

Haemorheological Changes in African Breast Cancer Patients

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ABSTRACT

Several Studies have indicated the existence of thrombo-embolic complications in cancer patients and that this could be associated with changes in haemorheological parameters. Packed cell volume (PCV), haemoglobin (Hb), relative plasma viscosity (RPV) and plasma Fibrinogen concentration (PFC) were measured in 50 healthy control women, 50 age-matched women with breast cancer, and 10 women with histopathologically proven benign breast tumour.

There were significant differences between the controls and breast cancer patients in all the parameters measured ($p < 0.05$). However, patients with cancer have significantly higher RPV and PFC ($P < 0.001$) respectively than controls. There was significant mean difference between pre and post mastectomy in fibrinogen concentration ($p < 0.05$) and this was observed over the 5-week study period. Since increased fibrinogen may give rise to increase fibrin formation which has been asserted as an independent cardiovascular risk factor for thrombo-embolic complications, African patients with breast cancer may well be predisposed to thrombotic complications during illness. The rheological assessment may offer valuable benefit for the management and early diagnosis of breast cancer in African women. (*Afr Reprod Health* 2008; 12[1]:84-89).

RÉSUMÉ

Modifications hémorhéologiques chez les cancéreuses Beaucoup d'études ont montré l'existence des complications thrombo-embolique chez les cancéreuses et qu'on peut lier ceci aux modifications dans les paramètres hémorhéologiques. Le volume globulaire concentré (VGC), l'hémoglobine (Hb), la viscosité du plasma relatif (VPR) et la concentration du fibrinogène du plasma (CFP) ont été mesurés chez 50 femmes en bonne santé comme femmes témoin, 50 femmes cancéreuses qui ont été appariées selon l'âge et 10 femmes qui souffraient de la tumeur du sein bénigne qui a été prouvée histopathologiquement. Il y avait des différences importantes entre les témoins et les patientes cancéreuses dans tous les paramètres mesurés ($p < 0,05$). Toutefois, les patientes cancéreuses ont une VPR considérablement plus élevé et la CFP ($P < 0,001$) respectivement que les témoins. Il y a une différence moyenne importante entre la pré et la post mastectomie dans la concentration du fibrinogène ($P < 0,05$) et ceci a été observé au cours des cinq semaines que l'étude a duré. Puisque l'augmentation du fibrinogène peut aboutir à l'augmentation de la formation de la fibrine qui a été acceptée comme un facteur indépendant de risque cardiovasculaire pour des complications thrombo-emboliques. Les patientes cancéreuses africaines pourraient bien être prédisposées à des complications thrombotiques pendant la maladie. L'évaluation rhéologique peut donner des avantages valables pour le traitement et le diagnostique anticipé du cancer du sein chez les femmes africaines. (*Rev Afr Santé Reprod* 2008; 12[1]:84-89).

KEY WORDS: *Perception and practice, menstruation, Nigerian school-girls*

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Introduction

Carcinoma of the breast ranks first amongst cancers in women in developed countries and similar importance is expected in developing countries as they adopt affluent life styles and fatty diet of the industrialized countries.¹ Over a century ago Armand Trousseau² suggested that a thrombotic diathesis was present in patients with cancer and other chronic disease and that this diathesis was due to changes in the properties of the blood. Hyperfibrinogenemia and concomitant hyperviscosity have been shown to be an important component of blood that influences its flow through capillaries.³ It is well established that the principal determinant of plasma viscosity is plasma fibrinogen concentration and red blood cell concentration.

Various abnormalities of coagulation factors and fibrinolysis in the cancer patient have been reported but none has addressed the importance of other factors that may induce thrombo-embolic state such as hyper viscosity despite its clinical importance in association with thrombus formation⁴ and in clinical practice.⁵

To date no study has examined the haemorheological response in breast cancer patients in Africa. In an attempt to address this neglect we designed the present study to measure plasma fibrinogen concentration and plasma viscosity and red cell concentration.

Materials and Methods Patients

Fifty women age range 25 to 45 years (mean \pm SD = 32.1 + 4.5 years) recently diagnosed as having breast cancer were studied. The patients were diagnosed by one of the authors from histological biopsy from the lump removed from the breast. None of the patients was receiving any medication for the duration of the illness. Patients studied were selected among cases at cancer clinics of the University of Benin Teaching Hospital, Benin City. Fifty normotensive women, in apparently good health, were included in the study as control. The group had a mean age (\pm

32.00 \pm 5.21 years, range 30 to 45 years). The women were not taking contraceptive pills nor transfused. Informed consent was obtained from all the subjects selected for this study.

