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RESEARCH ARTICLE

THE SERUM LEVELS OF MALONDIALDEHYDE, CHOLESTEROL AND TOTAL LIPIDS IN PATIENTS DIAGNOSED AS HAVING TYPHOID SALMONELLOSIS IN NSUKKA URBAN AREA, SOUTHEAST NIGERIA

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ABSTRACT

The sera of clinically confirmed typhoid patients in Nsukka urban area, along with healthy individuals were collected and analysed for MDA, total cholesterol and total lipid levels. Results showed total cholesterol levels in typhoid patients as 142.22± 29.83 and of healthy individuals as 211.19±22.02. It also showed total lipid levels as 128.98±3.39 and 154.95±11.40 in typhoid and healthy individuals respectively. Mean MDA levels were observed as 1.073±0.51 and 0.820±0.53 in typhoid and healthy individuals respectively.The results show that inflammation of the bowel caused by *Salmonella typhi* infection may lead to oxidative stress-mediated production of reactive oxygen species, causing lipid peroxidation in typhoid patients.

INTRODUCTION

Typhoid fever is a systemic disease caused by *Salmonella typhi,* a gram-negative bacillus that is motile due to its peritrichous flagella, affecting only humans. Typhoid fever is transmitted by food and water contaminated by faeces and urine of patients and carriers (Chin, 2000). Polluted water is the most common source of typhoid (Kapley *et al.,* 2001). In clinical practice today, certain aspects of typhoid fever continue to generate controversies. However, one indisputable fact is that the disease is still a major cause of morbidity and mortality in developing countries. Estimated that about 17 million cases occur annually worldwide (Chin, 2000) with approximately 600,000 deaths, several million of such cases occurring in Africa (Grange, 1994). Most developed countries saw declining rates of typhoid fever throughout first half of 20th century due to vaccinations and advances in public sanitation and hygiene. Antibiotics introduced in clinical practice in 1942 greatly reduced mortality (Kumar *et al.,* 2008). Typhoid salmonellosis is still endemic in developing countries (Muew and English, 2008) like Nigeria (Odugbemi *et al.,* 1994)

Clinical features include sudden onset of sustained fever, severe headache, and loss of appetite, gastroenteritis, constipation and / or non-bloody diarrhoea, cough, abdominal rose spots and mental confusion (Yano, 2002).

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There may be complications occurring two to five weeks into the disease condition having bacterial replication in the reticuloendothelial system and significant inflammation of the lymphoid organs of the small intestines presenting intestinal perforations and intestinal haemorrhages (Fru-Nsutebu *et al.,* 2003). Myocarditis, osteomyelitis, meningitis, mental dullness and even death (Yano, 2002; Kahn and Line 2005) can occur. The immune responses of humans to typhoid salmonellosis via inflammation of the bowel and subsequent activation of phagocytic leucocytes such as neutrophilic PMNs, eosinophils, monocytes and macrophages into the lamina propria of mucosal interstitum, lead to the oxidative stress-mediated production of reactive oxygen species (ROS), through respiratory burst (Riddell, 1988; Dennis, 1992). It is then accompanied by extensive mucosal injury including disruption of interstitial matrix, oedema, epithelial cell necrosis, erosion and ulcerations (Dennis, 1992; McDonald and Steidler, 2000). This suggests that *Salmonella typhi* may play an important role in the pathogenesis of interstitial and epithelial cell damage.

The immune responses due to inflammation of the bowel has been implicated in several forms of human diseases in relation to total lipid and cholesterol levels through the production of malondialdehyde (MDA) and other lipoperoxides. Oxidative stress is a disturbance in the 'prooxidant-antioxidant' balance in favour of the former leading to potential damage of macromolecules [13]. Reactive oxygen species (ROS) such as peroxides and free

radicals represent a class of molecules derived from the metabolism of oxygen and exists inherently in all aerobic organisms (Yoke, 2003). Oxidants such as hydrogen peroxide, superoxide radicals, hydroxyl radicals and lipid peroxides (LOOH) play an ever more important role in human diseases (Thompson, 1995). Mononuclear and polymorphonuclear leucocytes have the potential to synthesize and release a variety of potentially toxic agents including ROS into the extracellular environment where they may injure cells and tissues, when in large quantities. This study was designed to investigate the extent of involvement of oxidative stress in typhoid salmonellosis as well as compare its effect on total lipid and cholesterol levels in both infected and healthy individuals, being a measure of the health status of an individual.

MATERIALS AND METHOD

Sera obtained from the blood of one hundred and fifty two (152) clinically confirmed typhoid patients in the University Medical Centre, University of Nigeria, Nsukka over a period of four months as well as from donor healthy individuals were assayed for MDA (lipid peroxidation product), total lipid and total cholesterol levels. Subjects were of varying ages, sex, weight and different stages of typhoid salmonellosis infection. The design and conduct of the study were in accordance with the Helsinki declaration. Lipid peroxidation product, MDA was assayed using the method described by Wallin *et al.,* 1993 . This Principle is based on the reaction of thiobarbituric acid (TBA) with malondialdehyde (MDA) under slightly acidic conditions to produce a pink or red colour complex with absorbs at 532nm (Anosike *et al.,* 2008). The concentration of MDA is proportional to the level of peroxidation.

