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#### **EDITORIAL**

# AGING POPULATION AND DENTAL CARE IN SRI LANKA

The aging population is the most important demographic trend and most countries, including the Sri Lanka, have not prepared for it.

In Sri Lanka, 12.3% of the population is aged 60 or older, making it the country with the highest proportion of older adults in South Asia. Within 15 years 25% of the Sri Lankans will be over 60 years of age.

According to the World Bank, the demographic transition from a youth bulge to an aging creates several economic, health and social challenges.

First, the number of workers retiring will increase, while the number of people entering the workforce will decrease, resulting in lower productivity, lower taxes, lower national income, lower growth, and lower savings. Yet, a higher number of retired workers translates into increased burden for the public sector pension scheme, which now consumes almost 2% of the country's GDP and will already become fiscally unsustainable in less than a decade.

Second, an aging population will put pressure on the country's healthcare sector, which is already facing severe difficulties as a result of COVID-19. Indeed, the healthy life expectancy in Sri Lanka is 67.0 years which, based on an overall life expectancy of 77.3 years, translates into 10 years of healthy life lost with increased morbidity and disability that may require specialized and comprehensive care. Also

the share of females in the elderly population increases with age: from 54% in the 60–64 age group, to 58% in the 70–74 age group, to 60% in those aged 80 years and over. The share of females in the total population has increased over the years and currently is higher than males. Female share in total population was 47% in the 1946 census, which increased to 52% in 2012 (Department of Census and Statistics 2015).

The aging population also means there will be growing demand for aged-care services in the near future. This is crucial given that there is now limited availability of eldercare facilities: six public sector run elder care centers and 324 private or community run centers. Improving the quality and governance of these facilities will also be crucial.

Third, there is weak social protection for the elderly. For example, and while well-targeted, the cash transfer program for the elderly has limited coverage. In addition, private sector pension and savings schemes are fragmented and have limited coverage (most of the two-thirds of workers in the informal sector are excluded) and benefits. Relatedly, the social pension only covers half of those who are eligible, leaving many vulnerable workers without income in their retirement. Due to the unavailability of a systematic social security system, older people continue to work, often informally. All of which explains that poverty rates among the elderly are estimated to be higher than that of any other age group in Sri Lanka.

Given the above socio economic and health scenarios, let us consider the dental care deliver for an aging population.

Aging affects dental health of the people in many different aspects. Although the elderly are retaining their dentition longer than in the past, dental morbidity; prevalence of dental diseases continues to be high. Presence of root caries, periodontal disease and xerostomia are oral diseases that are found majorly affecting the older population. Many still hold the opinion that tooth loss is a normal part of the aging process and is not preventable. Others have adapted to a compromised oral health status and seek treatment only when an emergency arises.

Therefore, when treating elderly patients, dentist should be mindful of the following important aspects. Co-morbidities, nutrition in old age and its implications, changes in salivary glands and salivary secretion with aging, age changes in oral mucous membrane, changes in the teeth with aging, aging and periodontal disease, prosthetic considerations in geriatric dentistry and preventive dental care for elderly people.

Is Sri Lanka prepared for the aging population in the perspective of dental care delivery. The answer is a firm "No". The main health care service provider to the nation, Ministry of Health has no plans in its radar for provision of geriatric dental care. Private sector is no exception. The Faculty of Dental Sciences University of Peradeniya who had produced more than 98% of Dental Surgeon manpower in Sri Lanka, is yet to develop a formal training on geriatric dentistry for its undergraduates.

#### Dileep De Silva Shyama Banneheka

Editors - Sri Lanka Dental Journal

#### Oral manifestations of COVID-19 patients - a Sri Lankan perspective

#### P.V.K.S. Hettiarachchi, S.P.K.J. Subasinghe, D. Medagedara, R.D. Jayasinghe

#### Abstract

**Background:** Coronavirus disease 2019 (COVID-19) is reported with multifaceted manifestations, including the oral cavity. However, the association between oral lesions and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is still unclear and varies widely.

**Objective:** To identify the short-term oral manifestations and long-term oral complications of the COVID -19 patients among a Sri Lankan cohort.

Methods: A cross-sectional descriptive observational study in all the patients diagnosed with COVID-19 infection presented to a Respiratory Disease Treatment unit of a tertiary care centre in Sri-Lanka during the month of September 2021 was included in this study.

**Results:** One hundred COVID positive patients within the age ranging from 14-84 years were included in this study. Majority (72% each) complained of loss of taste and smell while the other complains in descending order were perceived dryness of the mouth (69%) for a mean of 4.9 days, pharyngeal soreness (46%), burning

sensation (25%), difficulty in swallowing (24%), halitosis (17%), pain and swelling in relation to salivary glands (13%), pain in the mouth at rest (9%), however, at the review appointment only 12 patients complained of loss of smell and taste. Only four patients' complaint of oral lesions at the initial visit and out of these 75% of the cases had aphthous type of ulcerations.

**Conclusions:** In the Sri Lankan context, patients infected with COVID-19 predominantly demonstrated general symptoms associated with the disease, however, the occurrence of oral lesions was not very common and severe.

**Key words:** COVID-19, Oral Manifestations, Corona Virus, Oral symptoms

#### Introduction

The emergence of severe acute respiratory syndrome corona virus 2 has resulted in an unprecedented global healthcare crisis. Majority of the cases are either asymptomatic or affected with mild symptoms, while a considerable fraction of cases develops severe respiratory symptoms, leading to acute severe respiratory distress (ASRD)<sup>1</sup>. However, there is enough evidence for us to believe that the disease that

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we are fronting is of complex nature which may cause harm to many other organs such as the cardiovascular system, gastrointestinal tract and kidneys leading to multiple organ failure<sup>2-4</sup>.

Many systemic diseases have oral manifestations including autoimmune, haematologic, endocrine and neoplastic processes<sup>5</sup>. At the same time viral infections that affect the head and neck area (eg- herpesviruses, human papillomavirus, and Coxsackie virus) may be responsible for primary lesions in the oral cavity, while viruses, like human immunodeficiency virus, affect the oral cavity due to the compromised state of the immune system<sup>6</sup>. Dysgeusia is the first recognized oral symptom of COVID-19 reported in 38% of patients, mostly in North Americans and Europeans, females, and patients with mild-moderate disease severity<sup>7</sup>. The mechanism of SARS-CoV invading the human cells has been extensively studied. SARS-CoV contains a receptor-binding domain (RBD) that specifically recognizes angiotensin-converting enzyme 2 (ACE2) as its receptor8. Therefore, a marked inflammatory response can be observed in organs and tissues such as the tongue mucosa and salivary glands which may contain higher number of cells with ACE2 receptors9-11. Further, this interaction may result in impairment of the taste bud sensitivity, leading to dysfunction in the gustatory responses<sup>12</sup>.

Since the emergence of the global COVID-19 pandemic, the scientific community has attempted to shed light on different presentations of the virus and the many symptoms the disease may cause. However, up to date there has been little information, mainly through case reports and case series, regarding oral complications caused by COVID-19. However, the association between these oral lesions and is still unclear and this fact was further highlighted by a systematic review which concluded further observational studies focusing on this issue and on the causal relationships between oral lesions and COVID-19 was a need of the hour <sup>13</sup>.

Due to the nature of our professional work, dental

care providers work in a very close proximity to the oral cavity of the patients. Therefore, it is the responsibility of the dental surgeons to report the findings of the possible oral manifestations in patients with COVID-19. As there is only very low level of evidence with limited number of cases and case series reported in the literature, we believe that the findings of this study will shed light on the oral manifestations of the Asian patients which may contribute differently to the scientific literature. Therefore, the main objective of the study was to identify the short-term oral manifestations and long-term oral complications of the COVID-19 patients among a Sri Lankan cohort.

#### Materials and methods

A cross-sectional descriptive observational study was conducted in all the patients diagnosed with COVID -19 infection with a positive rapid antigen (RAT) test or PCR presented to a Respiratory Disease Treatment unit, Teaching Hospital Kandy, Sri Lanka, a tertiary care centre during the month of September 2021. Patients who volunteered to participate in this study was included as the study sample, excluding patients who were seriously ill and not able to communicate due to severe COVID -19 pneumonia, patients with pre-existing oral lesions. Informed written consent was obtained by the PI, who was not involved in the provision of routine clinical care to the patient. Data collection included a brief oral examination which was conducted on the day of the admission by the principal investigator in accordance with the health guidelines published for prevention of spread of COVID-19, which included using proper PPEs where necessary. The recorded data included, demographic information, information regarding COVID-19 specific investigations, any oral symptoms, medications the patients on. The follow-up assessment was conducted via interviewing the patient over the phone. All the patients recruited for the study underwent the standard treatment protocols practiced at the Respiratory Disease Treatment Unit, National Hospital, Kandy, Sri Lanka.

Ethical clearance for the study was obtained from the Ethics Review Committee of the Faculty of Dental Sciences, University of Peradeniya.

#### Results

One hundred consecutive COVID-19 positive patients (64% males and 36% females) within the age ranging from 14-84 years with a mean age of 42.39 years were included in the study. In this sample majority (92%) were Sinhalese and 7 % were health care workers. Three quarters of the sample (75%) was confirmed with a positive rapid antigen test (RAT) while 22 % of the patients had a positive PCR result while 3 patients (3%) had undergone both investigations. Thirty nine percent (39%) of the patients were not vaccinated against COVID-19 when they developed the symptoms. Out of the 61 patients who were vaccinated, only 42.6% had completed both doses. All the patients experienced general symptoms associated with COVID-19 infection like fever, malaise, headache and etc while 69% of the patients have experienced oral symptoms. The mean duration of experiencing generalized symptoms was  $5.8 \pm 4.8$  days, while the mean number of days patients had experienced oral symptoms was  $4.8 \pm 3.5$  days. The mean duration from the date of last COVID-19 vaccination to the development of symptoms was  $65.5 \pm 49.4$  days. Only a minority of the sample demonstrated habits of smoking, alcoholism and betel chewing and it was found to be 18%, 23% and 12% respectively.

