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Assessment of salivary cortisol and dehydroepiandrosterone as oral biomarkers to assess stress in patients with recurrent aphthous stomatitis

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Abstract---Background: Recurrent aphthous stomatitis is a chronic inflammatory disease characterized by recurrent bouts of one or several shallow, rounded or ovoid, painful ulcers of oral mucosa that recur at intervals of a few days or up to 2–3 months and is of unknown etiology. The present study evaluated salivary cortisol and dehydroepiandrosterone as oral biomarkers to assess stress in patients with recurrent aphthous stomatitis (RAS). Materials & Methods: 84 patients of recurrent aphthous stomatitis (RAS) were

randomly divided into 2 groups of 41 each. Group I were RAS patients and group II were healthy control subjects. In all salivary cortisol and DHEA levels were measured. Results: DHEA levels 48–61 pg/ml was seen in 44% in group I and 10% in group II, <48 pg/ml in 24% in group I and 86% in group II, >61 pg/ml was seen in 32% in group I and 4% in group II. Salivary cortisol level >3 ng/ml was seen in 83% in group I and 28% in group II and between 1.2–3 ng/mL in 15% in group I and 74% in group II. Conclusion: RAS patients exhibited higher salivary cortisol and DHEA levels as compared to the healthy controls.

Keywords---anxiety, stress, recurrent aphthous stomatitis.

Introduction

Recurrent aphthous stomatitis (RAS) is defined as “a chronic inflammatory disease characterized by recurrent bouts of one or several shallow, rounded or ovoid, painful ulcers of oral mucosa that recur at intervals of a few days or up to 2–3 months and is of unknown etiology.”¹ The etiology and pathogenesis of RAS so far have remained elusive and the potential trigger factors reported are as follows: local trauma, anxiety and stress, vitamin and microelement deficiencies, increased oxidative stress, viral and bacterial infections, genetic predisposition, food allergies and hormonal and systemic diseases.² Psychological stress has been frequently observed during stressful situations such as school examination periods, family problems, new job, dental treatments or periods of significant changes in life.³ Cortisol & Dehydroepiandrosterone (DHEA) can be estimated in extracellular fluids such as blood, urine and saliva are closely related metabolic pathways and are involved actively in the growth and development, immune response, stress resistance and cardiovascular function of an individual.⁴ Alteration in cortisol and DHEA may indicate changes in adrenal function that can immensely affect the energy levels, disease resistance, emotional state and general sense of well-being of an individual.⁵ The present study evaluated salivary cortisol and dehydroepiandrosterone as oral biomarkers to assess stress in patients with recurrent aphthous stomatitis (RAS).

Materials and Methods

The present study consisted of 84 patients of recurrent aphthous stomatitis (RAS) of both genders. The consent was obtained from all enrolled patients. Data such as name, age, gender etc. was recorded. Patients were randomly divided into 2 groups of 41 each. Group I were RAS patients and group II were healthy control subjects. A thorough oral examination was carried out in all subjects. 2 mL of unstimulated whole saliva was collected and salivary cortisol and DHEA levels were measured using ELISA kit. Results thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I
Distribution of patients

Groups	Group I	Group II
Subjects	RAS	Control
M:F	16:25	18:23

Table I shows that group I had 16 males and 25 females and group II had 18 males and 23 females.

Table II
Assessment of dehydroepiandrosterone level in both groups

DHEA levels (pg/ml)	Group I	Group II	P value
48–61	44%	10%	0.01
<48	24%	86%	
>61	32%	4%	

Table II, graph I shows that DHEA levels 48–61 pg/ml was seen in 44% in group I and 10% in group II, <48 pg/ml in 24% in group I and 86% in group II, >61 pg/ml was seen in 32% in group I and 4% in group II. The difference was significant ($P < 0.05$).

