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Association Between Malondialdehyde and Glomerular Filtration Rate Among Patients Attending National Orthopaedic Hospital Dala- Kano, Nigeria

Adamu, S.M. ^{*1}, Wudil, A.M. ², Ibekwe, E.C. ¹, Koki, Y.A. ³, Adamu, S. ⁴, Abdullahi, S.A. ⁵ and Abbas, A.M. ⁶

Pathology Department, National Orthopedic Hospital Dala-Kano ¹, Department of Biochemistry, Bayero University Kano, Nigeria ², Pathology Department, Murtala Muhammad Specialist Hospital, Kano ³, Pharmacy Department, Infectious Diseases Hospital, Kano ⁴, Public health and Diagnostic Institute, Northwest University Kano ⁵ and Sir Muhammad Sunusi Specialist Hospital Kano ⁶.

Author for correspondence: shehumusayakasai@yahoo.com/+234-803-061-7330

Abstract

Estimated glomerular filtration rate is a direct measure of renal function. Malondialdehyde estimations can be used as a reliable tool to assess oxidative stress levels and finding its relationships with different disease patterns. This study is aimed at correlating malondialdehyde and eGFR as an index of lipid peroxidation induced kidney damage. A total of sixty (60) consenting subjects of both gender between the ages of 20 to 80 years were recruited. Kinetic Jaffe's method was employed for the estimation of creatinine. Estimated GFR was calculated using MDRD study equation. Malondialdehyde concentration was determined according to thiobarbituric acid reactive substances. Correlation coefficient ($r=0.334$) was observed between MDA (0.36 ± 0.31 nmol /ml) and eGFR (175 ± 52.10 ml/min/1.73m²) among the studied subjects. Mean MDA was higher in males (0.40 ± 0.35 nmol /ml) than in females (0.29 ± 0.22 nmol /ml), while eGFR was found to be higher in males (185.74 ± 54.40) than in females (152.06 ± 32.71). Correlation coefficient ($r = 0.335$ and 0.662) was observed in both males and females respectively. Positive association exists between malondialdehyde and eGFR among orthopaedic patients which is found to be stronger in females than males. Glomerular filtrates may produce reactive oxygen species even without kidney damage but aggravated to produce lipid peroxidation as metabolic products accumulates due to kidney dysfunction.

Key words: Creatinine, eGFR, Malondialdehyde and Kidney

Introduction

The oxidative stress depends on the excess production of free radicals known as reactive oxygen species (ROS) coupled with low concentration of antioxidants which induces lipid peroxidative tissue damage that plays a significant role in the pathogenesis of various diseases (Adamu *et al.*, 2016). The main cells damage results from ROS-induced alteration of macromolecules such as polyunsaturated fatty acids (PUFAs) in membrane lipids, essential proteins, and DNA. Additionally, oxidative stress and ROS have been implicated in disease states, such as Alzheimer's disease, Parkinson's disease, cancer, and aging (Alhassan *et al.*, 2016). Lipid peroxidation is the metabolic process in which ROS results in the oxidative deterioration of lipids which may significantly affect cell membrane structure and function (Vasilaki and McMillan, 2017). The PUFAs are major components of cell membranes and targets of free radical's attack, producing lipid peroxidative, secondary water soluble three carbons products with low molecular weight, reactive aldehyde known as malondialdehyde



(Raju *et al.*, 2013; Gwarzo and Muhammad, 2010). Malondialdehyde (MDA) is an end-product generated by decomposition of arachidonic acid and larger PUFAs through enzymatic or non-enzymatic processes (Ayala *et al.*, 2014). It has also been proposed that MDA could react physiologically with several nucleosides to form MDA-DNA adducts which may lead to mutations (point and frameshift), strand breaks, cell cycle arrest, and induction of apoptosis (Ayala *et al.*, 2014). Its estimation is an indirect assay of lipid peroxidation (Raju *et al.*, 2013).

Chronic kidney disease (CKD) is a pro-oxidant state and the degree of intracellular and extracellular oxidative stress is related to the severity of renal failure (Raju *et al.*, 2013). On the other hand, acute renal failure is commonly due to acute tubular necrosis (ATN), the latter representing an acute, usually reversible loss of renal function incurred from ischaemic or nephrotoxic insults occur singly or in combination. Such insults instigate a number of processes—haemodynamic alterations, aberrant vascular responses, sub-lethal and lethal cell damage, inflammatory responses, and nephron obstruction—that initiate and maintain ATN (Nath and Norby, 2000).

Renal damage or alterations in glomerular function affect the kidneys' ability to remove metabolic products from the blood into the urine and can be evaluated by measuring the glomerular filtration rate (GFR); the rate at which ultra-filtrate is formed by the glomerulus at approximately 120 ml per minute (Robert *et al.*, 2008; Nankivell, 2001). A more practical approach in the office is to estimate GFR (estimated GFR or eGFR) from the serum creatinine concentration, using either the Cockcroft-Gault or the Modification of Diet in Renal Disease (MDRD) study equations. The eGFR is a direct measure of renal function (Robert *et al.*, 2008; Nankivell, 2001). MDA estimations can be used as a reliable tool to assess oxidative stress levels and finding its relationships with different disease patterns (Singh *et al.*, 2014). Therefore, the aim of this study was to correlate malondialdehyde and

eGFR as an index of lipid peroxidation-induced kidney damage.