#### Oral Signs and Symptoms

The majority of the patients (72%) experienced both loss of smell as well as taste disturbances and this was the commonest oral complain that the patients complained of. Second commonest complain was the perceived dryness of the mouth and 69% of the sample experienced this. Thirdly, the pharyngeal soreness was experienced by 46% of the patients. Quarter of the sample was complaining of burning sensation and 24%, difficulty in swallowing. Other less common complaints observed in this study were, bad breath (halitosis) (17%), pain and swelling in relation to salivary glands, mainly the parotid in 13%, pain in the mouth at rest or while speaking in 9% and swelling below the jaw in 8% of the cases. Table 1 summarizes the complaints of the patients and the mean days the patient's experienced each of these symptoms. 11% the patients did not experience any symptoms related to the oral cavity.

**Table 1.** Summary of the oral signs and symptoms patients experienced and the mean days of the symptoms; SD - Standard deviation

Symptom	Present (%)	Absent (%)	Duration (days)	
			Mean	SD
Loss of smell	72	28	4.89	3.47
Taste disturbances	72	28	4.96	3.27
Dry mouth	69	31	5.10	3.79
Pharyngeal soreness	46	54	3.5	1.83
Difficulty in swelling	24	76	5	3.90
Halitosis	17	83	4.29	2.28
Pain and swelling in the salivary glands	13	87	4.77	4.75
Pain in mouth/speech	9	91	6	3.6
Swelling below the lower jaw	8	92	3.5	2.51

#### **Examination findings**

At the initial visit four patients demonstrated oral lesions, out of these patients three (75%) had oral ulcers (Figure 1) on tongue, throat and on buccal mucosa while a single patient had white plaques/coated tongue in addition to ulcers (Figure 2a). Out of the patients with oral lesions except the patient with ulcers on the tongue, all the others had complete resolution at on week. However, there were four new cases at one week and two of them had oral ulcers (Figure 2) while a coated tongue (Figure 2b) and presence of minor bleeding spots were reported by single patient each. However, other positive examination findings such as redness, intra oral swellings, or vesicles formations were not seen among this cohort of patients.

#### One week review interval

At one week review only 12 patients' complaint of loss of smell and out of this there were two (02) new patients who experienced loss of smell

who did not complaint about this at the day of the first examination. At the same time 12 patients' complaint of loss of taste, and out of this, 50% (06 patients) were experiencing both anosmia and ageusia persistently for one week, however, the change of the state of both anosmia and ageusia at one week was statistically significant at a value of P<0.05 (Table 2).

On the review appointment 14 patients were complaining of burning sensation, and of that 12 had persistent burning sensation and 57 (79.2%) had improvement of the symptoms from the initial visit. These values were also statistically significant at a P value of 0.05. Considering the pharyngeal soreness, a total of 9% complained of pharyngeal soreness at one week and out of these 4 patients (44.4%) had developed this later. However, the change of the pharyngeal soreness, difficulty in swallowing, halitosis, pain and swelling in the salivary gland at one week was not statistically significant at a P value of 0.05.

**Table 2.** Depicts the number of patients who persisted with the different oral complaints and the number of patients whom symptoms changed over the one week. The change of symptoms includes either complete resolution of the initial symptoms or development of the concerned symptom which was not present at the initial visit.

Complaint	Persistent of symp- toms complaint at the initial visit	Change of the sta- tus of symptoms at one week	P value
Loss of smell	36	64	P<0.05
Loss of taste	34	66	P<0.05
Dryness	41	59	P<0.05
Pharyngeal soreness	55	45	P = 0.97
Difficulty in swallowing	74	26	P = 0.89
Halitosis	83	17	P = 1
Pain and swelling in the salivary glands	86	14	P = 0.14
Pain in mouth/speech	89	11	P<0.05
Swelling below the lower jaw	92	8	P = 1

#### Discussion

Despite the fact that the COVID-19 pandemic has haunted the world for over a year, there is paucity of solid evidence on oral manifestations in patients with COVID-19 up to date. The number of studies reporting data on oral manifestations in COVID-19 is less and, has the main limitations of being available on the subjects from studies on mucocutaneous involvement or data gathered through patient questionnaires attributing to considerable risk of bias14. Further, adding to these limitations there is no consensus on the relationship between SARS-CoV2 infection and oral manifestations of COVID-19. A contributory factor for this may be the less involvement of the dentists during the pandemic owing to the fact that dental surgeries being classified among the professionals at a risk of potential exposure to SARS-CoV-2<sup>15</sup>. As a result, during the pandemic, the dental treatments were only limited to emergency care for trauma, pain, head and neck infections, and malignant tumours, primarily performed by Oral and Maxillofacial (OMFS) surgeons and oral medicine specialists in the hospitals. Further, studies show that other healthcare professionals pay less attention to the oral cavity in their examinations. The reduction in dental examinations of patients and the fact that the oral cavity is rarely observed by other healthcare workers could explain why there have been few reports regarding oral complications of COVID-1916.

The mostly reported general symptom was fever, cough, myalgias and loss of appetite and all most all the patients in this present sample also complained of these general symptoms. However, unlike the general symptoms many different types of oral lesions associated with COVID-19 infection is reported in the literature in COVID-19 confirmed and suspected individuals. It was interesting to note that in this present study also the commonest oral symptom reported were olfactory and gustatory dysfunction (72%) and the mean time that the patients experienced these symptoms were 4.89  $\pm$  3.47 and 4.96  $\pm$ 

3.27 respectively. Interestingly, our patients also complained of experiencing a transient dry mouth which persisted for a period of 5.10 days duration and this was the next commonest symptom (69%) following taste and smell disturbance. A meta-analysis reported the prevalence of 0.44 (95% CI 0.36–0.52). They further reported the less prevalence is more likely to be due to the underreporting of this xerostomia in smaller studies<sup>13</sup>. However, a recent review article by Amorim dos Santos et al., reported the triad of xerostomia, taste dysfunction, and oral mucosal lesions as common manifestations in patients with COVID-19. Pharyngeal soreness and difficulty in swallowing was reported by 46% and 24% respectively<sup>14</sup>.

Further, with regard to the oral mucosal lesions, the most common clinical pattern was aphthous ulcers, followed by herpes-like lesions, candidiasis, glossitis/depapillation/geographic tongue, parotitis, and angular cheilitis<sup>14</sup>. A clear relationship between COVID-19 and oral mucosal lesions is yet to be established and some publications state that the only oral symptom associated with COVID-19 is taste impairment probably as a result of an inflammatory response which affects the normal function of the taste buds <sup>14,17</sup>. However, there is still dilemma regarding the occurrence of other oral lesions, are they merely due to COVID infection or occurs in the background of an immune compromised person or as a co-infection or as an adverse reaction for the treatment received for COVID-19<sup>14,18,19</sup>. The patients present in this study were having mild to moderate symptoms and as mainly on inhalers and majority was otherwise healthy young patients, yet they have experienced, aphthous type of oral ulcers, white plaque/coated tongue, minor bleeding spots during the course of the disease and some of these lesions has occurred not immediately with the COVID infection but with a latent duration of one week. Majority of these oral lesions had disappeared within a duration of one week and this was in par with the other studies which reported a resolution time of 6 days to 2

weeks <sup>20-21</sup>. Further, in line with the literature our study also demonstrated the oral ulcers as one of the most common complications associated with COVID-19 confirmed individuals <sup>22</sup>. In addition, similar lesions which were described as "candidal plaque-like lesions" associated with COVID-19 in the previous studies were also observed in two individuals in this present study<sup>20,23</sup>. The main limitations of the study are: majority of the study population were including mild to moderately severe cases and due to the health regulatory guidelines a detailed oral examination including the periodontal assessment could not be carried out and post vaccination sample could not be assessed at the time of conducting the study majority of the patients had only received a single dose of vaccination.

#### **Conclusions**

This study reports various oral manifestations associated with COVID-19 confirmed patients



**Figure 1.** Different presentations of oral ulcers in the present sample

# who presented to a tertiary care hospital in Sri-Lanka. Gustatory impairment along with olfactory changes which is a symptom of COVID-19 was reported by majority of the patients. Even though, COVID-19 patients may present with ulcerative, erosive, vesicobullous and plaque-like oral lesions our cohort of patients only demonstrated these lesions very minimally. However, as there may be regional variations associated with the manifestations in the oral cavity, this knowledge is prudent in the dental health care professional's prior initiation of treatment in patients even though the oral manifestations are very minimal and less severe in the Sri Lankan patients.

#### Acknowledgements

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**Figure 2.** (a) white plaques/coated tongue like lesions on the first visit; (b) similar lesion present at one week interval

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#### Transformation of Management Information System in School Dental Services in Sri Lanka

Dileep De Silva, S.R. Weerasuriya, S.A.D.N. Amarasena, S.A. Muthuthanthri, H.G.T.I.D. Wijesiri, D.S.C. Colombathanthri

#### Abstract

The School Dental service has been operating for nearly 70 years in Sri Lanka. Monitoring and evaluation of the School services was started in 2007 using a paper-based reporting system. In order to mitigate the problems and shortcomings encountered in the paper-based system and to provide more accurate and timely data, web-based system was introduced in 2020. Web based system has given the opportunity for timely accurate data flow and enhance the analysis capacity to provide better information for decisions. All stakeholders in the school dental service have embraced the web-based system with much enthusiasm.

