The Relationship between Salivary IgA and White Oral Lesion in Bedridden Patients

Basma Ezzat Mustafa Al-Ahma[1], Nazih Shaban Mustafa[2*], Muhanad Ali Hamdon Kashmola[2], Salwana Binti Supa'At[3], Wan Noor Nazayan Bt. Wan Nik[4], Omar Abdul Jabbar Abdul Qader[2], Yunita Dewi Ardini[3], Mohamad Shafiq Bin Mohd Ibrahim[3], Muhammad Hazim Mohd Jefri[5], Amarul Firdaus Alias[5]

1. Department of Fundamental Dental-Medical Sciences, Kulliyyah of Dentistry, IIUM. 2. Department of Oral Maxillofacial Surgery and Oral Diagnosis, Kulliyyah of Dentistry, IIUM.
3. Peadiatric Dentistry and Dental Public Health, Kulliyyah Of Dentistry, IIUM ,
4. Prosthodontics- Kulliyyah Of Dentistry/ Kuantan Campus-IIUM 5. Kulliyyah of Dentistry, IIUM.

Abstract

The worldwide increase in the aging population poses tough challenges to the health care community. Indeed, older age has been associated with increased burden of chronic diseases. A decline in the protective functions of the oral mucosa could expose the aging individual to a variety of pathogens and chemicals that enter the oral cavity. The role of mucosal immunity in the defence against pathogens is well established. However, there does not seem to be much research on the relationship between salivary secretory immunoglobulin A (sIgA) and white lesion particularly among geriatric residents of long-term health care. Immunoglobulin A (IgA) is the dominant immunoglobulin isotype on oral mucosal surface where it acts as a first line of defence against microbial invasion. Recent investigations suggest that secretory IgA concentrations vary over the day due to a range of variables including dietary factors, daily mood, and exercise. The aim of this study is to investigate the relationship of sIgA level, and salivary pH with white lesion in bedridden patients. In this study, salivary IgA was determined by ELISA in samples of 34 elderly (60-80 years old) subjects grouped as male and female . Unstimulated saliva was collected, saliva flow, PH, and sIgA concentrations were measured. The results showed that the sIgA concentration was significantly higher in patients with white lesion (536.97±88.63) comparing to those with healthy mucosa (323.79±64.01) , and there is no significant difference of sIgA concentration between male (476.46±145.58) and female (396.83±108.09). We concluded that early detection of oral health problems especially white lesion can be determined by the assessment of the sIgA level. This would reflect the salivary IgA protective mechanism in patients with white lesion problems.

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Introduction

Elderly populations are mainly affected by non-transmissible diseases, which are quickly becoming the leading causes of disability and mortality, many of these diseases share common risk factors with different oral diseases. In addition to dental caries and periodontal disease, oral mucosal disease is another significant problem found in elderly populations. The oral mucosa performs essential protective functions that significantly affect the general health of an individual. As human beings age, the oral mucosa becomes more permeable to toxic substances and more vulnerable to external carcinogens. [1]

Secretory IgA (sIgA) is the predominant salivary immunoglobulin. Salivary glands are infiltrated by IgA-producing plasma cells, and ductal as well as acinar cells express receptors specific for polymeric IgA molecules. In addition, immune cells sensitized in one particular part of the mucosal immune system can populate the entire system far distal from the sensitization site. Thus, analysis of the immune response in saliva can provide a general picture of the function of

Corresponding author:
Assoc. Prof. Dr. Nazih Shaban Mustafa
Oral Maxillofacial Surgery and Oral Diagnosis,
Kulliyyah of Dentistry, IIUM.
E-mail: drbasma@iium.edu.my

the entire mucosal immune system.

Saliva is a complex mixture of secretions from parotid, submandibular, and sublingual glands and also from many minor glands. These glands provide the most important source of sIgA in the upper tracts. Many factors can influence the concentration of sIgA in saliva. A very important factor in determining the concentration of sIgA is salivary flow, which is controlled by a variety of factors including food ingestion, sensory stimulation, drugs, smoking, body positioning, stress, and degree of hydration.

Dietary factors, daily mood, and intense physical activity (training) may also influence sIgA concentration in saliva. [2]

Whole saliva is composed of secretions from salivary gland as well as from GCF, desquamated epithelial cells, microorganisms, and leukocytes. The pH of the saliva, determine its relevance to the oral health status and thus its suitability consider as a diagnostic marker of different diseases. [3,4]

Oral health problem especially white lesion which develops in patients while living in public or private care home are common even if these patients are bedridden and receiving home health care. [5]

Several studies indicate that nearly every component of the immune system undergoes age-associated alterations. [6]

The oral cavity may constitute a reservoir of pathogens responsible for many diseases in high-risk patients. [7] Oral hygiene, including professional oral care, has been shown to reduce the amount of bacteria in the oral cavity, [8] and daily oral care has been shown to decrease the frequency of fever and the mortality rate. [9]

Materials and methods

This cross-sectional study was conducted among a long-term-care forbidden residents in care home in Rumah Ehsan, Bandar Al Muktafi Billah Shah ,23400 Dungun, Terengganu, Malaysia. A total of 34 patients aged 60-80 years old were selected based on inclusive and exclusive criteria. Unstimulated saliva was collected, and salivary pH was measured. The samples were analyzed for determining the SIgA level.

