

The relationship between serum potassium levels and some chemical limitations in Rheumatoid arthritis from Qurna district, Basrah city

العلاقة بين مستويات البوتاسيوم وبعض المحددات الكيميائية في امصال مرضى التهاب المفاصل الروماتويدي من منطقة القرنة بمدينة البصرة.

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الخلاصة

الالتهاب المفصلي الروماتزمي هو عبارة عن التهاب مزمن غير معروف السبب يصيب مفاصل أجزاء الجسم المختلفة بصورة متوازية في الجهتين, في هذه الدراسة تم تقدير مستوى البوتاسيوم في مصل مرضى التهاب المفاصل ومدى علاقته ببعض المحددات الكيميائية لهؤلاء المرضى والتي منها , مستوى تراكيز النحاس , حامض اليورك , سرعة ترسيب كريات الدم الحمر, وعدد كريات الدم البيض, ونسبة الهموكلوبين , وعامل لروماتيزم, عامل التحديد البروتيني . أظهرت النتائج زيادة معنوية عالية في عدد كريات الدم البيض ومستوى حامض اليورك في مصل لمجاميع المرضى مقارنة بمجموعة السيطرة , بينما كانت مستويات سرعة ترسيب كريات الدم الحمر, ونسبة كريات الدم البيض, ونسبة الهموكلوبين , وعامل لروماتيزم, عامل التحديد البروتيني مرتفعة بفرق معنوي عالي في مجموعة الفعالة الثانوية عند مقارنتها مع مجموعة السيطرة . كما وجدت هذه النتائج إن مستوى تركيز البوتاسيوم في مصل المرضى اقل مما هو عليه في مصل مجموعة السيطرة , إما من ناحية مستوى تركيز النحاس لم يلاحظ أي فرق معنوي في مجاميع الدراسة .

Abstract

Rheumatoid arthritis is the chronic inflammatory arthropathy. Total serum potassium levels in patients with rheumatoid arthritis were determined in conjunction with total serum copper, serum uric acid, Rheumatoid factor (RF), C-reactive protein (CRP), erythrocyte sedimentation rate and Hemoglobin and WBC count,. There were significantly higher of white blood cell count (WBC) and uric acid levels in the total RA patient group and in the active subgroups than in controls($p \leq 0.05$). While Patients in the active subgroups had significantly elevated ESR, CRP, RF values than those in the corresponding inactive and control groups, The mean serum potassium concentration in all patients studies , which was significantly lower than that of control group($p \leq 0.05-0.01$), nevertheless no significantly association was recorded in the total serum copper concentration was observed. The results of this study support the hypothesis that low serum potassium level in rheumatoid arthritis and the correlation with copper level is one of the specific features of inflammation.

Introduction

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of unknown cause. It affects about 0.5% of the adult population and is 2-3 times more common in women than in men⁽¹⁾. Any joint may be affected but the disease is most commonly localized in hands, feet and wrists⁽²⁾. Other symptoms include fatigue, malaise and morning stiffness. Extra-articular involvement of organs such as the skin ,heart and eyes can be significant, thus RA may lead to considerable morbidity and is also associated with increased mortality⁽³⁾.

As strangely ,considerably less attention has been paid to divalent as opposed to monovalent cation metabolism in medicine ,this may be attributable to the earlier appearance of simple methods of measurement for the alkali metals (Na^+ , K^+ , Cu^{+2} .ie.) Rather than to their relative biological importance ⁽⁴⁾.An increased number of disease to day maybe associated with mineral deficiency, though metals deficiencies are associated with several arthritic conditions.

Many metals are intimately involved in numerous biological systems of relevance to patients with arthritis ranging over collagen and bone metabolism ⁽⁵⁾, complement system, lysosomal enzyme release and macrophage functions ⁽⁶⁾.

In the past arthritis was associated with old age in people's and there was a tendency to suffer it stoically as inevitable .While, the medical profession has intellectually a band oned an assumption that only people in old age are affected⁽⁷⁾.