#### Introduction

In 1921, New Zealand initiated the model of using school dental nurses in the oral health workforce, to provide an equitable service to children. Thereafter, other countries which were lacking an adequate oral health workforce, followed the New Zealand's model<sup>1</sup>. Currently in 54 countries, including Sri Lanka; school dental therapists are in the oral health workforce<sup>1</sup>. Most often, school dental therapists are utilized in school-based oral health programs for children, by the Government.

Deployment of School dental therapists in a large number of countries is a strong evidence that the dental therapists can provide care that is acceptable to and valued by the public<sup>2</sup>.

School Dental Services in Sri Lanka was officially established in early 1950s, with the aid of the Colombo Plan according to the New Zealand model. The first batch was six female dental nursing students and they were trained in New Zealand for two years. The school for dental nurses training was started in 1955 at Maharagama in a property donated by late Premier Sir John Kotalawela. Subsequently the Dental Nurses were renamed as school dental therapists<sup>2</sup>.

In the Sri Lanka, mostly a single School Dental Therapist (SDT) is employed in one School dental Clinic. There are few clinics where two therapists are attached. They provide preventative care for children between 3-13 years. Their target group for treatment is children in Grade 1, Grade 4 and Grade 7 classes in schools where there are more than 200 students, and in schools with less than 200 school children all the children

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under 13 years. The current norm for the target group is 2000 children per one School dental therapist. School dental service is technically supervised by Regional Dental Surgeons who function as the Regional Managers. Further the School Dental Therapists are under the administrative supervision of the Medical Officer of Health (MOH) and Regional Director of Health Services<sup>3</sup>. The Family Health Bureau, Ministry of Health has a supervisory role at the National level.

Currently the Ministry of Health has 443 School Dental Clinics manned by 365 School Dental Therapists (SDTs), throughout the country covering all 25 districts.

In a country which spends only around 2 % of GDP for state sector health services; it is not feasible and practical to provide a dental clinic to every school in the country. Therefore a "base school" is allocated to each School Dental Therapist, which is mainly the school where the dental clinic is situated along with several other schools in close proximity, called "feeder schools".

In a lower resource setting, like that of ours; it of paramount importance to monitor its health services to get the maximum of it. Hence the School Dental Service was monitored through a paper-based system since 2007, by the Family Health Bureau.

According to the guidelines on management information system developed by the Family health Bureau, the school dental therapists are requested to maintain six important records at the grass-root level. They are namely the Patient's consent form cum appointment card, Patient register (PR), Daily Record of treatment (DR), Patient's examination and history chart (HC), Monthly return and the Quarterly/Annual return. These records have been designed to serve two main purposes. Some records serve as a database on individual students/clientele. Others are used convey data and information to higher levels in

the health administrative system. The existing system mainly record quantitative data on service previsions.

Records maintained and procedure involved in the manual information system are described below<sup>4</sup>.

# 1 Information generation at the School Dental Clinic level

# (a) Patients' consent form cum appointment card - Health 1972

All children in the target group are given a consent form. The written consent is taken before the commencement of treatment using the consent form. This has two parts, the first part is used as an appointment card, and the second part is used to record medical history and the parents' consent to do dental treatments. The cards filled with the new registration number and the child's name are given to the teacher before screening is carried out to get the informed consent from parents. On the first day of screening the cards will be collected and the findings will be recorded in relevant places (DR, PR, HC) and appointment card part is given to the parent and the consent part will be kept with the School Dental Therapist.

#### (b) Register of Patients (PR)

Each School Dental Clinic maintains one patient register to register the children in the target group at the beginning of each year. A separate PR is maintained for each relief stations. The list of children in the target group should be obtained from the schools and the names are entered into the PR. A registration number will be assigned for each student of the target group, which will be maintained in all the other records. The registration number consists of 5 parts, which is unique for the entire country. For children in a base school, one registration number maintained throughout their career. However, for the children in outreach schools, new registration number is given each year. The PR will be updated on subsequent visits. The treatment need and treatment provided should be marked in shortened form in the given spaces. The date of treatment begun should be inserted in the relevant column and the treatment provided column should be updated until the treatment is completed.

# (c) The Daily Record of treatment (DR) - Health 1974

All the children who seek care in the clinic are entered in the DR of treatment book. Each SDTT maintains a separate book of DR of treatment. It is compulsory to fill the first four columns of the DR for all the children in the target group. During the initial screening, all the parts of the DR including the examination finding and treatment done will be filled. In the examination part, caries will be marked according dmft/DMFT index. Periodontal conditions, malocclusion, fluorosis, and other defects will be marked in summary forms. For subsequent visits, only the care provided part with the first four columns should be completed.

# (d) Examination and history chart (HC) - Health 1975

The patients' Examination and History charts are maintained only for students in the base school. It should be continued throughout all the target ages. There are provisions to record the intraoral condition at first, second and third examinations at grades 1, 4 and 7 respectively. Caries is recorded according to the Oral Health Surveys- basic methods. Recordings are made regarding d/D (decayed), m/M (missing due to caries), f/F (filled due to caries) and dmft/ DMFT (total number of teeth which are decayed, missing due to caries and filled due to caries). The condition of gums in each sextant, oral health habits (device and material used for brushing, frequency of brushing, sugar consumption), and description of treatment carried out are also recorded. These are recorded separately at all three examinations.

#### (e) Monthly return (MR) - Health 1982

The monthly work performance is compiled in the monthly return and triplicates the MR to be sent to the Medical Officer of Health (MOH) office and the Regional Director of Health Services (RDHS) office before the 5th day of next month. One copy

is kept at the clinic as the clinic copy. The DR entries are transformed into the monthly return at the end of each day. At the end of each month, all the entries will be compiled to generate a monthly summary in the form of row totals. Monthly return compiles administrative data, patient examination findings and the care provided entries. The MRs should be certified by the MOH before sending to the Regional Director's office.

#### (f) Quarterly return (QR)

At the end of each quarter, the QR is filled in triplicate based on monthly return totals, are sent to the MOH office, RDHS office with the certification by the MOH. The SDT keeps the third copy in the clinic. Moreover, SDT has to create an annual return based on QR summaries and send to the above authorities annually.

#### Information generation at the district level

At the RDHS office, supervising school dental therapist, and regional dental surgeon ensure the MRs and QRs are collected from all the SDTs in the district. At the RDHS office, SSDT and the RDS compile all the QRs and annual returns from the SDTTS in the district and prepare a district quarterly return and an annual return, which is sent to the FHB. A mid-year review is done in all districts based on data generated at the district level.

#### Information generation at the national level

At FHB, all the district annual returns are compiled and the data are disseminated at annual health bulletin published by the FHB annually. (Ministry of Health, 2013) An annual review is done based on the data generated each year.

There were numerous problems and gaps identified with this paper-based system. The paper document is less secure compared to an electronic system, manually managing is a very tough and time-consuming process, insufficient storage space, difficulty in modification of data, increase cost, accuracy such as data entering errors, individual errors in adding up numbers,

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as well as timeliness, were few issues with the paper-based system. As a result, all SDTs were burden with too much of paperwork.

As a solution for the gaps and problems identified, with the objective of improving the data management system of School dental services, paper-based system was transformed into a webbased electronic information system.

For this purpose, we utilized the already operative Electronic Reproductive Health Management Information System (eRHMIS) of the Family Health Bureau, modified to capture data from School Dental Services.

eRHMIS is a "District Health Information Software-2 (DHIS-2)" based Health Information Management System. It was developed and implemented to manage data from Reproductive, Maternal, New-born, Child, Adolescent and Youth Health (RMNCAYH) programmes in Sri Lanka since 2017. The system provides data access to regional, provincial and national level health authorities and allows flexible data analysis at each level<sup>5</sup>.

RMNCAYH data capturing was implemented in several phases. The first phase which include implementation of capturing aggregated reproductive health data from the field and clinic activities in all Public Health Midwife (PHM) areas of the country was completed in year 2017. Since then, seven main components are developed and implemented in the system at the national level. The School Dental Service was the one such component<sup>5</sup>.

In order to get better acceptance and active participation consultative meetings with experts in the field of Community Dentistry as well as with the ground level stakeholders were done before implementing the web- based system. Further all the service providers as well as the supervising officers were trained about the new implementation.

Web-based system was implemented island wide from 2020 by a General Circular (Circular No 02-156/2019) issued by the Director General of Health services.

With this initiative, the paperwork of SDTs were reduced to a greater extend, as the content of quarterly return reduced. Annual return was totally scrapped as it could be generated by the system. Further data entering and calculation errors were minimized as the system automatically sum-up the data entered. Mainly it facilitated data analysis at all levels of information flow hierarchy with ease and helped to produce informative tables and graphs. This motivated all the stake holders in School Dental service.

In the web-based system, the responsibility of monitoring and verifying the data is with Medical officer of Health at the MOH level and the Regional Dental Surgeon (RDS) and Supervising School Dental Therapist (SSDT) at RDHS level. Considering data security and confidential issues, the regional level data were made visible only at the RDHS level. Access to national level data for monitoring and evaluation purposes were limited to Family Health Bureau.

First annual review of school dental service using the data from eRHMIS was done in August 2021. e-RHMIS has addressed many of the short times in the manual paper-based system. Many stakeholders both at district and central level appreciated the system, while more importantly few short comings were identified.

