

Estimation of Pentraxin-3 (PTX3) in Rheumatoid Arthritis Males' patients (with and without) Type II Diabetes Mellitus in Iraq

Nashwa S. Sultan

Hamza2006n@gmail.com

Anwar F. AL- Taie

dr.anwar1979@yahoo.com

Department of Chemistry, College of Education for Pure Science Ibn Al-Haitham, University of Baghdad, Baghdad, Iraq

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Abstract

Rheumatoid arthritis is a chronic inflammatory autoimmune disease its etiology is unknown. The classical autoimmune diseases, have adaptive immune genetic associations with autoantibodies and major histocompatibility complex (MHC) class II such as rheumatoid arthritis (RA), diabetes mellitus type two (DM II). Serum of 99 males suffering from RA without DM II as group (G1), 45 males suffering from RA with DM II as group (G2) and 40 healthy males as group (G3) were enrolled in this study to estimation of alkaline phosphates (ALP), C-reactive protein (CRP) and Pentraxin-3 (PTX). Results showed a highly significant increase in PTX3 levels in G1 and G2 compared to G3 and a significant decrease in G1 comparing to G2. Results also revealed a significant increase in CRP levels in G1 and G2 when compared to G3, as well as a significant increase in G2 comparing to G1. Results showed a significant decrease in ALP levels in G1 and G2 while this phrase must no differences was observed between G1 and G2 and there was no significant positive correlation between PTX3 and ALP in sera of RA males' patients with and without DM II it be showed in our study.

Keywords: Rheumatoid arthritis; Diabetes mellitus; Pentraxin; C-reactive protein; alkaline phosphates; Methotrexate; folic acid omega 3

1. Introduction

Pentraxin are a family of evolutionarily conserved pattern-recognition proteins that are acute phase protein made up of five identical subunits. Based on the primary structure of the subunit that produced by immune and structural cells [1]. The Pentraxin are structurally unrelated to the collections and include small Pentraxin such as C-reactive proteins (CRP), serum amyloid protein (SAP) and such as PTX3 [1- 4]. The multifunctional properties of PTX3 can be at least in part explained by its capacity to interact with a number of different ligands a characteristic shared with CRP and serum amyloid protein (SAP) [4]. Recent studies have shown that PTX3 levels elevated in the presence of a bacterial infection [5]. It is a soluble inflammation and innate immunity [1]. Study demonstrated that PTX3 have a role in allergic asthma [6] so several kinds of cell types are confirmed to produce PTX3—vascular endothelial cells, vascular smooth muscle cells and monocytes pattern recognition receptor with non-redundant functions in macrophages. [1]. Acute-phase protein is a group of proteins that are synthesized in greater amounts include C-reactive protein (CRP) in Acute tissue damage, due to trauma Chronic inflammation and Malignant disease, [7, 8]. Acute phase

protein can include C-reactive protein (CRP) which available marker led to. Its concentration that increase 30-fold from a normal value of less than 5 mg/L during the acute phase response, rheumatoid arthritis and Crohn's disease [9]. Its measurement appears to be both more sensitive and more specific than measurements of the erythrocyte sedimentation rate (ESR) and plasma viscosity in this respect [9, 10]. Alkaline phosphates (ALP) comprise a group of enzymes that catalyze the hydrolysis of phosphate esters in an alkaline environment, generating an organic radical and inorganic phosphate [11]. Alkaline phosphates are derived from a number of different tissues, including the liver, the osteoblasts in bone and the placenta. Plasma activities rise in cholestatic liver disease because ALP synthesis is increased and the enzyme within the biliary tract is regurgitated into plasma [12, 13].

This study aimed to evaluate of Pentraxin-3 (Ptx3) in Iraqi males' patients suffering from RA with and without DM II. In addition to found correlation relation for ptx3 with ALP in RA patients with DM II and without DM II.

2. Methods

2.1. Patients Study

The samples of blood were collected from 188 males with age ranged between (18-67) years were enrolled in this study in medical city hospital in Baghdad, general hospital in Basra, teaching hospital and Al-salaams hospital in Mosul from October 2017 to April 2018. They were divided into three groups as follows: -

1. Rheumatoid arthritis patients without DM II as group one (G1) that consist of (99) males.
2. Rheumatoid arthritis patients with DM II as group two (G2) that consist of (45) males.
3. Healthy control groups as group three (G3) that consist of (40) males.

