

Pavle Picek<sup>1</sup>, Ana Andabak Rogulj<sup>2</sup>, Vanja Vučićević Boras<sup>2</sup>, Vlaho Brailo<sup>2</sup>, Livija Cigic<sup>3</sup>, Ivana Canjuga<sup>4</sup>, Blaženka Ladika-Davidović<sup>4</sup>

## Serumski i salivarni parametri kod oboljelih od rekurentnih aftoznih ulceracija

### *Serum and Salivary Parameters in Patients with Recurrent Aphthous Ulcerations*

<sup>1</sup> Dom zdravlja – istok, Zagreb  
Dental Unit Zagreb- East

<sup>2</sup> Zavod za oralnu medicinu Stomatološkog fakulteta Sveučilišta u Zagrebu  
Department of Oral Medicine, School of Dental Medicine, University of Zagreb

<sup>3</sup> Medicinski fakultet Sveučilišta u Splitu  
Medical School University of Split

<sup>4</sup> Klinika za stomatologiju Kliničkog bolničkog centra Zagreb, Hrvatska  
Dental Clinic, University Hospital Centre Zagreb, Croatia

<sup>5</sup> Zavod za onkologiju i nuklearnu medicinu KBC Sestara milosrdnica, Zagreb  
Department of Oncology and Nuclear Medicine, Clinical Hospital Centre Sisters of Mercy, Zagreb

#### Sažetak

**Svrha:** Rekurentne aftozne ulceracije (RAU) bolest je nepoznate etiologije koju posreduju T- limfociti, a uglavnom se pojavljuje uz neke druge bolesti poput imunodeficijenje, hematoloških deficit, preosjetljivosti na određenu vrstu hrane i gastrointestinalnih bolesti. Ipak, to što oboljeli od RAU-a imaju hematološke deficitne još je uvijek kontroverzno pitanje, kao i utjecaj stresa na pojave rekurentne aftozne ulceracije. **Ispitanici i postupci:** Od 30 bolesnika s RAU-om ( $36,27 \pm 15,308$  godina) i 30 kontrolnih ispitanika ( $29,83 \pm 9,082$  godina) uzeto je po pet mililitara krv kako bi se odredile vrijednosti željeza, vitamina B12 i folne kiseline te po dva mililitra sline zbog određivanja vrijednosti salivarne alfa-amilaze enzymskim imunotestom. Svi sudionici ispunili su i ljestvicu stresa. **Rezultati:** Prema rezultatima ovog istraživanja nije bilo razlike u vrijednostima serumskog željeza, vitamina B12 i folne kiseline između bolesnika s RAU-om i sudionika u kontrolnoj skupini. Osim toga nije bilo razlike ni u razini salivarne alfa-amilaze između bolesnika s RAU-om tijekom akutne faze i remisije u usporedbi s kontrolnom skupinom, kao što nije bilo razlike u broju stresnih dogadaja između 3 ispitane skupine. **Zaključak:** Kod oboljelih od RAU-a nije indicirano rutinsko određivanje navedenih hematoloških parametara. Nadalje, razina salivarne amilaze i ljestvica stresa ne pokazuju da su pacijenti s RAU-om više u stresu od sudionika u kontrolnoj skupini.

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#### Adresa za dopisivanje

Ana Andabak, dr. med. dent.  
Sveučilište u Zagrebu  
Stomatološki fakultet  
Zavod za oralnu medicinu  
Gundulićeva 5, 10 000 Zagreb  
Tel: + 1 4802 111  
Fax: + 1 4802 159  
anaandabak@gmail.com

#### Ključne riječi

stres; alfa amilaza; željezo; vitamin B12; folna kiselina; rekurentne aftozne ulceracije

## Uvod

Rekurentne aftozne ulceracije (RAU) bolest je posredovana T-limfocitima na još nepoznati antigen. RAU karakterizira povremena pojava ulceracija u usnoj šupljini. Iz literature je poznato da genetski čimbenici, imunodeficijenje, ciklička neutropenija, hematološki deficit, gastrointestinalne bolesti, trauma, preosjetljivost na određenu vrstu hrane i stres mogu pogodovati nastanku te bolesti (1).

Ipak, s obzirom na podatke iz literature još postoje kontradikcije o tome treba li takve bolesnike rutinski slati na pretrage kojima se određuju serumsko željezo, vitamin B12 i folna kiselina.

