

Relationship between serum concentrations of boron and inflammatory markers, disease duration, and severity of patients with knee osteoarthritis in Sulaimani city

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ABSTRACT

Background: Many trace elements in the biological system, including boron, are involved in various vital processes related to health and diseases. Boron has been proved to have a role in decreasing inflammatory pain, joint stiffness, and other disabling symptoms associated with osteoarthritis (OA). **Aims and Objective:** To evaluate the relationship between serum concentrations of boron with inflammatory markers, disease duration, and severity in patients with knee OA. **Materials and Methods:** A total of 43 patients with knee OA were clinically evaluated and serum boron concentrations were measured in addition to erythrocyte sedimentation rate (ESR) and total white blood cell (WBC) count; the results were compared with that of healthy controls. Boron levels were correlated with ESR, WBC, disease duration, and severity. **Result:** Serum boron levels were significantly lower in patients compared with controls, and found to be significantly correlated with disease duration and severity. No correlation was reported between boron and the inflammatory markers. **Conclusion:** Serum boron levels were significantly lower in patients with knee OA, and negatively correlated with the duration and severity of the disease.

KEY WORDS: Knee OA; Serum Boron; Disease Severity; ESR; WBC Count

INTRODUCTION

Osteoarthritis (OA) is the most common form of joint diseases, a source of daily pain, stiffness, and decreased range of motion and daily activities for millions of peoples worldwide. Multiple etiologies are suspected to contribute to the formation of OA, including defective articular cartilage structure and biosynthesis, joint trauma, joint instability, congenital and developmental

abnormalities, and inflammatory conditions.^[1] Oxidative damage to essential cell components caused by oxygen-free radicals is a mechanism in the pathobiology of degenerative joint disease.^[2] Many trace elements in the biological system, including boron, are involved in various vital processes related to health, ranging from skeletal structure support, neurotransmission, muscle contraction, enzyme/hormones homeostasis of mineral balance in human body.^[3,4] Boron is a water-soluble trace element mineral that is present in human and plant nutrition and critical to health.^[5] The biomolecules that contain boron as an important component are either directly involved in immune functions or affect many components of the immune system.^[6] Boron intake from dietary sources influences the activity of many biotransforming enzymes, especially those related to the metabolism of steroid hormones and several micronutrients, including calcium, magnesium, and vitamin D.^[7,8] Boron has been proved to have a role in decreasing inflammatory pain, joint stiffness, and other disabling symptoms

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associated with OA.^[9,10] The disabling symptoms of OA are often invariably related to joint inflammation, represented by inflammatory blood markers levels such as C-reactive protein and on erythrocyte sedimentation rate (ESR), and boron is involved in both mechanisms.^[11] Moreover, in 2013, Al-Rawi *et al.*^[12] have reported significant low serum level of boron in Iraqi patients with rheumatoid arthritis (RA). Many newly reported data regarding pre-osteoclastic cells (MC3T3-E1) indicated the regulatory role of boron on osteoclastic behavior, which could be considered as a promising primary evidence about the beneficial role of boron in the treatment of osteoarthritic lesions.^[13,14] This study was designed to measure serum boron level in patients with knee OA and to evaluate its relationship with disease severity and some inflammatory markers of OA.

MATERIALS AND METHODS

Study Design

This multi-center cross-sectional study was conducted in OA patients who referred to both private and public clinics within Sulaimani city region between December 2014 and April 2015. We screened patients with knee OA who are eligible to participate in the study, and then compared them with a conveniently matched group of healthy controls. Serum boron level was measured in both groups.

Sample Selection

A total of 43 knee OA patients were diagnosed by senior orthopedist according to the ACR Guidelines for Medical Management of Osteoarthritis of the knee 2000^[15] included in the study and compared with 18 healthy subjects recruited from the community matched in age and gender as a control group. The exclusion criteria of the study were the following: patients having comorbid diseases that affect immunity, overlapping with other connective tissue diseases, were alcohol drinkers, receiving a systemic therapy that may interfere with the inflammatory condition for the last 4 weeks before blood sample collection, and pregnant women. All patients and controls included in the study signed an informed consent form before participation. Ethical approval was obtained from the local Research Ethics Committee of Sulaimani University, Faculty of Medical Sciences, University of Sulaimani, Kurdistan, Iraq. Disease severity was ranked according to the Ahlbäck classification and the Kellgren and Lawrence system.^[16,17] Five milliliters of whole blood was collected from each subject utilizing standard procedures. Two milliliters of whole blood was kept in EDTA tube, which was used for ESR and hematological measurements. The other parts of blood samples were left to clot and the obtained serum was utilized for analysis of boron levels using ICP atomic absorption spectrophotometer (Perkin Elmer, USA).^[18]

