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Serum uric acid and C-reactive protein in psoriasis vulgaris

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Abstract
Psoriasis is a chronic, recurrent, immune-mediated inflammatory disease, with a recognised genetic predisposition, the primary immune defect appears to be an increase in cell signalling via chemokines and cytokines that act upregulating gene expression, causing keratinocyte hyperproliferation. Modest hyperuricaemia may be found and has been attributed to enhanced epidermopoiesis**.** CRP is an acute phase reactive protein, known as a systemic inflammatory biomarker, a lot of studies reported increased CRP concentrations in active psoriasis, and identified CRP as a marker for psoriasis severity. The purpose of this study is to determine the serum uric acid levels and CRP in plaque-type psoriasis patients, and to assess any relation between their levels severity of psoriasis disease, and psoriasis arthropathy.
Patients and Methods: A total of 123 Libyan patients with plaque type psoriasis with age ranging from 19-75 years. Severity of the disease is estimated by PASI score. Each patient investigated for CRP titer and serum uric acid levels. The data were statistically analyzed using SPSS version 22 programme.
Results: Out of 123 patients, 81(66%) were males and 42(34%) were females with mean age of 42.6 years. Hyperuricemia was detected in 7.1% of female patients and in 6.2% of male patients, The difference between mean level of uric acid in male and female highly significant (P value o.ooo1) and was not significant in relation to the disease severity in both genders (p value 0.675,, p. 0.350). The number of patients with arthropathy was 31(25.2%) with arthropathy and there was a significant correlation between hyperuricemia anf arthropathy (p =0.0001). Out of the total patients 29 (23.6%) had positive CRP titer and there is no significance relation between CRP titer and disease severity with p value= 0.341, but the significance correlation between CRP titer and psoriatic arthritis., out of 31 psoriasis patients with arthritis 18(58%) were with negative CRP titer, 13(42%) were with positive CRP titer, and out of 92 psoriasis patients without arthritis 76(82.6%) were with negative CRP titer, and 16(17.4%) were with positive CRP titer, p value=0.011(significant), so CRP titer in psoriasis patients with arthritis considered to be reliable assessment for psoriatic arthropathy. When we correlate CRP titer with serum uric acids levels in psoriasis patients, we found different results in male and female, there is significance relation between the hyperuricemia and high CRP titer in psoriasis male patients with p value = 0.001. Results of the present study thus, confirm that CRP and uric acid levels should be monitored in patients with psoriasis, and that psoriasis and psoriatic arthritis should be treated as a single disease entity with common inflammatory mediators and pathways.
Conclusions: Our data suggested that psoriasis vulgaris patients may have high levels of uric acid and positive CRP titres with a significant difference between genders and psoriatic arthritis but not with the disease severity.

Keywords: psoriasis vulgaris, uric acid, C-Reactive Protein (CRP), psoriasis area severity index (PASI)

Introduction

Psoriasis, is a chronic erythematosquamous dermatitis that affects about 2-3% of the population, is characterized by abnormal keratinocyte hyperproliferation, resulting in thickening of the epidermis and of the stratum corneum [1, 2]. The primary immune defect appears to be an increase in cell signalling via chemokines and cytokines that act up regulating gene expression, causing keratinocyte hyper proliferation. T lymphocytes and their cytokines and chemokines appear to be the driver of lesion development and persistence, although other cells, such as endothelial cells, dendritic cells, neutrophils and keratinocytes play also an important role, along with other cytokines and growth factors [3]. The Psoriasis Area Severity Index (PASI) is the most widely used measurement tool for psoriasis. PASI combines the assessment of the severity of lesions and the area affected into a single score in the range 0 (no disease) to 72 (maximal disease) [4]. The enzyme xanthine oxidase makes uric acid from xanthine and hypoxanthine, which in turn are produced from other purines. Xanthine oxidase is a large enzyme whose active site consists of the metal, molybdenum, bound to sulfur and oxygen [5]. Within cells, xanthine oxidase can exist as xanthine dehydrogenase and xanthine oxireductase, which has also been purified from bovine milk and spleen extracts [6]. Uric acid is released in hypoxic conditions [7]. Laboratory test results may vary depending on your age, gender, health history, the method used for the test, and many other factors The following are considered to be normal results for this test adult male 2.5-8mg/dl (150-480micromol/L), adult female 1.5-6mg/dL (90-360micromol\L) [8]. C-reactive protein (CRP) is a protein found in the blood, the levels of which rise in response to inflammation (i.e. C-reactive protein is an acute-phase protein). Its physiological role is to bind to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system via the C1Q complex [9]. Blood, usually collected in a serum-separating tube, is analysed in a medical laboratory or at the point of care. Various analytical methods are available for CRP determination, such as ELISA, immunoturbidimetry, rapid immuno diffusion, and visual agglutination [10]. A high-sensitivity

