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Determination of D-dimer Levels among Sudanese Patients with Rheumatoid Arthritis

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Abstract: *Rheumatoid arthritis is long lasting autoimmune disorder that primarily affects the joints and results in warm, swollen, and painful joints. This is a hospital based case-control study conducted in Wad Medani Teaching Hospital, Gezira State, Sudan from May to November 2018 on 50 cases (68% female; 32% male) and 50 normal healthy controls. The study aimed to determinate the levels of D-dimer in patients with rheumatoid arthritis. 2.5 ml venous blood was collected in tri sodium citrate anticoagulant. Platelet poor plasma was prepared by centrifugation of citrated blood at 2500 rpm for 15 minutes. D-dimer level was measured using sandwich immune-detection method. The results showed the level of D-Dimer was found to be normal in 31 (62%) of patients compared to 19 (38%) was high. A significant increase in the D-dimer level (mean: 512.08 ±278.55 ng/ml) in patients with rheumatoid arthritis were detected when compared with normal healthy control (mean: 281.44±84.44 ng/ml) (P value = 0.000). The study concluded that there was elevation level of D-dimer in patients with rheumatoid arthritis disease.*

Key words: D-dimer, Rheumatoid Arthritis, Sudan.

Introduction

The word arthritis literally means joint inflammation, which derived from Greek word "arthros" (joint) and "itis" means (inflammation) (Michael and Angelillo, 2009). Rheumatoid arthritis (RA) is a chronic, inflammatory, systematic autoimmune disease that initially affects small joints, progressing to larger joints and eventually the skin, eyes, heart, kidneys and lung. Often the bone and cartilage of joints are destroyed, tendons and ligaments become weaken. All this damage to the joints cause deformities and bone erosion, usually very painful for a patient (1). Most commonly involved are the small joints of the hands, feet and cervical spine, but larger joints like the shoulder and knee can also be involved. Synovitis can lead to tethering of tissue with loss of movement and erosion of the joint surface causing deformity and loss of function (2). RA primarily affects joints, but it also affects other organs in more than 15–25% of individuals (3). There are many possible triggers for rheumatoid arthritis including women, elderly age, HLA-DR4 and some environmental factor as smoking (4).

Diagnosis is made by clinical examination from an appropriate health professional, and may be supported by other tests such as X-ray, radiology and blood tests (presence of rheumatoid factor and/or anti-citrullinated protein antibodies (ACPAs, anti- CCP) (5).

Conn *et al*., found evidence of mild overcompensated intravascular coagulation and fibrinolysis in patients with RA (6). Recent studies identifying mechanisms for a functional role of coagulation factors beyond haemostasis have provided examples of interesting links between the coagulation system and innate immune activation. Furthermore, citrullinated fibrinogen is an important and early autoantigen in patients with RA carrying the HLA-DRβ1 shared epitope allele, which demonstrates an adaptive immune response to a coagulation factor in an inflammatory rheumatic disease (7). Etiology of RA is unknown but it is presumed to be an immunologic disease with contributing genetics factors. The dominant feature is inflammation, primary in synovium. The synovial membrane in RA becomes hyperplastic. There is an increased number of both type synoviocytes and is infiltrated with immune and inflammatory cells particularly macrophages, B-and T-lymphocytes, plasma cells and dendritic cells. Increased levels of cytokines are present which play a central role in the perpetuation of synovial inflammation. The persistence of the chronic inflammatoryresponse in conjunction with ongoing joint destruction (is finding in many patients with RA despite the use of effective anti-inflammatory agents and disease-modifying drugs) probably appears as a direct result of the sustained recruitment, inappropriate retention and impaired apoptosis. Increased levels of cytokines as IL-6 and TNF-α lead to elevated in D-dimer level (8).

D-dimer is a fibrin degradation product , a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two cross linked D fragment of the fibrin protein. D-dimer concentration may be determined by a blood test to help diagnose thrombosis. While a negative result practically rules out thrombosis, a positive result can indicate thrombosis but does not rule out other potential causes (8). Fibrinogen is a soluble plasma glycoprotein that is transformed into highly self-adhesive fibrin monomers after thrombin cleavage. D-dimer antigen as detected by commercially available assays can either be derived from the soluble fibrin polymers before their uptake in the clot or be the product of plasmin cleavage of the fibrin clot (9).