Over recent years there has been renewed debate about the nature of the association between raised serum uric acid concentration and many diseases for as RA. Observational studies show that serum uric acid in arthritis are interrelated in several races with a variety of geographic, ethnic characteristic.

One of clinical medicine's oldest tools the erythrocyte sedimentation rate (ESR), surpassed serum C- reactive protein (CRP) as a measure of rheumatoid arthritis activity and may be better for monitoring response to disease ⁽⁸⁾.

The chief objective of several studies was to compare the relative sensitivity to change of the ESR and CRP in RA. One reason for the lack of strong preference for either test may be that few comparisons of their evaluative properties have been done ⁽⁹⁾.

To our knowledge, changes in evaluation of potassium and some serum parameters levels have not been investigated in patients with RA in Iraq ,

In the present study we have focused attention their effect on total serum potassium, copper and we have also examined some inter-relationships between potassium, copper and rheumatoid factor, clinical index of activity.

Materials and Methods

The local ethics committee approved the study protocol. Patients with RA who attended the General Qurna hospital, from Basrah, Southran of Iraq. There were 120 patients of whom 49 males (mean age ,25.6 years ± 1.87 ,range 16 to 65 years) and 71 females (mean age 29.9 years ± 2.91 .range 20 to 74 years),as well as ,98 normal health subjects (42 males and 56 females) their aged from 19-71 years old. In all patients' routine biochemical analysis, CRP, and ESR were performed before the study and none of them had any systemic disease. All patients received non-steroidal anti-inflammatory drugs, and the treatment with these drugs was stopped 3-4 days before the study.

The patients were divided into two groups, active and inactive, with respect to CRP and ESR.A CRP titer >8 mg/L and ESR >20 mm/h were accepted as indicating the active stage of the disease.

Biochemical analysis:-

After on over night fast, blood was taken. clotted and immediately centrifuged to separate serum which was divide in several aliquots for determination of serum uric acid, potassium, copper, Rheumatoid factor (RF), Hemoglobin, C-reactive protein (CRP) ,their were performed by the enzymatic reagent standard kits.

Statistical analysis:-

Statistical evaluation was carried out with SPSS 10.0. The total patient group and the control group were compared with students (*t*) test. In all subgroups, parameters were subjected to Pearson correlation analysis ($p \leq 0.05$) was considered significant; data are a presented as Mean $\pm$ S.D in the tables.

Results

There was no statistically difference in age and sex distribution between control and patients and also among RA subgroups (table 1) ($p \leq 0.05$)

Table 1: Demographic features of the study groups

Parameters		Control	Patients of RA	
			Active	Inactive
Numbers		98	99	21
Age (years)		40.0±10.5(19-71)	49.8±9.8(19-70)	46±0.1(17-63)
Sex	Males	42	39	10
	Females	56	60	11
Disease duration(year)		/	9.8±0.3(1-23)	6.1±0.2(1-3)

Values are expressed as Mean ±SD. (range). (Student's *t* test).

Laboratory data are presented in (table 2, figure1). White blood cell count (WBC) and uric acid levels were significantly higher ($p \leq 0.05$ - 0.01) in the total RA patient group and in the active subgroups than in controls.

Table 2: Laboratory data of controls and all patients with RA

Parameters	Control (N=55)	Patients of RA	
		Active (N=99)	Inactive (N=21)
WBC count (x 10 ⁹ /L)	8.1±1.6	9.7±0.2	7.7±2
ESR(mm/h)	/	45±2.6*	13±5 ^a
CRP(mg/L)	/	50±4.7*	6±2.1 ^a
K	4.25±0.13	2.9±0.41*	3.9±1.2 ^a
Cu (µg/dl)	88.45±3.33	57.17±1.98**	82.45±1.77
RF	/	+ne	/
Uric acid mg/dL	/	5.81±2.1	/
Hemoglobin g/dL	12.9±102	11.3±1.8	12±2.34

Values are expressed as Mean ±SD. (range). Comparisons: * controls vs. total patients;

^a control vs. inactive/active, (* $p \leq 0.05$, ^a $p \leq 0.01$) (Student's *t* test). +ne= active value.