Methods

Venous blood was collected with minimal venous stasis, so that haemoconcentration was avoided. Six millilitres of blood was anticoagulated with solid potassium acetic acid (K+EDTA). Two mg/ mls of blood K+EDTA was used for plasma viscosity and haematocrit measurement⁶.

Another 4.5 mls of blood was treated with 0.5 ml of a 31.0 g/l sodium citrate solution for plasma fibrinogen determination.

Transparent plasma was prepared by centrifuging the blood in stoppered tubes, to prevent evaporation for five minutes at 3000g. The supernatant plasma was pipetted off and stored at room temperature (26°C - 28°C). Both plasma viscosity and fibrinogen concentration were measured within three hours of venipuncture.

Haematocrit was determined by the standard micro-haematocrit procedure. Haemoglobin concentration was measured by the cyanmethemoglobin method⁶ Plasma fibrinogen was determined by clot weight technique of Ingram.⁷ Plasma viscosity was measured by a syringe and needle capillary viscometer described by Reid and Ugwu.⁸ Measurements were made in duplicate and mean transit time was recorded. The ratio of transit time for the water to plasma and whole blood was computed and expressed as relative plasma viscosity (RPV) as recently reported.^{9,10} The respective coefficient of variation for plasma and water were 0.70% and 0.64% respectively.

The blood samples were collected from the breast cancer patients on a weekly basis for five weeks for the estimation of the packed cell volume (PCV), relative plasma viscosity (RPV) and fibrinogen concentration.

Statistics: Data were expressed as mean \pm SD and results were analyzed by parametric statistics (Student's t-test for paired data. A p value of <0.05 was considered significant.

Results

Table 1 shows the difference in PCV, RPV, and fibrinogen concentration between controls and patients with cancer of the breast. There was significant difference in all the hemorheological parameters measured between controls and PCV was higher in controls than in patients with breast cancer before mastectomy. However, patients with breast cancer had significantly higher fibrinogen concentration and plasma viscosity ($P < 0.001$) compared with controls respectively. Figure 1 to 3 showed the progressing changes in PCV, RPV and Fibrinogen concentration from the pre and post mastectomy during 5 weeks of study. Although, there were no significant changes in PCV and RPV there was consistent significant change ($P < 0.05$) between fibrinogen concentration over the period of study.

Discussion

Cancer of the breast ranks between the first and second most common malignancies in Nigerians and presents at a younger age than their Caucasian counterparts.^{11, 12, 13} These malignancies also present with a more histologically anaplastic and aggressive behaviour.¹³ Breast cancer and other malignant conditions are known risk factors in the development of thromboembolic disorders.¹⁴ In this study, patients with breast cancer had significant decreased packed cell volume, increased plasma viscosity and increased fibrinogen levels than controls. These results directly implicate the necessary blood properties capable of inducing thrombotic diathesis.^{4, 14, 15} These correlate with the previous work of Trosseau² which suggested an evidence of thromboembolic complications

of cancer patients in Caucasians. It has recently been shown that increase in fibrinogen level is an independent contributor to thrombus formation.⁵ From this study it would appear that the increase plasma viscosity is due to significant increase in plasma fibrinogen concentration. Theoretically, the increase in plasma viscosity could be due to either concentration of plasma volume or to an increase in synthesis of macroprotein which exert a strong influence on plasma viscosity.^{4, 14} Our results suggest increased fibrinogen levels as the predominant cause of elevation in plasma viscosity because plasma volume concentration would, of cause also cause an increase in haemoglobin which is significantly decreased in breast cancer patients in this study. The increased fibrinogen coupled with high plasma viscosity may progressively lead to thrombotic complications by increasing the viscous components of peripheral resistance leading to the decrease fluidity of blood⁵, which is a possible biological explanation for thromboembolic phenomenon in breast cancer patients. It should be emphasized, however, that the haemorheological results must be interpreted with caution since levels of these parameters may be raised in many clinical conditions in Africans.^{4, 9, 10} The effect of mastectomy from the figures indicate a reduction in fibrinogen level and increased packed cell volume over five weeks study suggesting that haemorheological risk factors may be a major determinant in the aetiology of thrombotic complications in cancer of the breast. These findings call for inclusion of rheological assessment of cancer patients at early stage since this may offer valuable benefit in the management and diagnosis of breast cancer.

