Evaluation of some hematological parameters and C-reactive protein among men and women with osteoarthritis

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Abstract
Osteoarthritis (OA) is a biomechanical phenomenon where the joints are susceptible to mechanical stress, resulting in reduced articular cartilage and changes in other knee tissue. It is characterized by joint pain, stiffness, loss of motion resulting in functional limitation, and disability. There are many risk factors lead to OA such as gender, aging, obesity, and joint injury. Blood samples obtained from 40 patients (23 females and 17 males) and 20 controls (10 females and 10 males), age years ranged (56.88 ± 2.57; 60.95 ± 1.57) in patients men and in women. (47.50 ± 1.50; 49.60 ± 1.30) in control men and women. The samples were collected from January to April 2019 in the Medical City, Baghdad. The study focuses on some hematological and C-reactive protein tests in patients with OA and controls. Erythrocyte sedimentation Rate (ESR) in patients men and women shows significant increase (P<0.01) in comparison with control ESR also increased significantly (p<0.05) in patient women (40.13 ± 6.43) in comparison with patients men (25.88 ± 6.38). Packed cell volume (PCV %) and hemoglobin (Hb) shows non-significant differences (P>0.05) in patients men and women in comparison with control while PCV (37.04 ± 0.98) and Hb (12.29 ± 0.32) in patients women decreased significantly (P<0.05) in comparison with patient men PCV (45.82 ± 1.06) and Hb (14.88 ± 0.38). In patients men (7.80 ± 2.62) and women (14.16 ± 2.15). The C-reactive protein (CRP) increased significantly (P<0.01) respectively when compared with control men (2.90 ± 0.45) and control women (3.12 ± 0.34). CRP in patients women (14.16 ± 2.15) shows significant increase (P<0.01) in comparison with patients men (7.80 ± 2.62).

Keywords: Osteoarthritis, Erythrocyte sedimentation rate, hemoglobin, hematocrit, anemia

Introduction

Osteoarthritis is the most prevalent type of joint degenerative diseases that lead to articular pain and failure in aging (Bitton, 2009; Pereira et al. 2015). OA is the cause of functional constraints and is characterized by progressive cartilage degeneration, osteophyte formation, narrowing of the joint space, subchondral bone sclerosis and tissue inflammation. Proliferation of synovial and cellular differentiation (Bitton, 2009; Bay-Jensen et al., 2011).

The erythrocyte sedimentation rate is an acute stage response surrogate marker. During an inflammatory reaction, growing fibrinogen levels, principle protein for coagulation while alpha globulins affect the sedimentation rate. Other than the acute phase reaction often and substantially affect the sedimentation rate (Takahashi et al., 2004). Patients with elevated ESR concentrations had considerably elevated concentrations of CRP, low concentrations of hemoglobin, low levels of hematocrit, elevated concentrations of platelets and low levels of albumin. Therefore, the levels of distinct parameters that directly affect its result must be taken into consideration for the interpretation of the ESR's outcomes. The size, shape, hematocrit, of red blood cells and sex and age affect the ESR (Paulus and Brahn, 2004; El Maataoui, 2015).

C-reactive protein versus erythrocyte sedimentation rate

CRP represents a stronger indicator of the acute phase reaction of successive patients with high levels of C-reactive protein or ESR (Feldman et al., 2013). Subjects which had high CRP and normal ESR are commonly infected (Osei-Bimpong et al., 2007). C-reactive protein is an acute amino acid protein serum 224-phase and one of the most widely used inflammation markers. Cytokines IL1β, IL6, the rate of CRP rises rapidly (Marnell et al., 2005). It is a parameter that enables the acute-phase reaction to be measured directly and quantitatively. The ESR is usually substituted by CRP calculation due to blood CRP concentrations increase more rapidly following infection that one widely used inflammation measurement is ESR, which indirectly tests the acute stage response. ESR is the distance that RBCs settling within one hour with in blood tube and measured by mm / h. Patients with elevated ESR concentrations had considerably elevated concentrations of CRP, low concentrations of hemoglobin, low levels of hematocrit, elevated concentrations of platelets and low levels of albumin. Therefore, the levels of distinct parameters that directly affect its result must be taken into consideration for the interpretation of the ESR's outcomes. The size, shape and hematocrit of the red blood cells, sex and age affect the ESR (Paulus and Brahn, 2004; El Maataoui, 2015). The aims of the study to investigate the effects of knee osteoarthritis in men and women on the some hematological parameters (Hemoglobin, Hematocrit, Erthrocyte sedimentation rate) and C-reactive protein (CRP).

Materials and Methods

Ten ml of venous blood were collected from each 40 patients (23 female; 17 male) with 20 control (10 female; 10 male) at Medical city of Baghdad province which their age ranged from 40 years to 70 years, 3 ml of the blood was transferred to Ethylene diamine tetra acet acid (EDTA) tubes for measuring ESR and transfer little of blood to capillary tube for measuring packed cell volume.
PCV%, 7 ml of the blood was used to obtain serum which separated by centrifugation 3000 r.p.m for 5 min, then they were kept in -20°C until the time use for other tests.