Graph II Assessment of dehydroepiandrosterone level in both groups

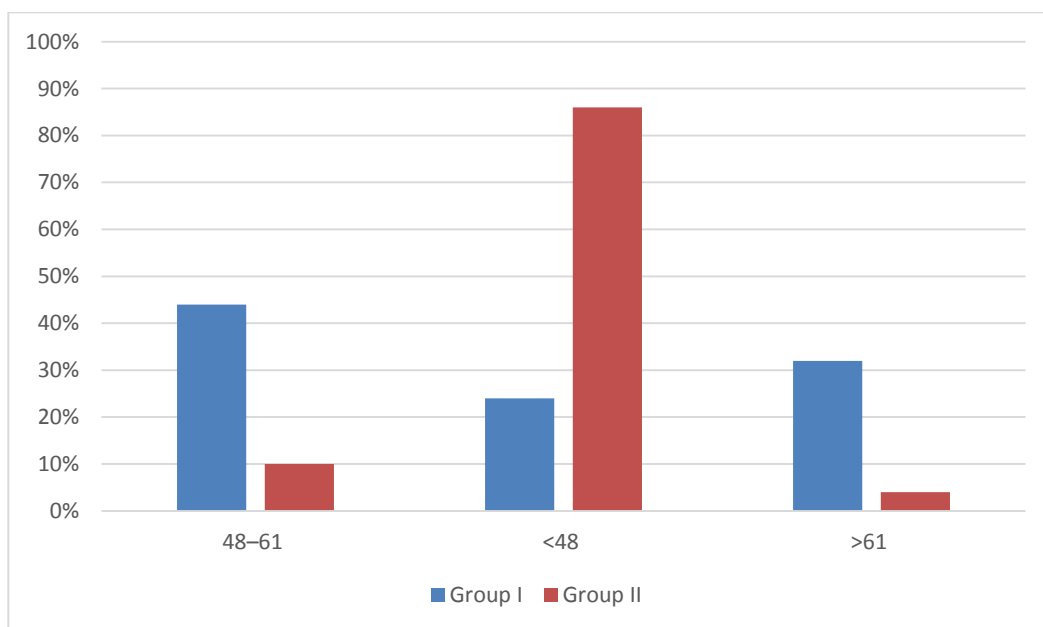
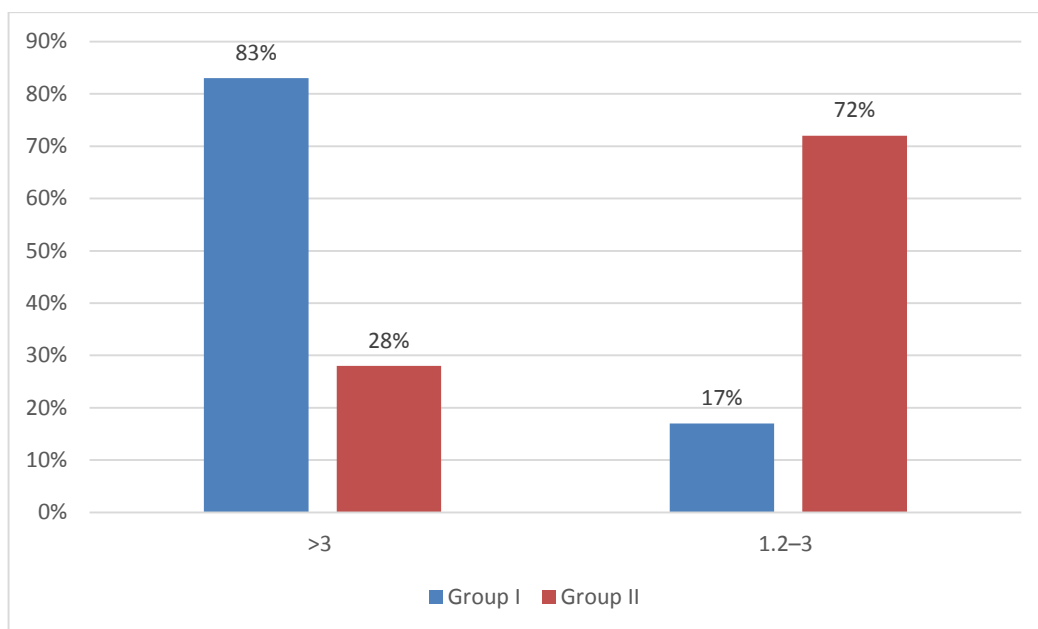


Table III
Assessment of salivary cortisol levels in both groups

Salivary cortisol levels (ng/mL)	Group I	Group II	P value
>3	83%	28%	0.05
1.2–3	17%	72%	

Table III, graph II shows that salivary cortisol level >3 ng/ml was seen in 83% in group I and 28% in group II and between 1.2–3 ng/mL in 15% in group I and 74% in group II. The difference was significant ($P < 0.05$).