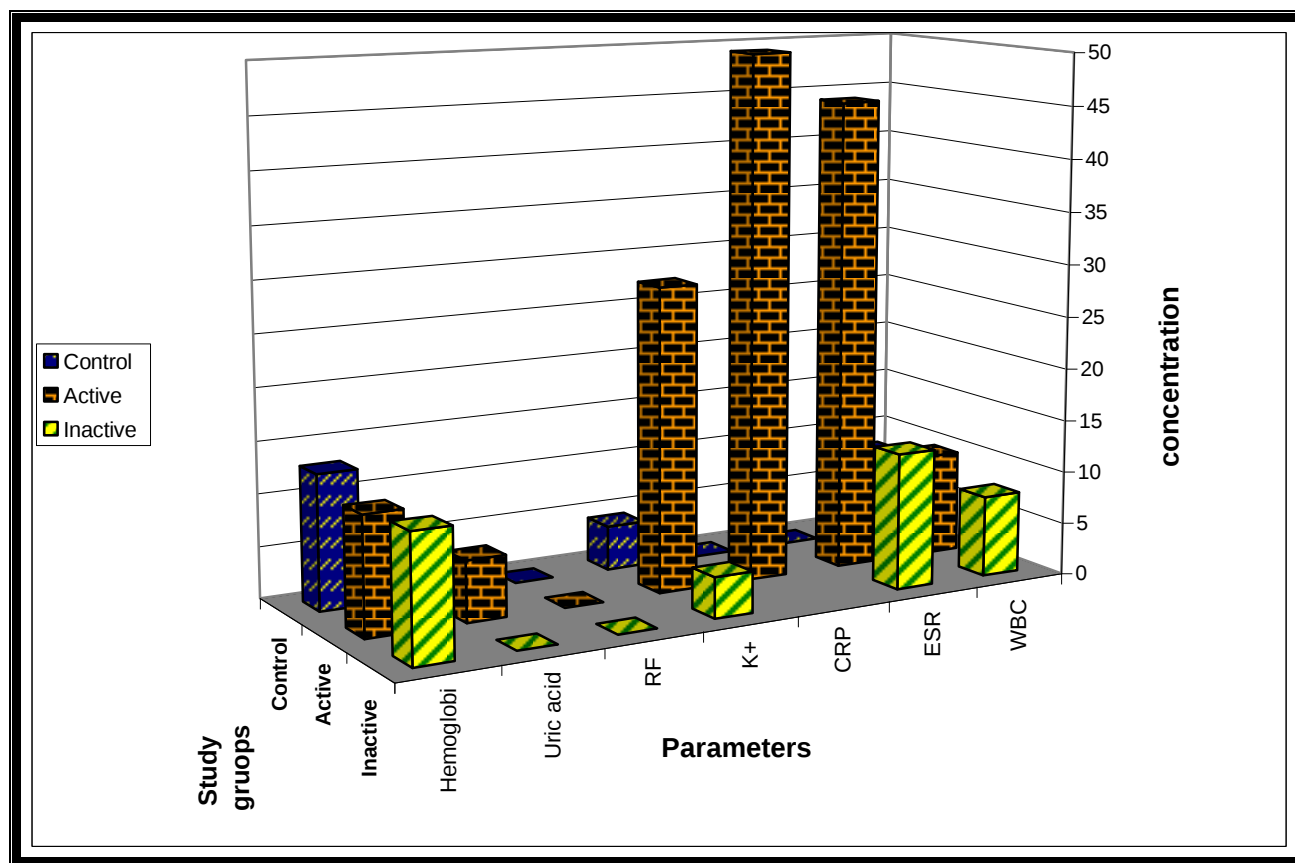


Figure1: Distribution of serum parameters in all study groups

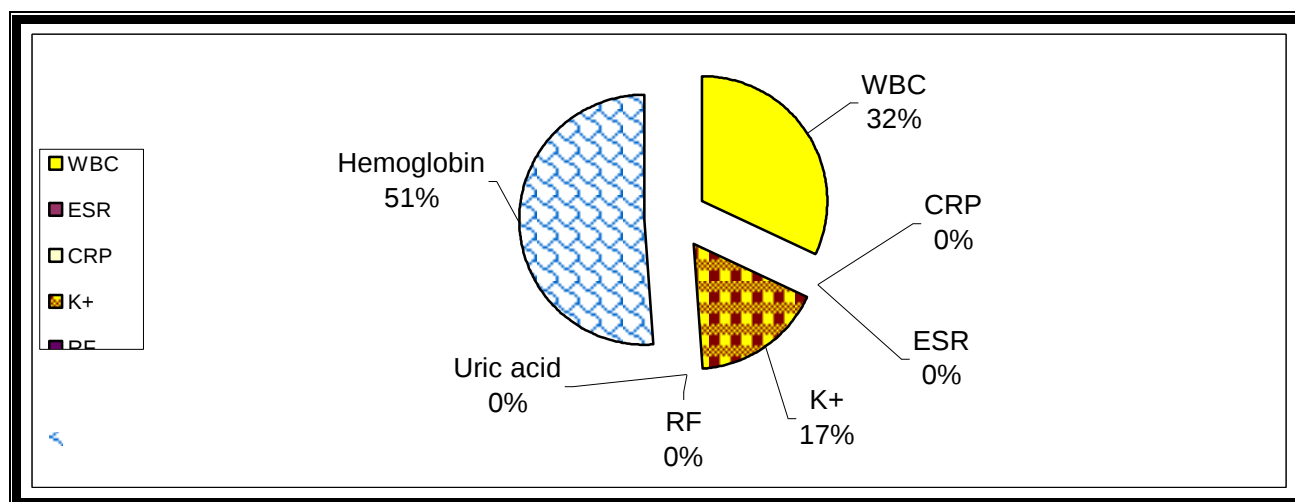


Figure2: Biochemical analysis distribution in control for this study

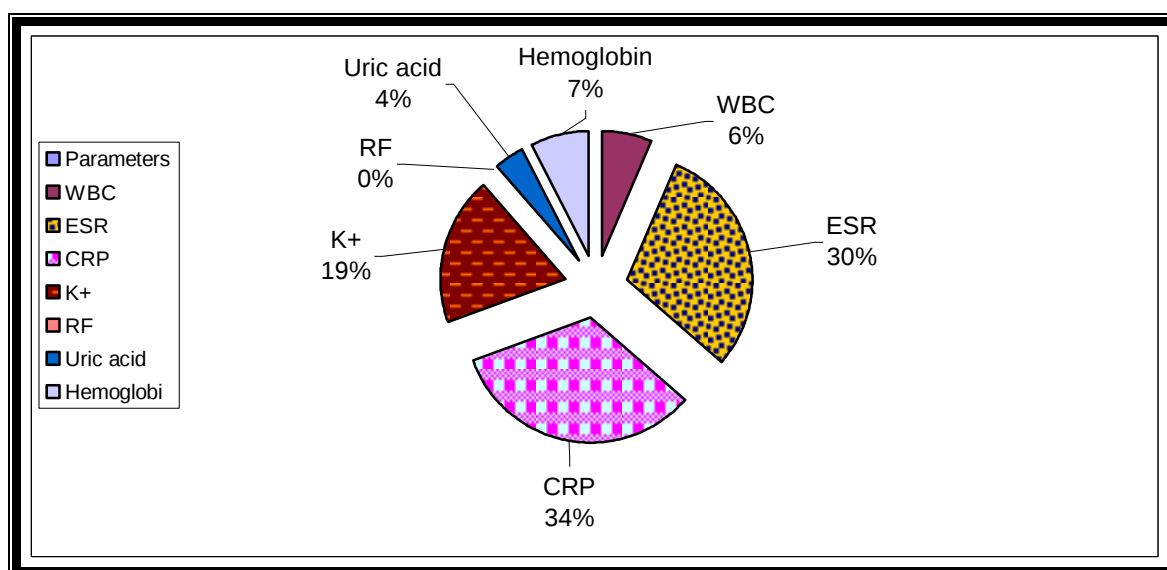


Figure3: Biochemical analysis distribution in active group for this study

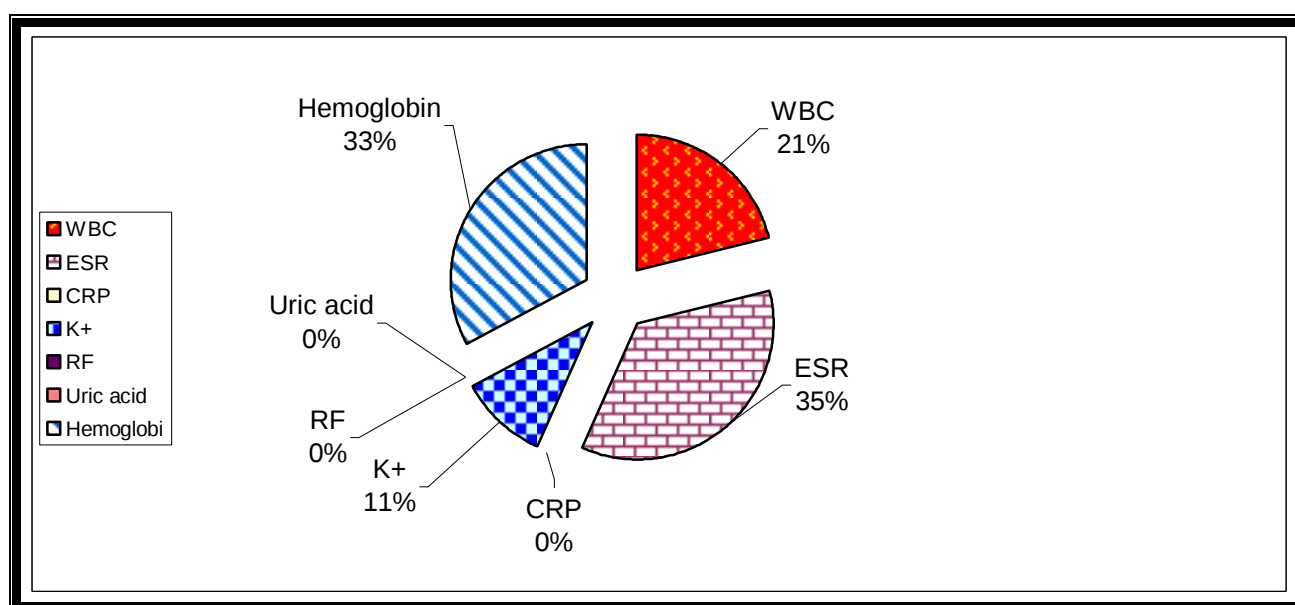


Figure4: Biochemical analysis distribution in inactive for this study

Patients in the active subgroups had significantly higher ESR, CRP, RF values than those in the corresponding inactive and control groups (table 2, figures2, 3, 4).

The mean serum potassium concentration in all patients studies, which was significantly lower ($p \leq 0.05$) than that of control group.

There is a significant correlation between serum potassium and uric and when males and females are considered as single group but when divided by sex, this significance disappears confirming the trend noted in the step-wise regression and principle component analysis .No significantly relationship was recorded in the total serum copper concentration ($p \leq 0.05$) was observed between that total patient group and the controls or among the patients subgroups (table 2).