CRP (hs-CRP) test measures low levels of CRP using laser nephelometry. The test gives results in 25 minutes with a sensitivity down to 0.04 mg/L. The aim of this study is to assess the level of uric acid and CRP titre in psoriasis vulgaris and to see any association with the disease severity and psoriatic arthropathy.

Materials and methods

A total of 123 Libyan patients with plaque type psoriasis attending the psoriasis clinic at dermatology department⁄ Aljumhouria hospital were included in this cross sectional study. Each patient exposed to detailed history and complete dermatological examination according to the prepared performa. Disease severity was assessed by PASI score where 1 to less than 10 is considered as mild, 10-20 moderate and more than 20 as severe disease (11). Blood sample then drawn from the patients and tested for C-reactive protein titre and serum uric acid. Serum uric acid level Laboratory test result may vary depending on age, gender, health history, the method used for the test, and many factors the following are considered to be normal results for this test adult male 2.5-8mg\L(150-480micromol\L), adult female 1.5-6mg\dl(90-360micromol\L). C-reactive protein titer normal concentration in healthy human serum is usually lower than 5mg\L. Data were analyzed using statistical package for social science (SPSS) version 22. Descriptive statistics, as mean, standard deviation, minimum and maximum value were used. Inferential statistics were used when needed, as t – test to find the difference between the means of the two groups, and Chi-square(x^2) to find the difference in the distribution of the variables between the two groups, P-value were considered significant when ≤ 0.05.

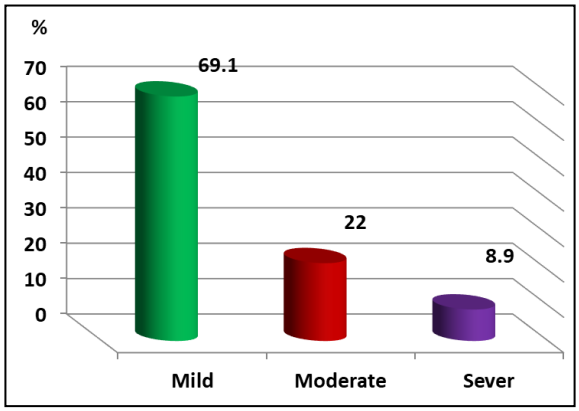

Fig 1: Severity of the disease according to PASI.

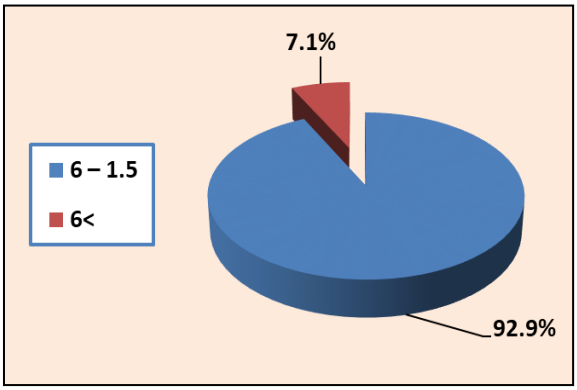

Fig 2: Uric acid levels in female psoriatic patients.