**Hematological tests**

1- ESR was measured and reported in millimeters per hour and ESR values were determined by the standard Westergren method (Patton et al., 1989). The normal values of ESR in Males (15 mm/hours) and (20 mm/hours) in females.

**Hemoglobin (Hb) test and Hematocrit, Packed cell volume (PCV)**

Measurement the hemoglobin was done by the method hemoglobin cyanide (cyanmethemoglobin), the spectrophotometer absorbance of the solution was measured at wavelength of 540 nm (Lewis et al., 2006). The following equation is then applied to calculate the hemoglobin concentration:

\[
\text{Hb (g/l)} = \frac{A_{(\text{at 540}) \text{ of test sample}}}{A_{(\text{at 540}) \text{ of standard}}} \times \text{concentration of standard} \times \frac{\text{Dilution factor (201)}}{1000}
\]

The normal value of Hb for Males (13.5-16.5 g/dl) and (12-15 g/dl) for female. PCV was measured by microhematocrit method, anticoagulant blood drawn into micro hematocrit tube (Turgeon, 2011). The normal value of PCV for Male (41-50 %) and (36-44 %) for females.

**Serological test**

**Detection of C- reactive protein (CRP):-**

This test was done by using BS 240 which are full automated biochemistry analyzer for the detection of CRP in serum according to Mindary company kit, the normal value of CRP (0-5) mg/l.

**Statistical Analysis**

The Statistical Analysis System- SAS (2012) was used to affect differential variables in the analysis. Test of Chi-square done for significantly comparison the percentage value. (ANOVA) or LSD to significantly compare the means.

**Results and discussion**

ESR in patients men (25.88±6.38) Table (1) increased significantly (p<0.05) when compared with control (9.30 ± 1.09) figure (1), while in patients women ESR (40.13 ± 6.43) increased significant (p<0.01) in comparing with control (13.80 ± 1.60). PCV% showed non-significant difference (p>0.05) in both patients men and women (45.82 ± 1.06; 37.04 ± 0.98) in comparison with control (45.60 ± 0.68; 39.10 ± 0.73) respectively. Hemoglobin also showed non-significant variations (p>0.05) in patients men (14.88 ± 0.38) and women (14.29 ± 0.32) when compared with control (15.17 ± 0.23; 13.00 ± 0.24) respectively. CRP (7.80 ± 2.62) in patients men increased significantly (p<0.05) with comparison with men control (2.90 ± 0.45) patients women (14.16 ± 2.15) increased significantly(p<0.01) when compared with control women (3.12 ± 0.34).
Table (1): Compare between Control and patients groups in ESR, PCV and Hb

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Men</th>
<th>LSD value</th>
<th>Women</th>
<th>LSD value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (Mean ± SE)</td>
<td>Patients</td>
<td>Control (Mean ± SE)</td>
<td>Patients</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>9.30 ± 1.09</td>
<td>25.88 ± 6.38</td>
<td>11.376 *</td>
<td>13.80 ± 1.60</td>
</tr>
<tr>
<td>PCV (%)</td>
<td>45.60 ± 0.68</td>
<td>45.82 ± 1.06</td>
<td>3.074 NS</td>
<td>39.10 ± 0.73</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>15.17 ± 0.23</td>
<td>14.88 ± 0.38</td>
<td>10.89 NS</td>
<td>13.00 ± 0.24</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>2.90 ± 0.45</td>
<td>7.80 ± 2.62</td>
<td>3.128 *</td>
<td>3.12 ± 0.34</td>
</tr>
</tbody>
</table>

* (P<0.05), ** (P<0.01), NS: Non-Significant.

(Mean ± SE) of men and women

Table (2): ESR increased significantly (p<0.05) in patients women (40.13 ± 6.43) in comparison with patients men(25.88 ± 6.38). PCV% in patients women (37.04 ± 0.98) decreased significantly(p<0.05) in comparison with patients men (45.82 ± 1.06). Hb decreased significantly(p<0.01) in patients women (12.29 ± 0.32) in comparison with patients men(14.88 ± 0.38). CRP (14.16 ± 2.15) increased significantly(p<0.01) in patients women in comparison with patient men (7.80 ± 2.62) figure 2
In our study table (1) ESR levels were found to be higher in the osteoarthritis patients than in the control group. ESR levels in osteoarthritis patients are used in studies as inflammation indicators (Hira and Tamam 2017). In patient’s women and men table (2) the ESR was elevated with decreased PCV% and hemoglobin among female’s patients. The causative of these changes can be multifactorial, as reported by disease involvement, drug-induced suppression of the bone marrow or defective erythropoiesis Harrison (2001) who researched OA's clinical characteristics. Red cells that may have induced secondary iron deficiency could also be prematurely killed, as was stated by some microcytic cells. This was the same thing. (Okoroiwu et al., 2016).