Total lipid levels were assayed using the method of Zollner and Kirsch (1962) which is based on the principle of colour reaction determined as absorbance at 530nm (Romeu-Moreno and Mas 1999), of unsaturated lipids with phosphoric acid-vanillin reagent. A modification of the Zak (1957) reaction technique was employed in the estimation of total cholesterol levels. It required that cholesterol be extracted from serum with ethanol. This extract is then reacted with a solution of $FeCl_3$ dissolved in phosphoric acid, and the resulting colour read-off in a spectrophotometer at 550nm against a known concentration that was treated in the same manner. Normal values for cholesterol tend to increase with age, but the average values range from 100 to 200mg/dl. Assay results were expressed as mean±standard deviation. Paired sample t-tests were used for comparisons of variables between typhoid and healthy individuals. Correlations were determined by Spearman correlation coefficient method. Results were considered statistically significant when $P < 0.05$.

RESULTS

The mean total lipid levels in typhoid patients were 128.98±3.39 and 154.95±11.40 in healthy individuals (Fig1). The mean total cholesterol levels in typhoid patients were 142.22± 29.83 and that of healthy individuals were 211.19±22.02 (Fig.2). The mean malondialdehyde (MDA) levels were observed as 1.073±0.51 and 0.820±0.53 in typhoid and healthy individuals respectively (Fig.3). Comparisons of the total lipid levels, total cholesterol and MDA levels showed a statistical significance between concentrations of total cholesterol ($P<0.01$) and total lipids ($P<0.00$). No statistical significance were observed in concentrations of MDA ($P<0.16$).

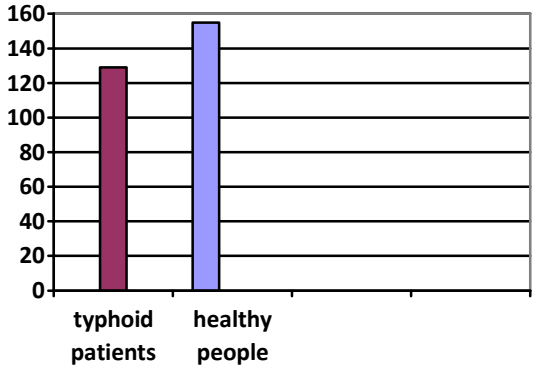

Fig. 1- Comparison of mean total lipid levels in healthy individuals and typhoid patients

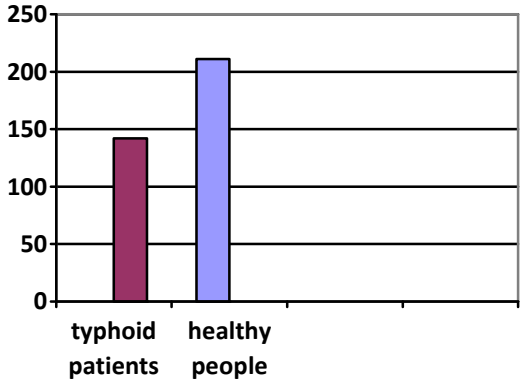

Fig. 2. Comparison of mean cholesterol levels in healthy individuals and typhoid patients

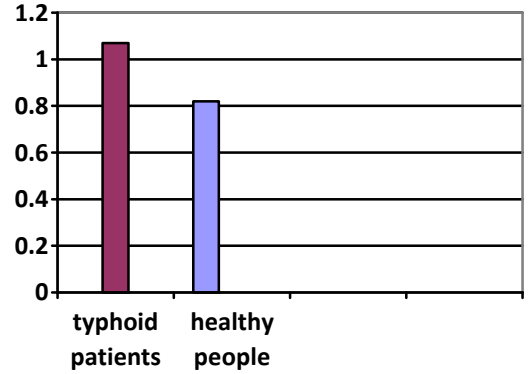

Fig. 3. Comparison of mean MDA levels in healthy individuals and typhoid patients.

DISCUSSION

Comparing healthy to presenting patients in Nsukka urban area, decline was observed in the mean total lipid levels (Fig1.) and mean total cholesterol levels (Fig. 2.) but the mean MDA levels indicated an elevation (Fig. 3). Lipid peroxidation results in oxidative modification of lipids and ultimately leads to the development of ulcers (Dennis, 1992). Typhoid fever is associated with inflammation and ulceration of the gut and liver of which oxidative lipid

modification plays an important role in exacerbating the disease.

One of the frequently used biomarkers giving an indication of lipid peroxidation is the serum concentration of MDA – a product of lipid peroxidation processes. MDA levels were observed to be higher in typhoid patients than in healthy individuals. This compares with previous works by Pranzy *et al*., 1999 showing higher MDA levels in malaria patients when compared to healthy individuals. The increased MDA levels could be due to the activation of the immune system which increases inflammation of the bowel as well as activation of phagocytes, mononuclear and polymorphonuclear leukocytes (PMNs) that have the potentials to synthesize and release potentially toxic agents such as reactive oxygen species (ROS). Furthermore, the study of Pranzy, 1999 on oxidative stress in malaria patients showed that cholesterol levels decreased tremendously in malaria patients when compared with healthy individuals. In this study, this decrease in cholesterol levels and total lipids were also observed, and may be attributed to lipid peroxidation, loss of appetite and diarrhoea which are classics in typhoid patients and partially due to the biosynthesis and activation of immune responses like prostaglandins, interleukins, interferons, tissue necrotic factor (TNF), etc. (Pranzy *et al.,* 1999). The decrease in the level of total cholesterol concentration in typhoid patients agrees with previous works done by (Khosla *et al*., 1991) in which low levels of HDL-cholesterol where observed in enteric fever patients. Results obtained therefore demonstrate the implication of oxidative stress in typhoid salmonellosis.

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