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Erythrocyte Sedimentation Rate and C-Reactive Protein Levels in Breast Cancer Patients in Benin City, Nigeria

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Abstract:
Introduction: *Inflammation has been shown to play a role in the pathogenesis of breast cancer. The inflammatory basis of breast cancer has not been evaluated in our environment.*
Objective: *The purpose of this present study is to compare the level of some systemic inflammation markers in patients with breast cancer to those of apparently healthy populace in Benin City, Nigeria.*
Methodology: *This is a case control study conducted in Benin City, Nigeria. Breast cancers patients recruited from central hospital Benin City and Controls from the general populace had their venous blood sampled and analyzed for Erythrocyte Sedimentation Rate (ESR) and C-Reactive Proteins (CRP) levels using standardized laboratory methods. Results were analyzed using SAS 2004 model.*
Results: *A total of 90 participants including 60 patient and 30 controls participated in this study. ESR and CRP were significantly elevated in Breast cancer patients (P<0.05). ESR correlated positively with CRP in the study populace.*
Conclusion: *These findings support the fact that inflammation plays a role in the pathogenesis of breast cancer. These markers may be useful in prognostication and monitoring of patients response to therapy.*
Keywords: *Breast cancer, C - reactive protein (CRP), Erythrocyte Sedimentation Rate (ESR), inflammation.*

I. Introduction

Breast cancer is the most common type of cancer in women and the leading cause of cancer-related death worldwide.[1] The exact cause of breast cancer is not completely known, it represents a complex interplay of genetic susceptibility and environmental factor and inflammation has been shown to underly the pathology of cancer.[2 - 4] The inflammatory response promotes carcinogenesis by damaging DNA, stimulating angiogenesis and cell proliferation, and inhibiting apoptosis. [5, 6]

Erythrocyte Sedimentation Rate (ESR) is a simple inexpensive index of measurement of chronic inflammation frequently ordered in clinical medicine[7.] In cancer management, a high ESR has been found to correlate with adverse prognosis in some specific cancers including solid organ and haematological malignancies.[10 – 12] The diagnostic use of ESR has been generally replaced by the measurement of C-reactive protein (CRP).

CRP is classical positive acute-phase protein displaying rapid and pronounced rise in plasma level in response to acute inflammation, infection and tissue damage[13, 14]. CRP is produced by the liver, predominantly under transcriptional control by the cytokine interleukin-6 originating from the site of pathology.[15]

Serum CRP has been shown to parallel carcinogenesis possibly as an expression of the host defense reaction or as paraneoplastic syndrome[16, 17]. Previous epidemiologic studies have reported that elevated CRP levels may be associated with poor prognosis of several types of solid cancers[18], including endometrial[19], cervical[20], colorectal, pancreatic, hepatocellular, esophageal, renal cell, bladder, prostate, ovarian and non small-cell lung cancer.[21, 22]

Breast cancer is characterized by significant histological inflammation. Emerging evidence suggest that inflammatory pathways also play an important role in the disease progression.[23 – 28] This study therefore aims to evaluate and compare the levels of some inflammatory markers (ESR and CRP) in breast cancer patients with those of a control population.

II. Methodology

` This is a case control study conducted in Central Hospital, Benin City, Nigeria over a 15 months period (1st July, 2011 to 31st October, 2012). The study populace include 60 females diagnosed of Breast Cancer (Case group) were recruited from the General Surgery Clinic of the hospital after obtaining their consent to participate in the study and 30 apparently healthy women as Controls.

Breast Cancer was diagnosed based on patient history, physical examination, breast tissue biopsy and histologic evaluation. Newly diagnosed patients who are yet to commence chemotherapy were recruited.

Patients with comorbid medical conditions associated with intense inflammatory changes were excluded from the study.

Sample collection and preparation

Venous blood was obtained from consenting participants into an anticoagulant bottle containing ethylene diamine tetracetic acid (EDTA) for ESR evaluation, and also into a sterile plain bottle for CRP level estimation. The sample for CRP was allowed to clot and retract, and then the serum harvested after centrifugation at 3000 rpm for 15mins.

ESR was evaluated immediately after sample was collected. Sera for CRP estimation were frozen at -20^0C till sufficient samples were collected for analysis. The sample for CRP were analyzed at the University of Benin Teaching Hospital, Benin City.

