Relation between serum visfatin and clinical severity in different stages of rheumatoid arthritis

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Objective

Visfatin is one of the recently discovered adipokines that plays important proinflammatory and catabolic roles in rheumatoid arthritis (RA). Proinflammatory cytokines, such as interleukin (IL)-1, IL-6, IL-15, IL-18, and tumor necrosis factor-α (TNF-α), induce a number of physiological changes that result in the characteristic signs of inflammation. As inflammation is the major factor leading to structural damage, it is critical to achieve rapid suppression of inflammation to maximize disease control. Therefore, early diagnosis and treatment of RA is of paramount importance. As information on the relation between visfatin and disease activity in RA patients is conflicting and little is known about its role in joint damage, the present study was designed to evaluate the role of serum visfatin as a recent proinflammatory marker in RA according to the activity scores of disease to assess the possibility of introducing serum visfatin in the diagnosis and monitoring of RA patients and to determine the correlation between its serum level and other cytokines (IL-6 and TNF-α) and other laboratory biomarkers.

Patients and methods

This study was carried out on a total of 80 individuals; 60 of these were (48 women, 80%, 12 men, 20%) diagnosed with RA according to the American College of Rheumatology/The European League Against Rheumatism 2010 criteria and 20 healthy individuals were included as controls (10 women, 50%, 10 men, 50%). RA patients were classified into three groups: group I (severe RA) included 20 RA patients, group II (moderate RA) included 20 RA patients, and group III (mild RA) included 20 RA patients according to clinical evaluation for disease activity assessed using a 28 joint disease activity score (DAS-28). Blood samples were obtained from patients and controls for complete blood count and erythrocyte sedimentation rate. The sera of patients were collected for enzyme-linked immunosorbent assay estimation of serum visfatin, IL-6, and TNF-α. C-reactive protein (CRP) and rheumatoid factor (RF) were determined using the turbidimetry quantitative method.

Results

Comparison of the RA and control groups showed that the mean serum levels of visfatin, platelets (PLT), ESR, IL-6, CRP, and RF were significantly higher in RA patients than in the control group. Comparison of the mild, moderate, and severe RA groups showed that the mean levels of visfatin and IL-6 were significantly higher in the severe RA group than the moderate RA group, which was significantly higher than that of the mild RA group. There was a significant positive correlation between serum visfatin and IL-6, ESR, CRP, TNF-α, and DAS-28 in the RA group.

Conclusion

Visfatin plays a role in the pathogenesis of RA and could be considered as a disease marker in RA and a marker of joint damage and hence as a potential therapeutic target for RA. The findings of the present study also indicate that serum visfatin and IL-6 might be of diagnostic value for RA; however, the combined diagnosis using serum visfatin, IL-6, and the RF test can improve the diagnosis of RA in the early stage. Further studies are required to determine the possibility of introducing visfatin as a potential therapeutic target especially in early RA to prevent erosions.

Keywords:
interleukin 6, rheumatoid arthritis, tunour necrosis factor-α, visfatin, DAS28

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Introduction

Rheumatoid arthritis (RA), the most severe of all joint diseases and also the most common systemic autoimmune disease, affects ~1% of the adult population [1]. The major features of RA are the activation and proliferation of synovial tissue and the degradation of

articular cartilage. Synovial fibroblasts and inflammatory cells, such as macrophage, play key roles in this process. Innate immunity also plays an important role in the pathogenesis of RA [2].

No single diagnostic test definitively confirms the diagnosis of RA. However, several tests can provide objective data that increase diagnostic certainty and allow disease progression to be followed [3].

Failure to diagnose or treat a patient with RA in the early stages of the disease increases the risk of progression to persistent joint inflammation and damage. However, aggressive treatment of patients with mild arthritis, which probably will not evolve to erosive forms, is also damaging. It exposes such patients to risks without proven benefits and represents the opposite of effective early treatment. Therefore, early diagnosis of those patients who will progress to more severe forms and consequently will require therapy that is more aggressive is essential [4].

Visfatin was originally identified as a secreted growth factor for early lymphocytes (pre-B-cell colony enhancing factor). Visfatin or pre-B-cell colony enhancing factor is a 52 kDa protein found in living species from bacteria to humans [5].