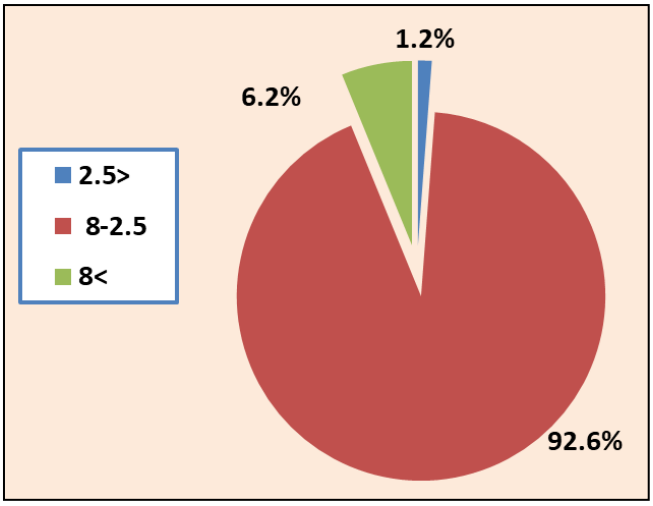

Fig 3: Uric acid levels in male psoriatic patients.

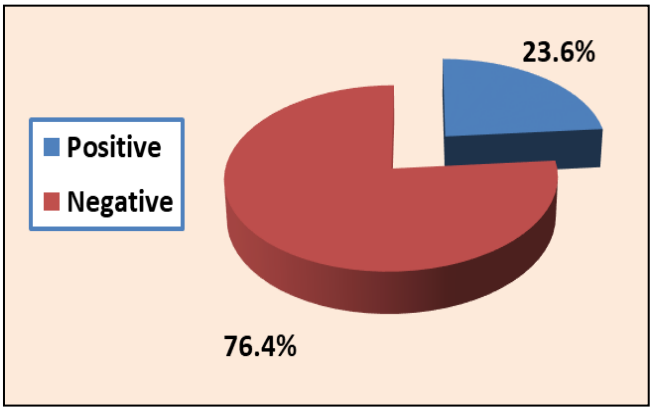

Fig 4: CRP titre in psoriasis vulgaris patients.

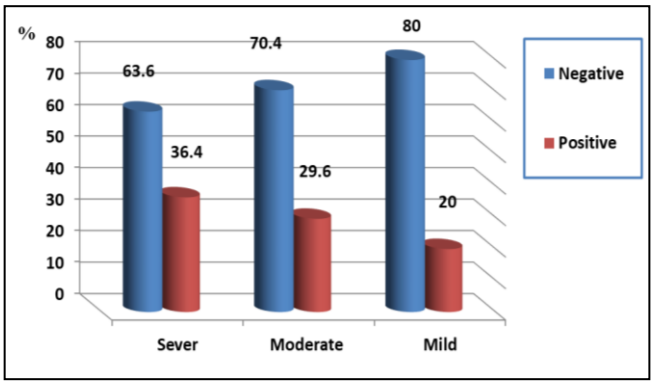

Fig 5: CRP titer in relation to psoriasis severity

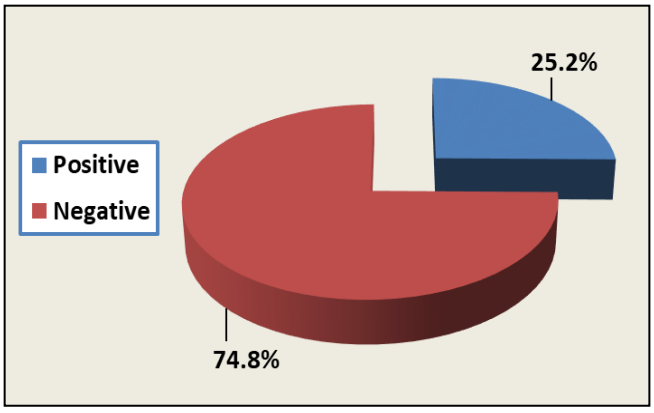

Fig 6: CRP titre in psoriasis patients with arthritis.