Compilato i suradnici (2) ustanovili su hematološke deficitne, odnosno nedostatak željeza, folne kiseline i vitamina

## Introduction

Recurrent aphthous ulceration (RAU) is a T-cell mediated disease to a still unknown antigen. RAU are characterized with periodic appearance of ulcerations in the oral cavity. Literature data indicate that genetic heritage, immunodeficiencies, cyclic neutropenia, haematological deficiencies, gastrointestinal diseases, trauma, intolerance to certain food types and stress might contribute to the RAU development (1).

However, so far published literature data revealed contradictory results regarding the fact whether RAU patients should be routinely sent to iron, vitamin B12 and folate assays.

Compilato et al. (2) reported that iron, vitamin B12 and folate deficiency was found in 56% of RAU patients and in

B12 kod 56 posto oboljelih od RAU-a, a u kontrolnoj skupini kod samo sedam posto sudionika. Isti autori (2) zaključili su da se oboljeli od RAU-a moraju rutinski poslati na pretrage željeza, folne kiseline i vitamina B12.

Burgan i njegovi kolege (3) istaknuli su da oboljeli od RAU-a češće imaju hematološke deficite, posebice manjak B12 u odnosu prema kontrolnoj skupini.

Koybasi i suradnici (4) pronašli su da je 35 posto bolesnika s RAU-om imalo manjak vitamina B12 u usporedbi s kontrolnom skupinom. Porter i njegov tim (5) istaknuli su da su ustanovili mnogo nižu razinu serumskog feritina kod oboljelih od RAU-a (11,6%) u odnosu prema kontrolnoj skupini (4,9%). S druge strane, Wray i njegovi kolege (6) nisu ustanovili čest deficit željeza kod oboljelih od RAU-a. Takav su nalaz potvrdili Piskin i suradnici (7), Olson i njegovi kolege (8) te Koybasi sa suradnicima (4).

Pojava rekurentnih afroznih ulceracija povezuje se sa stresom te smo ljestvicom stresa i mjerjenjem salivarne alfa-amilaze (ekvivalent je mjerenu razinu kortizola) pokušali ustanoviti jesu li oboljeli od RAU-a više u stresu od sudionika u kontrolnoj skupini. U nekoliko istraživanja nastanak te bolesti povezuje se sa stresom i anksioznosću, iako se dobiveni rezultati jako razlikuju. Naime, poznato je da se nastanak RAU-a povezuje sa stresnim situacijama, poput polaganja ispita, stomatoloških zahvata te velikih i važnih promjena u životu, poput novog posla, selidbe, obiteljskih problema, itd (9).

Istraživanje Galla i suradnika (10) pokazuje koliko psihološki stres može utjecati na pojavu RAU-a kao *trigger* ili modificirajući čimbenik, a ne uzrok bolesti jer nije ustanovljena izravna korelacija. Albanidou-Farmaki i suradnici (11) zaključili su da stres može biti jedan od etioloških čimbenika u nastanku RAU-a jer su razina salivarnog i serumskog kortizola te rezultati testova anksioznosti bili značajno viši nego u kontrolnoj skupini.

### Ispitanici i postupci

Prije početka rada Etičko povjerenstvo Stomatološkog fakulteta u Zagrebu odobrilo je istraživanje. Svi ispitanici sudjelovali su dobrovoljno, što su potvrdili potpisivanjem informativnog pristanka. Bili su također obaviješteni o tome što se želi postići istraživanjem i o načinu na koji se provodi. Nitko nije odbio sudjelovati.

Istraživanje je provedeno na 30 ispitanika oboljelih od RAU-a (20 žena i 10 muškaraca) liječenih 2010. i 2011. godine u Zavodu za oralnu medicinu Stomatološkog fakulteta u Zagrebu. Prosječni dobit oboljelih ispitanika iznosi je  $36,27 \pm 15,308$  godina, a onih u kontrolnoj skupini  $29,83 \pm 9,082$ . Dijagnoza RAU-a potvrđena je na temelju anamneze, kliničkog pregleda sluznice usne šupljine i ekskuluzije drugih oralnih bolesti.

