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CORRELATION OF PARAOXONASE 1 ACTIVITY WITH OXLDL LEVELS IN IRAQI DIABETIC FOOT PATIENTS

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ABSTRACT : Type 2 diabetes mellitus (T2DM) associated with reduced HDL-C level, induces change in HDL-C level, impairing cholesterol efflux and antioxidant capacity, which is associated with lower paraoxonase (PON1) protein expression and activity. This study aimed to assess PON1 activity in diabetic foot patients and explore the risk of cardiovascular disease. Iraqi patients with T2DM (n = 130) were enrolled after being divided into two groups; patients group with T2DM (n=22) and diabetic foot ulcer (DF) patients group (n = 108), which was classified to sub-groups according to Wagner classification. Also, a control group (n = 21) were used consisted of healthy subjects. Serum PON1 activity was measured using paraoxon as substrate. Oxidized low density lipoprotein (oxLDL) level was measured using ELISA kit. Results: The diabetic patients had significant lower paraoxonaseactivity, HDL-c level, while significantly higher levels of cholesterol, triglyceride, oxLDL, CRP, WBC was found when compared with control group. A significant negative correlation was found between PON1 activity and oxLDL level in patients groups. The increased oxLDL level and decreased PON1 activity in DF group is an indication of increased oxidative stress. Decrease activity of PON1 in DF group and its negative correlation with oxLDL level may increase their risk to CVD.

Key words : Type 2 diabetes mellitus, diabetic foot ulcer, paraoxonase 1, oxidized low density lipoprotein, cardiovascular disease.

INTRODUCTION

Foot ulcers are a major complication of diabetes mellitus, with high morbidity and mortality (Prompers *et al*, 2007; Bakker *et al*, 2012,). Hyperglycemia is the most important risk factor for the microvascular complications: retinopathy, nephropathy, neuropathy and diabetic foot ulcer (Klein *et al*, 1996). Diabetic foot is one of the heaviest and most debilitating financial burdens, not only for the sufferer, but also for the family and health system (Brito-Zurita *et al*, 2013; Odhayani *et al*, 2017). Some of the complications associated with diabetic foot include infections, ulcers, gangrene and extremity amputation in severe cases (Rubio *et al*, 2012).

Paraoxonase1 (PON1) (E.C. 3.1.8.1) catalyzes the hydrolysis of organophosphate esters; its name arises from its most commonly used *in vitro* substrate, paraoxon, but it also has arylesterase and lactonase activities (Furlong *et al*, 1989).

Human PON1 consists of 354 amino acids residues with a molecular mass of (43-45 KDa) (A°kar and Büyükleblebici, 2012) exclusively associated with high density lipoprotein (HDL) in association with human phosphate binding protein (HPBP) and small amounts of PON1 were detected in very low-density lipoprotein (VLDL) and postprandial chylomicrons (Draganov and La Du, 2004). Binding of PON1 to HDL is through hydrophobic N-terminus interaction to phospholipid and through PON1 Apo-A interaction. ApoA1 is the major protein in HDL that stabilizes PON1 and binds it with very high affinity (Morales *et al*, 2006). It catalyzes the hydrolysis of multiple substrates such as aryl ester, lactones and hydro peroxides (Dias *et al*, 2014).

Human PON1 mRNA was detected only in liver where, it is synthesized and then secreted into plasma (Reddy *et al*, 2001)

Paraoxonase1 (PON1) is a calcium dependent enzyme; it has two calcium binding sites, which are important for enzyme stability and catalytic activity (Ibrahim *et al*, 2017)

Alterations in circulating PON1 levels and activity have been reported in several diseases associated with both oxidative stress and inflammation, including