All patients in groups (G1) and (G2) were taking Methotrexate, Folic acid and Omega3 treatment, Smoker patients were excluded from this study ptx3 were estimated by ELASA kit No: YHB 2259Hu from China. CRP estimated by Latex method kit L21-V3 from UK and ALP estimated by a Colorimetric method according to kit from France. EC 3.1.3.

2.2. Statistical Analysis

The statistical analysis of this prospective study performed with the Graph Pad Prism® 7 and Microsoft Excel 2013. Numerical data with normal distribution were described as mean and standard deviation, Analysis of variance (ANOVA) used for multiple comparison using least significant difference.

Categorical data were described as count and percentage. Chi-square test or fisher exact test used to estimate the association between variables. The lower level of accepted statistical significant difference is bellow or equal to 0.05. Correlation of coefficient used for estimation of correlation between studied variables. Alan C.2007).

3. Results and Discussion

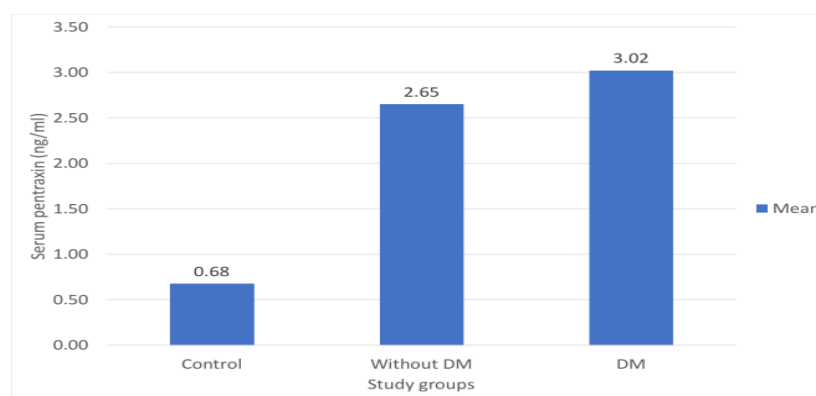
Table 1. and **Figures 2.** and **3.** showed levels of ptx3, CRP% and ALP for the studies groups, that results showed a highly significant increase in PTX3 levels in G1 and G2 compared with G3 and no significant decreasing in PTX3 levels in G1 compared with G2. Results also revealed a highly significant increase in CRP levels in G1 and G2 when compared to G3, as well as a highly significant increase in G2 comparing to G1. Results showed a highly significant decrease in ALP levels in G1 and G2 when compared with G3, and there were a highly significant different between G1 compared with G2.

Table1. Concentrations of Pentraxin3, CRP, and Alp in males' Iraqi patients and healthy control.

Groups	G1	G2	G3	P value		
				G1 & G2	G2&G3	G1&G3
Parameters	NO:99	NO:45	NO:40			
Ptx3 - μ g/ml	2.65 \pm 0.78	3.02 \pm 0.5	0.68 \pm 0.09	0.129 N.S	0.001 s	0.001 H.s
CRP IU/ml	47.2%	37.8%	0%	0.001H. s	0.001 H.s	0.001 H.s
ALP U/L	22.04 \pm 3.776	28.05 \pm 5.61	48.95 \pm 4.82	0.001H.s	0.001 H.s	0.001 H.s