Visfatin has shown both nuclear and cytoplasmic expression. Within the cell, it functions as a nicotinamide phosphoribosyl transferase, the rate-limiting step in a salvage pathway of nicotinamide adenine dinucleotide (NAD) biosynthesis. By virtue of this role, it can regulate the cellular levels of NAD and thus affect not only cellular energetics but also NAD-dependent enzymes such as sirtuins. It has been shown to be an adipokine expressed by fat cells and exerts a number of insulin mimetic effects [6].

Visfatin has been added to a growing list of adipocytokines with potent effects on immunity and inflammation in addition to their metabolic activities [7]. In CD14 (+) monocytes, visfatin induces the production of interleukin (IL-1β), tumor necrosis factor-α (TNF-α), and IL-6. Moreover, it increases the surface expression of costimulatory molecules CD54, CD40, and CD80 [8].

Rho *et al.* [9] reported that visfatin is induced by inflammation and immune activation. It enhances B-cell differentiation, initiation of cytokines and matrix metalloproteinases, and inhibits neutrophil apoptosis, thus playing a key role in the persistence of inflammation.

Visfatin is released by a variety of cells and elevated levels can be found in the systemic circulation of patients with various acute and chronic inflammatory diseases including RA, sepsis, acute lung injury, inflammatory bowel disease, and myocardial infarction [6].

A study of experimental animals proved that inhibition of visfatin led to markedly reduced inflammation, severity of arthritis, and cartilage damage in a collagen-induced arthritis model. They postulated that pharmacologic inhibition of visfatin led to reduced levels of intracellular NAD in inflammatory cells and decreased the production of TNF-α and IL-6 by such cells with clinical effects comparable with those of a TNF-α inhibitor in a murine arthritis model [10].

A large number of cytokines are active in the joints of patients with RA. It is now clear that these cytokines play a fundamental role in the processes that cause inflammation, particular destruction, and the comorbidities associated with RA. Following the success of TNF-α blocked as a treatment for RA, other cytokines now offer alternative targets for a therapeutic intervention or might be useful as predictive biomarkers of disease. The biologic contribution and therapeutic potential of the major cytokine families to RA pathology, is focusing on the TNF-α, IL-18, IL-6, IL-23, and IL-2 families [11].

TNF-α is now recognized as mediating a wide variety of effector functions relevant to the pathogenesis of RA, including endothelial cell activation and chemokine amplification, leading to leukocyte accumulation and probably attendant cardiovascular comorbidity; osteoclast and chondrocyte activation, promoting articular destruction; nociceptor sensitization; impaired cognitive function; and metabolic syndrome. These are all recognized components of the RA disease spectrum and explain the broad effects of TNF-α blockade in patients [12].

IL-6 is considered to play a central role in chronic inflammation and is expressed in excess at sites of inflammation. High levels of sIL-6R have been shown to correlate with the degree of joint destruction, in particular, in advanced stages of RA. IL-6 is a multitarget cytokine with activity relevant to RA. At the affected joints, IL-6 has a pivotal role in the inflammatory process, in osteoclast-mediated bone resorption, and in synovitis. IL-6 induces acute-phase proteins and contributes to the systemic manifestations of RA though hepcidin production (anemia) and acts potently in changing lipid concentrations (hypolipidemia). In addition, IL-6 may contribute to the induction and maintenance of the autoimmunity through B-cell activation and Th17 cell differentiation [13].

Aim of the study

The present study aimed to evaluate the role of serum visfatin as a recent proinflammatory marker in RA according to the activity scores of disease to assess the possibility of introducing serum visfatin in the diagnosis and monitoring of RA patients and correlate between its serum level and other cytokines (IL-6 and TNF-α) and other laboratory biomarkers.

Patients and methods

A total of 80 individuals, including 60 patients with the diagnosis of RA and 20 healthy individuals as controls, were recruited in this study. The study population was selected consecutively from among patients who presented to the outpatient of Rheumatology clinics of Al-Hussein and Sayed Galal hospitals. The RA group included 60 patients in age ranging from 18 to 60 years

(mean 45 years). There were 48 women and 12 men. Their duration of disease ranged from 1 year to 23 years. The diagnosis of RA was made on the basis of and confirmed according to the American College of Rheumatology (ACR)/The European League Against Rheumatism (EULAR) 2010 criteria [14].