Oral Health Unit of the Family Health Bureau together with Monitoring and Evaluation Unit of FHB are taking measures to address the identified short timings within 2022.

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#### Transformation of Management Information System in School Dental Services in Sri Lanka

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# An overview of implications of cardiovascular drugs in clinical dentistry Part II - antianginals and antihypertensives

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#### **Abstract**

Cardiovascular diseases are considered one of the major causes of morbidity and mortality. Out of all the cardiovascular diseases and conditions ischemic heart disease and hypertension are responsible for the increased prevalence of mortality among those patients. Therefore, dental practitioners should have an adequate knowledge about the pharmacological agents the patients take, their possible adverse effects and the drug-drug interactions (DDIs) that might give rise as a result of the drugs prescribed by the dentist. Moreover, dental practitioners should be knowledgeable of the medical emergencies and be able to manage them efficiently. Hence, this article aims to provide an overview of pharmacological agents that are commonly used in cardiovascular diseases, the risk they pose due to DDIs with agents prescribed for dental conditions, their possible effects on dental treatments and remediable measures needed to be taken to deliver dental treatments efficiently and safely.

#### Introduction

Due to the high commonality of the ischemic heart disease and hypertension in the general population dental practitioner will frequently encounter such patients in day-to-day practice. Patients with angina has been shown to develop medical emergencies in dental clinic more than other patients who are been treated for cardiovascular disorders<sup>1</sup>. Inadequate knowledge

on cardiovascular diseases and their treatments and incompetency in managing such patients make the general dental practitioners to refer those patients to hospitals for dental treatments<sup>2</sup>. However, it has been demonstrated that managing such patients in a dental practice set-up could be easily done without causing untoward risks to the patients<sup>1</sup>. This necessitates that dentists have an adequate knowledge on pharmacological agents including antiarrhythmics, antianginal drugs, drugs in heart failure, antihypertensives and antidyslipidemic drugs which are commonly used in managing conditions such as arrhythmia, angina, heart failure, hypertension and hyperlipidemia, respectively. In a previous paper we have discussed the dental management of patients on antiarrhythmic drugs and drugs used in cardiac failure. This overview is an attempt to discuss the dental management of patients on antianginal and antihypertensive drugs.

#### 1. Antianginal drugs

Angina is clinically defined as sudden, severe tightening type retrosternal/central chest pain which radiates to jaws and or arms. It is a clinical diagnosis and three subtypes have been identified including stable angina, unstable angina and variant angina. Unstable angina has a risk of developing into myocardial infarction (MI) where cardiac myocytes are dying due to myocardial ischemia. The diagnosis of MI is based on the clinical history, 12-lead ECG and elevated cardiac

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biomarkers such as troponin I, troponin T and creatine kinase-MB (CKMB). An acute coronary syndrome is an umbrella term for unstable angina, ST elevated myocardial infarction (STEMI) and Non-ST elevated myocardial infarction (Non-STEMI) which arises due to the rupture of an atherosclerotic plaque or partial or complete thrombosis of the infarct-related artery. Acute coronary syndrome is considered a medical emergency.

Pharmacological agents for symptomatic relief of angina include glyceryl trinitrate (GTN), β-adrenergic blockers, long-acting nitrates such as isosorbide mono nitrate (ISMN), and isosorbide dinitrate (ISDN), calcium channel blockers (CCBs), nicorandil, ranolazine and ivabradine. Aspirin and statins are considered as drugs with prognostic benefits. Antiplatelet therapy (e.g., aspirin, clopidogrel), antithrombins (e.g., heparin, low molecular weight heparin (LMWH)), glycoprotein IIB, IIIA inhibitors (e.g., abciximab, tirofiban), analgesics (e.g., morphine), β-blockers (e.g., atenolol, metoprolol), vasodilators (e.g., GTN, ISMN), statins and ACEIs are used in the management of MI.

β-blockers exert their effect in angina by inhibition of β1-receptor-mediated stimulation on heart rate and contractility thus facilitating oxygen supply to myocardium. Selective β-blockers such as metoprolol, atenolol and bisoprolol act on heart without affecting  $\beta$ -2 receptors on lungs and vessels. Carvedilol, propranolol and sotalol are considered as nonselective β-blockers. Nitro vasodilators such as GTN, ISDN, ISMN are metabolized into nitrites and nitrates resulting in both venous and arteriolar dilatation. Venous dilatation reduces venous pressure and preload and increases subendocardial blood flow whereas systemic arteriolar dilatation reduces the afterload, enhances cardiac output and reduces oxygen demand. These agents also facilitate coronary vasodilatation resulting in marked improvement in angina. Other than the aforementioned effects, they may act as potent antiplatelet agents as well<sup>3</sup>.

Antiplatelet drugs decrease the platelet aggregation and inhibit thrombus formation. Aspirin and clopidogrel are commonly used antiplatelets in patients having cardiovascular diseases. Dual antiplatelet therapy with aspirin and clopidogrel is considered as the standard treatment for such patients<sup>4</sup>. Platelet aggregation and vasoconstriction are induced by thromboxane  $A_2$  (TXA<sub>2</sub>) whereas prostaglandin  $I_2$  (PGI<sub>2</sub>) exerts an opposite effect. Synthesis of TXA, relies on the COX-1pathway whereas PGI is dependent on the COX-2 pathway. Even though aspirin blocks both pathways, COX-2-mediated PGI, deficiency is not sufficient to initiate thrombosis. Anticoagulants are used for both treatment and secondary prevention of acute coronary syndrome. LMWH is considered as the first-line antithrombotic therapy in the management of acute coronary syndrome and it can be administered subcutaneously as well as intravascularly. Warfarin, which is an oral anticoagulant, acts on the vitamin K pathway which is essential for the synthesis of factor II, VII, IX and X and endogenous anticoagulant proteins C and S<sup>5</sup>.

#### Implications in dentistry

Coronary artery disease is very common in the general population and therefore, it is likely that the dental practitioner may encounter such patients in day-to-day clinical practice. In such a situation obtaining a detailed clinical history including drug history is vital with special emphasis on anticoagulants because those patients are at a high risk of developing another MI within the first month following their initial diagnosis. Physical and emotional stress during dental treatment may precipitate an anginal attack in patients who are at a high risk of developing an angina. It is important that the dental practitioner should reduce the undue stress of the patient by giving relevant details regarding the procedure when necessary.

Apart from premedication with anxiolytics and sedatives (5-10mg of diazepam the night before

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and 1-2 hour before surgery), nitrous oxideoxygen sedation can be used to relieve anxiety after excluding possible contraindications such as significant cardiovascular depression<sup>6</sup>. Due to the high prevalence and seriousness, the dentist must be aware of the symptoms and the treatment for angina at the clinic and MI until the patient reaches the hospital. Angina pain may originate from the mandibular region with secondary radiation to neck or throat misleading that the pain is in dental origin. In the event of an initial attack such patients may present to a dental rather than a medical practitioner. In such instances, careful evaluation of the patient's symptoms is utmost important<sup>6</sup>. A detailed history should be obtained from the patient to reveal the type of angina, risk factors for angina, the time elapsed since the last attack, medications and the patient compliance. The patient should be advised to take the prescribed medications without interruption. If the patient has already been treated for angina, it is necessary to make sure that the patient has emergency medications such as GTN, in an easily accessible place prior to commencing the dental procedure. Apart from that, the emergency drug kit should be ready with drugs including nitroglycerin when treating such a patient after ensuring that the drugs have not been expired. MI may precipitate as a prolonged chest pain which does not subside with sublingual GTN unlike the transient anginal pain. In such an emergency situation a 300 mg tablet of aspirin should be given to the patient to chew as a first aid measure until the patient is taken to the hospital<sup>7</sup>. MI has been identified to occur more frequently during the early mornings and patients tend to experience stress and tiredness towards the late afternoon. Therefore, dental appointments in such patients who are at a high risk of developing a MI should be arranged during daytime avoiding early morning hours and late afternoon hours<sup>8</sup>. It is believed that dental procedures should be done after 6 months of a previous attack of infarction and not earlier than that. Until then dental treatments should be limited to emergency procedures mainly focusing on pain relief9. During the treatment of such a patient, placing the patient in supine or sitting position is important and change of position from a supine to sitting as well as to a standing position should be carefully carried out to avoid orthostatic hypotension. Blood pressure and saturation monitoring may be required during intraoperative period depending on the cardiovascular status of the patient. Proper administration of anesthesia is required when administering local anesthetic containing adrenaline to avoid inadvertent intravenous administration because adrenaline can induce an excessive workload on the heart. It is advisable to stick to the recommended doses of adrenaline which is about 0.04mg (2 injections containing 1:100,000 adrenaline). Administering nitrates as a preventive measure of developing an angina, before local anesthesia is practiced in some institutions<sup>8,10</sup>. If the patient develops a chest pain during the procedure, suspension of the procedure immediately and administration of a sublingual GTN tablet with nasal oxygen should be carried out. If pain is not subsided, a second sublingual GTN tablet should be administered after 5 minutes. Pain lasting more than 15 minutes may indicate an impending MI hence; the patient should be transferred to a nearby hospital immediately.

