

## Periodontal Health Status & Salivary Elements Analysis (Iron & Potassium) Among Group of Patients with Rheumatoid Arthritis & Chronic Periodontitis

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### ABSTRACT

**Background:** Periodontal diseases are common in the society & some researchers suggested an association between rheumatoid arthritis (RA) & periodontal diseases. The aim of the present study was to determine the periodontal health status in patient with RA & chronic periodontitis & compare it with those having chronic periodontitis only & determine the level of salivary elements; iron (Fe) & potassium (k) in both groups & compare it with control group & correlate between these salivary elements with the periodontal parameters plaque index (PLI), gingival index (GI), bleeding on probing (BOP), probing pocket depth (PPD) & clinical attachment level (CAL).

**Materials & Methods:** The samples were recruited from patients referred to department of rheumatology at Baghdad Hospital. Seventy five (75) patients participated in this study, twenty five of them had rheumatoid arthritis with chronic periodontitis; twenty five had chronic periodontitis only without arthritis & another twenty five patients were periodontally & systemically healthy (control group). The patients were with age range 40-50 years with no other systemic disease. Periodontal parameters were measured in all groups at four surfaces which include plaque index, gingival index, bleeding on probing, probing pocket depth & clinical attachment level. Salivary samples were collected under standardized condition & then analyzed for estimation of the level of potassium by using flame atomic absorption spectrophotometry (AAS) while the iron level by using spectrophotometric analysis.

**Results:** Patients with RA & chronic periodontitis had higher prevalence of site presenting dental, plaque, a higher rate of gingival inflammation & bleeding on probing, greater probing depth & clinical attachment level with a significant difference from the group of patients with chronic periodontitis alone without RA the results also revealed a higher concentration of iron & potassium among the rheumatoid arthritis group than the second & control group with a statistically highly significant difference between the three groups.

**Conclusion:** The results suggest higher potentiality for moderate to severe periodontitis involvement among RA patients with higher levels of salivary iron & potassium. The coexistence of RA & chronic periodontitis could possibly influence the inflammatory process & the pathogenesis of one disease on the other.

**KEYWORDS:** Rheumatoid arthritis, Chronic periodontitis, Salivary elements.

### INTRODUCTION

Periodontitis is an inflammatory disease of tooth supportive tissues & is characterized by destruction in periodontal ligaments & alveolar bone besides pocket formation & gingival recession.<sup>(1)</sup> Rheumatoid arthritis (RA) is thought to be an auto immune disease that affects several organs & systems & it is also associated

with destruction of joint connective tissue & bone.<sup>(2)</sup> It is a chronic destructive inflammatory disease characterized by the accumulation & persistence of an inflammatory infiltrate in the synovial membrane that leads to synovitis & the destruction of the joint architecture, deformity & loss of function (Figures 1,2).



(Figures 1&2) structural deformity of the hand joints. Permanent deformity is an unwanted result of the inflammatory process

An association between periodontitis & RA has been considered since 1820s. Both diseases are chronic & may present with bursts of disease activity. There is the possibility of a common genetic trait predisposing to both conditions (dysregulation of the inflammatory mechanisms). Porphyromonas gingivalis is a common pathogen in periodontal infection & it has

also been identified in synovial fluid. This periodontal pathogen may carry a unique risk for development of autoimmune antibodies associated with RA.<sup>(4)</sup>

Both periodontitis & RA present an imbalance between pro-inflammatory & anti-inflammatory cytokines which is responsible for the tissue damage. In this sense, both conditions are associated with

destruction of bones, mediated by inflammatory cytokines such as inter leukin-1, tumor necrosis factor- $\alpha$  & prostaglandin E<sub>2</sub>.<sup>(2,5)</sup> A bidirectional relationship of RA & periodontitis may involve RA affecting the pathogenesis of periodontitis & vice versa.<sup>(6)</sup>