Graph II Assessment of salivary cortisol levels in both groups



Discussion

RAS, the most common ailment affecting the oral cavity, is characterized by recurrent disruption of the oral mucosa in the form of painful ulcers. It is a diagnosis of exclusion, and other causes of ulcerative stomatitis should be explored before a diagnosis of RAS is made. RAS accounts for 25 percent of recurrent ulcers in adults and 40 percent in children.⁴ The severity of the stomatitis is represented by one of three subtypes. Minor RAS which is the most prevalent form and typically occurs in patients who are 5 to 19 years old⁶. Minor aphthae are usually confined to the lips, tongue, and buccal mucosa. Major RAS has a wider distribution is larger in size, (>10mm), and has a longer duration of outbreak. Minor aphthae typically resolve within 14 days of presentation and herpetiform RAS which presents with dozens of small, deep ulcers that often coalesce and therefore present as large ulcers with an irregular contour.⁷ The

present study evaluated salivary cortisol and dehydroepiandrosterone as oral biomarkers to assess stress in patients with recurrent aphthous stomatitis (RAS). We found that group I had 16 males and 25 females and group II had 18 males and 23 females. Mathew⁸ cited an increased frequency of RAS in men in the US adult population and South Indian population, respectively. The equal incidence among men and women in our study suggests that hormonal levels have a limited role in the multifactorial etiology of RAS. Mello et al⁹ in their studies reported salivary cortisol levels of 0.25–1.09 µg/dL, 0.35–1.47 µg/dL, and 0.30–3.20 µg/dL, respectively, in controls. This variation could be attributed to the varying populations and methodologies used.

We found that DHEA levels 48–61 pg/ml was seen in 44% in group I and 10% in group II, <48 pg/ml in 24% in group I and 86% in group II, >61 pg/ml was seen in 32% in group I and 4% in group II. Nadendla et al¹⁰ observed a highly significant difference in salivary cortisol levels between the RAS group (mean value: 1.73 ± 0.319 µg/dl) and healthy control group (mean value: 0.504 ± 0.129 µg/dL). It is suggested that prolonged stress leads to a persistent increase in the cortisol levels, which tend to dysregulate the various homeostatic mechanisms in the body by altering the local immune response in the oral mucosa. Although cortisol decreases the recruitment and activation of B lymphocytes, its main effects are exhibited on cell-mediated immunity. It causes suppression of immune system, decreases lymphocyte infiltration, lymphocyte and thymocyte populations (anti-mitotic), reduces differentiation and proliferation of local mast cells and production of nitric oxide and platelet-activating factor, stabilizes lysosomes and impairs phagocytosis.¹¹ Cortisol also suppresses synthesis and release of arachidonic acid (the key precursor for several inflammatory mediators) and decreases the production of gamma interferon and interleukins (ILs) (the critical mediators of immune response). The susceptible individuals might overreact to precipitating factors like mucosal microtrauma or food allergens, which could progress to ulcer development in RAS.¹² Aijaz et al¹³ found that 85% in group I (RAS) and 26% in group II (control) had salivary cortisol level >3 ng/ml and 15% in group I and 74% in group II had between 1.2–3 ng/mL. The difference was significant ($P < 0.05$). DHEA levels 48–61 pg/ml was seen in 54% in Group I and 5% in Group II, <48 pg/ml was seen in 20% in group I and 94% in group II, >61 pg/ml was seen in 26% in group I and 1% in group II.

Conclusion

Authors found that RAS patients exhibited higher salivary cortisol and DHEA levels as compared to the healthy controls.

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