Evidence of contributory role of inflammation in patients with knee osteoarthritis

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Abstract:

Background: Osteoarthritis (OA) is a debilitating degenerative joint disease particularly affecting weightbearing joints within the body, principally the hips and knees.

Objectives: We aimed to asses the inflammatory markers in the form of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) among patients with knee OA.

Patients and Method: The study included 90patients with knee OA, 30 patients with mild degree of OA&30 patients with moderate degree of OA &30 patients with severe degree of OA. CRP and ESR wereperformed and analyzed for all the included patients.

Results: the mean CRP of all studied patients was 5.1 ± 1.33 mg/L with minimum CRP value of 3 mg/dL and maximum one of 7 mg/dL.The mean ESR of all studied patients was 23.5 ± 2.04 mm/h with minimum ESR value of 20 mm/h and maximum one of 27 mm/h.Statistically significant difference (p= 0.028) between mild OA & severe OA groups as regard ESR, no other significant differences were observed.

Conclusions: The present study confirms the presence of inflammatory state among patients with knee osteoarthritis especially those with sever form.

Keywords: CRP, ESR, knee, Osteoarthritis.

Introduction:

Osteoarthritis (OA) is a degenerative joint disease characterized by articular cartilage degradation which can affect many joints in the body, but is particularly common in weight-bearing joints such as the knee and hip. The loss of cartilage can lead to joint space narrowing (JSN), pain, and loss of function and ultimately leads to the need for total joint replacement. There are a number of risk factors associated with OA, including genetic predisposition, obesity, age, and previous joint trauma. With obesity set to rise in future years,(**Salihu et al., 2009**) combined with OA being a frequent condition among the elderly and an ageing population (**Mabey,Honsawek 2015**), the prevalence of OA is expected to increase. An effective and reliable method for diagnosis and prognosis is needed, with increased demands on health services around the world.Radiography is routinely used to aid in the diagnosis of OA.However, radiographic imaging is ineffective at detecting and monitoring the biochemical changes within joint tissue which can occur long before symptoms present(**Swearingen et al.,2010**).Different compounds may show different biochemical marker properties at different stages of the disease, reflecting the pathophysiological changes occurring within the joint tissue.(**Lotz et al., 2013**) Therefore, characterization of potential biomarkers is important to ensure their appropriate and optimal use.The future challenge in the management of knee OA is to discover early tools for diagnosis, progression and monitoring of the disease, and to find effective therapeutic interventions. Biomarkers are among

possible tools. Since OA is related to inflammation, inflammatory biomarkers, such as C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) have been used to determine such relationship (**Fernandez-Cuadros et al., 2018**).

The ideal scenario, in terms of biochemical markers of OA, would be to have a non-invasive, reliable and valid biochemical marker or cluster of markers that could be measured to aid in the diagnosis and predict the development of OA in patients at an early stage before the disease becomes symptomatic. The ability to reduce the long-term effects of the disease could considerably reduce the substantial socioeconomic costs ofOA(**Ruiz D et al.,2013**).

This study aims to determine wheatehr there is a role of the inflammation in the pathogenesis of knee OA or not, via evaluation of CRP and ESR) in patients with various severities of knee OA.

Materials&Methods:

- **Study design:** Aprospective, hospital based study carried out on 90 patients with knee osteoartheits of whom; 30 patients with mild OA, 30 patients with moderate OA & 30 patients with severe OA. They wererecruited fromorthopaedic Surgery Department,Qena University Hospital, Egypt,during the period from February to July 2019.

- **Methodology:**

5 ml venous blood sample was collected from all included patients and divided into two parts; 3 mls were evacuated into plain tubes for CRP assay and 2 ml was placed into sodium citrate containing tubes for ESR measurements. For CRP assay, the blood samples were allowed to be clotted at room temprature for 20 min and then were centrifugated at 3000 rpmfor 10 minutes. The separated sera were used for CRP assays immediately by the semi-quantitative latex agglutination test (AVITEX CRP KITS: Catalog NO.OD023: supplied by Omega Diagnostics.UK). Antibodies to human CRP coat the AVITEX latex particles: when the latex suspension was mixed with the serum containing high CRP levels on a slide. Agglutination was seen within 2 min. and then serial dilutions of patient's serum in positive cases using isotonic saline were done to determine the CRP values. CRP consider normal if <6 mg/L. **ESR** assays were measured using (ESR STAT 6 Sed Rate Analyzer from HemaTechnologies, United States of America).ESR considered normal if ≤ 25 mm/h.

Statistical analyses:

Data were analyzed using Statistical Program for Social Science (SPSS) version 15.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.Independent-samples t-test of significance was used when comparing between two means. Level of significance was considered at $p<0.05$.

Results:Demographic data: 90 patients including(10 males and 80 females),mean age of all studied patients was 45.5 ± 10.6 years**.**

Laboratory data:As regard CRP, the mean CRP of all studied patients was 5.1 ± 1.33 mg/L with minimum CRP of 3 mg/L and maximum CRP of 7 mg/L.

As regard ESR, the mean ESR of all studied patients was 23.5 ± 2.04 mm/h with minimum ESR of 20 mm/h and maximum ESR of 27 mm/h. table (1).Statistically significant difference **(p-value = 0.028)** between mild OA & severe OA groups as regard ESR. Table (2).

Table (1): values of CRP and ESR of the studied patients.

Demographic & Clinical data		Studied patients (N = 90)
CRP(mg/L)	Mean ±SD	5.1 ± 1.33
	Min – Max	3 – 7
ESR(mm/hour)	Mean ±SD	23.5 ± 2.04
	Min – Max	20 – 27

Table (2): comparison of CRP and ESR among the studied patients as regard severity of OA.