Materials and Methods

This is a prospective study conducted among orthopaedic patients attending National Orthopaedic Hospital Dala Kano. A total of sixty (60) consenting subjects of both gender between the ages of 20 to 80 years were recruited after obtaining ethical clearance from the hospital research ethics committee. The sample size was determined from a standard formula for the calculation of minimum sample size as shown by Oyejide (1992) at 95 % confidence level using the prevalence of 3.6% as given by Alebiosu *et al.* (2006). Five (5ml) of blood sample was obtained by venepuncture from the antecubital vein of the forearm using disposable syringes and delivered in clean, labelled plastic centrifuge tubes. It was allowed to stand for 30 minutes for proper retraction and clotting and then centrifuged for five minutes at 3000 rpm, after which the serum was separated into dry and labeled sample tubes.

Kinetic Jaffe's method was employed for the estimation of creatinine using commercially prepared kit as approved by Rosano *et al.* (1990). Estimated GFR was calculated using MDRD study equation as given by Stevens *et al.* (2006). Malondialdehyde concentration was determined according to Thiobarbituric Acid Reactive Substances (TBARS) method as described by Ohkawa *et al.* (1979). The data was analyzed using the Statistical package for the Social Sciences (SPSS) Version 16.0 (2007). Pearson's correlation was carried out and data was presented as mean \pm standard deviation.

Results

Positive correlation ($r=0.334$) was observed between MDA (0.36 ± 0.31 nmol /ml) and eGFR (175 ± 52.10 ml/min/ $1.73m^2$) ($p<0.01$) among the orthopaedic patients as illustrated in Table 1. Table 2 shows association between MDA and eGFR in relation to gender. Mean MDA was higher in males (0.40 ± 0.35 nmol /ml) than in females (0.29 ± 0.22 nmol /ml), while eGFR was found to be higher in males (185.74 ± 54.40) than

in females (152.06±32.71). A positive correlation was observed in both males (r=0.335) and females (r=0.662) (p<0.05).

Table 1: Association between MDA and eGFR among the Studied Population

MDA (nmol/ml)	eGFR (ml/min/1.73m ²)	r
0.36±0.31	175±52.10	0.334

N=60; r = Pearson's Correlation, p<0.01

Table 2: Association between MDA and eGFR in Relation to Gender

Gender	MDA (nmol /ml)	eGFR (ml/min/1.73m ²)	r
Males	0.40±0.35	185.74±54.40	0.335
Females	0.29±0.22	152.06±32.71	0.662

Males (n=43); Females (n=17); r = Pearson's Correlation, p<0.05

Table 3: Occurrence of Glomerular Function among the Studied Subjects

eGFR (ml/min/1.73m ²)	Occurrence (%)
≤ 90	1 (1.70)
≥90	59 (98.30)

eGFR ≤ 90 ml/min/1.73m² = abnormal kidney function, eGFR ≥90 = normal kidney function, N=60

Discussions

Malondialdehyde appears to be the most mutagenic product of lipid peroxidation is widely used for many years as a convenient biomarker for lipid peroxidation of omega-3 and omega-6 fatty acids because of its facile reaction with thiobarbituric acid (TBA) (Ayala *et al.*, 2014). In this study, positive association between MDA and eGFR has been observed. This clearly indicated that the formation of ROS is evident in the kidney predominantly in the renal cortices (Raju *et al.*, 2013). Hence the filtration occurs within the glomerulus in the renal corpuscle (Saladin, 2004). ROS formation

results in morphologic lesions and in modifications of glomerular permeability to proteins through activation of proteases and reduction of proteoglycan synthesis. Additionally, they promote a reduction in glomerular blood flow and glomerular filtration rate through liberation of vasoconstrictory bioactive lipids and, possibly, inactivation of relaxing nitric oxide (Baud and Ardaillou, 1993). There are also evidences indicating that the inordinate or aberrant generation of ROS may contribute to the initiation and maintenance of ATN (Nath and Norby, 2000).



Genomic functional analysis demonstrated a clear deregulation of the mitochondrial respiratory machinery in the CKD patients closely associated with an enhanced oxidative stress (Granata *et al.*, 2009). Padalkar *et al.* (2012) reported the increased level of serum MDA in kidney disease patients which clearly shows that they were exposed to an increased oxidative stress via lipid peroxidation. De Vecchi *et al.* (2006) also confirmed the presence of lipid peroxidation in end state renal disease (ESRD). However, it has been shown that MDA levels are significantly raised in patients with chronic renal failure (CRF) due to glomerulonephritis, regardless of serum creatinine, which may suggest that oxidative injury is independent of any possible MDA retention due to renal impairment (Templar *et al.*, 1999). In contrast, this study considered orthopaedic patients with 98.30% having normal eGFR (Table 3), therefore, our findings suggest that glomerular filtrates may produce ROS even without kidney damage but aggravate to produce lipid peroxidation as metabolic products accumulates due to kidney dysfunction.

The observed positive association of MDA and eGFR in both gender is stronger in females than males. Ginsburg *et al.* (2001) concluded that there is a significant gender-specific differences in the susceptibility of lipids to peroxidation among athletes. These suggested that gender difference in the production and metabolic deactivation of reactive oxygen metabolite may be due to the nature of the gender response to the DNA-damaging effects of ROS (Nedelcu *et al.*, 2003; Brunelli *et al.*, 2014). However, glomerular histology of males and females in autopsy specimens detected no differences between genders regarding the development of glomerulosclerosis among humans (Gava *et al.*, 2001).

Conclusion and Recommendation

Positive association exists between malondialdehyde and eGFR among orthopaedic patients which is found to be stronger in females than males. Glomerular filtrates may produce reactive oxygen species even without

kidney damage but aggravate to produce lipid peroxidation as metabolic products accumulates due to kidney dysfunction. Further studies are suggested to ascertain the role of malondialdehyde as an index of lipid peroxidation induced kidney damage.

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