Nonselective β-blockers may induce hypertension in the presence of adrenaline containing local anesthetic agents. Therefore, careful use of recommended doses of adrenaline while monitoring the vital signs such as blood pressure and pulse rate is important as well as the reassessment of the patient every 3-5 minutes after each injection when administering adrenaline to a patient who is on a β-blocker. It is also advisable to avoid gingival retraction cord in such patients due to the same reason<sup>11</sup>. Longterm use of nonselective β-blockers may also increase systemic local anesthetic concentration resulting in hypotension and bradycardia. Since long-term use of NSAIDs may reduce the antihypertensive effect of β-blockers, paracetamol is preferred over NSAIDs as analgesics<sup>12</sup>. Oral manifestations of \beta-blockers include

angioedema, dry mouth, oral ulcers, lichenoid drug eruptions, lupus erythematosus, Stevens - Johnson syndrome, oculo-mucocutaneous syndrome and manifestations of β-blockermediated hematological disorders. Most cases of angioedema are reported within the first week of initiation of β-blockers and may resolve after discontinuation of the culprit β-blocker. Dry mouth may occur due to β-blocker-mediated reduction in total salivary protein content. Oral ulcerations may also be seen in patients who are on β-blockers. Agranulocytosis and thrombocytopenia are considered as β-blockermediated hematological disorders where mucosal lesions such as hemorrhage and petechiae may arise. Few cases of oral lichen planus have been reported in patients taking propranolol. Acebutolol, labetalol, practolol and propranolol may induce lupus erythematous skin eruption whereas labetalol and practolol may cause oculomucocutaneous syndrome resulting in recurrent ulceration of oral mucosa. Carvedilol which is a selective β-blocker may cause Stevens-Johnson Syndrome involving skin and oral mucosa which may arise within 4 weeks of initiation of the therapy<sup>13</sup>. Vasodilators are known to exacerbate postural hypotension especially in the elderly. This effect may be enhanced during the administration of central nervous system depressants during moderate to deep sedation. Therefore, caution should be practiced in such instances.

Aspirin doesn't pose a major risk for bleeding during minor dental procedures but maybe of concern during extensive surgery. Generally, antiplatelets are not discontinued during dental procedures involving single or multiple dental extractions given that appropriate local hemostatic measures are carried out<sup>14</sup>. But in unusual circumstances, it is advisable to withhold the antiplatelet therapy on the recommendation of the patient's cardiologist which is usually recommended 5 days before the invasive therapy<sup>15,16</sup>. Simultaneous use of clopidogrel with aspirin may further enhance the risk of excessive

bleeding. However, interruption of aspirin may induce myocardial infarction in patients who are on dual antiplatelet therapy, hence, cardiologist's recommendations play a major role in decision making whether to discontinue the antiplatelet therapy or not. Antiplatelets may rarely discontinue in patients with coronary stents especially drug-eluting stents. If the patient has high-risk factors for cardiovascular diseases, it is always advisable to discuss with the cardiologist and outweigh the risk of thrombosis and postoperative bleeding risk. If bleeding can be arrested with local measures coupled with platelet transfusion it is advisable to continue medications during the treatments. Concurrent administration of NSAIDs to a patient who is on antiplatelets has a 2-3fold risk of bleeding from NSAID-induced gastric ulcers. Monotherapy with low dose aspirin has not been shown to cause excessive bleeding during invasive dental therapy. Ibuprofen is considered as a competitive inhibitor of aspirin as ibuprofen has been shown to counteract the aspirin-induced COX-1 inhibition of TXA2. As a result, patients are advised to take aspirin early in the morning and to take ibuprofen 1-2 hours later because by that time antiplatelet effect of aspirin has been already established. Angioedema may also occur with aspirin therapy due to the overproduction of leukotrienes as a result the inhibition of the COX pathway and shifting the accumulated arachidonic acid towards leukotriene pathway. Hematological manifestations such as agranulocytosis may occur due to dipyridamole (antiplatelet/phosphodiesterase inhibitor) therapy which may be evident by oral manifestations<sup>13</sup>.

Patients who are on anticoagulants have to face several risks during dental treatments including the risk of excessive bleeding after an invasive dental procedure, thromboembolic events due to dose adjustments or discontinuation of anticoagulants during dental treatment and DDIs between anticoagulants and other drugs which are commonly prescribed during dental treatment such as sedatives, analgesics and antibiotics. Prior discussion with the patient's physician or

cardiologist about the planned invasive dental treatment of the patient is advisable to avoid the abovementioned potential risks. Warfarin therapy is monitored by measuring the prothrombin time (PT) and the results are reported as an INR. This is beneficial as small changes in anticoagulation may cause marked changes in PT and INR. Most clinicians consider that maintaining INR within the range of 2-3 is ideal for most medical conditions whereas it may be higher in patients having prosthetic heart valves. The values of INRs for various dental procedures and the management of bleeding is discussed in a previous article published in this journal<sup>17</sup> and elsewhere<sup>5</sup>. It is always advisable to discuss with the cardiologist or with the physician in situations where INR is maintained at a higher value of 3.5- 4.5 in patients having atrial fibrillation. An appointment with the physician or cardiologist should be made at least a week prior to the dental treatment because INR to establish may take days to a week. Bridge therapy is used in patients who are at risk of thrombosis due to the cessation of anticoagulant therapy or experience excessive bleeding if measures were not taken properly. Usually, injectable anticoagulants are given when oral anticoagulants such as warfarin are discontinued and INR is assessed 1-2 days before an invasive dental treatment if previous INR is inconsistent. On the other hand, patients whose anticoagulants are stabilized can be managed based on the INR value within a week. People with unpredictable high or low INR despite consultation with the medical team should have an INR on the day of the surgery and if the target values are not achieved, the treatment should be postponed. Vitamin K and local hemostatic measures and fresh frozen plasma should be reserved for an emergency bleeding in such patients during the procedure<sup>11,18</sup>. Intravenous heparin should be stopped 1-6 hours prior to the procedure and restarted after 1 hour, if necessary, by allowing the time to form the clot fully. Local hemostatic measures such as using an antifibrinolytic mouthwash containing tranexamic acid (4.5%) and packing the wound (e.g., socket)

with hemostatic agents such as oxidized cellulose, gelatin sponges, and micro crystalline collagen are adequate to arrest excessive bleeding<sup>5,7</sup> and protamine sulphate infusion can be used if there is more bleeding. Metronidazole, tetracycline and macrolides may enhance the anticoagulant effect of warfarin resulting in increased bleeding tendency. Therefore, those antibiotics should be avoided in such patients. Analgesics or anti-inflammatory doses of NSAIDs should be used cautiously with anticoagulants due to their synergistic effects. This is rarely seen with low dose aspirin. Therefore, monitoring is essential in patients receiving NSAIDs and anticoagulants together<sup>19</sup>.

#### 2. Antihypertensives

Hypertension is a commonly diagnosed disease worldwide which is associated with increased cardiovascular risk and mortality. It is defined as systolic blood pressure ≥140 mmHg and/ or diastolic blood pressure ≥90 mmHg. This is further divided into pre-hypertension (120- 139 mmHg/80-89 mmHg), grade 1 (140-159 mmHg/ 90-99 mmHg), grade 2 (160-179 mmHg/100-109 mmHg) and grade 3 (≥180 mmHg/≥110 mmHg)<sup>20</sup>. According to the etiology, it can be classified into primary hypertension which is the commonest type with no identifiable cause and secondary hypertension which has identifiable causes such as renal parenchymal diseases, pheochromocytoma, renal artery disease, Cushing's disease, and others. Secondary hypertension may progress into resistant hypertension with multiple cardiovascular and renal complications. Combination of ACEIs, ARBs, CCBs, diuretics and β-blockers are used in the management of hypertension. CCBs exert a vasodilatory effect, decrease the contractility of working cardiac muscles and slow SA node and AV conduction. They are mainly divided into two groups including dihydropyridines such as amlodipine and nifedipine and nondihydropyridines such as verapamil and diltiazem. Nifedipine acts more on vascular smooth muscles than heart whereas verapamil and diltiazem have

the same degree of effects on both heart and vessels <sup>21</sup>.

#### Implications in dentistry

The dental practitioner should take a detailed history including onset and progression of the disease, medications and patient's compliance, symptoms of end-organ damage among others in order to determine the type of dental treatment and possible complications which may arise during procedures due to the disease condition and DDIs<sup>12</sup>. This would help the dentist to deliver the dental treatment without untoward complications during and after the dental treatment. The patient should be advised to take their prescribed antihypertensives prior to the dental procedure. Hypertension is most of the time asymptomatic and patients are unaware that they have high blood pressure. Therefore, it is advisable and mandatory that dentists measure the patient's blood pressure in all new patients at each clinic visit. Routine measurement of blood pressure may enable the dentist to identify new patients having hypertension as well as reduce the risk of cardiovascular events and acute complications during dental treatment and at the same time allows the dentist to assess whether the condition is under control. Dental procedure should not be performed if the blood pressure is more or similar to grade 3 and it should be postponed until the control is achieved. It is better if the dentist can refer the patient to a physician for further assessment if the patient is newly diagnosed or if no adequate control has been achieved in a known hypertensive patient<sup>8,12</sup>. An accurate measurement of blood pressure is important for definitive diagnosis and to decide the treatment plan and this requires that blood pressure should be measured with a properly calibrated sphygmomanometer. It is always good that if the dental practitioner can advise the patients regarding possible side effects of abrupt withdrawing of antihypertensives of a patient's own accord. Withdrawal symptoms may occur with all antihypertensives but commonly encountered with centrally acting agents such as  $\alpha$ -methyldopa, clonidine, and guanabenz and with  $\beta$ -adrenoreceptor blockers. Abrupt discontinuation of higher doses of centrally acting antihypertensives can produce symptoms of sympathetic over activity such as agitation, headache, sweating, nausea and less commonly rapid changes in blood pressure. If  $\beta$ -blockers are suddenly stopped a sympathetic over activity as well as an acute exacerbation of the cardiac disease in patients with ischemic heart disease may occur<sup>22</sup>.