		Mild OA (n = 30)	Moderate OA (n = 30)	Severe OA (n = 30)	p-value		
					P1	P2	P3
CRP(mg/L)	Mean±SD	5.8 ± 1.2	4.9 ± 1.2	4.7 ± 1.4	0.129 NS	0.066 NS	0.731 NS
ESR(mm/hour)	Mean±SD	22.3 ± 1.7	23.8 ± 2.6	24.3 ± 1.2	0.092 NS	**0.028 S**	0.566 NS

S: p-value < 0.05 is considered significant.NS: p-value > 0.05 is considered non-significant.

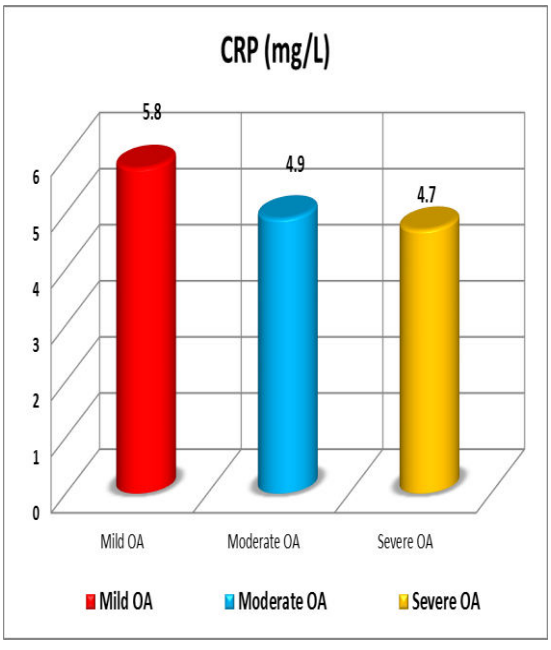

Figure (1): comparison of CRP as regard severity of OA.

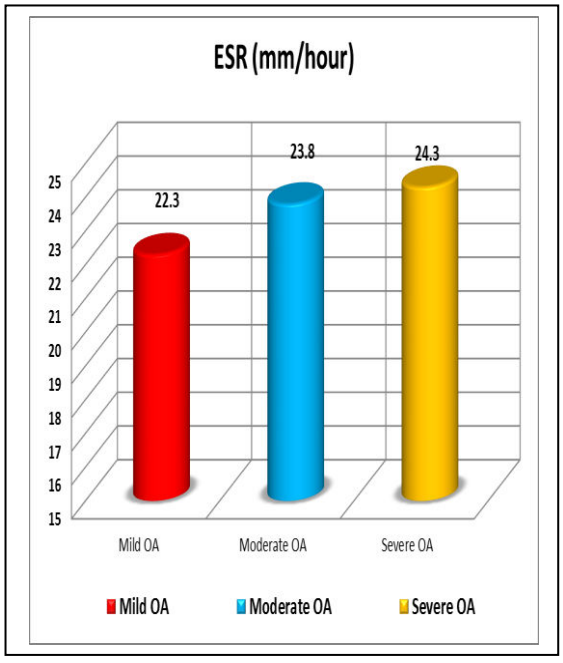

Figure (2): comparison of ESR as regard severity of OA.

Discussion:

Knee osteoarthritis (OA) is a major cause of pain and disability in subjects over 50 years with a significant impact on physical performance and quality of life (**Conrozier et al.,2019**).

Biomarkers of inflammation used in the study were CRP and ESR. These biomarkers are recognized as acute phase reactants or proteins. They indicate an inflammatory state, as in the case of rheumatic diseases. Erythrocyte Sedimentation Rate is cheap and commonly used in clinical practice. It mainly reflects fibrinogen concentration. Furthermore, CRP shows no variation with age, neither with erythrocytes morphology, nor with other protein variations. During inflammation, CRP concentration increases by 1000 folds; on the contrary, ESR increases by 2 to 5 folds. In an inflammatory process, such as orthopedic surgery, CRP reaches its maximum level at 24 to 48 hours and normalizes by the next week. On the contrary, ESR value is elevated after a week, and normalizes in the next 6 weeks (**Möller I et al., 2016**).

Several studies have observed that increased CRP levels are related to prevalence and progression of the knee or hip OA. With respect to OA, elevated CRP levels are related to synovial fluid IL-6 levels and to synovial infiltration, as well as with symptoms of pain and stiffness, radiographic grading, and disease progression (**Smith et al., 2012**).

Many researchers worldwide have suggested that CRP and ESR are closely related to radiographic knee OA, symptoms severity, and the progression of the disease. These biomarkers suggest that low-grade inflammation might be a direct pathway in structural and symptomatic changes on knee OA (**Zhu et al., 2016**)

In this study the mean of ESR for all studied patient was22.3 ± 1.7 mm/h which was condiered as normal and the mean of CRP for all studied patients was5.8 ± 1.2 mg/L which also consider within normal range.

When considering the degree of OA severity, there was only Statistically significant difference between mild OA & severe OA groups as regard ESR, otherwise all comparisons were statistically non-significant.

The results of the present study are in disagreement with **Levinger et al., 2011;Conde et al., 2011;sanchez-Ramirez et al.,2014.**On the other hand, **Santos et al., 2011;Ferrucciet al., 2012;Xu et al., 2014**did not find a significant correlation between inflammatory markers in plasma and knee osteoarthritis severity this is the same with our study result.

Conclusion:

In conclusion, in patients with knee OA, levels of serum CRP and ESR were not associated with degree of severity of OA. Moreover, ESR and CRP provide no additional diagnostic accuracy in the diagnosis of knee osteoarthritis.

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