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A Clinical Study of Oral Mucosal Changes Adjacent to Amalgam Restorations

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ABSTRACT

Amalgam has been widely used in dentistry and its components may cause some oral mucosal changes (OMC), commonly presenting as oral lichenoid lesions (OLLs), acute or generalized sensitivity reaction or amalgam tattoo. Our objective was to determine the demographic and clinical profile of patients with and without OMC adjacent to their amalgam restorations (AR) and to evaluate the prevalence and types of AR-related OMC and associated clinical parameters. *Materials and methods*: In this retrospective cross-sectional study, 83 outpatients attending the Primary Dental Care Unit at the Faculty of Dentistry, University Malaya were examined for the presence of AR-related OMC. The study period was from early to mid July 2016. Firstly, patients' personal details (age, gender, medical status, social habits) were analyzed and history of AR (the age, condition and number of restorations) was determined. Clinical examination of patient's oral cavity was carried out to detect any AR-related OMC. The data collected was analyzed using SPSS 12.0.1 *Result*: Approximately 14.6 % patients had OMC. OLLs and amalgam tattoo made up 1.2% and 13.4% respectively. Females (8.4%) had higher predilection and Chinese were more commonly affected (8.4%). Social habits were not associated with OMC. Certain systemic diseases, age (p=0.005) and duration of amalgam (p=0.007) in the oral cavity were significant risk factors for OMC. *Conclusions*: Present findings suggest that AR-related OMC is uncommon. Three key parameters namely systemic diseases, patient's age and duration of AR were identified as significant risk factors predisposing to the development of OMCs.

Keywords: Oral mucosal changes, amalgam restorations, oral lichenoid reactions, amalgam tattoo

INTRODUCTION

Dental amalgam is an alloy composed of a mixture of approximately equal parts of liquid mercury and a powder consisting of silver (~22-32%), tin (~14%), copper (~8%) and other trace metals, including zinc (1). Local toxic effects such as mercury vapour is released during insertion, condensation and carving of amalgam (2). Chewing during eating as well can release-mercury as a vapour or as a salt dissolved in saliva (3). The amount of mercury released is directly proportional to the amount of amalgam present and its total surface area (4, 5).

Components of amalgam may cause local side effects such as amalgam tattoo, or allergic reactions referred to as oral lichenoid lesions. Amalgam tattoo is the most common localized exogenous pigmented lesion in the mouth (6). It is caused by the implantation or passive transfer of dental amalgam into mucosal. Most of the time these amalgam restorations do not elicit a local inflammatory response, but occasional cases are associated with chronic inflammatory changes compatible with a foreign body reaction (7). Amalgam restorations may accidentally be implanted into adjacent gingival, buccal, palatal, or lingual

mucosa at the time of tooth restoration. Clinically, amalgam tattoo presents as a black, blue, or gray macules located in close proximity to a restored tooth that are asymptomatic and change little over time (8). Amalgam tattoos are common and benign, but appearance may mimic other pigmented oral lesions with more worrisome causes. The prognosis is good and generally no treatment **is** required for this lesion except for cosmetic concern and to exclude a melanoma.

Oral lichenoid lesions (OLL) is used to describe eruptions of the oral cavity having an identifiable aetiology, which are clinically and histologically similar to oral lichen planus (OLP) (9). OLLs form part of a heterogeneous group of chronic inflammatory diseases that are hard to differentiate from OLP. OLL of the oral mucosal caused by dental amalgam represent contact allergy which is the most common reaction to amalgam and OLL is generally a type IV sensitivity reaction as it takes a long period to develop, could be months to years. It is a type of cell-mediated response when certain dental restorative materials contact with oral mucosa resulting in immunologically mediated damage of the keratinocytes of the basal stratum of epithelium but this incidence of hypersensitivity to AR is rare (10). The lesions of OLLs are similar to OLP but OLLs can be differentiated from OLP lesions. OLL lesions are usually in close proximity with AR and they are usually localized asymmetrically. OLP lesions on the other hand are more widespread and bilateral with symmetrical occurrence. A detailed medical history and clinical and histopathological examinations are important in diagnosing an OLL. The differential diagnosis of OLLs from other oral diseases includes bullous diseases, leukoplakia, and lupus erythematosus, and final diagnosis is by histopathological examination (11, 12).