Kontrolnu skupinu činilo je 30 sudionika (20 žena i 10 muškaraca), inače zaposlenika i studenata Stomatološkog fakulteta u Zagrebu. Nitko od njih nije imao bolesti sluznice usne šupljine, što je potvrđeno kliničkim pregledom.

Svim ispitanicima uzeti su uzorci krvi iz antekubitalnih vena kako bi se dobole vrijednosti željeza, vitamina B12 i folne kiseline. Količina željeza u krvi određena je spektrofotometrijskom metodom. Vrijednosti vitamina B12 i folne kise-

only 7% of the controls. The same authors (2) concluded that patients with RAU should be routinely sent to iron, vitamin B12 and folate analysis. Burgan et al. (3) concluded that RAU patients more frequently have vitamin B12 deficiency than the healthy controls.

Koybasi et al. (4) reported that 35% of RAU patients had vitamin B12 deficiency when compared to the control group. Porter et al. (5) found out that serum ferritin levels were significantly decreased in RAU patients (11.6%) in comparison to the control group (4.9%). On the other hand, Wray et al. (6) did not confirm that patients with RAU are iron deficient. Such finding was confirmed by Piskin et al. (7), Olson et al. (8) as well as by Koybasi et al. (4).

The RAU appearance is said to be correlated with stress and that is why we measured levels of salivary alpha amylase in RAU patients. Only few literature data report connection between RAU and stress, despite the fact that RAU patients often report that stress preceded the RAU appearance. The RAU appearance is correlated with the period of university exams, attendance to the dental setting, and periods of major life events such as a new job, moving to new home, family problems, etc. (9). Gallo et al. (10) concluded that stress might be the precipitating factor in the RAU appearance. However, the direct relationship has not yet been established. Albanidou-Farmaki et. al. (11) concluded that stress might precede RAU development as salivary and serum cortisol as well as anxiety test were significantly higher when compared to the controls.

### Material and Methods

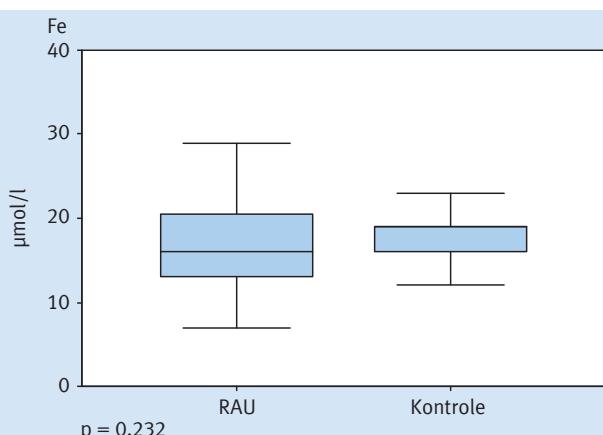
This study was approved by the Ethical Committee of the School of Dental Medicine in Zagreb. All subjects participated voluntarily and were informed about the purpose of this study. Their compliance was validated using questionnaires. None of the subjects refused to participate in this study. Research was conducted on 30 participants suffering from RAU (20 female and 10 male) who were treated during the years 2010 and 2011 at the Department of Oral Medicine, School of Dental Medicine in Zagreb. The mean age of participants suffering from RAU was  $36,27 \pm 15,308$  years, whereas participants of the control group were  $29,83 \pm 9,082$  years. The diagnosis of RAU was made on the basis of a detailed medical history, clinical examination and exclusion of other oral diseases. The control group consisted of 30 participants (20 female and 10 male) who were all employees and students of the School of Dental Medicine in Zagreb. The control group consisted of participants without oral diseases, which was confirmed by clinical examination. Blood samples were taken from antecubital veins in order to obtain the values of iron, vitamin B 12 and folic acid. Iron was measured by use of spectrophotometric method. Vitamin B 12 and folic acid levels were analysed on

line dobivene su na standardnim kitovima (Abbott IMx B12 and folate assay, Abbott Park, IL, USA) poluautomatiziranim analizom na uređaju IMx. Taj instrument automatski pipetira uzorak bolesnika i reagense te mjeri koncentraciju uporabom fluorescentnog signala. Analiza vitamina B12 sastoji se od uporabe mikropartikula presvučenih IF-om. Granica detekcije je 60 pg/ml i CV je sedam posto.