The antihypertensive effect of ACEIs, ARBs, diuretics and β-blockers is inhibited by the simultaneous administering of NSAIDs for more than 5 days. In such an instance paracetamol would be a better alternative. Adrenaline can be considered as a contraindication in hypertensive patients on nonselective β-blockers such as propranolol, adrenergic neuron blocking or noradrenaline depleting drugs such as reserpine or guanethidine. However, other vasoconstrictors can be used cautiously. Long-term use of guanethidine-related drugs with inadvisable adrenaline doses in local anesthetic preparations may enhance the effects of adrenaline in resulting cardiac arrhythmias and hypertensive crisis. Drugs such as propranolol block both β1 and β2-receptors and increase systemic vascular resistance due to exaggerated α effects of adrenaline with remarkable systemic vasoconstriction and pulmonary congestion<sup>23</sup>. To avoid any drug reaction with adrenaline in local anesthetics, it is advisable to measure blood pressure 5 minutes after injecting a small dose of about 1ml of 2% lignocaine with 100,000 adrenaline, depend on the dental procedure and the local anesthetic requirement. It can be assumed then that a hypertensive crisis with subsequent doses is unlikely to occur if no changes in blood pressure has been observed. Substantial amounts of adrenaline may be absorbed systemically from gingival retraction cords, adequate to cause changes in hemodynamic parameters. The amount depends on the length and concentration of the impregnated cord as

well as the duration it stays at the site of application. Moreover, good pain relief is often indicated in patients with hypertension because endogenous catecholamines may further enhance the condition in such a patient.

Methyldopa, clonidine, guanabenz and guanfacine (centrally acting antihypertensives) have more sedative side effects. Hence, the antianxiety agents and other central nervous system depressants should be used cautiously to avoid possible excessive central nervous system depression due to synergistic effects of drugs with similar effects. Careful positioning of patients from supine to stand should be exercised especially in those who are on antihypertensives since they are vulnerable to get an attack of orthostatic hypotension resulting in accidental falls during position changing. Hypertensive emergencies where blood pressure is more than 210mmHg/ 120mmHg can occur at any time during intraoperative period. In such a situation initial administration of frusemide and captopril is very important. If the blood pressure is not reduced within 30 minutes the patient should be taken to the nearest hospital immediately.

Usually, non-dihydropyridine CCBs and macrolides are metabolized in the liver by the same family of metabolizing enzymes called CYP3A4. Thus, people who are prescribed with clarithromycin or erythromycin may develop hypotension and shock if they are also on CCBs. Simultaneous administration of NSAIDs for more than 5 days will reduce the antihypertensive efficacy of CCBs as well. Gingival overgrowth is reported to be more prevalent among CCB users, especially with nifedipine and amlodipine and may affect the patient's appearance (esthetics), mastication, speech, oral hygiene and increased risk of bacterial infections. Strict oral hygiene with regular prophylaxis may reduce the occurrence of gingival overgrowth. CCBs especially nifedipine and diltiazem may induce angioedema of tongue and lips within the first week of therapy and reduces with discontinuation of treatment. Oral ulceration and lichen planus have been reported among diltiazem users and amlodipine users, respectively. Toxic epidermal necrolysis (TEN) and Stevens - Johnson syndrome can rarely occur with CCBs. Hypogeusia and hyposmia may occur with diltiazem whereas nifedipine may cause taste and smell distortion. Verapamil and nifedipine have the potential to reduce saliva protein and saliva output.

# 3. Antidyslipidemic drugs and dental implications

Atherosclerosis is caused by the development of fatty streaks and plaques in large and medium-sized arteries in the body. Therapeutic agents which are used in the management of dyslipidemia include fibric acid derivatives (e.g., gemfibrozil, clofibrate), nicotinic acid, bile acid sequestrants (e.g., cholestyramine), 3 hydroxy-3- methylglutaryl coenzyme reductase inhibitors (statins) (e.g., lovastatin, pravastatin, simvastatin, atorvastatin) and cholesterol absorption inhibitors. Macrolides and azole antifungals such as ketoconazole inhibit CYP3A4 resulting increased plasma concentration of statins and therefore, increase the risk of rhabdomyolysis and acute kidney injury. Tetracycline absorption may be reduced in patients who take bile acid sequestrants resulting in decreasing therapeutics doses of antibiotics. Simvastatin causes both angioedema and lichenoid eruptions involving skin and mucosa. Dry mouth, itchiness of tongue and lips and bitterness may also be seen among statin users.

#### Conclusion

Obtaining a detailed medical history and preassessment of the patient prior to dental treatment are essential to deliver safe and effective therapy. Details of current drug therapy will alleviate possible DDIs with the agents dentist may prescribe. Good communication with the patient's medical practitioner or cardiologist is vital if prior medical assessment is required before dental therapy. Patients may not to take their usual antihypertensive or antianginal on the day

of the dental appointment which may give rise to cardiovascular complications during therapy. Patients' compliance with their drug regimen and taking blood pressure before dental treatment may prevent possible complications. Pre-medication to reduce anxiety and proper pain management are necessary to avoid medical emergencies. Retraction cords impregnated with adrenaline should be avoided at all times in patient having ischemic heart disease and hypertension and. Appointments should be scheduled in the mornings to reduce anticipation stress and the stress due to actual therapy. Reducing the time taken to perform a procedure to a minimum is also important to prevent any possible medical emergencies.

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# Overlap of Sjögren's syndrome with rheumatoid arthritis and scleroderma

J.M.D.S.G. Jayasekara, J.M.M. Jayasinghe, J.M.R.P. Bandara

#### Abstract

Sjogren's syndrome which is characterized by xerostomia and dry eyes can occur in conjunction with other systemic auto immune diseases. This is a case report of a patient whose primary complaint was large and small joint pain for six weeks. In accordance with examination and investigations, patient had features of rheumatoid arthritis and scleroderma other than the Sjögren's syndrome which was diagnosed definitively with a lower labial gland biopsy. The diagnostic approach together with the clinical problems including increased prevalence of dental caries and oral candidiasis that arise from xerostomia are emphasized here. This case highlights the importance of clinical suspicion and subsequent correct diagnosis of Sjögren's syndrome in an instance where patient's primary concern is a symptom of other autoimmune disease. This will help to break off the disease progression which will ultimately improve the quality of life of the patient.

**Key words:** Sjögren's syndrome, overlap

#### Introduction

Auto immune diseases can be either systemic or organ specific. Systemic autoimmune disease is a more generalized form in which the body tissues are attacked by body's own adaptive immune response. Generally, systemic diseases are not purely categorized into one separate disease type such as polymyositis, rheumatoid arthritis etc. as they often share same clinical features with each other<sup>1</sup>. Frequently, patients present with milder incomplete forms of other auto immune diseases in addition to the disease in which the diagnosed criteria are fulfilled. With the progression of the disease, symptoms of one syndrome will overlap with symptoms of other diseases. Therefore, overlap syndromes can include features of two or more conditions. As many as 25% of patients with connective tissue diseases (CTD), present with overlapping clinical features<sup>2</sup>. Mixed connective disease (MCTD) and Undifferentiated connective disease (UCTD) are two entities of CTD. It is common to observe some patients who cannot be assigned to a single disease category in clinical practice and these patients are classified as having an undifferentiated connective tissue disease (UTCD)3. The most well characterized overlap syndrome, mixed connective tissue disease (MCTD), is defined by anti-RNP autoimmunity along with features of at least two of other connective tissue diseases<sup>4</sup>. Therefore, MTCD is one particular overlap. Common diseases associated with overlap syndrome are systemic lupus erythematosus, systemic sclerosis, polymyositis, dermatomyositis, rheumatoid arthritis and Sjögren's syndrome.

Sjögren's syndrome is characterized by xerostomia

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and keratoconjunctivitis sicca due to lymphocytic infiltration of salivary glands and lacrimal glands. Primary Sjögren's syndrome occurs in people with no other rheumatic disease. Secondary Sjögren's syndrome occurs in people who have another rheumatological diseases. We present a case with Sjögren's syndrome overlapping with Rheumatoid arthritis and systemic sclerosis.

#### **Case Report**

A 44-year-old mother of four children was admitted with the chief complaint of large and small joint arthritis for six weeks duration. Additionally, she had backache which was worse in the morning. Further, she has had dry mouth and irritation of both eyes for six months. She had developed dysphagia over the last three months. She had no preexisting auto immune diseases or a significant family history.

On examination she had depigmented area above the right eyebrow and mild swelling over the right parotid region. Her mouth opening was restricted significantly and could barely insert two fingers. Intraorally multiple dental caries was present and whitish plaque was noted on the dorsum of the tongue that could be wiped off. Skin over both upper limbs was thickened (Figure 1) and hardened and fingers were puffy. Distal and proximal interphalangeal joints of both hands were swollen and tender.



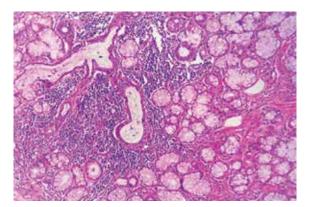
**Figure 1.** Skin darkening and thickening together with dactylitis

Investigations showed a high ESR (110 mm/hour). ANA and Rheumatoid Factor were positive. CPK was high (3265 U/L) which was suggestive of a concurrent muscle pathology. Ultrasound scan of the of neck showed enlarged right side parotid gland with altered architecture suggestive of Sjögren's syndrome. Labial biopsy from lower lip was taken and histopathological features were consistent with Sjögren's syndrome. Upper GI endoscopy showed GERD with erosions and ulcers in the distal esophagus. HRCT did not show evidence of interstitial lung disease.