Results

Among 123 Libyan psoriasis vulgaris patients, 81(66%) were males and 42 (34%) females. Their ages ranged from 19-75years (Mean age 42.6 years). Severe psoriasis was seen in 8.9%, and moderate in 22% while mild in 69.1% (Fig.1). Serum uric acid level in female patients was 1.5-6mg⁄dl in 92.9% and> 6mg⁄dl in 7.1% (Fig.2), The level of uric acid in males was <2.5 mg⁄dl in1.2%), 2.5-8 mg⁄dl in 92.6% and >8 mg⁄dl in 6.2% (Fig.3), So hyperuriceamia is seen in 7,1% of female patients and 6.2% of male patients The difference between mean level of uric acid in males and females has highly significant difference with p value 0.0001. The relation between hyperuriceamia and severity of psoriasis in female psoriatic patients was shown in Tab.1 in which out of 10 moderate psoriatic female patients, only 1(10%) were hyperuriceamic (uric acid > 6 mg⁄dl) out of 30 mild psoriatic female patient 2 (6.7%) were hyperuriceamic. So there is no statistically significant relation between hyperuriceamia in female patients and severity of the disease (p value 0.350). Also according to the data in Tab.2 comparing hyperuricemia in male patients with severity of the psoriasis, out of 17 moderate psoriatic male patients only 2 (11.8%) were hyperuriceamic (uric acid > 8mg⁄dl) and out of 55 mild psoriatic male patients 2(3.7%) were hyperuriceamic, and out of 9 sever psoriatic male patients 1(11%) were hyperuriceamic, which statistically not significant (p value 0.675). The Correlation between serum uric acid levels and psoriatic arthritis in male patients (Tab.3), out of 64 psoriasis male patients without arthritis 3 (4.7%) were hyperuricemic with serum uric acid >8mg⁄dl whereas out of 17 male psoriasis patients with arthritis 2(11.8%) were hyperuricemic (statistically significant, p value 0.0001).

The correlation between serum uric acid levels and psoriatic arthritis, in female patients shown in Tab.4, out of 28 psoriasis female patients without arthritis 2(7.1%) were hyperuricemic with serum uric acid levels >6mg⁄dl and out of 14 female psoriasis patients with arthritis 1(7.1) were hyperuricemic (statistically not significant, p value= 0.525). Figure.4 showed the distribution of CRP titre in psoriatic patients out of 123 patients 29 (23.6) had positive CRP titre (>5mg⁄dl) and 94 (76.4) had negative CRP titre. The relation between CRP titre and severity of the disease is shown in Fig.5 where out of 11 sever psoriatic patients 7 (63.6%) were negative CRP titre and 4 (36.4%) were positive CRP titre whereas out of 27 moderate psoriatic patients 19 (70.4%) were negative CRP titre, 8 (29.6%) were positive CRP titre. In our cross sectional study we studied the percent of psoriatic patients with arthritis, as shown in Fig.6 out of 123 psoriatic patients were 31 (25.2%) with arthritis, 92 (74.8%) without arthritis. The correlation between CRP titre and psoriatic arthritis, as shown in Tab.5 out of 92 psoriasis patients without arthritis 76(82.6%) were with negative CRP titre and 16(17.4%) were with positive CRP titre whereas out of 31 psoriasis patients with arthritis 18(58%) were with negative CRP titre and 13(42%) were with positive CRP titre, so there is significant correlation between CRP titre and psoriatic arthritis in psoriasis patients (p. value =0.011).