Statistical Analysis

All the results were expressed as mean \pm SD. The data were analyzed using GraphPad Prism 5.1 software (Graph Pad Software

Inc., San Diego, CA). Unpaired *t*-test with Welch's correction was utilized for statistical evaluation of the differences between the means. Pearson's linear correlation coefficient (*r*) was performed between serum boron and each quantitative independent variable, which is normally distributed, and Spearman's linear correlation coefficient between serum boron and disease severity because it is an ordered variable. A *P*-value < 0.05 was considered significant.

RESULT

Figure 1 indicates that ESR value in OA patients was significantly higher than that in controls (660%; $P < 0.001$), whereas Figure 2 shows that total white blood cell (WBC) count in patients with knee OA was significantly higher than that reported in healthy controls (14%; $P = 0.02$). Regarding serum boron levels, OA patients demonstrated significantly lower concentrations of serum boron (86%; $P < 0.0001$) compared to that of healthy controls (Figure 3). Figure 4 demonstrates weak positive and nonsignificant correlation ($r = 0.28$) between serum boron levels and ESR values in the studied OA patients. Meanwhile, serum boron levels were also poorly correlated with total WBC count in OA patients ($r = 0.17$; $P = 0.28$) (Figure 5). In Figure 6, serum boron levels showed high negative and significant correlation ($r = -0.47$; $P = 0.002$) with the duration of knee OA in the studied patients. Similarly, serum boron levels showed very high negative and significant correlation ($r = -0.8$; $P < 0.0001$) with the disease severity score in patients with knee OA (Figure 7).

DISCUSSION

The importance of the trace element boron in inflammatory diseases is related to its role in immune system functions and in

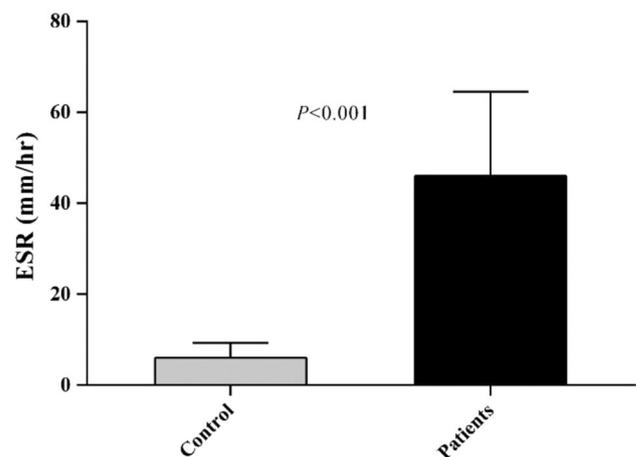


Figure 1: Erythrocytes sedimentation rate (ESR) of patients with knee osteoarthritis compared with control healthy subjects; $n = 43$ patients versus 18 healthy subjects. Data are expressed as mean \pm SD; results are significantly different according to unpaired *t*-test.

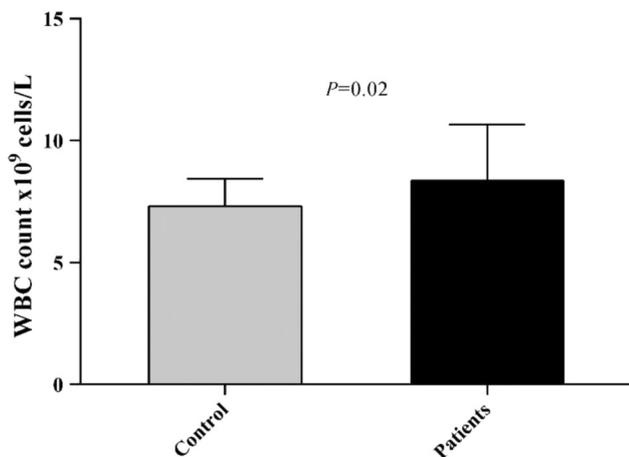


Figure 2: Total white blood cell (WBC) count of patients with knee osteoarthritis compared with control healthy subjects; $n = 43$ patients versus 18 healthy subjects. Data are expressed as mean \pm SD; results are significantly different according to unpaired t -test.

