Levels of pro-inflammatory mediators CRP, IL-1β and IL-6 in alkaptonuria patients

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Alkaptonuria (AKU; MIM no. 203500) is a recessive inborn error disorder in the phenylalanine and tyrosine metabolism pathway, arising due to the deficient activity of the enzyme homogentisate 1,2-dioxygenase (HGD). Consequently, the homogentisic acid (HGA; 2,5-dihydroxyphenylacetic acid) will deposit in the connective tissue of various organs, causing a pigmentation known as ochronosis, leading to dramatic tissue degeneration, inflammation and arthritis. The disease prevalence worldwide is estimated as an ultra-rare, although higher incidence rates are recorded in Jordan. Data regarding the levels of inflammatory mediators in patients suffering of the rare disease Alkaptonuria are limited. C-reactive protein (CRP), Interleukin-1 Beta (IL-1β) and Interleukin-6 (IL-6) are acute-phase markers associated with joint inflammation. The aim of the present study is to compare the serum levels of the pro-inflammatory mediators, CRP, IL-1β and IL-6 in alkaptonuria patients (n = 17) with those measured for age-matched healthy controls (n = 17). Moreover, we attempt to determine the association between cytokine levels with the disease severity score and age using the Spearman correlation and multiple linear regression. The results show that the serum concentrations of the IL-1 β, IL-6 and CRP are higher in AKU patients compared with healthy controls, with a significant difference in IL-6 ($p = 0.02$). Moreover, a positive correlation is found between the patients' serum IL-6 and patients' age and the AKU Severity Score ($ro = 0.73$ and 0.7, respectively; $p < 0.05$). Thus, the patients' IL-6 serum levels can predict the disease severity score in alkaptonuria patients ($p < 0.05$). These findings suggest that the IL-6 might play a role in the pathogenesis of inflammation in AKU patients and thus targeting it may be one mode of treatment in future. However, these findings need to be supported by further studies, conducted on a larger sample of patients.

Image

Variables	Patients n= 17	Control n= 17	Mann-Whitney U	p-value
	Mean±se	Mean±se		
Age (years)	38.7±1.66	37±1.49	49.5	0.5
IL-6 (pg/ml)	1.2±0.25	0.5±0.07	25.5	0.020*
IL-1β (pg/ml)	12.7±4.02	2.4±0.71	51	0.5
CRP (mg/ml)	9.1±3.61	2.3±0.47	46	0.3
disease severity score	33.1±1.94	-	-	-
HGA (g/day)	1±0.07	-	-	-

Table1: Age, serum cytokines levels, disease severity score and urine HGA levels in alkaptonuria patients and controls. Patient score and Urine HGA were null in controls.

Variables	Patient score r^0 , P-value	Patient age r^0, P-value
Disease severity score	1, -	0.4, 0.3
Patient age (years)	0.4, 0.3	1, -
CRP (mg/ml)	0.2, 0.6	0.5, 0.1
IL-6 (pg/ml)	0.698, <0.001*	0.732, <0.001*
Il-1Beta (pg/ml)	0.0, 1	-0.115, 0.7
HGA (g/day)	0.1, 0.7	0.2, 0.6

Table1: Table2: Correlation of the patients' serum CRP, IL-1β and IL-6 levels with the age and disease severity in the AKU patients.

Biography

Eman Albataineh has her expertise in Immunologic research projects about molecular immunology, allergic diseases epidemiology in Jordan as well as the Allergy-triggering factors and associated diseases. She has been working in research for 6 years in two different universities, i.e.; Jordan University of science and technology and Mutah University.