Discussion

For years arthritis was the poor relation of medical research .Its victims did not do something dramatic like die, as they often did with pneumonia or go insane as they did with syphilis, or bring tears to the eyes as with childhood diphtheria. Arthritis tended to be a disability of old folks with vague, sometimes disbelieved symptoms. That has changed and extensive, well founded research is being done now⁽¹⁰⁾.

Early literature on this subject was bedeviled by methodological problems which could go some way towards explaining the apparent discrepancies⁽¹¹⁾.

The results of this study confirm and extend our previous observation that the serum potassium concentration in patients with RA is low⁽¹²⁾. LaCelle's finding that the whole body potassium concentration is significantly lower in older arthritis, even if one assumed that the RA patients caused the potassium content rather than other way around⁽¹³⁾. This finding was in agreement with our results,. However ,one can not draw sure conclusions from low potassium serum of the blood content alone and is dependant on the status of hydrogen ion and chloride ,the reason is that serum can have wide swings in content⁽¹⁴⁾. In contrast, Alastar *et al.*,. Observed that mean total potassium concentration in serum was not significantly different in RA patients. Our justification, the causes which were responsible of disorder in potassium deficiency, there are several enzyme systems in the kidneys which are affected by a deficiency. The enzyme which reduces the amino acid glutamine to ammonia is one of them and its activity is increased⁽¹⁵⁾. The ammonium ion has a positive charge and is about the same size as potassium. Therefore this may be a mechanism for helping to prevent potassium loss by substituting ammonium. The ammonium is said to be synthesized in the mitochondria of the proximal tubule cells, excreted in part by the sodium-potassium-chloride co transporter, and then brought to the collecting duct and excreted⁽¹⁶⁾. In addition, Sckick, *et al.* demonstrated that everyone given 1.5 to 3 grams of potassium supplements per day had a complete healing of all arteries .The only consistent thing that happened during the course of the experiment was that his daily intake of potassium was raised⁽¹⁷⁾.

In our study we have shown the serum uric acid concentration that correlates significantly with serum potassium concentration in RA .many studies have been carried out to ascertain the influence of multitude of factors on serum levels of uric acid ,that showed serum uric acid level was positively associated with measures of blood pressure,obesity,geographical factor,height and weight of body, while we know of no tests reported in the literature testing in correlating between potassium and uric acid levels in RA patients .Uric acid is produced from the natural breakdown of your body's cells and from the foods.

Most of the uric acid is filtered out by the kidneys and passes out of the body in urine. A small amount passes out of the body in urine. But if too much uric acid is being produced or if the kidneys are not able to remove it from the blood normally, the level of uric acid in the blood increases. High levels of uric acid in the blood can cause solid crystals to form within joints, these uric acid crystals can build up in the joints and nearby tissues, forming hard lumpy deposits called tophi. High levels of uric acid may also cause kidney stones or kidney failure⁽¹⁸⁾.

We have demonstrated a significant relationship between ESR, CRP, and serum potassium concentration, and the inter-relationship extended in much the direction one would expect .When the body has any sort of inflammation, levels of C-reactive protein and ESR in the blood increase usually within 2 to 6 hours, these interesting findings are derived from a large number of clinical trials and appear to reflect real differences in the sensitivity to change of two measures⁽¹⁹⁾. The liver produces C-reactive protein (CRP) when there is inflammation somewhere in the body, of these data we found in agreement with our previous data.Paulus and Brahn pointed that ESR may be considered a less specific measure of the acute-phase response than CRP because its influenced by many factors other than systemic inflammation ,including age ,sex,red blood cell morphology, hemoglobin and rheumatoid factor, for this results were a bit surprising because the tendency in recent years has been to favor CRP than ESR⁽²⁰⁾.

From these our results suggest that the relationship between serum potassium concentration and several other test in arthritis panel is either weak or non-existent, we believe that further investigations with a larger patient population and many testing were warranted for the detection of subtler relationships. In addition, further studies of the relationships between RA and intracellular concentration of copper and potassium are needed.

