

Full Length Research Paper

## Evaluation of Chromium and Manganese level in Rheumatoid Arthritis Patients

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**Background:** The importance of trace element in Rh is great of interest because many of these trace elements are co-factors in metabolic processes involving collagen and bone structure, particular tissue or immune system function. In this cross sectional case control study, 55 subjects were studied, 30 of them were RA patients and 25 as healthy controls. The aim of this study was to evaluate the concentration of trace elements (manganese and chromium) in RA patients and apparently healthy control as well as the duration and complications of the disease. **Methods:** plasma chromium and manganese concentrations were determined using flame atomic absorption spectrophotometer (Buck Scientific 210/211 VGP Atomic Absorption-England). **Results:** The mean plasma manganese in RA patients when compared vs healthy controls observed statistical insignificant difference, whereas chromium presented, a low significance difference, p.value (0.819, 0.00), respectively. Our result findings reveals statistical insignificance differences in Mn levels in all of the durations period (<5 years, 5-10 years and >10 years), p.value was (0.5, 0.059, 0.48), respectively, while chromium mean levels of patients vs mean control group was significantly lower p.value (0.000, 0.000, 0.000), respectively. The levels of Mn in the 3 complication groups of RA disease (slight complication – moderate complication – sever complication) when compared with mean levels of the healthy control group revealed statistical insignificant, p.value was (0.8), furthermore the mean level of chromium was found significantly decreased among the 3 complication groups p.value (0.02). **Conclusion:** The mean plasma manganese in RA when compared vs healthy controls found statistical insignificant difference, whereas chromium presented, a low significance difference, p.value (0.819, 0.00), respectively. Chromium mean levels of patients vs mean control group was significantly low p.value (0.000, 0.000, 0.000), respectively. Manganese levels in the 3 complication groups was not statistically different when compared with controls p.value (0.8), chromium was found significantly decreased among the 3 complications groups with p.value (0.02).

**Key words:** Rheumatoid arthritis, metabolism, tissues, patients.

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### INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory, systemic disease that produces its most prominent manifestations in the diarthrodial (Michael *et al.*, 2010; Smith *et al.*, 1998).

The typical form of the disease is symmetrical, destructive and deforming polyarthritis affecting small and large synovial joints with associated systemic disturbances, a variety of extra-particular features and the presence of circulating anti globulins antibodies (rheumatoid factor) (Cerhan *et al.*, 2003). Many symptoms of

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RA are present before its diagnosis. Weight loss, fever, prolonged early morning stiffness, fatigue, generalized muscle weakness, low mood, and depression are often responsible for a significant loss in the quality of life of patients. Fatigue is reported in 40–80% of RA patients as their most disabling symptoms (Balsamo *et al.*, 2014). The importance of trace element in Rh is great of interest because many of these trace elements are co-factors in metabolic processes involving collagen and bone structure, reticular tissue or immune system function (Brig *et al.*, 2005). Trace elements are widely distributed in a variable proportion in the human body and they play a vital role in growth (Florianczyk *et al.*, 2008). Manganese is one of trace elements that are necessary for bone health, and its deficiency can lead to abnormal bone formation. An excess of Mn affects iron metabolism (poor iron metabolism, It is an essential part of many enzymes associated with protein and fat metabolism, energy production and bone formation, it's also required for the utilization of vitamin E and vitamin B1, formation of cartilage and synovial fluid of the joints and biochemically essential as the enzyme activator (Santamaria AB, 2003). It is an essential for synthesis of acid mucopolysacchride such as chondroitin sulphate which is utilized to form collagen, bone and cartilage, the strong fibrous connective material that build tissue, it's also involved in glycoprotein synthesis and it's a co-factor in phosphohydrolases and phosphotransferases involved in the synthesis of proteoglycans in cartilage (Gordon RF, 1977). Manganese is important in mental facilities and functions. It aids memory and modulates neurotransmitter activity related to nerve/muscle dysfunction and it's a part of enzymes involved in urea formation, pyruvate metabolism and galactotransferase of connective tissue biosynthesis (Chandra RK, 1990). In previous studies it was found that manganese level increase in RA patients (Satish & Reshu, 2009).