Materials and methods:

It is a hospital based case-control study conducted on Wad Medani Teaching Hospital, Gezira State, Sudan among Sudanese patients diagnosed with rheumatoid arthritis and matched healthy normal individuals with the same age and gender as control during the period from May 2018 to May 2019**.** Data were collected by questionnaire was designed to provide personal and medical information. Medical information were collected from hospital medical records. Sudanese patients diagnosed with rheumatoid arthritis were included and exclude any patients with liver disease, renal disease, hematological malignancy, and patients with thrombosis. Ethical Approval was obtained by the Research Ethical Committee from Ministry of Health, Gezira State and Faculty of Medical Laboratory Sciences, Gezira University. A 2.5ml venous blood was collected in tri sodium citrate container. Platelet poor plasma was prepared by centrifugation of citrated blood at 2500 rpm for 15 minutes. Then D-dimer level was measured by I-CHROMA^{TM}instrument. Data was analyzed using statistical package for social science (SPSS) computer program (version 20.0) and t- test used for calculation of the mean, and the significant is fixed at the value $p<0.05$.

Results:

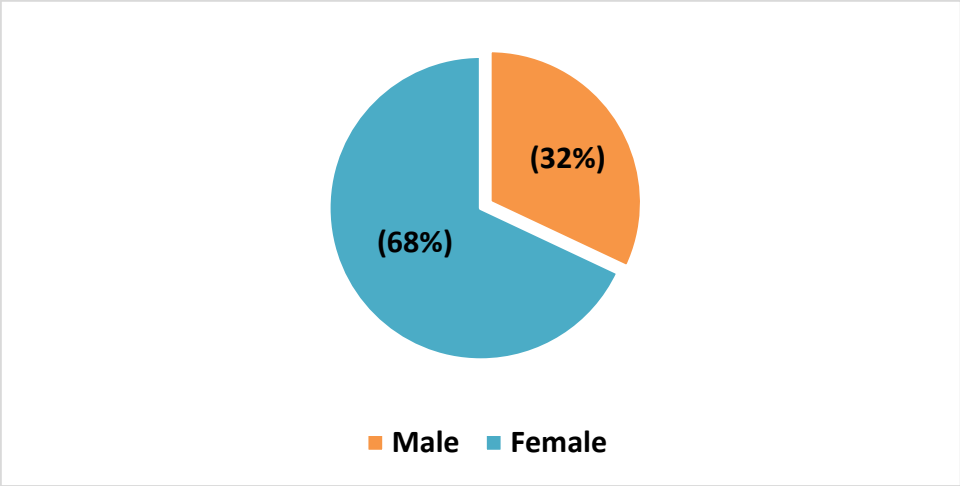

Figure 1. Distribution of study subject according to gender.

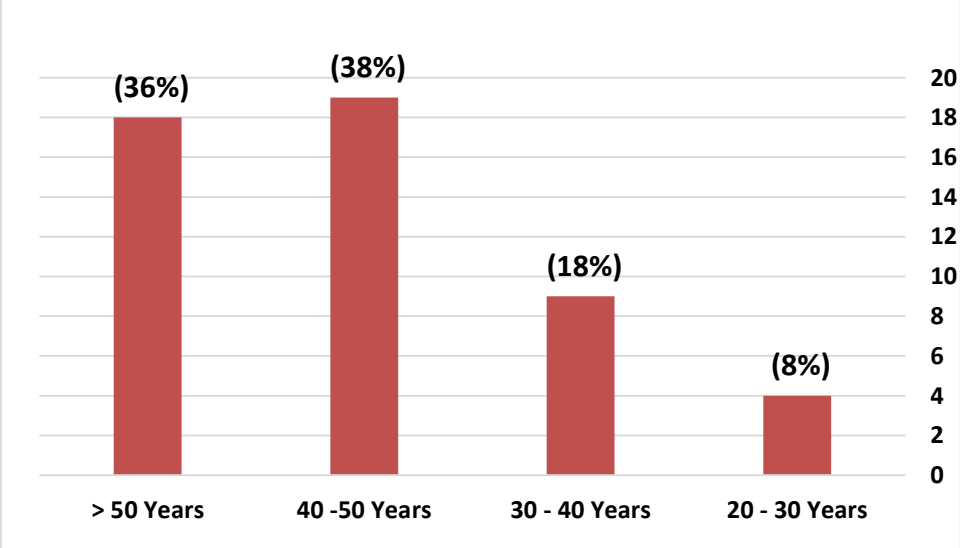

Figure 2. Distribution of study subject according to age groups.