G1 = RA without DM II, G2=RA with DM II, G3=healthy control

S= significant p value, H. s=high significant p value., N. S=non-significant

**Figure 1.** Pentraxin concentration - μ g/ml in males Patients and healthy control.

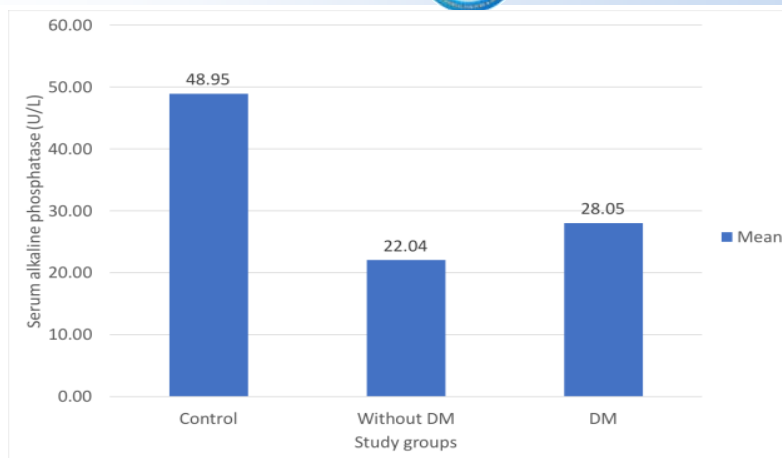


Figure 2. ALP activity U/L, in males' patients and healthy control.

Tables 2. and **3.**, **Figures 2.** and **3.** showed the level of Pentraxin-3 in sera of the RA patients without and with DMII, respectively. Groups Gg (Baghdad patients), Gb (Basra patients), and Gm (Mosul patients). The results of all groups in these tables and figures represent a highly significant different in PTX3 levels in RA patients without DMII in three cities (Gg, Gb, and Gm), while there were a highly significant different in PTX3 levels in RA patients with DMII between (Gg and Gb) and (Gb and Gm) cities, while there were no significant different between (Gg and Gm) cities when compared with others. The results also show a highly significant different in CRP levels in RA patients without DMII in three cities (Gg, Gb, and Gm) when compared with them. In addition to no significant different in CRP levels in RA patients with DMII between (Gg and Gb) and (Gb and Gm), while there was a significant different in CRP levels in RA patients with DMII between (Gg and Gm) cities.

Table 2. concentrations of Pentraxin-3, CRP, and ALP in three major cities of Iraqi patients of RA without DMII.

Groups Parameters	Gg	Gb	Gm	P value		
				Gg vs. Gb	Gb vs. Gm	Gg vs. Gm
Ptx3 µg/ml	2.63±0.72	1.58±0.5	3.75±1.01	0.001H.s	0.001 H. s	0.001 H.s
CRP IU/ml	39.6%	43.75%	58.33%	0.001H. s	0.001H. s	0.001H.s
ALP U/L	20.59 ± 3.33	23.3 ± 4.4	22.23 ± 3.60	0.002 s	0.071N.s	0.209 N.s

Gg=Baghdad patients of RA. without DMII , Gb=Basra patients with RA. without DMII

Gm =Mosul patients with RA. without DMII

The concentration of PTX3 and CRP were high in RA patient (with and without DMII) this results lead to expect that (PTX3 and CRP) may be a sensitive indicator of clinical arthritis.

Also, **Table 3.** and **Figure 4.** show no significant different in ALP levels in RA patients with DM II between (Gg and Gb) cities, and a highly significant decrease between (Gb and Gm), in addition to a significant different between (Gg and Gm) when compared with them.

Table 3. Concentration Pentraxin-3, CRP and ALK.P in Three major cities of Iraqi patients of RA with DM II.

Groups	Gg	Gb	Gm	P value		
				Gg vs. Gb	Gb vs. Gm	Gg vs. Gm
Ptx3 $\mu\text{g/ml}$	3.59 \pm 0.71	1.76 \pm 0.91	3.71 \pm 1.05	0.0001 H.s	0.001H. s	0.831 N.s
CRP IU/ML	33.3%	53.3%	26.7%	0.663 N.S	0.516N.S	0.032.S
ALP U/L	27.75 \pm 6.7	25.31 \pm 3.52	31.01 \pm 4.77	0.153N.s	0.001 H.s	0.021 s

Gg=Baghdad patients of RA. with DMII , Gb=Basra patients with RA. with DMII

Gm =Mosul patients with RA. with DMII

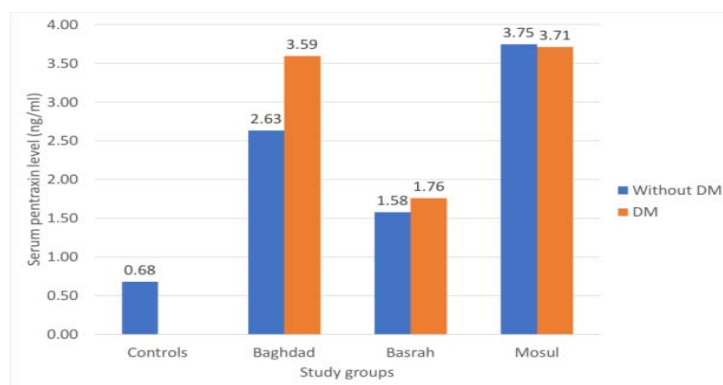


Figure 3. Pentraxin concentration - $\mu\text{g/ml}$, in males Patients of RA with and without DM II and healthy control.