OLLs are most commonly seen on the buccal mucosa and tongue where the covering mucosa comes in direct contact with the dental amalgam restorations. The gingivae, palate or floor of mouth are rarely affected as they are located further away from these restorations. Patients almost never have associated cutaneous symptoms (10). These lesions can be asymptomatic or present as a sore with symptoms of burning or as redness. Chronic lesions typically appear as erythematous areas, edematous, with desquamation and occasionally ulceration. Moreover, allergic contact stomatitis can present as erosions with rough surface and irregular borders usually surrounded by a red halo (13-16).

Patch testing is useful to identify patients suspected with hypersensitivity reactions to amalgam or mercury when earlier studies failed to differentiate OLP from OLL. Positive reaction would show skin reaction with erythema and effusion with possible papulo-vesicles (17-19). Resolution occurs after removal of offending AR. Therefore, AR should be replaced with other options of filling materials.

Epidemiological studies regarding the prevalence of different OMC adjacent to AR may vary in relation to our local population as ethnic, culture and demographic differences exist. The limited information has led us to conduct a study in this area. Data from this study can be used as local reference in the daily clinical practice and hopefully as a guide to gain some insights into the amalgam restorations and their potential impact on the surrounding oral mucosa by examining for clinical evidence of these changes, symptomology and co-morbidities if any.

The primary objective of our study was to determine the demographic and clinical profile of patients with and without OMC adjacent to AR. These were walk-in patients attending the Primary Dental Care Unit at the Faculty of Dentistry, University of Malaya. Kuala Lumpur. Malaysia. Other objectives included an evaluation on the prevalence and types of OMC related to AR and associated clinical parameters namely age, ethnicity, gender, medical status, oral hygiene as well as habits.

MATERIALS AND METHODS

Approval from the Research Ethics Committee (Ethics ID: DF OS1605/0017(U)), Faculty of Dentistry, University of Malaya, was obtained before the commencement of this study. A total of 200 outpatients receiving dental treatment at the Primary Dental Care Unit at the Faculty of Dentistry, University of Malaya from early to mid July (two weeks) year 2016 were targeted for this study. A total of 83 patients were recruited as study sample.

Before taking part in the study, consent was obtained from the participants after brief explanation by the examiners. All patients were interviewed by the examiners and were given a patient information sheet as a reference to this study. A pre-designed structured questionnaire with details on age, gender, race, and medical histories (underlying systemic diseases, hospitalization, allergies and medications) and habits was used.

A systemic comprehensive oral clinical examination was carried out by one of the examiners who was supervised and calibrated by an Oral Medicine specialist. Equipment such as dental lights, mouth mirror and gauze were used during the clinical examination. The examiner examined and assessed existing AR (age, number of teeth filled with amalgam, surfaces involved and condition of the amalgam). Any OMC adjacent to AR was identified. OLLs and amalgam tattoo associated with reactions

ENGLISH
Thank you for responding to this questionnaire. It will be completely confidential.

Age: _____ yrs old

Gender: Male ☐ Female ☐

Race: Malay ☐ Chinese ☐ Indian ☐ Others ☐

Registaration No. / IC: _____

Occupation: _____

Marital Status: Single ☐ Married ☐ Others ☐

Social Habits: Smoking ☐ Betel Quid Chewing ☐ Alcohol ☐

The following questions concern your amalgam fillings in your mouth.

1. How long are the amalgam fillings in your mouth? _____

2. Which tooth has amalgam fillings? Front, upper ☐ Front, lower ☐ Back, upper ☐ Back, lower ☐

3. Any problem(s) with your amalgam fillings?
Broken ☐ Fall off ☐

Figure 1: Questionaire (English version)

towards AR were clinically diagnosed according to the diagnostic criteria proposed by Cobos-Fuentes et al. (20). The clinical diagnostic criteria are as follow:

(A) OLLs
- Asymmetrical lesions and those in non-typical locations
- Direct topographic relation between lesion and causing material
- Variables manifestation such as stretch marks and plaques, or as erythematous, erosive atrophic or ulcerative lesions that are similar to those oral lichen planus (OLP)

(B) Amalgam Tattoo
- presents as a blue, black or slate grey flat spot (macule) on the oral mucosa
- commonly found on the gum near a tooth with an AR
- also present in roof of the mouth, inside of the cheeks and on the tongue

No radiographs, biopsies and laboratory tests (Patch/skin testing for mercury) were carried out in this study. Any suspicious lesion related to the amalgam fillings was photographed and shown to the Oral Medicine Specialist for her opinions to confirm/verify the diagnosis.

The records of 16 previous patients who presented with OLLs/amalgam tattoo, and seeking specialist treatment for OLP or oral lichenoid reaction (OLR) at the Oral Medicine Clinic in the Faculty of Dentistry, University of Malaya were retrieved and included in this study. All of these patients

failed to attend the follow-up and so only the old clinical summaries were obtained, leading to some incomplete data.

