Original Research Article

Oxidative Changes Among Women Suffering From Urinary Tract Infection in Enugu Metropolis, Nigeria.

ABSTRACT:

Background: The action of bacterial infection in the urinary tract can trigger the release of free radicals which could progress and overwhelm endogenous antioxidants, hence oxidative changes occur. This work aimed at estimating the level of oxidative stress markers, viz, oxidized low-density lipoprotein (Ox-LDL) and superoxide dismutase (SOD), among women suffering from urinary tract infections of bacterial origin in the Enugu metropolis.

Materials and Methods: Ethical approval was obtained from the Health Research and Ethics Committee (HREC) of the University of Nigeria Teaching Hospital (UNTH), Ituku–Ozalla, Enugu State. Informed consent was obtained from all recruited subjects. About forty (40) women diagnosed with UTIs at the UNTH were recruited for the study and twenty (20) women free of UTIs and who are not registered with UNTH were used as control for this study. Blood specimens were collected and analysed using the ELISA technique to check for Ox-LDL and SOD levels.

Results: The mean value of the antioxidant enzyme, SOD, was lower than that of the control which suggests a possibility of oxidative stress. However, Ox-LDL mean value was lower than that of the control population showing the absence of lipid peroxidation in all sampled populations, which may have been pronounced if the subjects had complicated UTIs like pyelonephritis.

Conclusion: This study showed a drop in the levels of an antioxidant enzyme among UTI patients placing the patients at risk of oxidative stress. Ox-LDL should be higher in the test than in the control population indicating lipid peroxidation. However, in this study, the Ox-LDL showed no increase in values. Oxidative stress should be looked out for by physicians when treating UTIs.

KEYWORDS:

Urinary Tract Infection, Superoxide Dismutase, Oxidized Low-Density Lipoprotein, Oxidative Stress.

BACKGROUND

Urinary tract infection is a common contagion among men and women but the incidence is quite high among women due to their anatomic and physiologic features such as shorter urethral length, shorter distance from the anus to the urethral meatus, and permissiveness of the vaginal and perineal environments to microbial colonization (Tsai et al., 2023 and Zhai et al., 2023). Urinary tract infections (UTIs) in women represent one of the most common disease entities in

both the ambulatory and hospital setting (Matulay et al., 2016). Nearly 60% of all women will experience at least one UTI in their lifetime leading to billions of dollars of healthcare spending (Matulay et al., 2016).

UTIs can be categorized into two: the uncomplicated and complicated UTIs. Uncomplicated UTI also known as uncomplicated cystitis, is an infection limited to the bladder or lower urinary tract. Uncomplicated cystitis is primarily observed in young, healthy women and very rarely requires hospitalization and parenteral antimicrobial therapy. Complicated UTI, on the other hand, is a broad term that encompasses various infections including complicated cystitis, pyelonephritis, and catheter-associated UTI (Steiger et al., 2017). Migration of the infection towards the kidneys leads to inflammation of the renal parenchyma causing pyelonephritis. Constant inflammation can lead to tubular damage generating interstitial oedema, nephritis and acute kidney injury, thus leading to systemic injuries and damages. Complicated disease most frequently occurs in older adults, those with underlying renal pathology, catheterization, and immune compromising conditions (Steiger et al., 2017).

Oxidative stress relates to increasing intracellular levels of reactive oxygen species (ROS), which is a heterogeneous group of highly reactive ions and molecules generated during univalent reduction of oxygen to water including superoxide anions, hydrogen peroxide, hydroxyl radicals, singlet oxygen and hypochlorous acid (Miyata et al., 2019). Normally, the production of ROS is low and the low levels of ROS are necessary for several biological processes, including intracellular differentiation and cell progression, arrest of growth, apoptosis, immunity and defence against microorganisms. However, oxidative stress caused by the increased formation of ROS and/or decreased antioxidant defence may lead to damage to biological macromolecules. This possible damage by ROS can be prevented by endogenous antioxidant enzymes such as catalase (CAT) and superoxide dismutase (SOD) (Kurutas et al., 2005). In bacterial infections oxidative stress arises, at least in part, from altered metabolic pathways and has also been implicated in organ damage and the development of malignancies (Ivanov et al., 2017). The action of bacterial infection in the urinary tract can, thus, trigger the release of free radicals which progresses and may overwhelm the antioxidants, thus leading to an imbalance between reactive oxygen species or oxidative radicals and antioxidants, hence oxidative changes occur.