Biochemical Assays:

Determination of ESR: ESR was determined using the Westerngreen method,[7] which measures the distance that erythrocytes have sediment after one hour in a vertical column of anticoagulated blood under the influence of gravity.

Determination of CRP levels: CRP level was determined using the immunoturbidimetric method[30.] In this method CRP sample binds to specific anti-CRP antibodies, which have been adsorbed to latex particles and the agglutination measured spectrophotometrically is proportional to the quantity of CRP in the sample.

Ethical Approval: The study was approved by the ethics committee of Central Hospital, Benin City..

Data analysis: Data were analyzed with SAS 2004 model. All results were expressed as mean ± standard error of mean. The difference in means between the two groups were compared with the student T test. Correlation between CRP and ESR was detremined using Pearson correlation coefficient. P value was set at 0.05.

III. Results

The mean age of the patient group was 55 ± 1.6 and the controls 51 ± 1.4 years. The ESR was significantly higher in breast cancer patients than in controls (47.5±7.3 versus 6.9 ± 0.5 mm/hr) ($P<0.05$). similarly CRP was significantly higher in breast cancer patients than in controls (73.8 ± 1.3 versus 9.0 ± 0.7mg/L) ($P<0.05$) as shown in "Table 1". A statistically significant positive correlation existed between ESR and CRP levels ($r=0.6004$), ($P< 0.001$) in all the participants.

IV. Discussion

The findings in this study showed statistically significant elevation of ESR levels of patients with breast cancer compared to that of the control subjects. High ESR levels have been found to correlate with overall poor prognosis for different types of cancer including breast. European studies of patients with Hodgkin's disease have suggested that an elevated ESR may still be an excellent predictor of early relapse, especially if the value remained elevated after chemotherapy or fails to drop to a normal level within six months after therapy.[9, 11]

Findings from this study also showed statistically significantly elevated CRP levels in breast cancer patients compared to the control subjects; this is probably due to the rise in the plasma concentration of interleukin 6 which is produced predominantly by macrophages during inflammation.[31] High serum CRP might reflect a high metastatic potential as inflammatory cytokines in general and CRP in particular are known to promote metastatic spread by stimulating angiogenesis, increasing vascular permeability, acting as an endothelial cell mitogen.[32] Results from prospective epidemiologic studies are conflicting, with some other studies showing an association between elevated CRP levels and poor prognosis [33, 34] and others showing no such association[35, 36]. The largest study asociating elevated CRP with poor prognostic outcome included 700 women treated for early stage breast cancer and wer found to have elevated levels of CRP measured two and a half years from the time of diagnosis. This was associated with reduced overall survival.[33]

Allin et al in another related study showed that invasive breast cancer patients with elevated CRP levels at diagnosis had a 1-7 fold increased risk of death from breast cancer compared to patients with low CRP levels at diagnosis.[37] Promising data on the prognostic significance of serum CRP in various malignancies have been reported.[38]

Akanni et al in Oshogbo, Nigeria reported a rise in CRP levels in patients with chronic myeloid leukaemia; they concluded that CRP could be a useful factor in determining disease progression or monitoring the effectiveness of treatment in leukaemic patients.[39] In another ralated study Ojo et al in Abeokuta, South Western Nigeria reported that patients with high CRP also correlated with elevated ESR as observed in the index study.[40]

V. Conclusion

It can be concluded that ESR and CRP are significantly elevated in patients breast cancer thereby affirming that inflammatory changes underly the pathogenesis of the disease. We therefore recommend another study to evaluate the prognostic potentials of these markers in breast cancer patients in our environment.

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Table 1: Age, ESR, and CRP levels of the Study Participants

Variables	Breast Cancer	Controls	P value
	Mean ± SEM (Range) n = 60	Mean ± SEM (Range) n = 30	
Age	55.0 ± 1.6 (45 – 65)	51.0 ± 1.4 (42 – 66)	>0.05
ESR	47.5 ± 7.3 (14 – 130)	6.9 ± 0.5 (3 – 13)	<0.05
CRP	73.8 ± 1.3 (59.9 – 82.8)	9.0 ± 0.7 (5.5 – 13.9)	<0.05