) respectively.
Conclusion: High OPN associated with hormone receptor and tumor stage in breast cancer patients.
Keywords: Osteopontin, BC, Hormone, Receptors

INTRODUCTION

Breast cancer (BC) is a major issue around the world and has the highest incidence and mortality rates of all malignancies in women worldwide [(1)],now that it has surpassed all cancer types as the most commonly diagnosed cancer [(2)]. BC global burden was increasedin 2020 to 2.3 million new cases, which is the fifth leading cause of cancer mortality worldwide [(2)]. BC accounts for 1 in 4 cancer cases and for 1 in 6 cancer deaths[(2)].

In Africa, the incidence of BC continues to increase in all regions of the continent reaching nearly 169,000 in 2018 and GLOBOCAN has estimated that by 2040 the number of incident cases could nearly double that of current estimation[(3)].

In Sudan, there is no national registry for cancer, thus hospital case series are used to derive estimates of cancer. Data from the Khartoum State Cancer Registry 2009-2010 demonstrated higher prevalence of BC among Sudanese women. Meanwhile the National Cancer Institute of the University of Gezira (NCI-UG) show that the incidence of breast cancer accounts for 34% of all cancers among female patients in2017[(4)].

BC molecular subtypes are: luminal A (ER and/or PR positive and HER2 negative), luminal B (ER and/or PR positive and HER2 positive), HER2-enriched (ER and PR negative, and HER2 positive), and basal-like breast cancer (approximates TNBC) [(5)]. About 10% to 20% of breast cancers are basal type "triple negative" because they are ER-, PR-, and HER2-[(5, 6).] Basal-like tumours are more common in African-American women, premenopausal women, and those with the BRCA1 gene mutation.[(7)]. In contrast to other breast cancer types, basal-like breast cancer patients have a poorer short-term prognosis [(8)].

According to studies, Sudanese women, as elsewhere in sub-Saharan African countries, are diagnosed at younger ages, with advanced stages, and with a higher tumor grade and lymph node involvement than western women. [(4)], Therefore, a full understanding of breast cancers is crucial to develop useful prognostic markers and therapeutic targets.

Recent evidence has highlighted OPN as a potential cancer biomarker and therapeutic target [(9).] In at least 30% of cancer patients, OPN gene is among the most highly expressed genes[(10, 11).]

Most osteopontin studies concluded that high levels of OPN were associated with adverse pathological and clinical outcomes in breast cancer patients and highlight OPN is a valuable breast cancer prognostic biomarker [(12)]. There for present study hypothesis that overexpression of OPN associated with high risk with breast cancer hormonal status.

MATERIALS AND METHODS

In a cross sectional study 178diagnosed breast cancer patients were enrolled from Radiation and Isotope centre at Khartoum (RICK). After informed consent samples were collected. Patients with bone disease, asthma, autoimmune disease and other types of cancer were excluded, all patients received chemotherapy and some on adjuvant therapy. Study population were classified according to immunohistochemistry results to 2 groups (triple negative and hormone receptor positive)
Demographic data (age, BMI, stage, hormone receptor, and duration of treatment) were recorded from the statistic department.
Ethics Approval: All procedures in this study were conducted in accordance with the ethics standards of the Institutional Review Board (AL-Neelain University) IRB serial No: NU-IRB-17-10-10-106 and national (National Health Research Ethics Committee – Sudan.All participants were informed by the aim of the study and the signed consent was obtained from each participant included.
Collection of the blood sample: A 2.5 ml of blood was withdrawn on EDTA container. plasma was obtained by centrifugation at 3000 rpm and kept at -20°.
OPN measurement: OPN level was measured by ELISA technique (Catalogue No.: 201-12-1526) (Sun Red – Shanghai).it uses a double antibody sandwich linked immunosorbentassay.OPN level was assayed according to the procedure provided by manufacture leaflet. The Chroma of colour is positively correlated with OPN concentration.
Statistical analysis: Data analysed using Statistical Package for Social Sciences (SPSS Inc, ver. 23, IL-Chicago- USA). The descriptive results were presented as frequency, and percentages. Chi squire was used to correlate between nominal variables. P-value of ≤0.05 was considered significant.

RESULTS

The demographic results showed that the percentage of triple negative is 30.3 % in Sudanese BC patients, while the hormone receptors positive is 69.7%. Meanwhile, 86 (48.3%) of the study population had high plasma OPN level > 55 ng/ml and 92 (51.7%) with OPN ≤ 55 of 178 patients. Age group ≤ 50 years were found to be 118 (66.3%) and > 50 years were 60 (33.7%). Of BC patients, 120 (67.4%) had normal BMI and 58 (32.6%) was overweight. Moreover, 92(51.7%) was received ≤ 4 treatment cycles and 86 (48.3%) Received > 4 treatment cycles, the results are presented in **Table 1**.