At the time of examination, all patients received information about the outcome of the clinical assessment, and their oral condition(s) (if present).

STATISTICAL ANALYSIS

Descriptive statistics were used to analyze the collected different data from each patient with SPSS 12.0.1 for Windows. Chi-square tests (Pearson Chi-Square) were applied to compare the occurrence of OMC adjacent to AR (OLLs and amalgam tattoo) with ethnicity, gender, medical histories, habits and conditions of AR. Simple logistic regression analysis is used to analyze the significant risk factor for OMC with patients' age, duration, total surfaces, number of teeth restored with amalgam. Mann-Whitney Test was applied to compare the occurrence OLLs and amalgam tattoo with age. The level of significance was set at $p<0.05$.

RESULTS

A total of 83 patients with AR participated in this cross sectional study. The results are summarized in Tables 2 to 9 and illustrated in Figures 1 to Figure 2. Table 2 shows the gender distribution of patients with and without OMC adjacent to AR. There were 26(31.3%) males and 45(54.2%) females that presented without OMC. Patients presenting with OMC comprised 8.4% female and 6% male respectively. According to the Pearson Chi-Square test, gender differences between patient with and without OMC adjacent to AR was not statistically significant ($p>0.05$).

Table 2: The distribution of oral mucosal changes according to gender.

Variable			Oral mucosal changes			
			No Nn (%)	Yes n (%)	Total	P*
Gender	Male	n	26 (31.3)	5 (6.0)	31 (37.3)	
	Female	n	45 **(54.2)**	7 **(8.4)**	52 **(62.7)**	0.738
Total		n	71 **(85.5)**	12 **(14.5)**	83 **(100)**	

*Pearson Chi-Square test

Table 3 shows the ethnic profile of patients with and without OMC adjacent to AR. In our study, only the Malays and the Chinese showed OMC with the Chinese showing a higher percentage (8.4%) followed by the Malays (6.0%). The ethnic differences in patients with and without OMC adjacent to AR was not statistically significant ($p>0.05$).

Table 3: The distribution of oral mucosal changes according to the ethnic group

		Oral mucosal changes			
Ethnic Group		**No Nn (%)**	**Yes n (%)**	**Total**	*p**
Malay	n	18 (21.7)	5 (6.0)	23 (27.7)	
Chinese	n	38 **(45.8)**	7 **(8.4)**	45 **(54.2)**	
Indian	n	9 **(10.8)**	0 (**0.0**)	9 **(10.8)**	0.312
Others	n	6 **(7.2)**	0 **(0.0)**	6 **(7.2)**	
Total	n	71 **(85.5)**	12 **(14.5)**	83 **(100)**	

*Pearson Chi-Square

Table 4 shows the mean age and range of the patients presenting with and without OMC adjacent to AR. The mean age of the patients with developed OMC adjacent to AR was 61 years with the youngest being 34 years old and the oldest 81 years old.

Table 4: Mean age and age range of patients with and without OMC adjacent to AR.

Variable	Oral mucosal changes		
	No	**Yes**	**Total**
Mean age (range) (yr)	42 (19-85)	61 (34-81)	45 (19-85)

Table 5 shows the habit profile in patients with and without OMC adjacent to AR. Two patients each presented with bruxism (2.4%) and smoking (2.4%) while none of the patients with alcohol consumption habit showed evidence of OMC adjacent to AR. According to Pearson Chi-Square test, alcohol-taking, smoking, and bruxism did not show any statistical significant differences in patients with and without OMC adjacent to AR ($p>0.05$). None of the patients have betel quid chewing habits.

Table 5: Habit profile of patients with and without OMC adjacent to AR.

Social habits		Oral mucosal changes No	Yes	*p**
		n(%)	n(%)	
Alcohol	Yes	4 (4.8)	0 (0.0)	0.399
	No	67 (80.7)	12 (14.5)	
Smoking	Yes	5 (666)	2 (102.4)	0.267
	No	66 (79.6)	10 (12)	
Betel quid chewing	Yes	0 (0.0)	0 (0.0)	Constant
	No	71 (85.5)	12 (14.5)	
Bruxism	Yes	6 (7.2)	2 (2.4)	0.372
	No	65 (78.3)	10 (12)	

*Pearson Chi-Square

Table 6 shows the prevalence of underlying systemic diseases in patients with and without OMC adjacent to AR. Various systemic diseases, including hypertension, hypercholesterolemia, endocrine disorders, infectious diseases, respiratory diseases and cardiovascular disorders were statistically significant (p<0.05) based on Pearson Chi-Square test. Other systemic diseases showed no significant associations.