Subject Recruitment and Oral Examination

This cross-sectional study consisted of a total of 34 subjects obtained from residents in Care Home in Rumah Ehsan, Bandar Al Muktafi Billah Shah ,23400 Dungun, Terengganu, Malaysia with the age range from 60-80 years old. All subjects were gave a written consent prior to participation. The subjects were excluded if they are unable to read, listen to the instructions given throughout the procedures, and have congenital abnormalities, undergone chemotherapy and radiotherapy, mentally illness, on antibiotic treatment within 3 previous months, on chronic medications that cause the hyposalivation or suffer from upper respiratory tract infection in past two weeks. The oral mucosa was screened by oral medicine specialist and recorded for each patient.

Saliva pH Determination and Saliva Collection

Salivary pH was determined using litmus paper (MACHEREY-NAGEL is certified according to the medical device directive ISO 13485) placed on the floor of the mouth for 5 seconds. Subjects were instructed not to eat/drink/brush teeth 30 minutes prior to the procedure. The whole unstimulated saliva was collected using spitting method. Subjects were asked to spit their saliva in the saliva container until the volume is adequate for analysis. The container was then kept in the icebox up to 2 hours. It was then stored in the freezer at -20degree Celsius until analyzed.

Lab Procedure

The samples then thawed and centrifuged for 5 minutes at 3.5 rpm at 9 degrees Celsius to remove the mucin and debris. The supernatant was collected and assay was carried out by Human s-IgA (Secretory Immunoglobulin A) ELISA Kits from Elabscience®. All reagents, standard solutions, and samples were prepared as instructed in the manual provided by the kits. Duplication was done for each standard and samples. The process was followed as instructed in Kit's Manual. Optical Density was determined using a Microplate Reader at 450nm immediately. The results obtained were tabulated and analysed.

Results

As seen in Table 1 and figure 1, There is a statistically significant difference ($p < 0.05$) of mean IgA concentration between the group with white lesion (536.97±88.63), comparing to the

other group which are without white lesion (323.79±64.01), according to the independent t test analysis. while there is no statistically significant differences (p > 0.05) of mean IgA concentration between male (476.46±145.58) and female (396.83±108.09) as shown in table 2 and figure 2.

Variable	Mean (SD)		Mean difference (95% CI)	*p* value
	No	Yes		
IgA concentration (ng/dl)	323.79(64.01)	536.97(88.63)	-213.18(-267.81, -158.55)	0.00

Table 1. Comparison of mean IgA concentration between no white lesion and presence of white lesion.

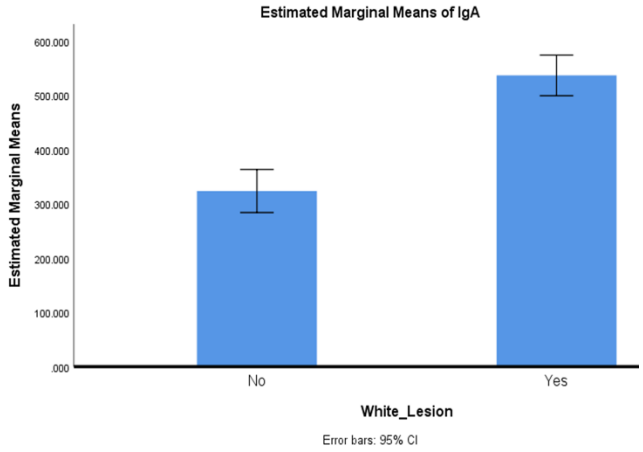

Figure 1. Bar graph of mean IgA concentration between no white lesion and presence of white lesion.