Table 1: Serum uric acid levels in female patients in relation to disease severity.

Level of uric acid	Severity of the disease					
	Sever		Moderate		Mild	
	No.	%	No.	%	No.	%
1.5 – 6	2	100	9	90	28	93.3
>6	0	0	1	10	2	6.7
Total	2	100	10	100	30	100

Table 2: Serum uric acid levels in male patients in relation to disease severity.

Level of uric acid	Severity of the disease					
	Sever		Moderate		Mild	
	No.	%	No.	%	No.	%
<2.5	0	0	0	0	1	1.8
2.5 – 8	8	88.9	15	88.2	52	94.5
>8	1	11.1	2	11.8	2	3.7
Total	9	100	17	100	55	100

Table 3: Serum uric acid levels in male patients in relation to arthritis.

Level of uric acid	Arthritis in psoriasis male patients			
	Negative		Positive	
	No.	%	No.	%
<2.5	1	1.6	0	0
2.5 – 8	60	93.7	15	88.2
>8	3	4.7	2	11.8
Total	64	100	17	100

Table 4: Serum uric acid levels in female patients in relation to arthritis.

Level of uric acid	Arthritis in psoriasis female patients			
	Negative		Positive	
	No.	%	No.	%
1.5 – 6	26	92.8	13	92.8
>6	2	7.1	1	7.1
Total	28	100	14	100

Table 5: CRP titre in psoriasis with and without arthritis

CRP titre	Arthritis in psoriasis patients			
	Negative		Positive	
	No.	%	No.	%
Negative	76	82.6	18	58
Positive	16	17.4	13	42
Total	92	100	31	100

Discussion

Psoriasis is a chronic, recurrent, immune-mediated inflammatory disease, with a recognized genetic predisposition. The primary immune defect appears to be an increase in cell signalling via chemokines and cytokines that act up regulating gene expression, causing keratinocyte hyperproliferation. T lymphocytes and their cytokines and chemokines appear to be the driver of lesion development and persistence, although other cells, such as endothelial cells, dendritic cells, neutrophils and keratinocytes play also an important role, along with other cytokines and growth factors [12, 13]. Studies conducted in the second half of the 20thcentury, which aimed to determine the relationship between hyperuricemia and psoriasis, produced conflicting results [14].

It also suggested that the most reasonable explanation for elevated uric acid in psoriasis seems to be a combination of genetic predisposition and hyperalimentation [15]. However the study by Goldman m. on Uric acid in the etiology of psoriasis suggested that psoriasis occurs as a result of disorder of purine metabolism and monosodium urate crystals may be responsible for the cell proliferation that is characteristic of psoriatic plaques [16].

Uric acid is the final product of purine nucleotide catabolism. In particular, purine nucleotides are derived from both endogenous (de novo molecule synthesis and nucleic acid breakdown) and exogenous sources (alimentary

intake) [17, 18].