Periodontitis might interfere with the pathogenesis of RA through bacteremia, presence of inflammatory mediators, bacterial antigens & immunoglobulins in the serum, while RA may influence the pathogenesis of periodontitis through its motor & emotional impairment. Motor impairment may make it more difficult to perform adequate oral hygiene. The salivary flow reduction due to medication or secondary Sjogren syndrome may increase supra gingival plaque formation in these individuals. Also psychological alterations found among RA patients were suggested as risk indicators for periodontitis.<sup>(7,8)</sup>

### Iron, Potassium & RA:

Iron is an essential element for nearly all living organisms by participating in a wide variety of important metabolic processes, such as oxygen transport (binding & release of hemoglobin), DNA synthesis, electron transport, lipid metabolism, photosynthesis & gene regulation.<sup>(9,10)</sup> The role of iron in patient with RA had been studied by spectrometric analysis & showed elevated concentration of iron in the synovial fluid of RA patients than normal subjects<sup>(11)</sup>. Also it has been found that patient with RA had low levels of iron in the serum which will lead to development of anemia termed as anemia of inflammation (AI).<sup>(12)</sup>

Potassium is a very important mineral for the proper function of all cells, tissues & organs in the human body. It is also an electrolyte that conducts electricity in the body. It is the major intra cellular ion that is crucial to heart function & plays a key role in skeletal & smooth muscle contraction. Also it has been suggested that increasing consumption of foods rich in potassium may play a role in osteoporosis prevention particularly among elderly women.<sup>(13,14)</sup> It has been found that patients with RA have lower salivary & serum potassium concentration than healthy subjects.<sup>(15)</sup> According to the National health & Nutrition Survey –III, serum of the patients with RA have been tested for potassium & they found 18% appeared to be in the normal range.<sup>(16)</sup>

According to our knowledge there is no study that determine the concentration of iron & potassium in the saliva of patients having both rheumatoid arthritis & chronic periodontitis, so it was decided to conduct this study to determine the periodontal health

status of those patients & measure the concentration of these two salivary elements & correlated with the periodontal parameters (PLI, GI, BOP, PPD & CAL).

### MATERIALS & METHODS

**Human sample:** subjects included in the study were drawn from patients attending the department of Rheumatology & dental department at Baghdad hospital from the period between June to September 2011. The sample is composed of 75 patients. The inclusion criteria for the total sample were: both genders, age between 40-50 years, must have not less than 4 periodontal sites with pocket depth of 4mm or greater, had good general health with no history of systemic disease (except RA) & had normal weight & length according to Body Mass Index (BMI) which is defined as weight in kilogram divided by the square of height in meters & its normal value is 18.5-25 because increase or decrease in weight may be a risk factor of RA. The exclusion criteria included: smoking, patients who undergone periodontal treatment &/ or antibiotic therapy for the last 3 months, females with pregnancy, breast feeding, postmenopausal status & contraceptive pills intake.

### Design of the Study:

All the individuals were informed of the purposes of the investigation. A questionnaire was designed & it include name, age, sex, medical & dental histories, use of medication & smoking. The sample was divided into 3 groups:

1. The first group was 25 patients (3 males & 22 females) diagnosed to have RA & chronic periodontitis. The diagnosis of RA was done according to the Revised criteria for the classification of RA of the American College of Rheumatology 1987,<sup>(17)</sup> also according to the laboratory investigation (ESR, Latex test). It was the first time for the patient to be diagnosed as having RA. The criteria for classification of RA include the following:
  - Morning stiffness in & around Joints lasting at least 1 hour before maximal improvement
  - Soft tissue swelling (arthritis) of 3 or more Joints areas observed by a physician
  - Swelling (arthritis) of the proximal interphalangeal, metacarpophalangeal or wrist joints
  - Symmetric swelling (arthritis)
  - Rheumatoid nodules
  - The presence of Rheumatoid factor
  - Radiographic erosions &/or periarticular osteopenia in hand &/or wrist joints

Criteria 1 through 4 must have been present for at least 6 weeks. RA is defined by the presence of 4 or more criteria.