different metabolic processes in joint tissues.^[19] Boron, among many other trace elements is found in bone structures in very minute quantities.^[20] Although body content of boron is minute, its critical role for many metabolic and vital functions in many tissues and cells is highly appreciated.^[6] Many studies have previously reported the relationship between serum boron levels and many diseases and disorders of inflammatory bases, including RA and OA, and the data presented in this study was in tune with those reported by many others.^[21,22] The significant influence of boron is particularly important because it regulates inflammatory reactions in arthritic states by downregulating certain enzyme systems, enhancing significantly their activities at the inflammatory sites,^[23] inhibiting the inflammatory stress,^[24] and affecting the production of inflammatory cytokines by

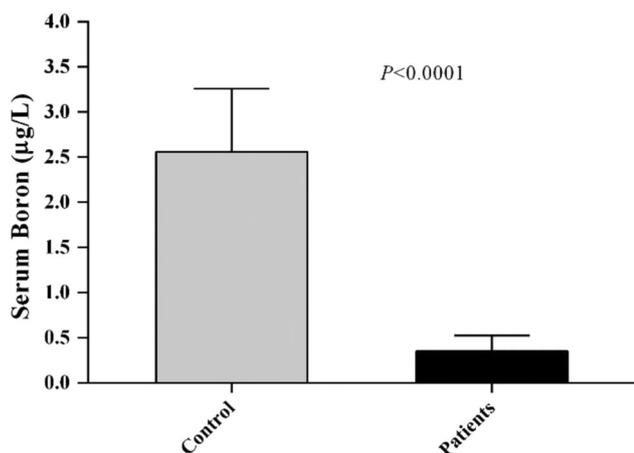


Figure 3: Serum boron levels of patients with knee osteoarthritis compared with control healthy subjects; $n = 43$ patients versus 18 healthy subjects. Data are expressed as mean \pm SD; results are significantly different according to unpaired t -test.

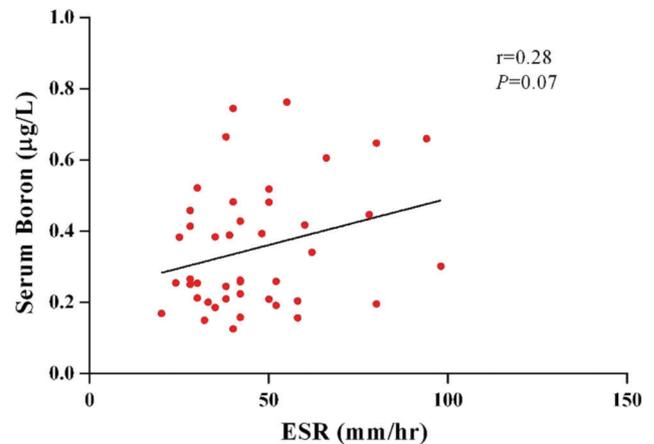


Figure 4: Correlation between serum boron levels and erythrocytes sedimentation rate (ESR) of patients with knee osteoarthritis; $n = 43$ patients. r = Pearson correlation coefficient.

cartilage cells and cells involved in the inflammatory response.^[10] This study showed that serum boron levels were significantly lower in OA patients compared to controls. Havercroft and Ward^[25] reported that boron concentrations in bone and synovial fluid were lower in RA patients than in healthy controls. Although the biological role of boron is mostly related with the inflammatory processes, this study did not reveal significant correlation between serum boron levels and the markers of inflammation (ESR and WBC count); this could be attributed to small sample size of patients and/or influence of treatment with anti-inflammatory agents, mostly used by those patients. However, this study revealed highly significant negative correlation between serum boron levels and duration and disease severity in patients with knee OA, which was not in tune with the finding of

