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Indices of thrombotic risk in patients who have undergone treatment for breast cancer

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ABSTRACT

The purpose of treatment is to alleviate the burden of morbidity and reduce mortality, therefore treatment-associated risks are of great interest. Surgical removal of breast tumour and chemotherapy are quite integral in halting disease progress. However, these treatment strategies appear to be associated with the risk of activated coagulation. This study purposively enrolled 60 female breast cancer patients consisting of 30 subjects each in pre-treatment and post-treatment groups at a tertiary hospital in Nigeria. The Quick's One-stage method was used for PT and APTT tests, while enzyme-linked immunosorbent assay was used for D-Dimer assessment. Data analysis was carried out on statistical package for social sciences (SPSS) version 20.0. A p-value ≤ 0.05 was considered significant. Mean values of PT, APTT and D-Dimer of breast cancer patients were compared to values from control subjects. The PT was significantly prolonged in the breast cancer patients compared to that of controls ($p = 0.009$). D-Dimer was also significantly raised in the breast cancer patients compared to the value for controls ($p = 0.001$). The breast cancer patients were further categorized into pre-treatment and post-treatment groups. All measured parameters were observed to be more significantly ($p = 0.001$) deranged in the post-treatment group compared to the pre-treatment group. This study concludes that there is evidence of increased thrombotic risk in breast cancer, particularly among those who have undergone surgical and chemotherapeutic treatment.

Keywords: Breast cancer, activated coagulation, thrombosis

INTRODUCTION

Breast cancer awareness and detection have been receiving impressive attention in recent years [1-3]. More importantly, medical care for the condition holds more optimistic outlook with the increasing availability of treatment centers and therapies. As more patients are being managed for breast cancer, research opportunities have emerged for better understanding of the disease as well as possible risks inherent in the treatment approaches utilized at present. Biomedical variations occasioned by the occurrence of breast cancer have been reported [4-5]. The contributions of cancer pathophysiology as well as the impact of treatment have been adduced in support of observed derangements. While the purpose of treatment is to alleviate the burden of morbidity and reduce mortality,

treatment-associated complications bear further concerns worth investigating. Undoubtedly, the dilemma in weighing between the benefits and adverse effects of the various options in medical care remains a sensitive aspect of medical practice. Studies, thus, provide the necessary evidence for advancing favorable decisions for the good of patients.

The risk of thrombosis in association with cancer has often been considered in the light of persistent inflammatory processes. This notwithstanding, vascular trauma in relation to treatment of breast cancer has been implicated as a possible avenue for thrombogenesis [6-8]. Breast cancer management entails the consideration of different approaches such as chemotherapy and surgery. Surgical removal of breast tumour and administration of cytotoxic drugs are quite integral in halting the progress of the condition and ultimately preventing metastasis with its debilitating consequences. Timely execution of these treatment strategies impacts positively in breast cancer treatment and therefore, both are commonly adopted in managing breast cancer patients. However, the associated risk of activated coagulation via vascular injury and stimulation as well as general induction of a hypercoagulability state remains to be fully investigated. So far, thrombosis in breast cancer has been reported to associate with poor prognosis [5, 9-10]. This study assessed breast cancer patients for indices of thrombotic risks sequel to surgical and chemotherapeutic interventions.

Materials and methods

This study purposively enrolled 60 female breast cancer patients consisting of 30 subjects each in pre-treatment and post-treatment groups. The patients were accessing medical care at University of Calabar Teaching Hospital in Calabar, Cross River State of Nigeria. Ethical considerations were duly observed and approval obtained from the institution's committee on ethics. Informed consent was also obtained from the study participants.

Blood sample was collected from each participant to obtain citrated plasma for the selected coagulation studies. The Quick's One-stage method was used for PT and APTT tests, while enzyme-linked immunosorbent assay was used for D-Dimer assessment. Data analysis was carried out on statistical package for social sciences (SPSS) version 20.0. Student t-test was used as the statistical tool to analyse the difference between means. A p-value ≤ 0.05 was considered significant.