Lipid peroxidation is one of the most important expressions of oxidative stress induced by ROS (Kurutas et al., 2005). The oxidized low-density lipoprotein (Ox-LDL) is an indicator of lipid peroxidation. The Ox-LDL is elevated in oxidative stress associated with a variety of pathological conditions such as atherosclerosis, inflammation, chronic renal failure, acute myocardial and cerebral infarctions, etc (Itabe, 2012). Hence, Ox-LDL is likely to be pronounced in cases of complicated UTI such as pelvic inflammatory disease and pyelonephritis. A build-up of oxidative stress and lipid peroxidation may lead to chronic systemic injuries secondary to urinary tract infections. This study investigated the levels of Ox-LDL and SOD which could serve as a prognostic tool to address the susceptibility or predisposition of women with urinary tract infection to some systemic disease. There is a paucity of literature addressing oxidative changes in UTIs, hence the need for the study.

METHODS

Research Design

This research was carried out on women with urinary tract infections registered with the University of Nigeria Teaching Hospital (UNTH), Ituku-Ozalla, Enugu State, Nigeria. The subjects were chosen using a simple random sampling technique.

Study Population

About forty (40) women diagnosed with urinary tract infections (UTIs) at the University of Nigeria Teaching Hospital (UNTH) were recruited for the study. These patients were further divided into two groups: Group One comprises of twenty (20) patients with Gram-negative urinary tract infections and Group Two comprises of twenty (20) patients with Gram-positive urinary tract infections. Also, twenty (20) women who were not suffering from UTIs and who were not registered with UNTH were used as a control group for this study.

Duration of Study

This research was carried out from July to September 2021.

Inclusion and Exclusion Criteria

The inclusion criteria used for this study include women diagnosed with Gram-positive and Gram-negative bacterial-related UTIs, women between the ages of 18 and 55 years and women who are not on antimicrobial therapy already. However, women below 18 years and above 55 years of age, women with viral or fungal-related UTIs, women on antimicrobial therapy and women with hypertension, cardiomyopathy, diabetes mellitus, tuberculosis, obesity and HIV/AIDS were excluded from the study. Moreso, women with no sort of UTIs, be it of bacterial, viral or fungal origin, between 18 – 55 years, not on any antimicrobial therapy and not admitted to the hospital, were recruited as the control group for this study.

Ethical Consideration

The following ethical considerations were undertaken during this study: Ethical approval was sought and obtained from the Health Research and Ethics Committee (HREC) of the University of Nigeria Teaching Hospital, Ituku–Ozalla, Enugu State, Nigeria. Each patient signed a voluntary informed consent form before participating in the study. Participants' privacy and confidentiality were maintained and only data obtained from this study were presented.

Specimen Collection

The serum level of oxidized low-density lipoprotein (Ox-LDL) and serum level of superoxide dismutase (SOD) were estimated in each of the blood specimens collected. About 5ml of venous blood was collected aseptically by venipuncture from each consenting subject and dispensed into a plain project bottle and transported to the laboratory within 30 minutes. The blood specimens

were centrifuged at 500 × g for 5 minutes and the serum was transferred into labelled sterile cryovials and stored at -20^{o}C until ready for analysis. Each specimen was labelled with the subject's initials and laboratory identification number.

Method of Sample Processing

The Enzyme-Linked Immunosorbent Assay (ELISA) technique was used to determine the concentration of human ox-LDL and SOD in the samples. The ELISA kits were procured from the Elabscience kit. The tests were carried out according to the manufacturer's instructions. The optical densities (OD) were read at 450nm wavelength using a microtitre plate reader and reported as concentrations of ox-LDL and SOD in pg/ml.