References

- 1-Administration NF, 2005: Swedish Nutrition recommendations objectified in National Administration
- 2-Abernathy PP, *etal* .2003:Healthy body: an alternative perspective .*AM.J ClinNutr*.447-452
- 3-Baumgartner RN, 2000: Body composition in healthy aging. *Ann N Y Acad*, 904:437-445
- 4 Brown DH, Buchanan WW, el-Ghobarey AF, Smith WE, and Teape J,1997: Serum copper and its relationship to clinical symptoms in rheumatoid arthritis. *Ann Rheum Dis*. Apr;38(2):174–176.
- 5- Fernandez-Madrid F, Prasad AS, and Oberleas D, 2003: Effect of zinc deficiency on collagen metabolism. *J Lab Clin Med*. Nov; 78(5):853
- 6- Yamamoto K, Takahashi M, 1999. Inhibition of the terminal stage of complement-mediated lysis (reactive lyses) by zinc and copper ions. *Int Arch Allergy Appl Immunol*.; 48(5):653–663
- 7- Holman RL,.1985 :Arteriosclerosis - the lesion. *American Journal of Clinical Nutrition* 8; 85- 94
- 8- Hogevik H, Olaison L, and Anderson R, I, 2001: C-reactive protein is more sensitive than erythrocyte sedimentation rate for diagnosis of infective endocarditis. *Infection*; 25 (2): 82-85
- 9- Ward MM, 2004: Relative sensitivity to change of the erythrocyte sedimentation rate and serum C-reactive protein concentration in rheumatoid arthritis. *J Rheumatol*
- 10 Arnett FC Koopman WJ, ed, 2005: Arthritis and allied conditions: a textbook of rheumatology, 13th edn. Vol. 1. Baltimore: *Williams & Wilkins*.;1197–208.
- 11- Aaseth J, Munthe E, Førre O, and Steinnes E,1987: Trace elements in serum and urine of patients with rheumatoid arthritis. *Scand J Rheumatol*.;7(4,):237–240. [[PubMed](#)].
- 12- Repo H, Leirisalo-Repo M, and Koivuranta-Vaara P, 1984: Exaggerated inflammatory responsiveness plays a part in the pathogenesis of HLA-B27 linked diseases-hypothesis. *Ann Clin Res*; 16:47–50.[[Medline](#)]
- 13- LaCelle PL, *etal*. 1994: An investigation of total body potassium in patients with rheumatoid arthritis. Proceedings of the Annual Meeting of the American Rheumatism Association, *Arthritis and Rheumatism* 7; 321.
- 14- Luke RG, Wright FS, Fowler N, Kashgarian M and Giebisch GH, 1998: Effect of potassium depletion on renal tubular chloride transport in the rat. *Kidney International* 14; 414-427
- 15- Iacobellis M, *etal*. 1987; Free amino acid patterns of certain tissues from potassium and/or protein - deficient rats. *Amer. Journal Physiology* 185 ;275
- 16- American Medical Association ,2004 ;Handbook of Nutrition, 2nd Ed. Blakiston Co., NY
Amlal H Wang Z & Soleimani M 1998 Potassium depletion down regulates chloride - absorbing transporters in rat kidney. *Journal of Clinical Investigation*. 101; 1045-1054
- 17- Shick BM, *etal* .1997: Periarteritis nodosa and temporal arthritis. *Collected Papers of the Mayo Clinic* 49; 381
- 18- Chercey CC, and Berger BJ, 2004: Laboratory Tests and Diagnostic Procedures, 4th ed. *Philadelphia: Saunders*.
- 19- Saadeh C, 1998: The erythrocyte sedimentation rate: old and new clinical applications. *South Med J*; 3: 220-5.
- 20- Paulus HE, and Brahn E.,2004 :Is erythrocyte sedimentation rate the preferable measure of the acute phase response in rheumatoid arthritis. *J Rheumatol* May; 31(5):838-40