Serum Lactate And Uric Acid Levels In Patients With Breast Cancer In Benin City, Nigeria

[1]J.O Idemudia, [1]K. Atoe, [2]O. Eboreime

1. Department of Chemical Pathology, University of Benin Teaching Hospital Benin City.
2 Department of Surgery, Central Hospital, Benin City.

Abstract
Breast cancer is one of the most common cancers in women of the developed and developing countries. Development of cancer produces oxidative stress which increases the disease progression. The metabolic effect of breast cancer was examined in this study by comparing some biochemical parameters of patient with breast cancer with those without the disease. Serum lactate and uric acid levels were measured using standardized laboratory methods from venous blood obtained from participants. Results showed a significant increase in lactic acid and uric acid levels ($P<0.05$) of patients with breast cancer compared to the control. There's also a significant positive correlation ($P<0.001$) between serum lactic acid and uric acid level in the study population. The results suggested that patients with breast cancer undergoing oxidative stress can benefit from exogenous antioxidants as an adjuvant therapy.

Key word; Breast cancer, oxidative stress, uric acid, lactic acid, antioxidant.

Introduction
Breast cancer is the most common type of cancer in women and is a leading cause of cancer related death worldwide[1]

Experimental investigations as well as clinical and epidemiological studies implicate the involvement of oxygen derived radicals such as singlet oxygen, superoxide anions, hydrogen peroxide and hydroxyl radical in the etiology of cancer[2,3].

Correspondence to:

Dr. J.O. Idemudia
Department Of Chemical Pathology,
University Of Benin Teaching
Hospital Benin City.
Phone Number: 08023349492
E-mail: Osagiep2001@yahoo.com

Free radicals are formed in both physiological and pathological conditions in mammalian tissues and a subtle balance exit between the generation and eradication as the human body is equipped with certain enzymatic and non-enzymatic antioxidant system[4,5], these antioxidants are known to dispose, scavange, and suppress the formation of free radical or oppose their action and they increase with the severity of the disease[6,7]. Oxidative stress ensures when these antioxidant mechanisms are overwhelmed by excessive reactive oxygen and nitrogen species generation that damage membrane lipids, proteins and nucleic acid[8]. Studies indicated increased levels of oxidative stress markers in breast cancer patients[9,10].

Epidermiological studies have revealed that low levels of essential antioxidants in circulation are associated with an increased risk at cancer[11].

Uric acid has been demonstrated to be an important antioxidant and a free radical scavenger in human. It is one of the major radical trapping antioxidant in plasma and is reported to protect the erythrocyte membrane against lipid peroxidation[12]. Urate also possesses antioxidants activity[13], it has been found to protect ascorbate against oxidation by cupric ion and iron induced oxidation[14]. Uric acid interacts with peroxynitrite to form a stable nitric oxide donor, thus promoting vasodilation and reducing the potential for peroxynitrite induced oxidative damage[15]. Thus uric acid could be expected to protect against oxidative stresses.

Cancer is a proliferating and invasive disease known to cause severe tissue damage through oxidative stress mechanism. Tumour cells respire anaerobically with increase cell tumour and generation of lactic acid and hence lactate dehydrogenase activity can serve as a marker for the detection of cancer risk, population screening, diagnosis, staging and prognosis. It can also predict the response of occult metastatic disease and monitor the course of the disease[16]. Lactate dehydrogenase however is a less specific marker compared to several tumor markers in vogue.

The aim of the present study is to evaluate the variations in the levels of lactic acid and alteration in oxidant-antioxidant status by measuring the serum

lactate acid and uric acid levels in breast cancer patent compared to the control subject who are without the disease.

Patients and methods

A total of 60 participants were recruited for this study from the female surgical ward, Central Hospital Benin City from 1st July, 2011 through 31st October, 2012 (15 months). 30 of these women (50%) had breast cancer and were both pre menopausal and post menopausal age group with a mean age of 55±1.6 years (range 45 – 64). The other 30 participants (50%) were age matched healthy subjects with mean age 54±1.4years (Range 42 – 66) which we considered as control. Patients suffering from diseases of any origin other than breast cancer were excluded from the study

Due permission was obtained from the management of Central Hospital Benin City and participation was voluntary.