Data Analysis

The data were analysed using analysis of variance (ANOVA). Statistical analysis of difference was estimated using ANOVA and correlation and values were reported as Mean±SEM. The statistical package for social sciences (SPSS) version 18 was used. A value of $p<0.05$ is considered significant.

RESULTS

Table 1: Percentage of causative organisms in the women diagnosed with UTI.

	Isolated Organism	Number of Isolates	Percentage %
Gram +ve	*Staphylococcus aureus*	14	70
	Streptococcus spp.	4	20
	Enterococcus feacalis	2	10
Gram –ve	*Klebsiella* spp.	2	10
	Escherichia coli	16	80
	Proteus spp.	2	10

Table 2: Oxidized Low-Density Lipoprotein and Superoxide Dismutase values among Gram-positive UTI patients, Gram-negative UTI patients and control group.

	Control n=20	**Gram +ve UTI n=20**	**Gram -ve UTI n=20**	**P-value**
Ox-LDL (pg/ml)	3900.05±292.89	3854.05±49.52	3798.44±96.35	0.06
SOD (pg/ml)	4064.99±344.66	3790.44±600.62	3651.01±120.21	0.00

Both Gram-positive and Gram negative bacteria from UTI patients (and Gram-negative UTI patients) showed decreased Ox-LDL mean difference when compared to control, but did not show statistically significant difference ($P>0.05$). There was, however, a significant ($P<0.05$) mean difference in SOD among the control group compared to both Gram-positive UTI patients and Gram-negative UTI patients respectively.

DISCUSSION

Reactive oxygen species such as superoxide radicals, are thought to underlie the pathogenesis of various diseases. Oxidative stress is seen as a situation where there is increased formation of ROS and/or decreased antioxidant defence, an important feature of many diseases and in severe cases, uncontrolled lipid peroxidation is induced (Ciragil et al., 2005). To check for possible oxidative stress in UTIs in this study, the SOD, an endogenous antioxidant enzyme, and Ox-LDL, a marker for lipid peroxidation were quantitatively measured. The study showed a significantly decreased mean value of SOD among the test groups compared to the control group. However, lower SOD mean value was seen in Gram-negative bacteria UTI infections which are the commonest causative agents of UTI, than in UTIs caused by Gram-positive bacteria. In the studies of Kurutas et al. (2005) on the effects of oxidative stress in urinary tract infection, two antioxidant enzymes measured, catalase (CAT) and SOD, were significantly decreased in the urine samples of patients with UTI compared to negative urine culture. Also, a study by Ciragil et al. (2005) on the effects of oxidative stress in urinary tract infection during pregnancy shows reduced CAT and SOD values in pregnant women with UTI compared to pregnant women without UTI and non-pregnant women.

Ox-LDL is an indicator of lipid peroxidation, a product of severe oxidative stress. In this study, there was a decrease in the mean value of Ox-LDL in patients with UTI compared to the control. In the case of oxidative stress, it is expected to have higher Ox-LDL in patients with UTI than in the control subjects. But given the fact that Ox-LDL is seen in conditions such as atherosclerosis, inflammation, chronic renal failure, acute myocardial and cerebral infarctions, etc (Itabe, 2012), its mean value is likely to increase mainly in cases of complicated UTI with kidney involvements such as pyelonephritis, renal failure, or other severe forms such as pelvic inflammatory disease. A mean value lower than that of the control values could mean that non of the patient is suffering from a complicated form of UTI. Therefore one can deduce that non of the patients recruited for this study had a complicated UTI. However, the studies of Ciragil et al. (2005) and Kurutas et al. (2005) revealed significant lipid peroxidation as shown by increased levels of malondialdehyde (MDA), another marker for lipid peroxidation, among UTI patients.

CONCLUSION

Oxidative stress can underlie urinary tract infection as seen in this study, and also lipid peroxidation in many serious cases, which can further diminish the levels of antioxidant enzymes. A build-up of ROS and lipid peroxidation could lead to systemic injuries secondary to UTIs and so checking for and treating oxidative stress while handling cases of UTI by clinicians, in addition to an antimicrobial regimen, should be seriously taken into cognizance.

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