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Research article

NON-ENZYMATIC ANTIOXIDANTS LEVELS IN HYPERTENSIVE, CANCER, TUBERCULOSIS AND HIV PATIENTS

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ABSTRACT: This study was carried out on 300 subjects to ascertain the levels of non-enzymatic antioxidants (vitamin C, reduced glutathione and uric acid levels) in hypertensive, cancer, tuberculosis and HIV patients. Study group comprises of sixty subjects from each group and sixty healthy subjects also served as control. The non-enzymatic antioxidants monitored were vitamin C, reduced glutathione and uric acid levels. The biochemical parameters were measured with standard methods. A Student t test was applied to assess the statistical difference of the above biological parameters between diseased patients and control group. We observed a very low level of vitamin C in cancer patient and the patients with HIV infection when compared to control group ($P<0.05$). Similarly, a significant reduction of serum reduced glutathione particularly in cancer and HIV patients when compared to control group was also observed. ($P<0.05$). Hyperuricemia was also observed in patients with cancer cells and those with HIV. We have observed very low levels of non enzymatic Antioxidants, thus creating oxidative stress, which might be playing an important role in progression of these diseases.
Key words: Uric acid, Ascorbic acid, glutathione and antioxidant.

INTRODUCTION

HIV/AIDS has become a chronic rather than an acutely fatal disease in many areas of the world (UNAIDS. 2006)·In Nigeria, an estimated 3.6 percent of the population are living with HIV and AIDS [22]. Approximately 220,000 people died from AIDS in Nigeria in 2009 [23]. With AIDS claiming so many lives, according to the latest data from the Nigerian government, the country now accounts for around 10 percent of the global HIV burden (UNAIDS, 2010). Conversely, Tuberculosis co-infection is one of the leading causes of sickness and death in those with HIV/AIDS being present in a third of all HIV infected people and resulting in 25% of HIV related deaths. HIV is also the most important risk factors for tuberculosis. The two most common cancers associated with HIV/AIDS are Kaposi's sarcoma and AIDS-related non-Hodgkin's lymphoma. Apart from diseases caused by bacteria and virus , oxidative stress which is caused by reduction in antioxidants is thought to contribute to the development of a wide range of diseases including Alzheimer's disease [3, 13] and Parkinson's disease [26]. The pathologies caused by diabetes might result to hypertension [5, 7], rheumatoid arthritis [11], and neurodegeneration in motor neuron diseases [4]. In many of these cases, it is unclear if oxidants trigger the disease, or if they are produced as a secondary consequence of the disease and from general tissue damage [19]. One case in which this link is particularly well-understood is the role of oxidative stress in cardiovascular disease. Here, low density lipoprotein (LDL) oxidation appears to trigger the process of atherogenesis, which results in atherosclerosis, and finally cardiovascular disease [1, 20].

However oxidative damage to DNA leads to cancer and his can only occur due to depletion of antioxidants such as Ascorbic acid, glutathione, vitamin E and others. Vitamin C and GSH are important antioxidants which protect the cells from toxins such as free radicals. [12]. The different antioxidants are present at a wide range of concentrations in body fluids and tissues, with some such as glutathione or ubiquinone mostly present within cells, while others such as uric acid are more evenly distribute .The relative importance and interactions between these different antioxidants is a very complex question, with the various metabolites and enzyme systems having synergistic and interdependent effects on one another. [2, 17].The action of one antioxidant may therefore depend on the proper function of other members of the antioxidant system [21] .The amount of protection provided by any one antioxidant will also depend on its concentration, its reactivity towards the particular reactive oxygen species being considered, and the status of the antioxidants with which it interacts [21].

Glutathione, an antioxidant, helps protect cells from reactive oxygen species such as free radicals and peroxides. Glutathione is also nucleophile at sulfur and attacks poisonous conjugate acceptors. Glutathione, a major endogenous antioxidant produced by the cells, participating directly in the neutralization of free radicals and reactive oxygen compounds, as well as maintaining exogenous antioxidants such as vitamins C and E in their reduced (active) forms. Through direct conjugation, Glutathione detoxifies many xenobiotics (foreign compounds) and carcinogens, both organic and inorganic. It is essential for the immune system to exert its full potential, e.g. In modulating antigen presentation to lymphocytes, thereby influencing cytokine production and type of response (cellular or humoral) that develops, In enhancing proliferation of lymphocytes thereby increasing magnitude of response, In enhancing killing activity of cytotoxic T cells and NK cells, and also in regulating apoptosis, thereby maintaining control of the immune response. Glutathione plays a fundamental role in numerous metabolic and biochemical reactions such as DNA synthesis and repair, protein synthesis, prostaglandin synthesis, amino acid transport and enzyme activation. Thus, every system in the body can be affected by

the state of the glutathione system, especially the immune system, the nervous system, the gastrointestinal system and the lungs [8, 9].