Svakom sudioniku u istraživanju uzeta su dva mililitra sline, te su vrijednosti salivarne alfa-amilaze određene enzymskim imunotestom.

## Rezultati

Normalnost distribucije testirana je Shapiro-Wilksovim testom. Budući da vrijednosti nisu bile normalno distribuirane, za analizu su odabrane neparametrijske metode. Vrijednosti salivarne alfa-amilaze izražene su kao medijan  $\pm$  standardna pogreška. Razlike među skupinama testirane su Kruskal-Wallisovim testom. P-vrijednosti manje od 0,05 ( $p<0,05$ ) smatrane su statistički značajnima.



**Slika 1.** Razina serumskog željeza kod oboljelih od RAU-a i sudionika u kontrolnoj skupini

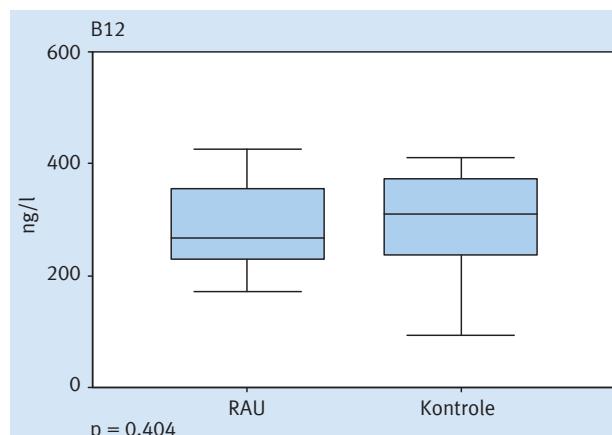
**Figure 1** Serum iron levels in patients with RAU and controls.

the standard kits (Abbott Imx B12 and folate assay, Abbott Park, IL) using semi-automated analysis on IMx instrument. This instrument automatically pipettes patient sample and reagents in order to measure the concentration of vitamin B12 and folate by use of the fluorescent signal. Vitamin B12 analysis consists of usage of microparticles coated with IF. The detection limit is 60 pg/ml and CV is 7%.

Every participant gave a sample of saliva (2 ml) in order to determine salivary alpha amylase levels by the use of enzyme immune test.

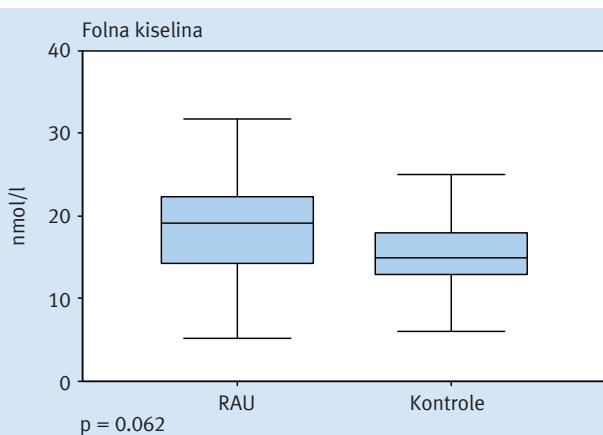
## Results

Normality of distribution was tested by Shapiro Wilks test. Due to abnormal distribution of the data, the non-parametric methods were used. Values of alpha amylase were expressed as median  $\pm$  standard error. Differences between groups were tested by Kruskal Wallis test; p values lower than 0.05 ( $p<0.05$ ) were considered statistically significant.



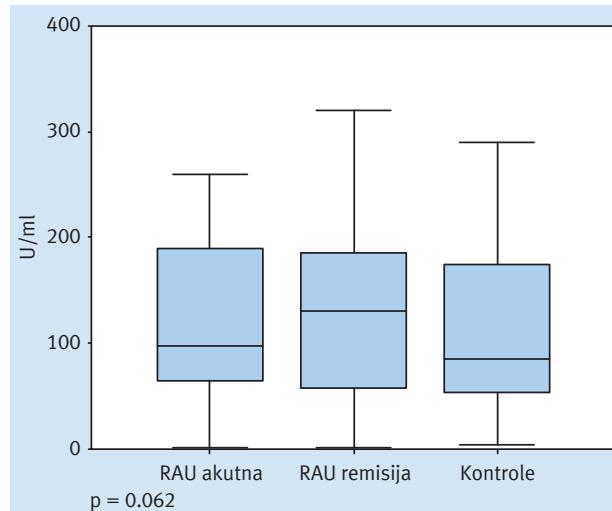
**Slika 2.** Razina vitamina B12 u serumu oboljelih od RAU-a i sudionika u kontrolnoj skupini