Variable	Mean (SD)		Mean difference (95% CI)	*p* value
	Male	Female		
IgA concentration (ng/dl)	476.46(145.58)	396.83(108.09)	79.63 (-9.94, 169.21)	0.08

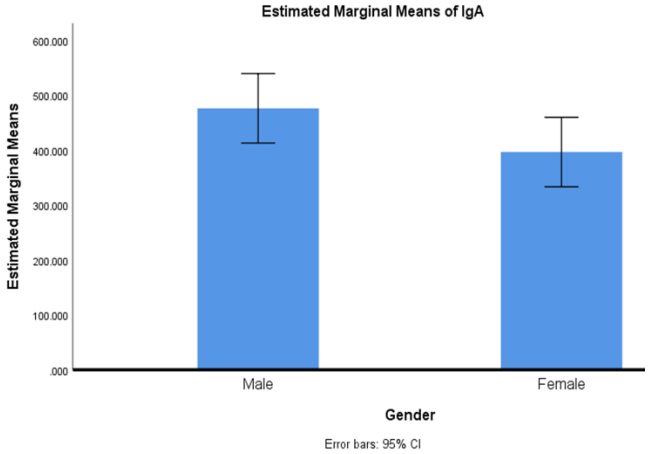

Table 2. Comparison of mean IgA concentration between male and female.

Discussion

The main finding of this study is that sIgA secretion rate from unstimulated saliva is significantly higher in elderly subjects with oral white lesion compared to the subjects free of oral white lesion. The sIgA secretion rate from unstimulated rather than stimulated saliva was chosen for this study because it provides information about the usual level of sIgA that continuously bathes the mucosal surfaces.

This may be due to the primary function of sIgA in opsonization of foreign invaders at the port of entrance to the body and blockade of their infectivity. The synthesis of sIgA may be used to follow the cooperation between T and B cells in the mucosal immune compartment.

Oral diseases such as dental caries, gingivitis, periodontitis and oral malodour are always initiated at the interface between microbial ecosystem and host tissue. Changes in microbial and environmental dynamics in microbial ecosystems may increase the potential for pathogenicity within a microbial ecosystem and subsequently initiate and promote oral diseases. These successional changes have recently and tentatively been referred to the ecological plaque hypothesis.[10] Hence, the properties of the environment determine, which microorganisms can occupy which site while the metabolic activities of those microbial communities subsequently modify the properties of the environment.[11]

The oral epithelium has been reported to become thinner with age, and collagen synthesis by connective tissue decreases. As a result, decreased tissue regeneration and disease resistance would be expected. [12]

Diagnosis of oral white lesions might be quite challenging. These lesions represent a wide spectrum of lesions with different aetiology and various prognoses. The diagnosis of white lesions varies from benign reactive lesions to more serious dysplastic and carcinomatous lesions. While there are some classic features that help distinguish these lesions, similar features may give rise to some complications in diagnosis. Efforts should be made to establish a definite diagnosis to prevent time elapse in treatment of patients with more serious lesions.[13,24]

Secretory IgA is the main immunoglobulin in secretions, including saliva. It is the first line of

defence of the host against pathogens which invade mucosal surfaces. [14] Some studies have also demonstrated a lower incidence of caries as a result of a high salivary IgA concentration.[15] In addition, low levels of salivary IgA has been presented as a risk factor for upper and lower respiratory infection and have also been associated with an increased risk for periodontal disease and caries. [16]

Use of saliva as a diagnostic fluid meets the demands for being inexpensive, non-invasive and easy-to-use diagnostic methods. [17]

As a clinical tool, saliva has many advantages over serum, including ease of collection, storing and it can be obtained at low cost in sufficient quantities for analysis. [18] Physical parameters like salivary pH, buffering capacity, flow rate, viscosity and chemical assays like salivary hormones, antibodies and tumor markers are gaining importance in the diagnosis of many systemic disorders. [19] Numerous studies have shown the effectiveness of oral care in the elderly suffering from various diseases. [20,21]

The diagnosis of active phases of inflammatory oral diseases and the identification of patients at risk for active disease represents a challenge for clinician,[22] [23]

Salivary IgA antibodies could help oral immunity by preventing microbial adherence, neutralizing enzymes, toxins and viruses; or by acting in synergy with other factors such as lysozyme and lactoferrin .[14]

Use of sIgA as an immune marker has numerous advantages over measurement of T and B cells in the blood.

Compared to the blood tests, collection of saliva is without any risk for the subjects under study. SIgA synthesis rate is high and half-life is short, thus any change in sIgA concentration can be observed immediately and directly correlated with the causative agent or procedure. SIgA synthesis is T cell dependent and changes in synthesis can be correlated directly to T and B cell activation. there is cooperation between distant compartments in the mucosal immune system, and therefore, the findings in saliva may be generalized to the entire mucosal system.

Conclusion

In our society, there is a growing number of elderly people with a higher risk of illness and infection (oral mucosal lesions) it will become increasingly important to be able to easily evaluate immune status and find a way in which to improve it. Early detection of oral health problems especially white lesion can be determined by the assessment of the sIgA level. This would reflect the salivary IgA protective mechanism in patients with white lesion problems.

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Declaration of Interest

The authors declare that they have no conflict of interest.