RA patients were classified into three groups: group I (severe RA) included 20 RA patients with disease activity score-28 (DAS-28) range (5.22–7.32) (17 women and three men), group II (moderate RA) included 20 RA patients with DAS-28 range (4.00–4.96) (15 women and five men) and group III (mild RA) included 20 RA patients with DAS-28 range (2.35–3.20) (16 women and four men). The control group included 20 healthy individuals who ranged in age from 24 to 57 years (mean 43 years). There were 10 women and 10 men.

All patients with RA had received medications previously. The drugs taken at the time of sampling included 5 mg of prednisolone, methotrexate varying from 7.5 to 15 mg/week, 200 mg hydoxychloroquine, and NSAIDs.

All patients were subjected to complete assessment of history and a full clinical examination with a special focus on the musculoskeletal system.

Disease activity was measured by DAS-28 in RA, consisting of a 28 tender joint count (range 0–28), a 28 swollen joint count (range 0–28), erythrocyte sedimentation rate (ESR), and an optional general health assessment on a visual analogue scale (range 0–100) [15]. The DAS-28 has a continuous scale ranging from 0 to 9.4, and usually shows a Gaussian distribution in RA populations. The level of disease activity can be interpreted as low (DAS-28 $\leq$ 3.2), moderate (3.2 $<$ DAS-28 $\leq$ 5.1), or high (DAS-28 $>$ 5.1). A DAS-28 less than 1.2 corresponds to being in remission according to the ARA criteria [16].

Weight and height were measured for each individual, and then the BMI was calculated as follows: BMI = body weight in kg/height in m^2 [17].

Laboratory investigations

Sample collection

Five milliliters of blood was withdrawn from each patient into two tubes.

Two milliliters of blood was immediately citrated for a complete blood count using a Coulter device and the ESR was determined using the westergren method.

Three milliliters of blood was allowed to clot, and was centrifuged 1 h later for 15 min; the serum collected was stored at -30°C for determination of the following.

Serum visfatin was measured by visfatin C terminal using a solid-phase enzyme-linked immunosorbent assay (ELISA) Kit (Phoenix Pharmaceuticals Inc., Burlingame, California, USA) [7].

Serum C-reactive protein (CRP) was assessed by turbidimetry quantitative determination [18].

Serum rheumatoid factor (RF) was assessed by turbidimetry for quantitative determination [19].

Serum TNF-α was determined using a solid-phase ELISA Kit (Phoenix Pharmaceuticals Inc.) [20].

Serum IL-6 was determined using a solid-phase ELISA Kit (Phoenix Pharmaceuticals Inc.) [21].

Statistical methods

Graph Pad Prism program version 5.0 was used for analysis of data. Data were summarized as mean $\pm$ SD. One-way analysis of variance was used for analysis of more than two variables, followed by the Tukey's post-hoc test for the detection of significance. Simple linear correlation (Pearson's correlation) was also carried out. *P*-value of up to 0.05 was considered significant [22].

Results

The mean of PLT was significantly higher in RA patients than in the control group, whereas there was no significant difference in age, BMI, white blood cells, red blood cells, and hemoglobin between RA patients and the control group.

The mean ESR, CRP, RF, serum visfatin, and IL-6 were significantly higher in RA patients than in the control group, whereas there was no significant difference in TNF-α between RA patients and the control group.

The mean levels of CRP, serum visfatin, and IL-6 were significantly higher in the severe RA group than the moderate RA group, which were significantly higher than those in the mild RA group. There was no significant difference in ESR, RF, and TNF-α between the groups studied.

There was a significant positive correlation between serum visfatin and ESR, CRP, IL-6, TNF-α, DAS-28, and the visual analogue scale pain score in RA patients. However, there was no significant correlation between serum visfatin and age, duration of disease, and BMI in RA patients.

Discussion

RA is the most common autoimmune chronic inflammatory arthritis, whose main characteristic is persistent joint inflammation that results in joint damage and loss of function [23]. Early diagnosis of RA is a major challenge for clinical rheumatologists. This is because there is considerable evidence that early treatment with disease-modifying antirheumatic drugs leads to a better disease outcome. As current predictors of joint destruction in RA have low specificity, serological biomarkers reflecting bone and cartilage destruction have been proposed as tools in assessing the prognosis of this disease [24].

Cytokines regulate a broad range of inflammatory processes that are implicated in the pathogenesis of RA. In rheumatoid joints, it is well known that an imbalance between proinflammatory and anti-inflammatory cytokine activities favors the induction of autoimmunity, chronic inflammation, and thereby joint damage [25].