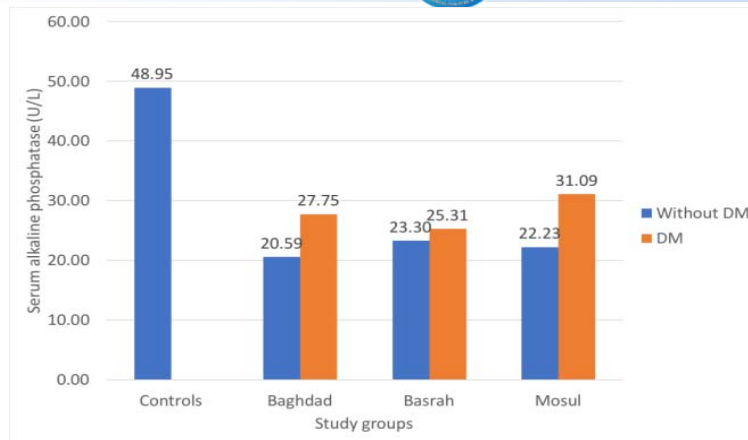


Figure 4. ALP activity U/L in males' patients of RA with and without DM II in three Iraqi cities.

Table 4. correlation between PTX-3 and ALP in RA patients with and without DM II.

		ALP	
ptx-3	R	0.271	Without DM II
	P	0.072	
ptx-3	R	0.04	With DM II
	P	0.633	

RA is an inflammatory disease characterized by chronic inflammation of the synovium, particularly of small joints, which of then leads to destruction of at articular cartilage and juxta auricular one [14]. **Table 1.** showed the level of pentraxin-3 (PTX3) in sera of G1, G2. Results of all groups represent significantly a High levels of PTX3 in G1 and G2 as a compared with G3. Pentraxins are a group of highly conserved as a modulators of inflammatory processes that primarily produced and released by vascular cell wall study revealed that elevation in (PTX3) level in patients with RA due to the PTX3 belongs to a super family of phylogenically conserved multiservice proteins, with includes short and long Pentraxin3. Combination of PTX3 and CRP could serve as better differential diagnostic markers for RA [15]. c-reactive protein a markers of system inflammation elevated CRP levels have also been linked to an increased risk of later development of diabetes [16]. and it being strongly predicting for the future development of RA in CRP is a sensitive marker of systemic inflammation and is elevated in patients with RA [17]. As the have suggest ALP are most effective in an alkaline medium [14]. Infect the level of serum ALP is increased in disorders characterized by accelerated bone turnover. For a long time, the diagnose is of RA was mainly based on clinical manifest a torn sand ALP may add useful information for assessing fracture risk and for monitoring osteoporosis in RA patient [17]. RA is the main causes of increased level of ALP because affect the wrist and small joints of the body besides the joints [18], but in and present study showing decrease in ALP in patients of RA with and without DM II that is due to all patients taking a Methotrexate a drug for treatment and taking (omega3 and folic acid) [19-20]. Provide that omega 3 influence ALP activities [19]. Methotrexate is the most important drug modifying anti rheumatic for the treatment of RA and currently considered as the central drug for the standard care and the management of RA [21]. Omega 3 is found primarily in fatty fish with high oil content. It's widely used in the treatment of chemotherapy

as a common consist of multidrug regimens [22]. Folic acid As an antagonist agonist which inhibits de novo synthesis of the nucleoside thymidine a prerequisite for DNA synthesis. Folic acid would be useful in reducing toxic manifestations that occur during long term treatment with low-dose MTX for RA [23].

4. Conclusions

This study is the first that observe the elevation of PTX3 levels in serum of Iraqi male's RA patients with and without DMII in three cities (Baghdad, Basra and Mosel) therefore indicated that Ptx3 may be a good biomarker for RA with and without DMII.

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