Factors that contribute to hyperuricaemia include genetics, diet, alcohol consumption, obesity, renal insufficiency, insulin resistance, hypertension, as well as the use of some drugs. The underlying mechanisms that cause hyperuricaemia may be under excretion of uric acid due to defective renal clearance, overproduction of uric acid, or a combination of the two. Many drugs – notably diuretics, ciclosporin, nicotinic acid, vitamin B12,chemotherapeutic agents, salicylates (low dose) and levodopa –have been reported to alter the abovementioned processes and cause hyperuricemia [19, 20]. of the 123 psoriasis patients, the hyperuricemia present in 7.1% of female psoriatic patients, 6.2% of male psoriatic patients, The difference between mean level of uric acid in male and female highly significance difference with p value 0.0001, mean 5.84 mg⁄dl, minimum 2.4 mg⁄dl, maximum 14 mg⁄dl. The statistical data about the severity of the disease, in our study show 8.9% had sever psoriasis, 22% moderate psoriasis, 69.1% with mild psoriasis. We compare the severity of the disease with hyperuricemia, which is differ according to level of uric acid in male and female. However serum uric acid levels didn't show significant relation with severity of the psoriasis disease on both gender (p.value 0.350 in females and 0.675 in males), this finding was in agreement with the results obtained by Ashishkumar *et al* [21]. As they found that serum uric acid, not correlate with surface area severity index but it was in disagreement with results obtained by Kwon HH *et al* on the correlation of serum uric acid with disease severity in 198 Korean patients with psoriasis suggested that serum uric acid concentration in patients with psoriasis is positively associated with PASI, extent of skin involvement for both genders independently ($p<0.05$) [14]. Also disagreement results obtained by Marym *et al* on serum uric acid levels in patients with psoriasis suggested that serum uric acid levels exacerbate by increase in the severity and duration of psoriasis, in psoriatic arthritis and in patients with non-plaque type psoriasis [22]. We notice that in our study in plaque type psoriasis patients with arthritis in relation to uric acid levels, of the 123 psoriasis patients were 25.2% with psoriatic arthritis and 74.8% without psoriatic arthritis. the study show the relation between uric acid levels and psoriatic arthritis we found significant correlation between arthritis in male psoriatic patients and hyperuricemia with p value 0.0001(significant), this was in agreement with results obtained by Choi *et al*, have shown that increased levels of uric acid can lead to type of arthritis, which associated with psoriasis skin disease. They further suggested that hyperuricemia in these patients, is a result of increased purine catabolism due to rapid epidermal cell turnover. These workers also reported that uric acid levels are elevated in psoriatic patients, with comparatively more rise in those who develop psoriatic arthritis. It has also been suggested that combined assessment of CRP and uric acid, in patients of coronary artery disease with low levels of other markers, provides incremental information for risk of further complications [23].

But those finding was disagreement with result obtained by Lambert JR et.al as they found that hyperuricemia not common characteristic for psoriatic arthritis [24]. Research over recent years has highlighted that psoriasis is associated with other immune mediated inflammatory conditions including inflammatory bowel disease, and ankylosing spondylitis and cardiovascular disease [12, 13]. CRP is an acute phase reactive protein, known as a systemic inflammatory biomarker. Serwin reported increased CRP concentrations in active psoriasis [25].

Uysal et.al identified CRP as a marker for psoriasis severity (26) In our cross-sectional study for the C-reactive protein titer in 123 psoriasis patients, we found 23.6% with positive CRP titer and 76.4% with negative CRP titer. Our study show the relation between the serum uric acid and CRP titer in psoriasis disease. We found that male psoriasis patients with high uric acid levels, also had high CRP titer with p value 0.001(significant), this suggested that hyperuricemia in male associated with high CRP titer.

But when we correlate the severity of psoriasis disease with CRP titer,in our studies there is no correlation between CRP titer and severity of psoriasis disease the p value = 0.341(not significant), This finding was in disagreement with result obtained by Papys *et al* as they found a significant association between psoriasis disease severity and elevated CRP levels [27]. Several other studies have also reported a correlation between increased levels of CRP and PASI as the results obtained by Gerkowicz *et al*, Coimbra *et al*, [28, 29]. Thus, CRP can be considered as a useful marker of disease severity that could be used to monitor the disease course and its treatment. In our study we found correlation between CRP titer and psoriatic arthropathy. This indicate the need for CRP titer in assessment of psoriatic arthropathy, this results was in agreement with study obtained by Punzi *et al*, they have shown that the determination of ESR and/or CRP is frequently disappointing in psoriatic arthropathy, since they are both elevated in only half of the patients with psoriatic arthropathy [30]. Recently, it was noted that elevated serum levels of uric acid are associated with factors that contributeto metabolic syndrome, including: hypertriglyceridemia, obesity, hypertension and diabetes [31, 32].

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