Biochemical analyses were done at the Department of Chemical Pathology, University of Benin Teaching Hospital.

Sample Collection and Preparation

Blood was obtained by venous puncture from participants into a sterile tube, allowed to clot and retract. Serum was separated by centrifugation at 3000rpm for 15 minutes. The sera were harvested and stored frozen at -20^{0}c until analysis was carried out.

Biochemical analysis

Determination of serum lactate levels

Serum lactate levels was measured by the direct enzymatic method[17,18,19], in which lactate oxidase catalyzes the oxidation of lactic acid to pyruvate and hydrogen peroxide. Peroxidase then catalyzes the reaction of hydrogen peroxide with a hydrogen donor, in the presence of 4 – aminophenazone, to form a dye. Colour intensity, measured at 550nm, is proportional to the lactate concentration in the sample.

Using this method, the normal reference range is 0.5 – 2.2 mmol/L.

Determination of Uric Acid

Uric acid was measured in serum by the colorimetric method[20]. In this method, uric acid is converted by uricase to allantoin and hydrogen peroxide, which under the catalytic influence of peroxidase, oxidizes 3,5 – Dichloro -2- hydroxybenzenesulfonic acid and 4 – aminophenazone to form a red-violet quinoneimine compound. The intensity of colour formed is directly proportional to the amount of uric acid present in the sample.

Using this method, the normal reference range is 3.4 – 7.4mg/dL.

Statistical analysis

Data analysis was conducted using the general linear model of SAS (statistical analysis for agric and sciences) 2004 model. All results are expressed as mean± standard error of mean. Multiple group comparism were performed by one way ANOVA followed by Duncan test. Pearson correlation coefficients was employed to ascertain the associations between the various biochemical parameters.

Results

The mean serum lactate level in breast cancer patients was 7.581±0.126mmol/L and that of the control subject was 3.168±0.359 mmol/L.

The disparity between the control and breast cancer serum lactate levels was statistically significant P (<0.05).

The mean serum uric acid levels in breast cancer patients was 10.164±0.499mg/dL and that of the control subjects was 6.436±0.145mg/dL and the differences seen was statistically significant P (<0.05).

Table 1 and figure 1 are tables and histogram respectively showing the mean levels of the biochemical parameters of the patient versus the control.

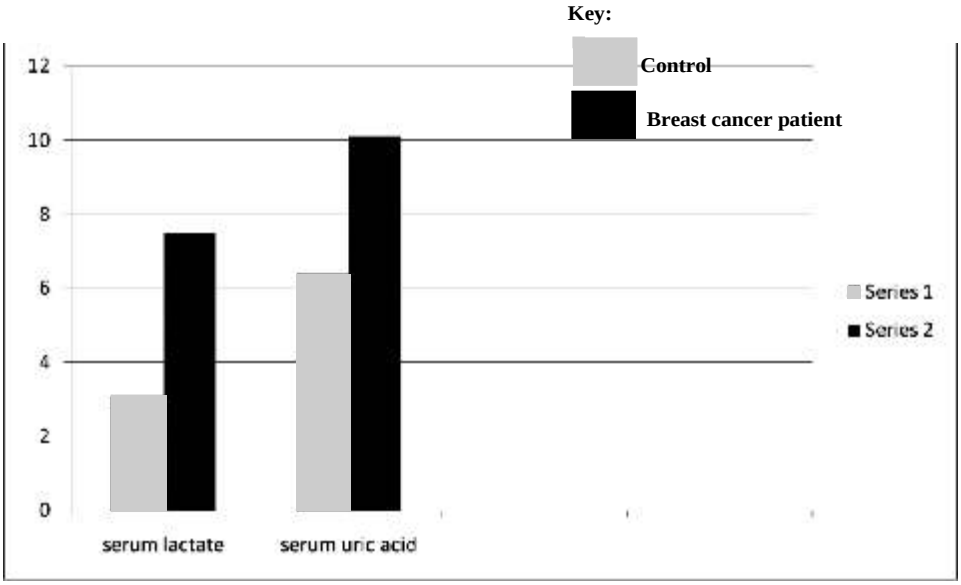
Correlation of the patient serum lactate acid levels and uric acid levels was positive at P<0.001. r=057197