**Figure 2** Vitamin B 12 serum levels in RAU patients and controls.



**Slika 3.** Razina folne kiseline u serumu oboljelih od RAU-a i sudionika u kontrolnoj skupini

**Figure 3** Folic acid serum levels in RAU patients and controls.



**Slika 4.** Koncentracije salivарне alfa-amilaze u svim trima skupinama испитаника

**Figure 4** Salivary amylase concentrations in all three groups

**Tablica 1.** Vrijednosti promatranih parametara kod ispitanika i u kontrolnoj skupini  
**Table 1** Values of observed parameters in RAU patients and control group

	Ispitanici • RAU patients	Kontrole • Controls	p
Željezo • Fe (median ± SEM)	16 ± 1.17	19 ± 0.91	0.232
B <sub>12</sub> (median ± SEM)	268 ± 17.05	310 ± 27.91	0.404
folna kiselina • Folic acid (median ± SEM)	19.2 ± 1.44	15 ± 1.10	0.062

**Tablica 2.** Koncentracije salivarne alfa-amilaze kod pacijenata s RAU-om i sudionika u kontrolnoj skupini  
**Table 2** Salivary alpha amylase concentrations in RAU patients and controls

Salivarna alfa- amilaza • Salivary alpha amylase (median ± SEM)	RAU patients		Kontrolna skupina • Controls 85 ± 29.6
	Akutna faza • Acute phase 97 ± 21.6	Remisija • Remission 130 ± 26	

Nisu pronađene statistički značajne razlike između skupina (p=0,723) • No significant differences were observed between the three groups (p=0.723).

## Rasprava

Barnadas i suradnici (12) zaključili su da bolesnici s RAU češće imaju nedostatak željeza, vitamina B12 i folne kiseline, iako – kada se promatraju navedeni elementi – pojedinačno nema razlike u odnosu prema bolesnicima s ostalim oralnim bolestima.

Porter i suradnici (5) istaknuli su da su razina hemoglobina i indikatori stanja crvenih krvnih stanica bili normalni kod bolesnika s RAU-om. Ipak, kako se nije istraživala razina željeza, vitamina B12 i folne kiseline dopuštaju mogućnost da su neki bolesnici imali manjak tih elemenata.

Piskin i suradnici (7) istraživali su kod 35 bolesnika s RAU-om razinu željeza, folne kiseline i vitamina B12 te ustanovili da je razina serumskog vitamina B12 kod njih bila znatno niža u odnosu prema 26 kontrolnih ispitanika.

Burgan i suradnici (3) istaknuli su da je od 143 bolesnika s RAU-om njih 14 posto bilo anemično, 16,8 posto imalo je sniženi serumski feritin, 26,6 posto imalo je sniženi serumski vitamin B12, a 4,9 posto sniženu razinu serumske folne kiseline. U kontrolnoj skupini je 10,5 posto sudionika bilo anemično, 9,8 posto imalo je sniženu razinu serumskog feritina, 12,6 posto imalo je sniženi serumski vitamin B12, no nitko nije imao manjak serumske folne kiseline.

Ustanovljena je velika razlika između ispitne i kontrolne skupine kad je riječ o razini folne kiseline. Kako navode Thongprasom i suradnici (13), serumska razina vitamina B12 bila je unutar normalnih raspona i u ispitnoj i u kontrolnoj skupini kao i hemoglobin i hematokrit. Ti rezultati u suprotnosti su s rezultatima iz ovog istraživanja jer u našem uzorku nije bilo značajnih razlika između oboljelih od RAU-a i kontrolne skupine, a s obzirom na vrijednosti serumskog željeza, vitamina B12 i folne kiseline.