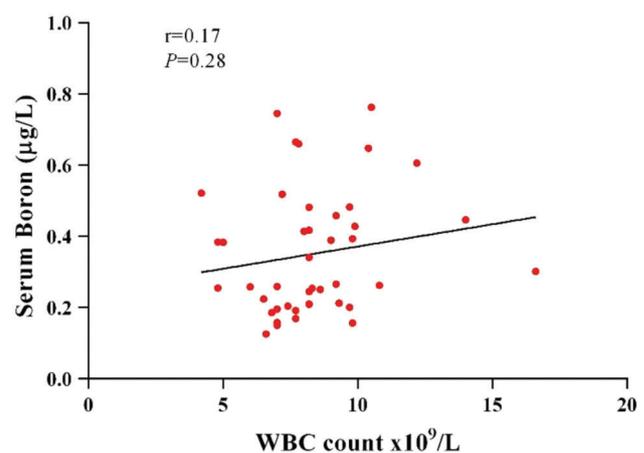


Figure 5: Correlation between serum boron levels and total white blood cell (WBC) count of patients with knee osteoarthritis; $n = 43$ patients. r = Pearson correlation coefficient.

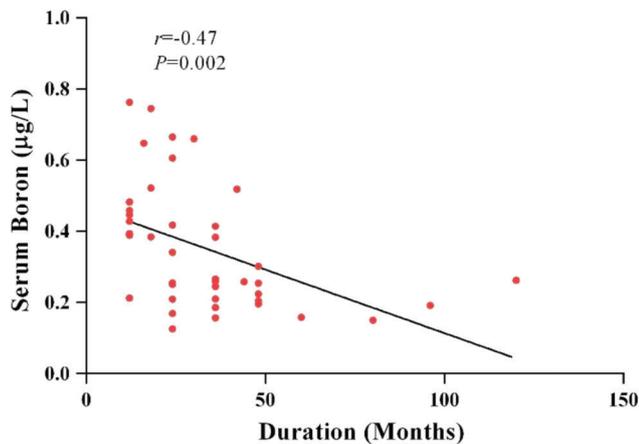


Figure 6: Correlation between serum boron levels and disease duration (months) of patients with knee osteoarthritis; $n = 43$ patients. $r =$ Pearson correlation coefficient.

Al-Rawi *et al.*^[12] in RA patients; this may be attributed to the complicated immune-based etiology of RA compared with OA. Previous studies have demonstrated the effects of boron as potential anti-inflammatory agent with the ability to modulate key markers associated with inflammation-related conditions such as OA.^[26–28] Such findings shed a light on the relationship between serum content of boron and disease severity, which could be of significant importance in the treatment follow-up when boron is therapeutically utilized in cases of OA or RA. Although small sample size of included patients and use of markers with low sensitivity are the major limitations of this study, the outcome encourages utilization of larger scale of patients and longer period follow-up to support the reported data. In conclusion, serum boron levels were significantly lower in patients with knee OA, and negatively correlated with the duration and severity of the disease.

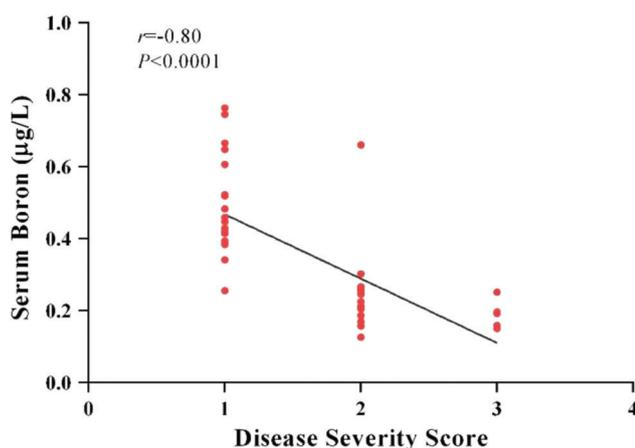


Figure 7: Correlation between serum boron levels and disease severity score of patients with knee osteoarthritis; $n = 43$ patients. $r =$ Spearman correlation coefficient.

CONCLUSION

Serum boron levels were significantly lower in patients with knee OA, and negatively correlated with the duration and severity of the disease.

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