#### **Discussion**

Sjögren's syndrome can affect at any age, but in majority the symptoms start to appear during the ages of 45-55yrs<sup>5</sup>. Female predilection is also noted<sup>6</sup>. It has two forms as Primary and secondary Sjögren's syndrome. The symptoms of the latter coexist with the presence of other systemic connective tissue diseases.

There are no separate classifications for secondary Sjögren's syndrome. For a definitive diagnosis, a positive labial biopsy is emphasized in the literature<sup>7</sup>. In this patient, labial biopsy showed salivary acinus with periductal lymphocytes aggregations and proliferative changes of ducts. (Figure 2) When performing the biopsy sample from the bottom of the lower lip should be taken so that minor salivary glands are included for



**Figure 2.** Periductal lymphocytic aggregates and proliferative changes of ducts in labial salivary glands

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the histopathological examination. In addition to the minor salivary gland histopathological features, ultrasonography is also used in some diagnostic systems as altered architecture could be suggestive of Sjögren's syndrome<sup>8</sup>. There were multiple hypoechoic areas noted in the left parotid gland of this patient which is a main feature. Schirmer's test is another investigation that can be carried out to diagnose, although it was not attempted in this patient. This test involves putting a strip of paper under the lower eyelid, waiting five minutes, then measuring how much moisture was absorbed by the paper which is indicative of the tear production.

Sjögren's syndrome overlapping with rheumatoid arthritis (RA) is not uncommon. The incidence ranges from 3.8% - 38.7% in different parts of the world. When the chief complaint of a patient is related to joint pain, possibility of having Sjögren's syndrome may go unnoticed. Thus, major problems associated with that are overlooked.

In this case, Increased prevalence of dental caries can be attributed to the decrease salivary flow. In addition to the dental caries, she presented with oral candidiasis on the dorsum of the tongue. Decrease salivary flow is directly associated with oral candidiasis <sup>10,11</sup>. Saliva has many constituents such as histatins which has anti-fungal properties and thus in the absence of adequate saliva, *Candida* spp can grow.

This patient underwent upper gastrointestinal endoscopy mainly for two reasons. One is to exclude esophageal candidiasis and secondly to identify any abnormality since she complained of dysphagia. Further she was having scleroderma features in the upper limb including sclerodactyly and puffy fingers. GI manifestations such as microstomia, esophageal fibrosis and burns due to reflux disease are commonly seen in the setting of systemic sclerosis. Therefore, exclusion of such manifestations is also of great importance specifically in this case.

#### Conclusion

When a patient has significant clinical features of a single autoimmune disease or overlap syndrome, symptoms of Sjögren's syndrome may be overlooked. Specially if the signs and symptoms of Sjögren's syndrome is minimal and nonspecific. This may lead to deterioration of clinical picture and irrecoverable damage, especially in oral health. Therefore, clinical suspicion is imperative in timely diagnosis and management of Sjögren's syndrome.

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# Oral submucous fibrosis in a 19-year-old male: An exceptional case emphasizing behavioural risk factors

Venuri Rekogama, S.A.K.J. Kumara, B.S.M.S. Siriwardena

#### **Abstract**

Children and adolescence are now reported with oral submucous fibrosis (OSF) due to chewing areca nut or areca containing products. OSF is a chronic inflammatory disease which is characterized by stiffening of oral mucosa due to loss of fibroelasticity that has a potential for malignant transformation. More than 60 cases have been reported in the literature. Although cases reported from western countries, all are from South Asian nationals. A 19-year-old boy presented with a difficulty in mouth opening and burning sensation to spicy food with pallor oral mucosa. Most posteriorly, fibrous bands were palpable with depapillation of the tongue. Habit intervention, methyl prednisolone intralesional injections, nutritional supplements, and mouth opening exercises showed favourable improvement. This case report with the evidence of literature highlights the lack of awareness among general public about the causative factor being areca for oral submucous fibrosis and the fact that it is a potentially malignant disorder which is a problem that should be addressed immediately.

**Key words:** Oral submucous fibrosis, Young, Areca nut, betel quid, areca products.

#### Introduction

Oral submucous fibrosis (OSF) is a potentially

malignant disorder in the oral cavity which presents due to a chronic, insidious change in the submucosal tissues<sup>1</sup>. It is characterized by loss of fibroelasticity leading to progressive stiffening of oral mucosa and ultimately resulting in reduction in mouth opening<sup>1,2</sup>. The hallmark of the disease is said to be the presence of fibrous bands in the lips, cheeks and soft palate. The disease manifestations also include burning sensation to spicy food, gradual depapillation of the dorsum of the tongue, blanching and ulceration of the oral mucosa, appearance of tough and leathery texture of mucosa<sup>2,3</sup>. Mostly people older than 40 years of age are affected as the majority nevertheless, recent studies have found evidence that younger people are also affected and those below 21 years of age have developed the disease within a shorter duration than the older individuals<sup>3</sup>.

OSF is typically encountered in south and southeast Asian populations thereby suggesting a distinct geographical and ethnic predisposition<sup>2,3</sup>. However, recent updates have shown that it has spread to Europe and North America as well due to migration of people of Asian descent<sup>2,4</sup>. A significant risk of 7.6% (7% -13%) for malignancy has been divulged with OSF<sup>4</sup>. In certain studies, it was revealed that it has taken about 3 to 16 years for malignant transformation after diagnosis of OSF in usual cases which involves older people with a peak incidence of 35-54years<sup>4,5</sup>.

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In 1952, Schwartz pioneered the discoveries of oral submucous fibrosis in five Indian females and termed the condition as "Atrophia Idiopathica tropica mucosae oris". Over time, this condition evolved as a clinicopathological entity rather than an idiopathic one.

OSF is believed to be of multi-factorial origin where the risk factors are consumption of chilli, betel chewing, tobacco smoking and due to deficiencies in vitamin B, folic acid, Iron and protein and genetic predisposition to the disease. Now, it has become evident through various studies that the sole etiological factor for this condition is consumption of areca nut<sup>1,5</sup>. Studies have disclosed that only 1-2% betel chewers acquire the disease although over 600 million are speculated to be betel chewers worldwide indicating a genetic predisposition to the disease.

Based on the constituents of areca and genetic predisposition to the disease, various mechanisms and biological processes have been proposed for the pathogenesis of the disease<sup>1,6</sup>. Alkaloids, Tannins, Arecoline and copper which are the main substances in areca<sup>7,8</sup> alters the collagen metabolism. In addition, arecoline has an antiproliferative and cytotoxic effect on endothelial cells which results in reduction in vascularity ultimately causing atrophy of epithelium and creating a hypoxic surrounding that predispose the tissue to carcinogenesis<sup>1</sup>.

Histopathological features are in accordance with pathogenesis of the disease which includes increased deposition of collagen in the extracellular matrix, reduced vascularity and inflammatory cells, subepithelial hyalinization<sup>6</sup>. Alterations are seen in both epithelium and the connective tissues. Marked atrophy and complete loss of rete ridges become evident in the epithelium<sup>1</sup>. In very early stages, in the connective tissues, fibroblastic activity is strong and fine fibrillar collagen appear in the extracellular matrix and with time, plump fibroblasts in moderate numbers and inflammatory infiltrates

of polymorphonucleocytes; predominantly eosinophils appear along with dilated and congested blood vessels. When the disease progresses, collagen get moderately hyalinized, fibroblastic activity becomes less significant, blood vessels become constricted and the inflammatory exudates mainly lymphocytes and plasma cells remain. In advanced stages completely hyalinized collagen, obliterated or highly constricted blood vessels are seen<sup>1,7</sup>. In later stages the hyalinized collagen extends up to muscles from submucosa entrapping and destroying them1. OSF can be graded from 1-5 developed using mainly clinical/physical features<sup>7</sup>. So far there is no proper management protocol and currently many treatment options are carrying out such as cessation of habit, physical therapy, medical and surgical intervention<sup>8,9</sup>.

This report presents an unusual case of OSF which has developed during a very short course of time after exposure to areca in a younger patient and a review of literature outlining clinical features, etiopathology and pathogenesis.

#### Case

A 19-year-old male patient with a complaint of burning sensation and restriction of mouth opening presented to the oral and maxillofacial clinic. He had aggravation of burning sensation to spicy food since few months back. Patient initiated the risk habits 2 years ago and continued until the symptoms appeared recently. During the course of time, he had experienced a progressive reduction in mouth opening (Figure 1).

Patient used to consume about 3 self-prepared betel quid with all 4 ingredients (betel leaf, slaked lime, tobacco and areca nut) which is a routine quid by majority. Every day he used to keep the quid for about one hour, mostly in the right side, posterior buccal pouch region. He had practiced the habit to stay awake while studying and his father was also a betel chewer for a long period. The patient did not have any other harmful habits and the medical history was nothing significant.

On examination, maximum extent of mouth opening was recorded as 22mm from upper to lower incisor. Intra orally pale, glossy bilateral buccal mucosa mostly on the right side (Figure 2), pale upper and lower labial mucosa, lips, floor of the mouth and palate along with leathery texture of mucosa and in addition depapillation of the tongue was observed. Few firm bands were palpable mostly on the right side most posterior part of buccal mucosa.