Chromium is one of the newer essential trace elements. Have a great role in maintaining good health; Chromium may have a function in the control of glucose and lipid metabolism (Jonathan CL, 1981). The basis for the suggestion that Chromium may effective in prevention of rheumatoid arthritis is that post menopausal women taking a Chromium supplement exhibited increased plasma dehydroepiandrosterone, a precursor of estrogen, which inhibits bone loss, and decreased urinary calcium and hydroxyproline excretion, which are indirect rather variable indicators of bone loss (Carl & Edward, 2008). Chromium supplementation should view as only one of a number of speculative methods that may help in maintaining healthy bones (Hathcock JN, 2004). In previous studies it was found that chromium level decreases in RA patients (Hansson *et al.*, 1975). Case control study involved 30 RA patients of both genders. The proposal of the study was approved through an ethical committee of Alneelain University, college of Medical Laboratory Sciences. All patients were and selected through direct questionnaires after filing an informed

consent, from Omdurman Military Hospital and Omdurman Teaching Hospital, part of Khartoum state. The study period spanned from (October to December, 2015). The aim of this study to assess the concentration of trace elements (chromium and manganese) in RA patients as well as correlations between these apparently healthy subject and compare them.

## Patients

All patients with Rheumatoid arthritis were participated in this study, 25 were females and 5 males, and 25 as healthy controls 20 females and 5 males. All patients had fulfilled the American College of Rheumatology (ACR) criteria (Arnett *et al.*, 1988) for RA diagnoses were selected by physician rheumatologist.

## Samples collection and preparation

A volume of 3 ml of venous blood sample was collected from all patients in lithium heparin containers. Using a disposable syringe and aseptic standard non traumatic vein puncture technique was applied, blood was emptied into a sterile containers. And then centrifuged at 4000 rpm for 10 minutes, then the plasma was separated and transferred into a new container and processed. Plasma was stored at -20°C until analysis.

## Analysis of Trace Elements

### Determination of chromium and Manganese

Plasma chromium and manganese concentrations were determined using flame atomic absorption spectrophotometer (Buck Scientific 210/211 VGP Atomic Absorption-England). Plasma samples were diluted with deionized water. The analysis was performed against control sample, standard prepared in glycerol to approximate the viscosity characteristics of diluted samples. For determination of plasma chromium, samples were diluted 1:5 with deionized water. The plasma samples for manganese estimation were diluted 1:10.

### Inclusion criteria

Only diagnosed RA patients by physician rheumatologist

### Exclusion criteria

Any Pregnant patients or had recent infection or autoimmune overlapping was excluded from this study.

### Statistical Analysis

The results of serum element concentrations were expressed as a mean  $\pm$  standard deviation. The level of significance was determined by employing pooled t-test,

**Table 1:** shows a comparison of the plasma mean trace elements concentration (Cr and Mn) in patients with rheumatoid arthritis and control group

	Study group	Mean $\pm$ SD	P. Value
Mn	Patients NO 30	0.34 $\pm$ 0.23	0.819
	Control NO 25	0.35 $\pm$ 0.15	
Cr	Patients NO 30	0.02 $\pm$ 0.01	0.00
	Control NO 25	0.07 $\pm$ 0.04	

**Table 2:** shows a comparison of the means of the trace bioelements (Mn and Cr) levels of the three durations in RA patients

Trace elements	Durations No 30	Controls No 25	Sig
	<5 years	Control mean $\pm$ SD	P.value
Mn mean $\pm$ SD	0.39 $\pm$ 0.25	0.35 $\pm$ 0.15	0.50
Cr mean $\pm$ SD	0.03 $\pm$ 0.01	0.07 $\pm$ 0.04	0.000
	5 – 10 years	control	p.value
Mn mean $\pm$ SD	0.26 $\pm$ .10	0.35 $\pm$ 0.15	0.059
Cr mean $\pm$ SD	0.02 $\pm$ 0.01	0.07 $\pm$ 0.04	0.000
	>10 years	control	p.value
Mn mean $\pm$ SD	0.42 $\pm$ 0.41	0.35 $\pm$ 0.15	0.48
Cr mean $\pm$ SD	0.02 $\pm$ 0.008	0.07 $\pm$ 0.04	0.000

only when p-value less than 0.05, considered as statistically significant.

## RESULTS

In this cross sectional case control study, 55 subjects were studied, 30 of them were RA patients and 25 as healthy controls. Table 1 demonstrates the distribution pattern of the quantitative parameters (the mean of the Bioelements) in RA patients, and control group. In this study mean plasma level of Cr was significantly lower when compared with the mean of the control group, whereas Mn mean levels revealed the statistical insignificant value, p.value (0.00, 0.819), respectively.