It is important to mention for future researches that a new criterion of classification of RA had been developed in 2010.<sup>(18)</sup>

This new classification system redefines the current paradigm of RA by focusing at earlier stages of disease that are associated with persistent &/or erosive disease, rather than defining the disease by its late-stage features. This will refocus attention on the important need for earlier diagnosis of the disease to prevent or minimize the occurrence of the undesirable sequelae of the disease.<sup>(18)</sup>

2. The second group of the sample was 25 patients that had chronic periodontitis without RA. The patients had at least 4 sites with probing depth of 4mm or greater with clinical attachment loss of 1-2mm or greater.
3. The third group was another 25 patients with healthy periodontium & systemically healthy. The three groups were uniform with regard to age & sex. It is important to mention that women are more affected with RA than men in a ratio of 3:1 & has a peak incidence of onset in women in the fourth & fifth decades of life,<sup>(19)</sup> so our sample had more females than males (4 males & 22 females).

**Collection of Saliva:** Unstimulated salivary sample was collected. The patients were asked not to eat or drink except water one hour before collection & sited in a relaxed position. The saliva was collected in the floor of the mouth & then the patient let it drool passively over the lower lip into a cylinder until 5ml was collected. Then salivary samples were taken to the laboratory of poisoning center in the specialized surgery hospital, & centrifuged at 4000 rpm for 15min. the clear supernatant was separated by micropipette & stored at (-20Co) in a deep freeze till being assessed.

**Clinical Periodontal Examination:** All the patients underwent an oral examination by an experienced periodontist. The periodontal parameters that had been calibrated include:

1. PLI of Silness & Loe 1964.<sup>(20)</sup>
2. GI of Loe & Silness 1967.<sup>(21)</sup>
3. Bleeding on probing (BOP): a blunt periodontal probe was inserted to the bottom of periodontal pocket. If bleeding occur within 30 sec. after probing, the site was given a positive score (1) & a negative score (0) for the non bleeding site.<sup>(22)</sup>

4. Probing pocket depth (PPD): The distance from gingival margin to the most apical penetration of the periodontal probe was recorded.
5. Clinical attachment level (CAL): was calculated by adding the values of probing depth & the distance between the cement enamel junction (CEJ) & the gingival margin (GM), when the gingival margin was located apically to the CEJ. When the GM was located coronal to the CEJ, the value of the CEJ-GM distance was subtracted from the value of probing depth.

**Biochemical Analysis:** Frozen salivary samples were allowed to thaw & come to room temperature. The salivary elements F & K were analyzed at the poisoning consultation center/surgical specialty hospital. Potassium ion determined using flame atomic absorption spectrophotometer (Buck scientific, 210 VGP, USA) procedure by air-acetylene. The concentration level was expressed as (mmol/L) unit.

The method used to determine the level of salivary iron was by colorimetric method. A ready-made kit (Linear chemicals-Spain) was used according to the manufacturer instruction. The intensity of the color is proportional to the amount of iron in the sample & it was read at a wave length of 560 nm. The concentration level was expressed as  $\mu\text{mol/L}$  unit.

**Statistical analysis:** The data were processed & analyzed using the statistics package for social science SPSS Inc., version 17 for windows XP & excel 2007. Both descriptive & inferential statistics were used. *t*-test, chi-square, anova tests were used where indicated level of significance was 0.05.

## RESULTS

Seventy five patients were involved in this study & were subdivided as follows:

- 25 patients with rheumatoid arthritis & chronic periodontitis (RA group)
- 25 patients with chronic periodontitis only (CP group)
- 25 patients were periodontally & systemically healthy (control group).
- Table 1 showed that the mean PLI in RA group (1.837) was significantly higher than the CP group (1.149).
- Table 2 showed that the mean GI in RA group (1.319) was significantly higher than CP group (1.141).
- Table 3 showed than number & percentage of bleeding sites in RA group which was higher (70.1%) than CP group (55.8%) with significant difference.
- Mean PPD & CAL among RA group was found higher than CP group with a highly significant dif-

ference as seen in tables 4&5.