Za 58 oboljelih od RAU-a ustanovljeno je da im je trajanje epizoda, broj ulceracija i razina боли bila jako snižena nakon pet i šest mjeseci terapije vitaminom B12, neovisno o tome jesu li prije bili deficijentni ili ne. Tijekom petog mjeseca liječenja najveći dio bolesnika s RAU-om iz ispitne skupine bio je bez rekurentnih aftoznih ulceracija (74,1% versus 32,0%;). Kako izvještava Carrozzo (14), liječenje vitaminom B12 jednostavno je, jeftino i bez rizika te se čini da pomaže oboljelima, neovisno o razini serumskog vitamina B12.

## Discussion

Barnadas et al. (12) reported that patients with RAU are prone to iron, vitamin B12 and folate deficiencies although when the investigated factors were analysed separately, there were no significant differences between patients with RAU and patients with other oral diseases.

Porter et al. (5) concluded that haemoglobin levels as well as other parameters regarding red blood cells were normal in patients with RAU. However, they did not look for iron, vitamin B12 and folate.

Piskin et al. (7) found vitamin B12 deficiencies in patients with RAU but none of the tested patients had either iron or folic acid deficiency.

Burgan et al. (3) reported that patients with RAU were iron, vitamin B12 and folate deficient, whereas in the control group, none of the participants were folate deficient.

Significant difference between study and control group was found regarding serum folate levels. However, serum vitamins B12 as well as haemoglobin and haematocrit levels were within a normal range in both groups, which was reported by Thongprasom et al. (13). This result is in contrast with the results of this study as there were no significant differences between patients with RAU and controls regarding serum iron, vitamin B12 and folate levels.

Carrozzo (14) concluded that patients with RAU should be given vitamin B12 regardless being deficient or not because the duration of RAU episodes, number of ulcerations and pain scores were significantly decreased after the 5<sup>th</sup> and 6<sup>th</sup> month of replacement therapy with vitamin B12.

Compilato et al. (2) found that out of 32 patients with RAU, 56.2% had haematinic deficiencies. Therefore, the same authors (2) concluded that in every patient with RAU, serum iron, vitamin B12 and folate should be determined.

Volkov et al. (15) reported that vitamin B12 therapy is efficient, cheap and without any side effects in patients with RAU, regardless of their vitamin B12 status, since significant number of patients with RAU were disease free after vitamin B12 therapy (1000 mcg during six months).

Gulcan et al. (16) found that 37 patients with RAU out of 72 were vitamin B12 deficient. Their results are in contrast with the results of this study since only two patients with RAU were vitamin B12 deficient. The same authors (14) also

Compilato i suradnici (2) su, prateći 32 bolesnika s RAU-om, ustanovili kod njih 56,2 posto hematološke deficite u odnosu prema sedam posto sudionika u kontrolnoj skupini, što se pokazalo statistički značajnom razlikom. Kod oboljelih od RAU-a koji nisu imali obiteljsku predispoziciju, pojavila se nakon nadomjesne vitamske terapije potpuna rezolucija RAU-a. Osobama s RAU s obiteljskom predispozicijom, nakon nadomjesne terapije bolest se rijede pojavljivala i bila je slabijeg intenziteta. Nakon logističkog regresijskog modela zaključeno je da je samo obiteljska predispozicija povezana s nastankom RAU-a. Isti autori (2) istaknuli su kako su svakom bolesniku s RAU-om potrebna rutinska hematološka testiranja i testovi razine željeza, folne kiseline i vitamina B12.

Rezultati dvostrukoga slijepog placebo-istraživanja Volkova i suradnika (15) pokazuju da je između 31 bolesnika s RAU-om u posljednjem mjesecu uzimanja vitamina B12 (tj. tijekom petog mjeseca) postojala znatna razlika u odnosu prema sudionicima u kontrolnoj skupini koji su također patili od RAU-a, ali nisu dobivali terapiju vitaminom B12. Naime, znatan broj osoba više nije imao RAU. Isti autori (13) zaključuju da je liječenje vitaminom B12 (1000 mcg tijekom šest mjeseci) jednostavno, jeftino i nerizično, a učinkovito ako osoba pati od RAU-a, neovisno o razini serumskog vitamina B12.