References

1. Jainkittivong A., Aneksuk V., Langlais R. P. Oral mucosal conditions in elderly dental patients. *Oral Dis.* 2002;8: 218–223.
2. Miletic I. D., Schiffman S. S., Miletic, V. D., Sattely-Miller E. A. Salivary IgA secretion rate in young and elderly persons. *Physiol. Behav.* 1996;60: 243–248.
3. Handayani F. T., Widyaningsih P. N., Arjadi F. Effect of Different Types of Sleep Deprivation and Sleep Recovery on Salivary Ph. *J. Vocat. Heal. Stud.* 2021;4: 95-99.
4. Khan R. S., Khurshid Z., Akhbar S., Moin S. F. Advances of salivary proteomics in oral squamous cell carcinoma (OSCC) detection: An update. *Proteomes* 2016;4: 1–11.
5. Fukuyama H., Ishida T., Tachibana H., Iga C, Nakagawa H., Ito A, et al. Clinical evaluation of bedridden patients with pneumonia receiving home health care. *J. Japanese Respir. Soc.* 2010;48: 906–911.
6. Pawelec G. Immunity and ageing in man. *Experimental Gerontology* 2006; 41(12): 1239-1242.
7. Inglis T. J. J., Sherratt M. J., Sproat L. J., Hawkey P. M., Gibson J. S. Gastroduodenal dysfunction and bacterial colonisation of the ventilated lung. *Lancet* 1993;341: 911–913.
8. Abe S., Ishihara K., Okuda K. Prevalence of potential respiratory pathogens in the mouths of elderly patients and effects of professional oral care. *Arch. Gerontol. Geriatr.* 2001;32(1): 45-55.
9. Yoneyama T. *et al.* 7~-Archives of. *Gerontol. Geriatr.* 1996;22: 11–19.
10. Iacopetti I. *et al.* Salivary pH, calcium, phosphorus and selected enzymes in healthy dogs: A pilot study. *BMC Vet. Res.* 2017;13: 330.
11. Morozumi T. *et al.* Salivary pathogen and serum antibody to assess the progression of chronic periodontitis: a 24-mo prospective multicenter cohort study. *J. Periodontal Res.* 2016;51(6): 768-778.
12. Cueto A. *et al.* Prevalence of oral mucosal lesions in an elderly population in the city of Valparaiso, Chile. *Gerodontology* 2013;30: 201–206.
13. Doria A. *et al.* SLE diagnosis and treatment: When early is early. *Autoimmun. Rev.* 2010;10: 55–60.
14. Marcotte H., Lavoie M. C. Oral Microbial Ecology and the Role of Salivary Immunoglobulin A. *Microbiol. Mol. Biol. Rev.* 1998;62(1): 71-109.
15. Hashizume L. N., Schwertner C., Moreira M. J. S., Coitinho A. S., Faccini, L. S. Salivary secretory IgA concentration and dental caries in children with Down syndrome. *Spec. Care Dent.* 2017;37:115–119.

16. Russell M. W., Kilian M., Mantis N. J., Corthésy B. *Biological Activities of IgA*. *Mucosal Immunology: Fourth Edition* vols 1–2. Elsevier, 2015;1:429-454.
17. Wang Q., Yu Q., Lin Q., Duan Y. Emerging salivary biomarkers by mass spectrometry. *Clin. Chim. Acta* 2014;438: 214–221.
18. Baliga S., Muglikar S., K. R. S. pH: A. diagnostic biomarker. J. of I. S. of P. 2013 J. Salivary pH: A diagnostic biomarker. Journal of Indian Society of Periodontology. *A diagnostic biomarker. J. Indian Soc. Periodontol.* 2013;17(4): 461.
19. Ngamchuea K., Chaisiwamongkhol K., Batchelor-mcauley C., Compton R. G. Correction: Chemical analysis in saliva and the search for salivary biomarkers - a tutorial review. *Analyst* 2018;143: 777–783.
20. Akutsu Y. *et al.* Pre-operative dental brushing can reduce the risk of postoperative pneumonia in esophageal cancer patients. *Surgery* 2010;147: 497–502.
21. Seguin P. *et al.* Effect of Oropharyngeal povidone-iodine preventive oral care on ventilator-associated pneumonia in severely brain-injured or cerebral hemorrhage patients: A multicenter, randomized controlled trial. *Crit. Care Med.* 2014;42: 1–8.
22. Hirschfield GM., Beuers U., C. C. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: the diagnosis and management of patients with primary biliary cholangitis. *J Hepatol.* 2017;67: 145–72.
23. Barros S. P., Williams R., Offenbacher S., Morelli T. Gingival crevicular fluid as a source of biomarkers for periodontitis. Periodontology 2000. 2016;70(1): 53-64.
24. Mortazavi H., Safi Y., Baharvand M., Rahmani S. Diagnostic features of common oral ulcerative lesions: an updated decision tree. International journal of dentistry. 2016; 3.