Regarding the K ion concentration among the three groups, it was found that the mean level of K ion in both RA group & CP group was higher than the control group expressed in  $\mu\text{mol}/\text{c}$  (table 6). Inter group comparison of K level concentration revealed a highly significant difference between different groups (table 7). Also comparison between the three groups by applying F test revealed a highly significant difference (table 8).

The mean concentration of salivary iron in RA group was found much higher than both CP & control group expressed in  $\mu\text{mol}/\text{c}$  (table 9). Inter group comparison revealed a highly significant difference between different groups (table 10) & by applying (Table 1) Mean and SD of Pl among group I and group II

Groups	Mean	SD	t-test	P-value	Sig
Group I	1.837	0.255	7.981	0.001	HS
Group II	1.149	0.113			

$P < 0.01$  highly significant

(Table 2) Mean and SD of GI among group I and group II

Groups	Mean	SD	t-test	P-value	Sig
Group I	1.319	0.076	8.641	0.002	HS
Group II	1.141	0.069			

(Table 3) Number and percentage of bleeding sites among group I and group II

Scores of BOP	Group I		Group II		Chi-square	P-value	Sig
	No.	%	No.	%			
0	582	29.9	828	44.2	79.81	0.049	S
1	1364	70.1	1044	55.8			

\* $P < 0.05$  Significant

(Table 4) Mean and SD of PPD among group I and group II

Groups	Mean	SD	t-test	P-value	Sig
Group I	6.065	0.547	12.146	0.028	S
Group II	4.296	0.479			

(Table 5) Mean and SD of CAL among group I and group II

Groups	Mean	SD	t-test	P-value	Sig
Group I	4.472	0.408	5.618	0.007	HS
Group II	3.684	0.569			

(Table 6) Mean and SD of K ion concentration among the three groups

Groups	Mean (mmol/L)	SD
Group I	11.424	2.06
Group II	10.553	1.992
Group III	9.112	1.368

F test the comparison between the three groups was found highly significant (table 11). The correlations between clinical periodontal parameters & salivary constituents K & iron among RA & CP groups were shown in table 12. In this table the correlations between K & iron levels & plaque index in both groups were mostly weak in negative direction, while the correlations with GI were varies between weak not significant positive & negative directions.

The only significant strong negative correlation was found between the level of salivary ZK ion among RA group & bleeding on probing (-0.608).

Negative & positive weak non significant correlations were also found between K & iron levels of both groups with PPD & CAL

Table (7) Inter group comparison of K level concentration

Groups	t-test	P-value	Sig
GroupI&groupII	6.239	P<0.01	HS
GroupI&groupIII	4.596	P>0.01	HS
GroupII&groupIII	6.501	P<0.01	HS

(Table 8) Comparison between the three groups regarding the K ion concentration

Groups	ANOVA F-test	P-value	Sig
GroupI,II,III	40.183	P<0.01	HS

(Table 9) Mean and SD of Fe ion concentration among the three groups

Groups	Mean(μmol/L)	SD
GroupI	9.504	3.428
GroupII	5.913	3.559
GroupIII	2.80	1.104

(Table 10) Inter group comparison of Fe level concentration

Groups	t-test	P-value	Sig
GroupI&groupII	2.478	0.021	S
GroupI&groupIII	6.096	P<0.01	HS
GroupII&groupIII	4.159	P<0.01	HS

(Table 11) Comparison between the three groups regarding the Fe concentration

Groups	ANOVA F-test	P-value	Sig
GroupI,II,III	19.97	P<0.01	HS

(Table 12) Correlation between clinical periodontal parameters and biochemical parameters

			PI	GI	BOP	PPD	CAL
Group I	K	r	-0.262	0.123	-0.608	0.088	-0.213
		p	0.206	0.557	0.001	0.676	0.307
	Fe	r	-0.178	-0.138	-0.246	-0.257	0.193
		p	0.396	0.510	0.235	0.214	0.350
Group II	K	r	-0.303	-0.101	-0.142	-0.268	0.125
		p	0.140	0.630	0.497	0.196	0.552
	Fe	r	-0.151	0.181	0.068	-0.117	0.193
		p	0.471	0.387	0.748	0.578	0.354