Table 1. shows the levels of PCV, RPV and PFC in controls and patients with cancer

	Controls	Cancer Patients
Packed cell volume (%)	37.75 ± 1.2	29.30 ± 1.5*
Relative plasma viscosity (sec.)	1.56 ± 0.26	1.98 ± 1.60*
Fibrinogen concentration (g/l)	2.61 ± 0.39	6.80 ± 1.82**

* = $P < 0.05$ compared with controls

** = $P < 0.001$ compared with controls

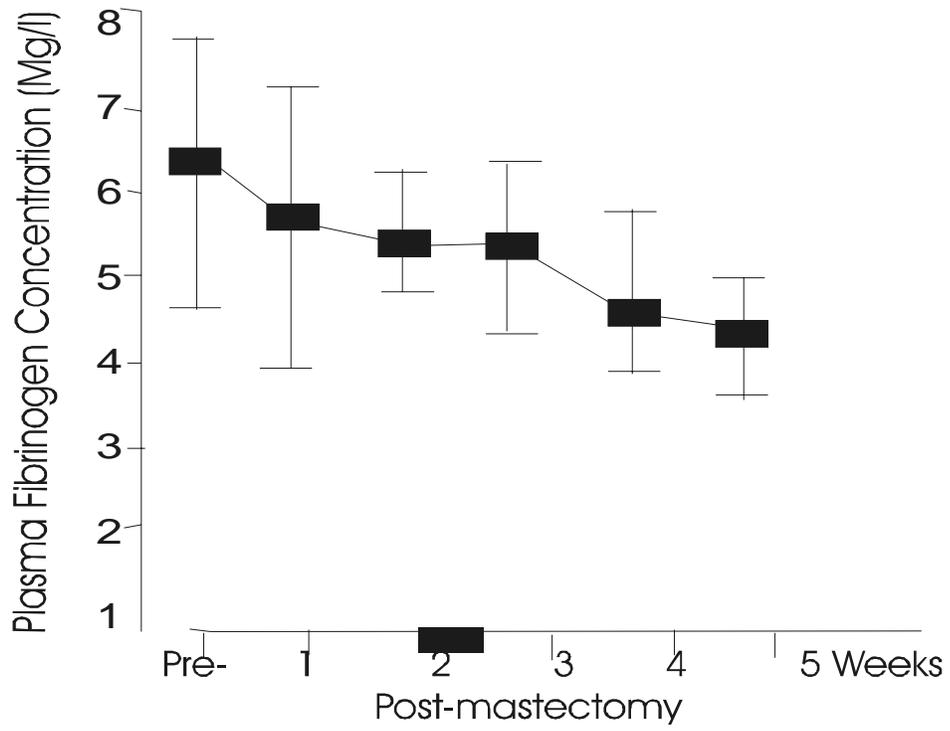


fig II

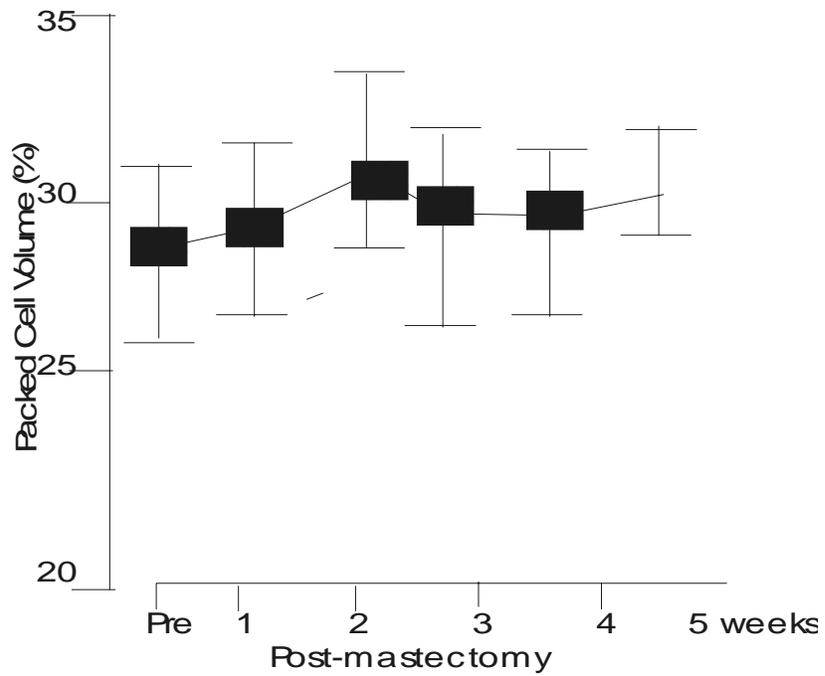
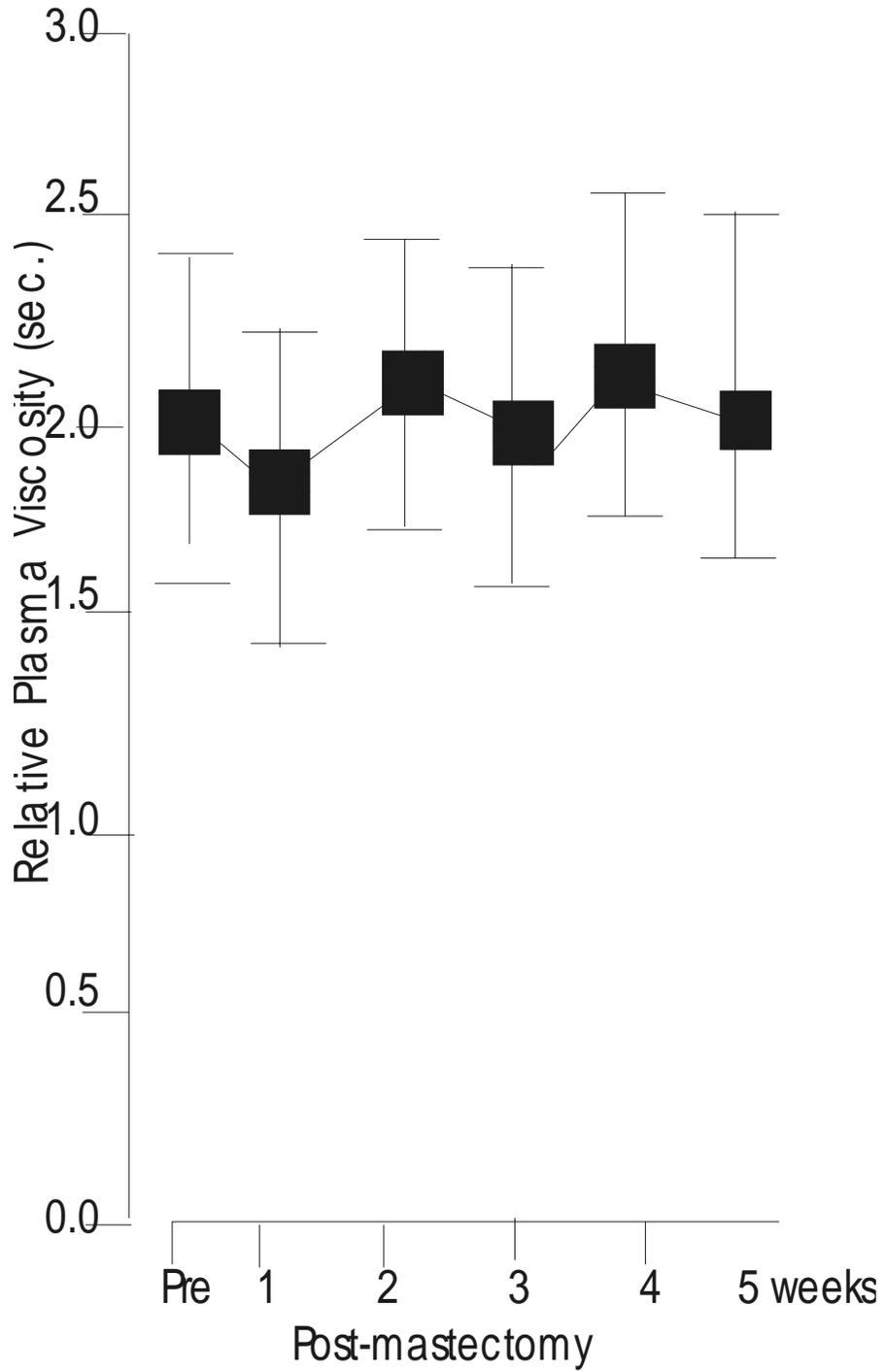


Fig. III



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