High levels of visfatin in plasma and synovial fluid have been found in RA patients [26]. In the last few years, visfatin has generated considerable interest because of its role in the development of RA [9].

The present study aimed to evaluate the role of serum visfatin as a recent proinflammatory marker in RA according to the activity scores of disease to assess the possibility of introducing serum visfatin in the diagnosis and monitoring of RA patients and to determine the correlation between its serum level and other cytokines (IL-6 and TNF-α) and other laboratory biomarkers.

In the present study, comparison between the RA and the control groups showed that the mean serum level of PLT was significantly higher in the RA group than in the control group (Table 1).

These data were in agreement with those of Jian *et al.* [27], Gülsüm [28], and Gasparyan *et al.* [29], who had found that PLT was significantly higher in the RA group than the control group and was increased with the severity of RA disease.

In the present study, 80% of the patients in the RA group were women. These data are in agreement with the fact that women are affected by RA approximately three times more often than men [30].

Visfatin was reported to be an adipocytokine with proinflammatory and immunomodulating properties. However, the pathological role and clinical relevance of visfatin in the setting of RA are still unclear [31].

In this study, serum visfatin levels in RA patients were significantly higher than those in the controls (Table 2), and were significantly higher in the severe RA group than the moderate RA group, which was significantly higher than that of the mild RA group (Table 3).

These findings are in agreement with those of Otero *et al.* [32], who investigated plasma levels of adipocytokines (leptin, adiponectin, visfatin, and resistin) in patients with RA in comparison with levels estimated in healthy controls, and found that patients with RA showed considerably higher plasma levels of leptin, adiponectin, and visfatin than healthy controls, but no marked difference was observed in resistin levels between both patients and controls.

Moreover, further research has shown that this adipocytokine was upregulated in the synovial fluid of RA patients and indicated synovial fibroblasts as the major visfatin-producing cells in the rheumatoid synovium [31,33].

Recently, Senolt *et al.* [34] showed that serum visfatin levels were significantly higher in patients with RA compared with healthy controls and decreased significantly following treatment with anti-B-cell therapy.

As inflammation plays a critical role in the pathophysiology of RA, the measurement of the acute-phase response is used as a surrogate marker of inflammation. The acute-phase reactants, CRP and ESR, are easy to determine, routinely available, and the most widely used biological markers for assessing disease activity and inflammation in RA [35].

In the present study, the mean serum level of ESR was significantly higher in the RA group than in the control group (Table 2).

This was also in agreement with Jian *et al.* [27] and Nalesnik *et al.* [36], who found that the level of ESR in active RA patients was higher than that in the normal control group.

In the current study, the mean serum level of CRP was significantly higher in the RA group than the control

Table 1 Mean ± SD of demographic data and complete blood count in the rheumatoid arthritis and control groups

Group variables	RA ($N=60$)	Controls ($N=20$)	*P*-value
Age (years)	45.1 ± 11.8	42.6 ± 8.5	0.831
BMI (kg/m^2)	22.26 ± 3.55	23.1 ± 3	0.670
WBCs (K/μl)	9.28 ± 5.75	7.7 ± 1.8	0.106
RBCs (K/μl)	4.72 ± 0.62	5.0 ± 0.48	0.241
Hb (g/dl)	11.95 ± 1.54	12.33 ± 1.47	0.987
PLT (μl)	381.25 ± 171.85	203.85 ± 39.87	0.0001

Hb, hemoglobin; RBCs, red blood cells; WBC, white blood cells.

Table 2 Mean ± SD of laboratory data in the rheumatoid arthritis and control groups

Group variables	RA ($N=60$)	Controls ($N=20$)	*P*-value
ESR (mm/h)	43.75 ± 24.9	14.25 ± 6.65	0.0001
CRP (mg/l)	37.26 ± 20.3	1.67 ± 0.83	0.0001
RF (IU/ml)	91.8 ± 83.0	0.61 ± 0.24	0.0001
Serum visfatin (ng/ml)	18 ± 5.14	4 ± 1.2	0.0001
IL-6 (pg/ml)	47.0 ± 14.8	2.8 ± 0.9	0.0001
TNF-α (pg/ml)	78.63 ± 31.6	48.88 ± 16.9	0.108

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; RF, rheumatoid factor; TNF-α, tumor necrosis factor-α.