RESULTS

In Table 1, mean values of PT, APTT and D-Dimer of breast cancer patients were compared to values from control subjects. The PT was significantly prolonged in the breast cancer patients compared to that of controls ($p = 0.009$). D-Dimer was also significantly raised in the breast cancer patients compared to the value for controls ($p = 0.001$).

The breast cancer patients were further categorized into pre-treatment and post-treatment groups. All measured parameters were observed to be more significantly ($p = 0.001$) deranged in the post-treatment group compared to the pre-treatment group (Table 2).

Table 1: Coagulation parameters of test and control subjects

Parameters	Breast cancer patients (n = 60)	Control (n = 60)	P value
PT (Sec)	12.52 ± 1.14	12.05 ± 1.12	0.009
APTT (Sec)	35.40 ± 1.44	35.33 ± 1.05	0.773
D-Dimer (pg/ml)	3610.93 ± 531.43	2105.87 ± 139.77	0.001

Values are expressed as Mean ± Standard deviation; PT = Prothrombin Time; APTT = Activated Partial Thromboplastin Time

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Table 2: Coagulation parameters of test and control subjects

Parameters	Post-treatment Breast cancer patients (n = 30)	Pre-treatment Breast cancer patients (n = 30)	P value
PT (Sec)	13.20 ± 1.06	12.23 ± 1.14	0.001
APTT (Sec)	36.17 ± 1.12	35.03 ± 1.33	0.001
D-Dimer (pg/ml)	4104.37 ± 208.14	3117.50 ± 165.85	0.001

Values are expressed as Mean ± Standard deviation; PT = Prothrombin Time; APTT = Activated Partial Thromboplastin Time

DISCUSSION

Indices of thrombotic risk were assessed in breast cancer patients in this study. The parameters of interest comprised PT, APTT and D-Dimer. Significantly prolonged PT and elevated D-Dimer were recorded in the breast cancer patients compared to values for controls. Prothrombin time is an indication of the extrinsic and common pathways of the pre-coagulant state. Prolonged PT could result from a number of factors that generally reflect insufficiency or inhibition of associated clotting factors. Previous studies on breast cancer in the study locality pointed towards heightened inflammatory and thrombotic risks [4,11]. Prolonged PT as observed in the present study is attributable to depletion of clotting factors due to an activated coagulation state. This is further corroborated by the finding of significantly elevated D-Dimer alongside the prolonged PT. Plasmin mediates the breakdown of blood clot in a process termed fibrinolysis. Various degradation products of fibrinogen and fibrin have been described including D-dimer. This product is among the smallest degradation products that are resistant to further plasmin activity [12]. It is considered more specific in that only fragments originating from fibrin polymers that had undergone factor XIII mediated cross-linking retain an intact covalent bond between two adjacent D domains; hence the term D-dimers. It is considered to reflect ongoing activation of the haemostatic system and more specifically represent breakdown products of cross-linked fibrin clot formation. The utility of D-Dimer in clinical practice is extensive including; screening of deep vein thrombosis, pulmonary embolism and disseminated intravascular coagulation [12-14].

When the breast cancer patients were separated into pre-treatment and post-treatment groups, all measured parameters were observed to be more significantly ($p = 0.001$) deranged in the post-treatment group compared to the pre-treatment group. The pathogenesis of venous thrombus formation as represented by the Virchow's triad includes venous stasis, hypercoagulability and endothelial damage/ activation [15-16]. Obviously, surgical operation and chemotherapy are capable of eliciting thrombosis via Virchow's triad. It is therefore imperative that adequate monitoring for thrombosis be ensured in the management of breast cancer patients, especially as the condition is still plagued with high mortality [17-23].

CONCLUSION

This study concludes that there is evidence of increased thrombotic risk in breast cancer, particularly among those who have undergone surgical and chemotherapeutic treatment.

CONFLICT OF INTEREST

Authors declare no conflict of interest

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