Table 2 describes the mean levels of trace elements (Cr, Mn) among the different duration groups. The duration was divided into 3 groups, the first one less than 5 years, second from 5 to 10 years and the third one more than 10 years.

Table 3 describes the mean patient's plasma levels of trace elements (Mn, Cr) in the complication groups. The mean level of the trace element chromium of the 3 complication groups revealed a lower statistical significant difference when compared with the control group, meanwhile manganese Mn was not significantly different among the 3 complication groups. The complications encompass 3 groups according to severity of disease.

Group1 have slight complication: (pain in joint, morning stiffens, fatigue, fever). Group 2 has a moderate complication (swelling in joint of the hand or foot or knee, shoulder tenderness). Group 3 has a severe complication: (deformation of joints or affect other organ).

Table 1 represents the comparison of mean plasma trace Bioelements of patients and control group.

## DISCUSSION

This study was performed to assess and compare the concentration of trace elements (chromium and manganese) in RA patients and apparently healthy subjects. The importance of trace element in RA is great of interest because many of these trace elements are co-factors in metabolic processes involving collagen & bone structure, particular tissue or immune system function (Brig *et al.*, 2005). Manganese is a required mineral in the metabolism of protein, fat, healthy immune also required in normal bone growth, energy production (Huda *et al.*, 2010).

A deficiency of Manganese concentration may affect brain health, skeletal, cartilage formation and antioxidant enzyme superoxide dismutase (SOD) which prevents damage by superoxide free radicals (De Carvalho *et al.*, 2010). The estimated result of mean plasma manganese in RA patients listed in Table 1 when compared vs healthy controls observed statistical insignificant difference, whereas chromium presented, a low significance difference, p.value (0.819, 0.00), respectively, and this was confirmed by (fig 1) that observed the comparison of mean Bioelements between patients and control. The findings of manganese mean level are inconsistent with the 2 past researchers' findings (Huda *et al.*, 2012), the first who had expressed, very little information on literature about this point who had found it significantly higher among RA patients, and chromium was consistent with that previously (Hansson *et al.*, 1975) who had found the chromium levels decreased significantly in RA patients.

The explanation for this significant reduction of chromium is not fully understood and the scientific researchers were carefully reviewed and detected there was no any information about this point. In table (2) we evaluated the effect of durations (<5 years, 5-10years, >10years) on the manganese and chromium concentrations and compare the result with mean levels of healthy controls. Our result findings reveal statistical insignificance differences in Mn levels in all of the durations period (<5 years, 5-10 years and >10 years), p.value was (0.5, 0.059, 0.48), respectively,, while chromium mean levels of patients vs mean control group was significantly lower p.value (0.000, 0.000, 0.000), respectively.

When we evaluate the effect of complications (slight complication – moderate complication – sever complication)

**Table 3:** shows the comparison of trace bioelements concentrations (Manganese and Chromium) on the RA patients

Trace element	Slight no 5	Moderate	Severe	Controls	p. values
Mn	0.32±.18	0.31±.22	0.37±.30	0.35±.15	0.8
Cr	0.016±.008	0.026±.009	0.03±.011	0.07±0.04	0.02

on the manganese concentration and compare the result with healthy control group, (Table 3) revealed statistically insignificant, the p.value was (0.8), that is means the complication of RA not affects significantly on manganese concentration, furthermore the mean level of chromium was found significantly decreased among the 3 complications groups with p.value (0.02).

### CONCLUSION AND RECOMMENDATIONS

The mean plasma manganese in RA when compared vs healthy controls found statistical insignificant difference, whereas chromium presented, a low significance difference, p.value (0.819, 0.00), respectively. Chromium mean levels of patients vs mean control group was significantly low p.value (0.000, 0.000, 0.000), respectively. Manganese levels in the 3 complication groups was not statistically different when compared with controls p.value (0.8), chromium was found significantly decreased among the 3 complications groups with p.value (0.02). Although, noticed that there was a minor decrease among individual patients in manganese concentration in about 50%, and in 44% of healthy controls, the reduction of manganese in healthy control, meaning that the Sudanese individual may have low manganese concentration but this suggests must be confirmed by prospective large sample size and need further researcher work to confirm it.

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