Table 3 Mean ± SD of laboratory data of rheumatoid arthritis patients in relation to the severity of disease

Group variables	Severe RA ($N=20$)	Moderate RA ($N=20$)	Mild RA ($N=20$)	*P*-value
ESR (mm/h)	45.19 ± 25.58	46.63 ± 25.65	37.53 ± 23.391	0.536
CRP (mg/l)	50.33 ± 18.09[a]	34.88 ± 16.89[b]	16.77 ± 12.84[c]	0.0001
RF (IU/ml)	115.49 ± 76.87	79.13 ± 53.09	65.26 ± 51.32	0.124
Serum visfatin (ng/ml)	22 ± 7.21[a]	17 ± 4.91[b]	9 ± 2.14[c]	0.0001
IL-6 (pg/ml)	71.16 ± 36.00[a]	34.56 ± 23.32[b]	19.56 ± 16.12[c]	0.0001
TNF-α (pg/ml)	61.9 ± 31.62	97.99 ± 35.86	84.20 ± 36.52	0.771

Superscript alphabets indicate significance.
CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; RA, rheumatoid arthritis; RF, rheumatoid factor; TNF-α, tumor necrosis factor-α.

group (Table 2), and the mean serum level of CRP in the severe RA group was significantly higher than that in the moderate RA group, which was significantly higher than that in the mild RA group (Table 3).

These results are in agreement with those of Al-mesry *et al.* [37], who found that CRP is a protein produced by the liver in response to tissue injury, infection, and inflammation.

Also, Morovic-Vergles *et al.* [38] showed that the serum CRP level was higher in RA and reflected a higher inflammatory activity in RA and CRP level increase by increasing of disease activity in RA patients.

RF is a very old serological marker for the diagnosis of RA. RF is considered as a nonspecific marker of RA because it is also found in other collagen vascular disease [39].

In the present study, RF was significantly higher in the RA group than in the control group. These data were in agreement with those of Novikov *et al.* [40], who found a variety of extra-articular features typical of RA and associated with the presence of RF in the serum.

The results were in agreement with those of Khalifa and Abdelfattah [41] and Hui *et al.* [42], who found that there was a difference in the RF levels between the RA and the non-RA groups.

IL-6 is a multifunctional cytokine that regulates immune response and induces an acute-phase response. Despite the important physiological activities of IL-6, deregulated overproduction of IL-6 is pathologically involved in various immune-mediated inflammatory diseases including RA [43].

In the present study, the serum level of IL-6 was significantly higher in RA than in the control group and the level of IL-6 in the severe RA group was significantly higher than that in the moderate RA group, which was significantly higher than that in the mild RA group.

These results were in agreement with those of Fonseca and Santos [44], as they found that IL-6 is a cytokine that can facilitate autoimmune phenomena, amplify acute inflammation, and promote a chronic inflammatory state in RA patients; also, Cronstein [45] found that IL-6 is an important cytokine present in elevated levels in patients with RA. The biological activities of IL-6 contribute toward both systemic and local RA symptoms.

Also, Katz [46] and Hwang [47] found that IL-17, IL-1β, and TNF-α can induce IL-6 production according to disease activity.

The DAS is widely used to quantify disease activity and gauge the response to treatment [16].

Assessment of disease severity relied on the evaluation of pain using the joint affection score (DAS-28) and laboratory evaluation of ESR and CRP levels. This combination aided patients' selection and was in agreement with the finding of Klarenbeek *et al.* [48], who compared nine disease activity indices versus the ARC/EULAR remission criteria in RA and attempted to relate these indices to physical function and joint damage progression, and found that clinical DAS and simplified DI were the most stringent definitions of remission, and DAS-28 and DAS-28-CRP had the highest proportions of remission; they concluded that for all indices, higher levels of disease activity were associated with decreased physical functioning and more radiological damage progression.

Table 4 Correlation between serum visfatin and other parameters studied in the rheumatoid arthritis group

	Serum visfatin (ng/ml) in the RA group	
Variables	*r*-value	*P*-value
Age (years)	0.208	0.152
BMI (kg/m^2)	0.285	0.134
Duration of disease (years)	0.328	0.074
ESR (mm/h)	0.42	0.01
CRP (mg/l)	0.49	0.001
IL-6 (pg/ml)	0.51	0.0001
TNF-α (pg/ml)	0.44	0.001
DAS-28	0.57	0.0001
VAS pain score	0.49	0.001

CRP, C-reactive protein; DAS-28, disease activity score-28; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; RA, rheumatoid arthritis; TNF-α, tumor necrosis factor-α; VAS, visual analogue scale. $P \leq 0.05$ is considered to be significant.