Gulcan i suradnici (16) su među svim ispitanicima – a bila su 72, kod njih 37 dokazali nedostatak vitamina B12 (manje od 140 pg/mL), a 35 je imalo normalnu razinu cijanokobalamina (više od 140 pg/mL). To je također u suprotnosti s rezultatima u ovom istraživanju jer se kod oboljelih od RAU-a u ovom istraživanju nije pronašao znakovit deficit B12 u odnosu prema kontrolnoj skupini. U obje je skupine nakon terapije vitaminom B12 ustanovljen znatan porast vrijednosti toga vitamina u serumu. Kod tih osoba znatno je pala učestalost RAU-a – kod 96 posto nastalo je poboljšanje, a četiri posto sudionika nije reagiralo na terapiju. Isti autori (16) zaključuju da cijanokobalamin koristi bolesnicima s RAU-om čak ako su njegove vrijednosti u serumu normalne jer je kod oboljelih vjerojatno potrebna veća zaštita oralne sluznice, što se postiže većim dozama cijanokobalamina.

Kako navode Koybasi i suradnici (4), kod 34 bolesnika s RAU-om jedino je ustanovljen znatan manjak serumskog vitamina B12 u odnosu prema sudionicima u kontrolnoj skupini, a s obzirom na sve druge obavljene hematološke teste, poput folne kiseline, kalcija i fosfora u serumu. To je u suprotnosti s rezultatima našeg istraživanja.

Rezultati istraživanja MacPhaila i Greenspana (17) pokazuju da manjak vitamina B12 ili folne kiseline nije bio znakovit čimbenik rizika za nastanak RAU-a, što je u skladu s rezultatima ovog istraživanja.

Olson i suradnici (8) ustanovili su kod 90 bolesnika s RAU-om poremećaj u kompletnoj krvnoj slici i serumskom željezu, no nitko nije imao poremećaje u serumskom vitamINU B12 ili razini folne kiseline bilo u serumu bilo u eritrocitima. Isti autori (8) zaključuju kako oboljelima od RAU-a, osim kompletne krvne slike, nije indicirano određivanje željeza, folne kiseline ili vitamina B12. Takav se nalaz slaže s rezultatima ovog istraživanja jer nije bilo značajnih razlika u razini željeza, vitamina B12 i folne kiseline između oboljelih od RAU-a i sudionika u kontrolnoj skupini.

reported that 90% of patients were free of RAU after vitamin B12 replacement therapy.

Koybasi et al. (4) found that patients with RAU suffered from vitamin B12 deficiency; however none of the patients had folic acid deficiency. The latter finding is in concordance with the results of this study.

MacPhail and Greenspan (17) concluded that vitamin B12 or folate deficiency is not an important factor in patients with RAU, which is in concordance with the results of this study.

Olson et al. (8) found abnormalities in complete blood count and serum iron levels in patients with RAU. However, none of the tested patients was either vitamin B12 or folate deficient. The same authors (8) concluded that vitamin B12 and folate levels should not be routinely recommended in RAU patients.

Tang et al. (18) reported that psychological disturbances caused by stressful life events in persons with certain personalities might lead to the RAU appearance. The results of this study showed that there were no differences in the number of stressful life events between patients with RAU and controls. McCartan et al. (19) concluded that average cortisol values were significantly increased in RAU patients and therefore suggested that stress might have an important role in the RAU aetiology, especially in persons who are prone to anxiety.

This finding is in contrast with the results of our study since there were no differences between patients with RAU and controls regarding stress scores.

Soto-Araya et al. (20) found that RAU are significantly correlated with stress and anxiety.

Albanidou-Farmaki et al. (11) found that salivary and serum cortisol levels were increased in RAU patients when compared to the controls. This finding is in contrast with the results of this study since we found no significant differences in salivary alpha amylase levels between patients with RAU and the controls. Pedersen (21) reported that the level of psychological stress was not significantly different in patients with RAU, either during the acute phase or during the remission period. This result is again in concordance with the results of our study since there were no significant differences in salivary amylase levels between the two phases of RAU and in comparison to the controls. Activity of salivary alpha amylase might reflect catecholamine serum levels in various stress situations (22). Patients with chronic pain have significant association between salivary alpha amylase levels and pain scales (23). Therefore, we determined salivary alpha amylase levels in order to investigate whether patients with acute RAU are more stressed in comparison to the ones during remission period and the controls which wasn't confirmed by this investigation. So far, in the published literature there are no data regarding salivary alpha amylase in oral diseases, i.e. RAU disease.