Discussion

The findings of the present study suggest a significant

Table 1: Biochemical parameters of patients with breast and control

	Serum lactate mean ±SEM mmol/L	Serum uric acid mean± SEM mg/dL
Normal subject/control	3.168±0.359	6.436±0.145
Breast cancer patient	7.581±0.126	10.164±0.499



Histogram showing serum lactate level and uric acid level of breast cancer patient vs control

increase in serum lactate concentration of breast cancer patients compared to the control subjects.

A retrospective study on serum lactate dehydrogease level of breast cancer patient with bone metastases receiving treatment with bisphosphonate was carried out and analysis shows that lactate dehydrognase level correlate strongly with survival in patients with bone metastases and comfirms its relevance as a prognostic fator[21]. Sandhya Mishra et al reported in their study that 70% of patients without metastasis had lactate dehydrogenase above normal subject[22].

Kher et al correlated post treatment decreased in ferritin and lactate dehydrogenase levels with response to therapy; however persistent rise observed in few cases was attributed to recurrence metastasis[23].

From our study, we noticed statistically significant increase in serum uric acid levels of patients with breast cancer compared to the control subjects. Study carried out by sreenivasa Rao et al revealed that serum uric acid levels were increased by 16% to 45% as the disease progresses from stage 1 to stage IV (16%, 39%, 41% and 45%), when compared to normal control[24]. The elevated concentration of serum uric acid level in breast cancer patients may be viewed as an index of increased antioxidant defense to compensate the loss of other antioxidant mechanism.

In contrast to our result, Nagini et al[25] reported, decreased serum uric acid levels in oral cancer patients.

Krishna veni et al also reported an increase in serum uric acid levels in breast cancer patients[26]. This is also in agreement with our studies.

Conclusion

From this present study, we can conclude that evaluation of serum lactic acid in patient with breast cancer suggests a release by the cancer cells and this can be of value in assessing the effectiveness of therapy. It can also be of diagnostic and prognostic markers for breast cancer patient.

Also findings in this study showed elevation of uric acid level (systemic antioxidant), we can conclude that administration of exogenous antioxidants may be of great benefit as adjuvant therapy to breast cancer patients as this may prevent oxidative damage caused by oxidative stress from the tumour cells.

References

1) Coughlin, S.S., and Ekwveme D.U. (2009) Breast cancer as a global health concern. Cancer epidemiology 33,315-318, doi:10.1016 /j. Canep. 2009.10.003.

2) Oberley LW, Oberley TD, Free radicals, cancer, and aging. In; Johnson JE jr, Walford R, Harman D, Miguel J (eds). Free radicals, Aging and Degenarative disease, Alan R Liss, New York 1986,325-71

3) Fisher SM, Floyd RA, Copeland E.S, Workshop report from the division of research grants, national institute of health. Oxy radicals in carcinogenesis a chemical pathology study section workshop cancer Res 1983,43:5631-34

4) Faruk Tas, Hansel H, Belce A, Ilvan S, Argon A, Camlica H, Topuz E. Oxiddative stress in breast cancer. Med Oncol 2005;22(1):11-15

5) Portakal O, Ozkaya O, Inal N, Bozan B, Kosan M, Sayek I. Co enzyme Q10 concentrations and antioxidants status in tissues of breast cancer patients.

Clinical Biochemistry 2000;33(4);279-84

6) Singh R, Singh RK, Mahdi AA, Singh RK, Kumar A, Tripathic AK. Circadian periodicity of plasma lipid peroxides and other antioxidants as putative markers in gynecological malignancies. In vivo 2003; 17:593-600.

7) Galleotti T, Masotti L Borrello S. Oxy-radical metabolism and control of tumour growth. Xenobiotica. 1991; 21,1041-51.