To focus more on the relation of visfatin with damage of joints and other inflammatory markers, the current study found that there was a positive correlation between serum visfatin and DAS-28 in RA patients (Table 4).

These findings were in agreement with the findings reported by Rho *et al.* [9] that visfatin concentrations were associated with higher Larsen scores, and this association remained significant after adjustment for age, race, sex, disease duration, BMI, and inflammation.

These findings suggest a role for visfatin as a mediator of joint damage in RA. These results are supported by experimental animal research that suggested that visfatin modulated inflammatory responses and radiographic joint damage in animal models [10].

The current study also showed that there was a positive correlation between serum visfatin and IL-6 and TNF-α in RA patients (Table 4).

Recently, Klein-Wieringa *et al.* [49] found that the levels of IL-6, TNF-α, visfatin, and adiponectin were associated positively with radiographic progression over 4 years and this association was independent of BMI, and concluded that adipokines are predictors of radiographic progression in RA.

In addition, Nowell *et al.* [33] reported that the production of visfatin was significantly upregulated by IL-6 in human synovial fibroblast cell lines by a pathway dependent on a signal transducer and activator of transcription 3.

The current study also showed that there was no significant correlation between serum visfatin and age, duration of disease, and BMI in RA patients (Table 4).

These findings are in agreement with those of Gonzalez-Gay *et al*. [50] and Senolt *et al*. [34], who found that serum levels of visfatin did not correlate with BMI, age, and duration of disease in patients with active RA in contrast to the case in non-RA individuals. This indicates that visfatin is an adipocytokine whose production in RA patients related principally to the disease process as part of the systemic inflammation and bone destruction, suggesting a role for visfatin in the pathogenesis of RA.

The current study also showed that there was a positive correlation between serum visfatin and both CRP and ESR in RA patients (Table 4).

These findings are in agreement with another study that reported that visfatin was correlated with serum markers of inflammation (CRP and ESR) as well as clinical DAS [31].

The mechanism by which visfatin plays a destructive role in joints of RA patients is through activation of the transcription factors NF-κB and activator protein 1 and induction of IL-6, IL-8, MMP-1, and MMP-3 in RA synovial fibroblasts as well as IL-6 and TNF-α in monocytes of these patients [51].

These findings indicate that visfatin has a catabolic function in cartilage and may play an important role in the pathophysiology of arthritis. There is evidence for an important function of innate immunity in the pathogenesis of RA [31], although a study by Luk *et al.* [6] showed that visfatin plays a role as a novel mediator of innate immunity. Taken together, these findings suggest that visfatin is involved in proinflammatory activity, innate immunity, and cartilage-catabolic functions in the processes of RA [26].

Conclusion

Visfatin plays a role in the pathogenesis of RA and can be considered as a disease marker in RA and a marker of joint damage and hence as a potential therapeutic target for RA.

The findings of the present study also indicate that serum visfatin and IL-6 might be of valuable diagnostic value for RA; however, the combined diagnosis using serum visfatin, IL-6, and the RF test can improve the diagnosis of RA in the early stage. Further studies are required to determine the possibility of introducing visfatin as a potential therapeutic target especially in early RA to prevent erosions.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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العلاقة بين مصل الفسفاتين ودرجة الخطورة الاكلينيكية فى مرض الروماتويد المفصلي بمراحله المختلفة

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يعتبر الفسفاتين من أحدث الاديبوكينات التى لها دور هام كعامل مبدئى للالتهاب بالاضافة الى دوره التقويضى فى مرض الروماتويد المفصلي . و تساهم بعض السيتوكينات مثل (الانترلوكين 1 و6 و15 و18 و عامل الورم التحللى ألفا) فى بعض التغيرات الفسيولوجية التى تؤدى بدورها الى الالتهابات المفصلية . ونظرا لان هذه الالتهابات هى التى لها الدور الاساسى فى احداث الاضرار الهيكلية فى هذا المرض ,فإن القضاء عليها مع التشخيص والعلاج المبكريساهم بقدر كبير فى درجة التحكم فى مرض الروماتويد المفصلي لما لذلك من أهمية. ولذا كان الهدف من هذا البحث هو تقييم دور الفسفاتين كعامل مبدئى حديث للالتهاب ودرجة ارتباطه بدورة الطور المرضى للروماتويد الفصلى , بالاضافة الى علاقته بغيره من السيتوكينات مثل (الانترلوكين 6 و عامل الورم التحللى ألفا) لبحث امكانية استخدامه فى التشخيص و المتابعة لمرضى الروماتويد المفصلى.