## DISCUSSION

Periodontal disease & its mechanism of inflammatory reactions result in the destruction of tissue & bone in a pattern similar to that which mediate destruction of soft tissue & erosion of bone in rheumatoid arthritis. In both conditions a persistent inflammatory reaction occurs in areas composed of connective tissue & bone with the activation of complement, production of cytokines & release of other inflammatory cell products.<sup>(6,23)</sup>

The literature regarding the relationship between periodontal disease & rheumatoid arthritis is controversial. The methodologies applied in the studies are as diverse as their results & conclusions.<sup>(7)</sup> When compared saliva constituents with other studies, one must keep in mind differences in age groups, type of saliva collected (stimulated or non-stimulated), way of collection, flow rate, diet that may affect composition of saliva, the variation in sampling procedure as well as technique of analysis which may

explain the differences in the result of the studies.<sup>(24)</sup>

In this study & regarding the periodontal health status of the two main groups which were the RA group & CP group, it was found that both mean plaque & gingival indices & the number & percentage of bleeding sites were significantly higher in RA group than CP group & this could be attributed to the stiffness of hand muscles & inability of the patient to remove all dental plaque which is the main causative factor of gingival inflammation, so this reduction in hands muscle function lead to difficulty in performing adequate oral hygiene. Moreover, interesting observations regarding the complexity of the oral & systemic challenge provide unique mechanisms by which dysregulation of host responses could occur.<sup>(7,25)</sup> The higher levels of periodontal inflammation in RA patient group than other groups are in conformity with Mirrielees 2010.<sup>(26)</sup>

The mean values of PPD & CAL in RA group were significantly higher compared to CP group & this could be related to local & systemic factors. The local factor is dental plaque & the systemic factor is the defect in the immune system which could result in inflammatory-mediated destruction predisposing them to periodontitis due to an unbalanced cytokine expression profile.<sup>(2,7)</sup> Regarding the salivary concentration of K ion & iron in the RA group which had at the same time chronic periodontitis. We could not find a similar study which measures the concentration of these two elements in the saliva of patients having both these diseases to compare with it. The researchers either measure the levels of these elements in one of these diseases or measure them in the serum & not saliva. However, in this study, it was found that the mean K ion concentration was higher in RA group than the chronic periodontitis group & the control group. This result disagrees with the study done by Rastmanesh R 2009<sup>(15)</sup> who found lower salivary & serum K concentration in patients with RA. An explanation for this difference is that in the previous study, the patients had only RA without chronic periodontitis. So the coexistence of RA & periodontitis would offer an interesting opportunity to study the possible influence of periodontal inflammatory process on RA progression. Regarding the salivary iron concentration of patients with RA & CP, it was found higher than the second group & higher than the control group. In a possible explanation for this result, we have to know the following: during inflammation, T cells & macrophages produce a number of cytokines which influence the metabolism of iron, affecting its

cellular uptake, transport, storage as well as its absorption.<sup>(27)</sup> This will result in the development of anemia of inflammation (AI) which is most common condition in patients with rheumatic disease & it is characterized by low to normal serum iron levels, low serum iron binding capacity & normal to elevated ferritin concentrations (Ferritin is iron storage protein).<sup>(11)</sup> Transferrin which is the iron transport protein have the function of controlling the level of iron in biological fluids, it allow ferric iron to remain soluble & facilitates the cellular import of iron.<sup>(28)</sup> Transferrin has an extremely high affinity for binding iron, it contain two specific high affinity iron binding sites. Transferrin was found localized within the cells of striated ducts, in some intercalated ducts as well as in serous acinar cells of salivary glands of patients with RA, & because transferrin has a high affinity for iron, this could explain increase iron in saliva of patient with RA.<sup>(29)</sup>

## CONCLUSION

In conclusion, patients with RA have a higher level of periodontal inflammation, higher levels of salivary iron & potassium than patients without RA.

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