Tang i suradnici (18) ustanovili su da psihološki poremećaji uzrokovani različitim događajima mogu kod nekih ljudi potaknuti RAU. Rezultati ovog istraživanja pokazuju da nije bilo razlike u broju stresnih događaja između oboljelih od RAU-a i onih u kontrolnoj skupini.

McCartan i suradnici (19) zaključili su da stres može imati važnu ulogu u etiologiji RAU-a, posebice kod osoba sklonih anksioznosti. Ovaj nalaz nije u skladu s rezultatima toga istraživanja jer nije bilo razlike u razini stupnja stresa između osoba s RAU-om i kontrolne skupine.

Soto-Araya i suradnici (20) ustanovili su povezanost između stresa i anksioznosti kod bolesnika s RAU-om.

Rezultati istraživanja Elene Albanidou-Farmaki i suradnika (11) pokazuju da stres može biti uključen u patogenetu RAU-a jer su koncentracija salivarnog i serumskog kortizola i stupanj anksioznosti bili znatno veći kod oboljelih u odnosu prema sudionicima u kontrolnoj skupini.

U istraživanju Lidiye Pedersen (21) sudjelovala su 22 bolesnika s RAU-om te im je u akutnoj fazi i u remisiji ispitivan stupanj psihološkog stresa i vizualna analogna ljestvica, no nisu ustanovljene razlike između dviju faza bolesti s obzirom na spomenute parametre. Zato autorica zaključuje kako nema povezanosti između psihološkog stresa i recidiva RAU-a.

Istaknuto je da aktivnost salivarne alfa-amilaze može biti pokazatelj razine kateholamina u plazmi u različitim stenskim uvjetima (22). U istraživanju na bolesnicima koji pate od kronične boli ustanovljena je značajna povezanost između razine salivarne alfa-amilaze i ljestvice boli (23). Zato smo oboljelima od RAU-a odredili vrijednosti salivarne alfa-amilaze kako bismo vidjeli koliko su ti pacijenti u akutnoj fazi bolesti u stresu, što rezultati našeg istraživanja nisu pokazali. U literaturi nema podataka o vrijednostima salivarne alfa-amilaze kod oralnih bolesti, odnosno RAU-a.

## Zaključak

Rezultati ovog istraživanja pokazuju kako oboljeli od RAU-a ne trebaju rutinski obavljati testove određivanja serumskog željeza, vitamina B12 i folne kiseline. Razine salivarne alfa-amilaze i ljestvica stresa ne upućuju na to da su pacijenti s RAU-om više u stresu od sudionika u kontrolnoj skupini.

## Conclusion

The results of this study suggest that routine screening of serum iron, vitamin B12 and folate in patients with RAU is not indicated. Levels of salivary amylase and stress scores in RAU patients do not indicate that they are more stressed out when compared to the controls.

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## Abstract

**Purpose:** Recurrent aphthous ulceration (RAU) is a T-cell mediated oral disease, sometimes concomitant to other systemic diseases such as immunodeficiencies, haematological disturbances, and sensitivity to certain types of food, gastrointestinal diseases and stress. However, there are still conflicting data regarding haematological deficiencies and stress in RAU patients. **Material and Methods:** From 30 patients with RAU (age range  $36.27 \pm 15.308$  years) and from 30 controls (age range  $29.83 \pm 9.082$  years), a 5 ml of venous blood was taken in order to determine levels of serum iron, vitamin B12 and folate. Furthermore, all participants filled out the stress scale and 2 ml of their saliva was taken to determine levels of salivary alpha amylase by enzyme immune test. **Results:** The results of this study show that there are no significant differences between patients with RAU and controls regarding levels of iron, vitamin B12 and folate. There were no significant differences in salivary amylase levels and stress scores between patients with RAU during acute phase and remission period and as well as compared to the controls. **Conclusion:** We might conclude that patients with RAU are not to be sent routinely to the screening of serum iron, vitamin B12 and folate. It should be pointed out that salivary amylase levels do not indicate that patients with RAU are more stressed out than controls.

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## Address for correspondence

Ana Andabak Rogulj, DMD  
University of Zagreb  
School of Dental Medicine  
Department of Oral Medicine  
Gundulićeva 5, Zagreb  
anaandabak@gmail.com

## Key words

Stomatitis; Aphthous; Stress; Iron;  
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