Initially, habit intervention with NPT (Nystatin, Prednisolone, Tetracycline) mouth wash for 3 weeks, a vitamin supplement for 1 month was prescribed. Incisional biopsy was done after antifungal treatment from right buccal mucosa and histopathology revealed features of OSF with mild epithelial dysplasia in a single focus (figure



Figure 1. Reduced mouth opening

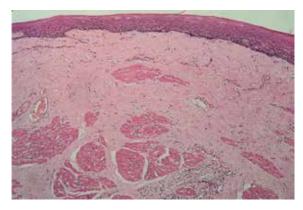


Figure 3a. Atrophic epithelium with dense fibrosis with muscle atrophy Histopathology with mild dysplasia

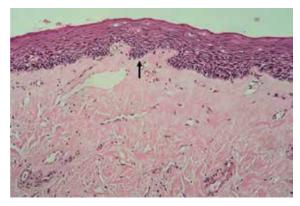
3a, 3b). Depo-medrol (methyl prednisolone) intralesional injection was given once and advised to follow several mouth opening exercises and a month later, the mouth opening was increased up to 25mm. in follow-up visits more 2 doses of Depo-medrol with exercises was given and 35mm mouth opening was achieved. Consent was given by the patient to use his data as a research material.

#### Discussion

Oral submucous fibrosis is a debilitating, potentially malignant disorder which is developed due to an imbalance in collagen metabolism resulting in excessive deposition of collagen in submucosa and later in deeper tissues causing loss of fibroelasticity<sup>1, 3,9</sup>.



**Figure 2.** Pale and glossy buccal mucosa. Note stains on teeth due to the abit



**Figure 3b.** Early budding retes (arrow) with subepithelial hyalinisation

The peak incidence of this condition was found to be 35-54 years of age through studies carried out in kerala<sup>5</sup> and as per a study done in Taiwan disclose that the mean age of occurrence of the disease has increased from 1996 to 20139. A wide variation in preponderance to a particular sex was recorded in different studies. Accordingly, the general predilection to females was thought to be associated with the deficiencies in iron and vitamin B complex in Indian women<sup>4</sup>. Yet, a survey done in Manipal, India recorded a propensity for male patients with OSMF<sup>10</sup>. Another, carried out in Gujarat, India in2015 involving 170 patients showed that 98.58% were male while only 2.42% were females where 22% were between 11 and 20 years, with the highest percentage of 52% were between 21 and 30 years and only a 5% between 31 and 40 years of age suggesting increased incidence of the disease in the age range 21 to 30 which is in agreement with findings of study done in Gujarat, through which it was discovered that about 85% of the patients were younger than 35 years<sup>9</sup>. At the same time, it shows that incidence of the disease in teenagers is not very frequent. Thereby, this patient who is a 19 year old male is also quite unusual as it is an early presentation of the condition in comparison to the literature.

More than 60 cases have been reported in the literature below 20 years (table 1). Within that early OSF cases have been reported in preschoolars<sup>2,4,5</sup>. There were 22 females and 36 males with M:F ratio of 1.7:1. All of them used areca either traditional way or as commercial areca product. Younger children mostly used sweetened areca. Accordingly, there is an increase in the incidence of the disease in young people, which is questionable whether this is due to the upsurge in commercial availability of areca for youngsters and the fact that it is an addictive substance.

**Table 1.** OSF in younger age group of patients reported in the literature (less than 20 years)

<b>Author and Year</b>	No. of	Age (Mean/	Gender	Habit
	<b>Patients</b>	range in years)		
Sirsat and Khanolakar (1962)	4	1-10 yrs	*	*
Anil S, Beena V.T (1993)	1	12	F	Areca nut chewing
Mundra et al. (1999)	1	8	F	Areca nut chewing
Shah et al (2001)	1	11	F	Areca nut chewing
Yusuf H, Yong SL (2002)	1	12	M	Areca nut chewing (gutkha)
Hazarey et al. (2007)	1	4.5	F	Areca nut chewing
Yazdanpanah et al (2009)	1	17	M	Areca products
Sitheeque et al. (2010)	5	3	M	Areca nut chewing
		3	M	Areca nut chewing
		3	M	Areca nut chewing
		3	F	Areca nut chewing
		2	F	??
Agrawal et al. (2011)	1	9	F	Areca nut chewing
Dhariwal et al. (2012)	2	10	M	Areca product (gutkha)
		12	F	Areca product (Pan masala)
Gupta et al (2013)	2	10	M	Areca nut chewing
		11	F	
Deshpande et al (2013)	1	14	F	Areca nut

# Oral submucous fibrosis in a 19-year-old male: An exceptional case emphasizing behavioural risk factors

Duggirala et al (2015)	3	9	F	Areca product (sweet supari)
2 4881414 20 41 (2010)		13	M	Areca nut
		15	F	Areca product (sweet supari)
Khandelwal et al (2017)	1	14	M	Areca nut chewing (gutkha)
Talla et al (2019)	1	5	F	Areca nut
More et al (2020)	36	12	M	Areca product (Flavoured)
		11	F	Areca product
		11	M	Areca nut
		14	M	Areca product (Gutkha)
		14	M	Areca product
		9	M	Areca nut
		14	M	Areca nut
		10	F	Areca product
		13	M	Areca product
		14	M	Areca product
		13	M	Areca product
		14	F	Areca product
		15	M	Areca product (pan masala)
		10	F	Areca product
		15	M	Areca product (Mawa)
		16	M	Areca product (pan masala)
		11	M	Areca product
		16	M	Areca nut
		14	M	Areca product
		14	F	Areca product
		12	M	Areca product
		14	M	Areca nut
		13	F	Areca product
		15	M	Areca product (Mawa)
		15	M	Areca product (pan masala)
		11	M	Areca product
		12	M	Areca nut
		15	M	Areca product (Gutkha)
		13	F	Areca product
		14	M	Areca product (Mawa)
		10	F	Areca product
		15	M	Areca product (pan masala)
		13	M	Areca nut
		12	F	Areca product
		15	M	Areca product (pan masala)
		14	M	Areca product (Mawa)

(\*unknown 4)

The commonest site involved is buccal mucosa and vestibule, however site varies depending on the way the contents are chewed and duration of the habit<sup>4,5</sup>. In most studies bilateral involvement is frequent. In this case right side buccal mucosa was affected more, probably the patient kept the quid in the right-side buccal vestibule for about an hour Furthermore this patient is a student engaged in studies and subjected to stress, certain deficiencies in vitamins and minerals may have contributed to the progression of the disease.

The time taken for the onset of the disease in this case which is 2 years is in line with the existing literature which indicates that to be as 2 to 5 years<sup>4</sup>. At the same time certain literature depicts that period of onset is associated with the age where there is a quick onset in younger patients (3.5 years) compared to older ones (6.5 years)1 which is again reflected in this particular case. The severity and the time taken to develop the disease depends on frequency and duration of consumption and the way in which areca is consumed<sup>1-3</sup>. It was revealed that time and frequency play an important role and commercial preparations which have high concentrations of areca have high potential to have the disease at a short duration than the self-prepared conventional betel quid<sup>2</sup>. This patient had been a daily consumer of self-prepared betel quid who developed OSF within a short period.

Although, histopathological studies do not play a prominent role in provisional diagnosis of the disease it is of utmost importance in definitive diagnosis, disease progression, prognosis of the disease and to assess malignant transformation<sup>5</sup>. This case revealed mild degree of dysplasia with other characteristic OSF features.

At present, treatments advocated are concerned in controlling the signs and symptoms, terminating the progression of the disease, improve the restricted mouth opening and reduce the risk of malignant transformation<sup>9</sup>. Although not many studies were conducted considering

habit intervention as primary management, it is vital to proceed with habit intervention educating and motivating the patients to cease the consumption of areca which is addictive thus terminating the progression of the disease8. Yet, no accurate measurement is introduced to check its effects and evidence of cessation. Several studies were carried out based on variety of medical interventions. Those include immunomodulators, corticosteroids, proteolytic enzymes, hyaluronidase which are administered as either systemically, topically, intralesionally or orally8. In addition, as antioxidants, nutritional supplements are also used. These are used as single agents or in combination<sup>8</sup>. The treatments provided to this patient are consistent with the currently available options mentioned in the literature which was effective.

#### **Conclusions**

There seem to be an upsurge of incidence of the disease in young people with the increase in commercial availability of areca. The disease development can be rapid specially, in daily consumers of betel quid. Lack of awareness among general public about the causative factor being areca for OSF which is an OPMD which should be addressed immediately. Furthermore, it is of great necessity of a new drug to evolve which can be used to treat this debilitating disease.

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1979; 37(6): 407-9.

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Lemanek K. Adherence issues in the medical management of asthma. J Pediatr Psychol [Internet]. 1990 [cited 2010 Apr 22];15(4):437-58. Available from: http://jpepsy. oxfordjournals. org /cgi / reprint / 15 / 4 / 437 (If available, mention the DOI number at the end of the URL)

#### Unpublished article

Barker DS. Lucas RB. Localised fibrous growth of the oral mucosa. J Dent Res 1965: in press.

#### Books and other monographs

Becker A. Orthodontic treatment of impacted teeth. 3<sup>rd</sup> ed. Oxford, United Kingdom: Wiley-Blackwell:2012

#### Chapter in an edited book

Boyde A. Amelogenesis and the structure of enamel. In: Cohen B. Kramer KH (eds). Scientific Foundations of Dentistry. London: William Heinemann Medical Books Ltd.; 1976.p 335-352.

#### Chapter in a non-edited book

Speroff L, Fritz MA. Clinical gynaecologic endocrinology and infertility. 7<sup>th</sup> ed. Philadelphia: Lippincott Williams and Wilkins; 2005. Chapter 29, Endometriosis; p.1103-33.

#### No author given

International statistical classification of diseases and related health problems, 10<sup>th</sup> revision, vol J. Geneva: World Health Organisation, 1992; 550-564.

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