Uric acid is by-far the highest concentrated antioxidant in human blood. Uric acid (UA) is an antioxidant oxypurine produced from xanthine by the enzyme xanthine oxidase, and is an intermediate product of purine metabolism .The effects of uric acid in conditions such as atherosclerosis, ischemic stroke, and heart attacks are still not well understood, with some studies linking higher levels of uric acid with increased mortality (Proctor ,1994) and other studies showing no association [18, 15, 25] first noted over two decades ago "the well-established association between high urate levels and atherosclerosis could be a protective reaction (antioxidant) or a primary cause (pro-oxidant)". This might be due to uric acid being activated as a defense mechanism against oxidative stress, but instead acting as a pro-oxidant in cases where metabolic derangements shift its production well outside of normal level [25, 21, 18].

It is in recognition of this fact that the present study was undertaken to estimate the serum levels of non enzymatic antioxidants like Vitamin C, reduced glutathione and uric acid to evaluate the total antioxidant capacity in patients with HIV, Cancer, Tuberculosis and those who are hypertensive.

MATERIAL AND METHODS

Study group comprises of sixty subjects from each disease group (hypertensive, cancer, tuberculosis and HIV patients) and sixty healthy subjects also served as control totaling 300 subjects of which subjects were attending Nnamdi Azikiwe University Teaching Hospital, Nnewi. Nigeria. The non-enzymatic antioxidants monitored were vitamin C, reduced glutathione and uric acid levels. The biochemical parameters were measured with standard methods. From both control and study groups, 5 ml venous blood was taken with heparinised syringe and centrifuged .The serum vitamin C was estimated by [16] method in which ascorbic acid reacts with dinitrophenylhydrazine to form a colored complex whose absorbance was read at 520 nm. Reduced glutathione was estimated by [10] method in which GSH reacts with di-thionitrobenzoic acid to form yellow colored complex whose intensity was read at 412 nm. Uric acid was measured using [6] method .uric acid reacts with uricase to form a red quinoneimine compound which was read at 520 nm.A Student t test was applied to assess the statistical difference of the above biological parameters between diseased patients and control group.

RESULT AND DISCUSSION.

We observed a very low level of vitamin C in cancer patient and the patients with HIV infection when compared to control group (P<0.05) Table. Similarly, a significant reduction of serum reduced glutathione particularly in cancer and HIV patients when compared to control group was also observed. (P < 0.05) Table-1. One thing that is common about these diseases is that they generate a lot of free radicals. Glutathione and Ascorbic acid are free radical scavengers' .However, with this function they stabilize the system and prevent radical damages to tissues' which incidentally fasten disease progression. Cancer and HIV generate a lot of free radicals; it is not surprising that Glutathione and Ascorbic acid are highly depleted in these disease conditions in this study.

Table-1: Ascorbic acid GSH and Uric acid levels in Hypertensive, Cancer, Tuberculosis, HIV Patients and Control.

Parameters	Ascorbic Acid (mg/dl)	GSH (mg/dl).	URIC ACID (mg/dl)
Hypertensive	o.48± 0. 05*	0.40 ± 0.06*	6.16 ± 1.40 *
Cancer	0.32± 0.02***	0.28 ±0.03***	9.60±2.60***
Tuberculosis	0.42± 0.03**	0.35± 0.04**	7. 38 ± 1.80**
HIV Positive Subjects	0.38± 0.04**	0.38±0.05 **	8.20±2.08**
Control	0.84± 0.07	0.75± 0.10	5.61 ± 1.30

*Significant difference P <0.05

Though glutathione is the most essential and powerful antioxidant which enables other antioxidants, like vitamins A and C, to continuously Perform their antioxidant activities effectively [8]. As antioxidants neutralize the free radicals, they themselves are consumed. Reduced glutathione allows antioxidants to be restored to their standard electron configuration and become active antioxidants once again [9]. When GSH levels are high, this process takes place almost immediately after an antioxidant donates an electron. As a result, GSH allows the body to maintain the levels of other functional antioxidants. However, reduced glutathione itself is depleted as it performs its various functions. The depletion in plasma GSH levels might be the key point in depletion of other antioxidants and creation of oxidative stress like environment. The significant reduction in the levels of ascorbic acid and GSH especially in cancer and HIV patients was due to oxidative stress.

Hyperuricemia was also observed in patients with cancer cells and those with HIV. The higher uric acid level may be due to the oxidative damage to cells causing an increase in cell turnover and muscle wasting as seen in cancer and HIV patients as well. This shows that these diseases are associated with increase cell turnover as suggested by [24]. The variation may also be due to the degree of dehydration as suggested by [14] because the climate condition in this part of the country is extremely hot which might increase cell turnover resulting to hyperuricaemia.

We have observed very low levels of non enzymatic Antioxidants, thus creating oxidative stress, which might be playing an important role in progression of these diseases.

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