8) Halliwell, B. and Gutteridge, J.C, (1995) The definition and measurement of antioxidants in biological systems, Free Radical Biology and Medicine, 18,125-126.doi:10,1016/0891-5849(95)91457-3

9) Kasapovic J., Pejie S., Stojiljkovic, V., Todorovic. A., Radosevic-Jelic. L., Saicie, Z.S and Pajovic S.B. (2010). Antioxidant status and lipid peroxidation in the blood cancer patients of different ages after chemotherapy with 5-fluorouracil, doxorubicin and cyclophophamide.

10) Yeon J.Y., Suh, Y.J., Kim, S.W., Baik, H.W., Sung, C.S., Kim H.S and Sung, M.K. (2011) Evaluation of dietary factors in relation to the biomarkers of oxidative stress and inflammation in breast cancer risk. Nutrition, 27, 912-918. Doi:10,1016/j:nut.2010.10.012

11) Diplock AT, Antioxidant nutrients and disease prevention: an overview. AMJ clin Nut;53,1991,189-193.

12) Wayner DM, Burton GW, Ingold KU, Barclay LRC, and Locke S.J., (1987). The relative contribution of vitamin E. Urate, ascorbate and proteins to the total peroxy radical trapping antioxidants activity of human blood plasma. Biochem Biophys Acta 924:408-419.

13) Nagini S, Shreeram S. Ramachandran CR, Ramachandran V. Plasma concentration of lipid peroxides carotene urate and ceruloplasmin in patients with oral squamous cell carcinoma 1997; J Biochem Mol Biol and Biophys :1:235-239.

14) Sevanian A. Davies KHA, Hochstein P. conservation of vitamin C by uric acid in blood. J free Rad Biol Med 1985:1:117-120

15) Skinner KA. White CR. Tan S, Barnes S, Kirk M, Darley Usman V, Parks DA., (1998). Nitrosation of uric acid by peroxynitrite, formation of a vasoactive nitric oxide donor. J Biol Chem. 273:24491-7.

16) Linbiom A. and Liljegreen. A. (2000) Tumour markers in malignancies. B.N. J., 320,424-27.

17) Gutmann, I., Wahlefeld A., Methods of enzymatic analysis, 2nd Ed. Academic press, New York 1974,1464.

18) Noil, F., Methods of enzymatic analysis, 2nd Ed. Academic press, New York 1974, 1465.

19) Tietz, N.W., fundamental of clinical chemistry, 4th Ed., W.B. Sanders company, Philadelphia, 1996,367.

20) Fossati, P., Prencipe, L., and Berti, E., Clin, Chem. (1980) 26/2,227-231.

21) Janet E. Brown, Richard J, Crook, Allan Lipton, Robert E. Coleman. Serum lactate dehydrogenase in prognostic for survival in patients with bone metastases from breast cancer; A retrospective analysis in bisphosphonate treated patient. Clin cancer Res; (2012)18(22);1-8

22) Sandhya Mishras D.C. Sharma and Praveen Sharma. (2004). Studies of Biochemical parameters in Breast cancer with and without metastasis. Indian Journal of Clinical Biochemistry. 19(1) 71-75.

23) Kher, A., Maghe, E. and Deshpande, A. (1997) significance of serum ferritin and lactate dehydrogenase in benign and malignanet discase of breast Indian J. Pathol. Microbiol. 40(3),321-6

24) Screenivasarao C.S and sarala Kumari D. ; Changes in serum ascorbate, urate and copper levels in woman with carcinoma of the breast. International journal of research in Biological Science 2012;2(3):103-106

25) Nagini S. Shreeran S, Ramachandian CR, Ramachandian V. Plasma concentration of lipid peroxide carotene urate and ceruloplasmin in patients with oral squamous cell carcinoma 1997; J Biochem Mol Biol and Biophys:1;235-239

26) Krishna Veni: G., bhaskar Rao. D., Munikumar D., Usha B., Murali Krishna V., Raghava Rao. Clinical evaluation of oxidative stress in women with breast cancer. Recent research in science and technology 2011,3(1);55-58.