The increase in ESR is an alternative that affects the sedimentation rate during an inflammatory reaction, increased levels of fibrinogen, the main clotting protein, and alpha globulins. There is a higher rate of erythrocyte sedimentation(Harrison, 2015). Arthritis and other rheumatic diseases are a major concern in public health and are estimated to affect over 21 per cent of adults (Helmick et al., 2008). The most common type of arthritis, osteoarthritis (OA), is a main cause of inability (Brooks, 2002 and Gupta et al., 2005). In table (2)it seems that women were severely affected than men in reduction of PCV% and Hb, 30-60 per cent of patients are estimated to be anemic (Wilson, et al,2004 and Borah and Iqbal ,2007. The bleeding from gastrointestinal (GI) associated with non-steroidal anti-inflammatory drug (NSAID) (Hawkey, 2006 and Stefanova et al., 2018).
Chronic disease anemia in OA another major cause of anemia in iron supplemented patients is that this typically non responsive to iron supplementation (Nissenson et al., 2003 and Weiss et al., 2005). In a sample of 225 RA patients, chronic disease anemia represents 77% and iron deficiency anemia accounted for 23 percent of the anemia (Borah and Iqbal, 2007). Sex also seems to affect the prevalence of disease; women OA appears to affect more than men, and it has been estimated Women are up to three times more likely to develop RA than men. (Zlateva et al., 2010).

Women showing anemic than men, especially during menstruation or pregnancy, when iron needs increase. (Sharma, 2003). In postmenopausal women at cross-sectional study with Hb below 14 gm / L was correlated with reduced overall health, physical function and fertility outcomes. A major clinical improvement in functional results was observed for every 2 grams of hemoglobin. Participants in OA are also at a higher risk of becoming a woman Non-steroidal anti-inflammatory drugs affecting badly outcomes for each level of Hb in comparison to not reporting NSAIDS use. OA treatments are designed to relieve pain in patients and improve their function and quality of life (QoL). (NSAIDS) are often used and are associated with varying levels of blood loss and anemia due to drug-related GI toxicity. (Eaton, 2011).

Increased of CRP in patients men and women in our results was supported by Sanchez-Ramirez et al. (2014). Their study examined the combination of serum inflammatory markers (i.e. CRP and ESR) with muscle strength in the knee OA community. They found that elevated inflammatory serum markers (i.e. CRP > 3 mg / l and ESR zwischen20 mm / h) were associated with lower muscle strength of the knee in patients with OA. The increased levels of CRP both in patients men and women means the In many aspects of the inflammatory process, C-reactive protein plays an important role by connecting to microorganisms and damaged cellular components through phosphocholine, It is part of the innate immune response. This results in an additional activation and phagocytosis. Although complementary C-reactive protein activation increases inflammation and tissue damage, it also has some anti-inflammatory effects activation(Harrison, 2015). In our study, ESR and CRP levels were found to be higher in the osteoarthritis patients than in the control group. This is in accord with previous studies. ESR and CRP levels in osteoarthritis patients are used in studies as inflammation indicators(Lange-Brokaar et al., 2012). The CRP in erosive and non-erosive hand osteoarthritis CRP levels in the EOA were 4.7 (2.4–6.9) mg / l and in the non-EOA group 2.1 (0.5–4.9) mg / l (p = 0.001).

The increasing in hsCRP in EOA indicates the existence of inflammatory activity in this type of arthropathy and the likelihood that there will also be a systemic aspect of a serious local injury, such as OA. (Punzi et al., 2005). It is widely known that nearly all CRP serum concentrations are derived from liver development with inflammatory cytokines, especially interleukin (IL-6), are primarily responsible for their synthesis. (Punzi et al., 2002).Hematological markers for studying inflammatory and immunological profile in knee idiopathic OA included serum levels of ESR, CRP, RF. In 83.3 percent of cases, ESR was more than 20 mm / hour.
In 5 (8.3%) patients, serum RF was positive and negative in 55 (91.7%) patients. Positive CRP (> 3 μg / ml) was found in 8 (13.3%) patients and negative (<3 μg / ml) was found in 52 cases. This retrospective research has been carried out for 2 years in 60 patients in comparison with 60 as control without signs of OA (Joshi et al., 2016). Kozijn et al., 2019 reported Human CRP expression resulted in the aggravation of OA by increasing cartilage degeneration and osteophytosis. Increased monocytes recruitment of classical and non-classical types might be a mechanism of CRP action which is involved in aggravating this process. These findings suggest interventions selectively directed against CRP activity could ameliorate metabolic OA development. As 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 (Malathi, 2017).

We concluded from this present study that hematological changes in hematocrit and hemoglobin reduced significantly among OA patients while ESR and CRP increased significantly in knee OA.

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References


• Sanchez-Ramirez Diana C.; Marike van der Leeden; Martin van der Esch, Leo D Roorda, Sabine Verschueren, Jaap H van Dieën, Joost Dekker, and Willem F Lems. (2014). Elevated C-reactive protein is associated with lower increase in knee muscle strength in patients with knee osteoarthritis: a 2-year follow-up study in the Amsterdam Osteoarthritis (AMS-OA) cohort. Arthritis Research and Therapy, 16:R123.