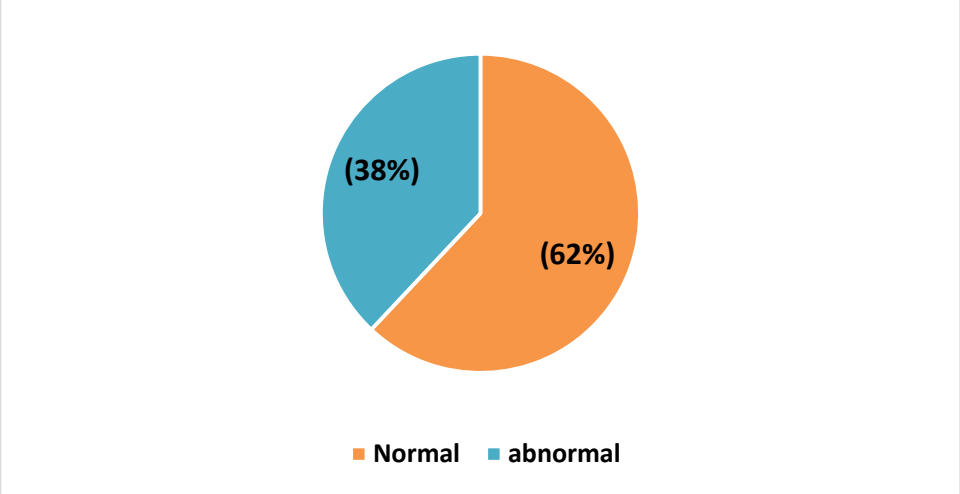

Figure 3. Distribution of study subject according to result of D-dimer level (ng/ml).

Table 1. Comparison of D-dimer level between patients and control groups.

Groups	N	Mean ng/ml	S. D ng/ml	*P value*
Patients	50	512.08	278.55	
Control	50	281.44	84.44	**0.000**

Table 2. Comparison of D-dimer level between male and female patients.

Gender	N	Mean ng/ml	S. D ng/ml	*P value*
Male	16	525.50	263.67	
Female	34	505.76	288.92	0.718

Table 3. Comparison of D-dimer level between age groups of patients.

Age groups	N	Mean ng/ml	S. D ng/ml	P value
20 - 30 Years	4	332.50	109.78	
30 - 40 Years	9	326.89	161.56	
40 -50 Years	19	471.26	270.42	0.278
> 50 Years	18	687.67	267.49	

Discussion:

Rheumatoid arthritis (RA) is a chronic, inflammatory, systematic autoimmune disease that initially affects small joints, progressing to larger joints and eventually the skin, eyes, heart, kidneys and lung. Often the bone and cartilage of joints are destroyed, tendons and ligaments become weaken (1).

Aside from roles in fibrin homeostasis, several of the coagulant and fibrinolytic proteases are important mediators of inflammation in diseases such as asthma, atherosclerosis, rheumatoid arthritis, and cancer (10).

This is hospital based case-control study conducted in Wad Medani Teaching Hospital Gezira state – Sudan in a period from May 2018 to November 2018. The study aimed to determination the level of D-dimer concentration in Sudanese patients with rheumatoid arthritis and compared to healthy normal control. Data were collected using structured questionnaire. A total of 100 samples were collected (50 patients and 50 controls). From 50 patients; There were 16 males (32%) and 34 females (68%), their age ranged between (20 to 70 years). The results showed 31 (62%) patients with normal D-dimer level compared to 19 (38%) patients with abnormal D-dimer level.

There were significant increasing in D-dimer levels for patients (mean = 512.08 ± 278.55 ng/ml) compared to control (mean = 281.44 ± 84.44 ng/ml) (*P value* = 0.000). This finding agree with previous studies that reported elevation of D-dimer among patients with rheumatoid arthritis when compared to healthy normal control (11-13).

There was no significant difference in D-dimer level between males and females (*P value* = 0.718). This result agree with study done in china (11).

There was no significant difference in D-dimer level between different age groups (*P value* = 0.278), despite increasing in D-dimer level in rheumatoid arthritis patients with their age groups (20 – 30 years), (30 – 40 years), (40 – 50 years) and (>50

years)(D-dimer level = 233.50 ± 109.78 ng/ml, 326.89 ± 161.56 ng/ml, 471.26 ± 270.42 ng/ml and 686.67± 267.49 ng/ml respectively). This finding agree with study done in china respectively (11).

Conclusion:

The study concluded that there was elevation level of D-dimer in patients with rheumatoid arthritis disease.

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