

INFLUENCE OF TNF- α IN HEMOPHILIC ARTHROPATHY

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ABSTRACT : Hemophilia is characterized by frequent bleeds particularly in joints (hemarthrosis) leading to devastating effects on all joint components, resulting in synovitis, osteochondral degeneration and ultimately end stage haemophilic arthropathy. Since few published data exist about the influence of TNF- α in haemophilic arthropathy, the present study is conducted to investigate its serum level in hemophilic patients. The study has been carried out on Iraqi patients with hemophilia in the National Center of Hematology, Mustansiriyah University. Fifty-seven male patients involved in this study with age ranged from (7-45) years. 43 of them were diagnosed as hemophilia A, while 14 were hemophilia B. Along with patient group, 20 healthy subjects with matched age and gender were involved as control group. The presence and severity of arthropathy among patients was determined based on FISH and activated partial thromboplastin time (aPTT) in hemophilic patients, while TNF- α was determined in the serum samples of healthy and patient subjects.

Results revealed that the serum level of TNF- α in HA patients (10.3 ± 0.69 pg/ml) is significantly ($p < 0.0001$) higher than those in control (5.8 ± 0.17 pg/ml) and in HB patients (6.2 ± 0.28 pg/ml) and has significant positive correlation ($r=0.3458$, $p=0.01$) with age of hemophilic patients. It can be concluded that this marker plays a pivotal role in deterioration of joints condition particularly in HA patients.

Key words : Hemophilia, hemarthrosis, TNF- α , aPTT, FISH.

INTRODUCTION

Hemophilia arthropathy usually begins with proliferative synovitis that shares some similarities with rheumatoid arthritis (RA) and osteoarthritis (OA), but in haemophilic patients may be more complex (van Vulpen *et al*, 2015; Oldenburg *et al*, 2016). The presence and severity of arthropathy complication among patients was determined by using Functional independence score in hemophilia (FISH) for assessing musculoskeletal function of hemophilic patients and degree of limitation of their movement (LOM) through measuring the patient's independence in performing seven activities under three categories: self-care (grooming and eating, bathing and dressing), transfers (chair and floor) and mobility (walking and step climbing) (Poonnoose *et al*, 2007). However, recent advances in technology have made musculoskeletal ultrasound (US) as an attractive alternative for several reasons (Doria *et al*, 2015), but has potential difficulties because it is operator dependent, non-visualization of internal bone structure, bone edema, and do not penetrate deeper structures such as cruciate ligaments in the knee (Rowbotham and Grainger, 2011);

Hall *et al*, 2014). Recently, analysis of biomarkers of joint disease biomarkers might be useful in monitoring the impact of joint bleed and evaluation of treatment of such bleeds (van Vulpen *et al*, 2015). In patients with rheumatoid arthritis (RA) or osteoarthritis (OA), the cytokine tumor necrosis factor-alpha (TNF- α) is recognized as a crucial pathogenic orchestrator (Pulles *et al*, 2017), while in patients with haemophilia may be more complex than in patients with RA or OA (Oldenburg *et al*, 2016). Tumor necrosis factor alpha (TNF- α) is one of the 19 ligands within the tumor necrosis factors superfamily (Bodmer *et al*, 2002). TNF- α plays a key role in the inflammatory response, which is the first protective barriers in the body (Zelová H and Hošek, 2013). As our knowing, there is no previous Iraqi study focused on the molecular basis of hemophilic arthropathy, therefore, the present study aimed to identify the role of proinflammatory cytokine TNF- α as a predictive biomarker that indicate the presence of arthropathy in hemophilic patients when the musculoskeletal ultrasound (US) is not available.