تضمن البحث 80 شخص مقسمين إلى مجموعتين المجموعة الاولى هي مجموعة مرضى الروماتويد المفصلى و تتكون من60 شخصاً (48إناث80٪ و 12 ذكور20٪), والتي تنقسم الى ثلاث مجموعات صغيرة حسب معدل نشاط المرض الى (أ) مجموعة مرضى الروماتويد المفصلي من الدرجة الخطرة وعددهم 20 مريض و مجموعة مرضى الروماتويد المفصلي من الدرجة المتوسطة وعددهم 20 مريض و مجموعة مرضى الروماتويد المفصلي من الدرجة المعتدلة وعددهم 20 مريض وذلك بالمقارنة بالمجموعة الثانية الضابطة و تتكون من 20 شخصاً سليم ظاهريا(10 إناث 50٪ و 10 ذكور50٪).

واستند البحث في تشخيص الروماتويد المفصلي على المعايير التي أكدتها الكلية الأمريكية للروماتيزم والمؤسسة الأوروبية ضد الروماتيزم.

تضمنت البيانات الوصفية لأفراد هذا البحث؛ العمر والجنس ومؤشر كتلة الجسم، وشملت الفحوص المعملية للمجموعات قياس صورة الدم الكاملة ومعدل ترسيب كرات الدم الحمراء و مصل الفسفاتين والبروتين المتفاعل ج وعامل الروماتويد و الانترلوكين 6 وعامل الورم التحللى ألفا.

وقد أظهرت النتائج ارتفاعا فى متوسط معدل ترسيب الكرات الحمراء و مصل الفسفاتين وعامل الروماتويد و الانترلوكين 6 و متوسط البروتين المتفاعل ج ارتفاعا ذا دلالة إحصائية في مرضى الروماتويد المفصلى عن المجموعة الضابطة .

وبالنسبة للمقارنة بين الثلاث مجموعات المنبثقة عن مرضى الروماتويد المفصلى فقد أظهرت النتائج ارتفاع متوسط مصل الفسفاتين و الانترلوكين 6 و متوسط البروتين المتفاعل ج ارتفاعا ذا دلالة إحصائية في مرضى الروماتويد المفصلى من الدرجة الخطرة بالمقارنة بالمرضى ذوى الدرجة المتوسطة و المعتدلة . بالاضافة الى وجود علاقة طردية ذات دلالة إحصائية بين مصل الفسفاتين وكل من (البروتين المتفاعل ج و معدل الترسيب و الانترلوكين 6 وعامل الورم التحللى ألفا و مقياس نشاط المرض ذا الرقم 28 العالمي)

نستنتج من هذه الدراسة أن مصل الفسفاتين له دور هام فى تطور الألية المرضية لمرضى الروماتويد المفصلى حيث ثبت وجود علاقة وثيقة بين مصل الفسفاتين و نشاط مرض الروماتويد المفصلي مما يؤكد إمكانية استخدامه كعلامة تحليلية كيميائية للالتهاب مما يساعد في تقديم معلومات إضافية بشأن نشاط المرض مع الدلالات التقليدية كمعدل ترسيب كريات الدم الحمراء والبروتين المتفاعل ج . بالاضافة الى ان مصل الفسفاتين و الانترلوكين 6 قد يكونا ذا قيمة تشخيصية لمرض الروماتويد المفصلي ، ومع ذلك، فإن الجمع بين التشخيص باستخدام مصل الفسفاتين و الانترلوكين 6 و عامل الروماتويد يزيد من خصوصية التشخيص خاصة فى الحالات المبكرة. كما يوصى البحث بمزيد من الدراسات لاكتشاف إمكانية استخدام الفسفاتين كأحد الاهداف العلاجية خاصة فى الحالات المبكرة لمرضى الروماتويد المفصلى لتجنب حدوث التقرحات (التآكل) بالمفاصل.