Patients with triple negative represent about 30.3 % of the total BC patients, out of these; about 66.7 % have OPN levels of> 55, while in hormone receptor positive group 40.3 %.

Chi‑square results showed that there are significant associations between OPN, Hormone receptor status, and stage (*P value* = 0.00 and 0.011) and (OR = 1.65,1.60), respectively. Whereas no associations were observed between OPN, age, BMI and number of treatment doses (*P value* 0.34, 1.00, 0.65) and (*OR*= 0.858, 1.00, 1.07) receptively, the results arepresented in Table 2.

Table 1: Basic Characteristics Data of Breast Cancer Patients

Frequency (%)	Classes	Characteristic
54 (30.3 %) 124 (69.7%)	Triple Negative Hormone. R Positive	Hormone. R Type
92 (51.7%) 86 (48.3%)	≤ 55 > 55	OPN
84 (47.2%) 94 (52.8%)	Early Late	Stage
118 (66.3%) 60 (33.7%)	≤ 50 > 50	Age (years)
120 (67.4%) 58 (32.6%)	Normal Overweight	BMI
92 (51.7 %) 86 (48.3 %)	<4 (cycles) > 4 (cycles)	No. Treatment cycles

Table 2: Frequencies, Percentages and adjusted Odd ratios (95% confidence interval) of age, stage, number of treatment dose and Osteopontin for comparison of Triple negative and Hormone receptor positive

CI(lower-upper)	OR		P Value	OPN	Characteristic
	≤ 55	> 55			
1.24 - 2.19	1.65	0.00	36 (66.7%) 50 (40.3%)	18 (33.3%) 74 (59.7%)	Status Triple negative Hormone receptor positive
1.09- 1.94	1.60	0.01	32 (38.1%) 54 (57.4%)	52 (61.95) 40 (42.6%)	Stage Early Late
0.63 -1.16	0.85	0.34	54 (45.8%) 32 (53.3)	64 (54.2%) 28 (46.7%)	Age (years) ≤ 50 > 50
0.43 - 1.21	1.00	1.00	58 (48.3%) 28 (48.3%)	62 (51.7%) 30 (51.7%)	BMI Normal Overweight
0.79 -1.45	1.07	0.65	46 (50 %) 40 (46.5%)	46 (50 %) 46 (53.5%)	Treatment dose ≤ 4 (Cycles) > 4 (Cycles)

OPN = Osteopontin, OR = Odds ratio, CI = Confidence Interval

DISCUSSION

Breast cancer is the most diagnosed and most mortal cancer among women[13]. In this study we focused more in triple negative breast cancer (TNBC). TNBC is a very aggressive BC subtype of BC, absence of effective therapies, and whose underpinning mechanisms remain unclear [14, 15]. Recent studies detected that OPN's role in tumor progression could potentially improve cancer therapy and facilitate development of a new anticancer agent [16].

The results of this study indicated that a higher incidence of breast cancer in younger women (<50 years), the same findings were reported before in study done African women residing in western countries [17]. The same observation was also being been reported in women of African descent residing in western countries [18]. The reasons for the younger age distribution of African women with breast cancer might be due to higher prevalence of early childbearing among African women compared to Caucasian.

Other study done by Palmer et al [19] reported that multiparity increased breast cancer risk prior to age 45, and multiparity was common in African women less than 45 years.

The present study detected that high OPN level associated with hormone receptor status and tumour stage in breast cancer patients. Whereas triple negative have higher risk for increase OPN level more than hormone receptor positive BC patients. This in agree with previous studies which concluded that patients with overexpression develop predominantly triple-negative tumours; and Tumor aggressiveness and a poor prognosis are linked to OPN overexpression [20]. Furthermore, high OPN is more common in late stage more than early stage [21, 22]. This distinction may be due to genomic composition and differential gene expression even in those primary tumours with similar histology [23]. Therefore, OPN blocking could be a useful therapeutic target.

This is first investigation of the relationship between hormone receptor status and Osteopontin level in Sudan, although no association were detected between OPN level, demographic variables (age, BMI), and treatment dose.

Finally, cohort studies examining the prognostic significance of OPN and OPN spliced variants, particularly OPN-C, may produce significant new methods for assessing BC.

CONCLUSION

The data of present study suggests that, triple negative and late stage BC patients areexpressingmoreOPN level. Therefore, triple negative patients at higher risk to have aggressive and resistance BC.

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