Table 6: Prevalence of underlying systemic diseases in patients with and without OMC adjacent to AR.

Systemic diseases		Oral mucosal changes No	Yes	p*
		n (%)	n (%)	
Allergy	Yes	10 (12.0)	3 (3.6)	0.336
	No	61 (73.5)	9 (10.8)	
Arthritis	Yes	1 (1.2)	0 (0.0)	0.679
	No	70 (84.3)	12 (14.5)	
Asthma	Yes	4 (4.8)	0 (0.0)	0.399
	No	67 (80.7)	12 (14.5)	
Blood disorders	Yes	2 (2.4)	0 (0.0)	0.556
	No	69 (83.1)	12 (14.5)	
Cancer	Yes	1 (1.2)	1(1.2)	0.148
	No	70 (84.3)	11 (13.3)	
Cardiovascular	Yes	4 (4.8)	4 (4.8)	**0.003**
diseases	No	67 (80.7)	8 (9.6)	
Diabetes Mellitus	Yes	6 (7.2)	3 (3.6)	0.088
	No	65 (78.3)	9 (10.8	
Endocrine	Yes	1 (1.2)	3 (3.6)	0.000
	No	70 (84.3)	9 (10.8)	
Gastrointestinal	Yes	8 (9.6)	2 (2.4)	0.595
diseases	No	63 (75.9)	10 (12.0)	
Hypercholesterolemia	Yes	5 (6.0)	5 (6.0)	**0.001**
	No	66 (79.5)	7 (8.4)	
Hypertension	Yes	11 (13.3)	5 (6.0)	**0.034**
	No	60 (72.3)	7 (8.4)	
Infectious diseases	Yes	0 (0.0)	1 (1.2)	**0.014**
	No	71 (85.5)	11 (13.3)	
Respiratory diseases	Yes	2 (2.4)	2 (2.4)	**0.038**
	No	69 (83.1)	10 (12.0)	

*Pearson Chi-Square. Bold font indicates statistical significance (p<0.05)

Table 7 shows the types of medication taken among patients with and without OMC adjacent to AR. Miscellaneous drugs (6.0%) and antihypertensive drugs (4.8%) were the two most common prescriptions taken, followed by antihypercholesterolemia drugs (3.6%) and antidiabetic drugs (3.6%), among patients with OMC adjacent to AR. Pearson Chi-Square test disclosed that differences in the medications were statistically significant (*p*<0.05).

Table 7: Medication taken by patients with and without OMC adjacent to AR.

		Oral mucosal changes		*p**
Medications		**No**	**Yes**	
		n (%)	**n (%)**	
Antihypertensive drug	Yes	7 (8.4)	4 (4.8)	**0.027**
	No	64 (77.1)	8 (9.6)	
Antihypercholesterolaemia	Yes	4 (4.8)	3 (3.6)	**0.010**
	No	67 (80.7)	9 (10.8)	
Antidiabetic drug	Yes	3 (3.6)	3 (3.6)	**0.026**
	No	68 (81.9)	9 (10.8)	
Miscellaneous drug	Yes	9 (10.8)	5 (6.0)	**0.013**
	No	62 (74.7)	7 (8.4)	

*Pearson Chi-Square

Table 8 shows the simple logistic regression analysis with the characteristics of AR. It was found out that the duration of amalgam in the oral cavity is a significant risk factor for the OMC adjacent to AR. A patient with an increase of one year duration of amalgam in the oral cavity has a 1.066 times higher risk in having OMC (95% CI, 1.021, 1.112, p=0.004). The number of teeth restored with amalgam (p=0.232) and the total surfaces of amalgam (p=0.379) are not a risk factor for OMC adjacent to AR. In patient with OMC, the average number of teeth restored with amalgam was six (1-13), while the mean total number of surfaces sealed with AR was ten (2-23). On an average, AR had been in the mouth for 27 years, with five years of most recent placement and oldest was 50 years.

Table 8: Simple logistic regression analysis on the characteristics of AR.

AR characteristics	With OMC (mean, range)	Without OMC (mean, range)	Total (mean, range)	Odd ratio	p value
Teeth with fillings (n)	6 (1-13)	5 (1-14)	5 (1-14)	1.126	0.232
Total surfaces with fillings (n)	10 (2-23)	8 (1-29)	8 (1-29)	1.040	0.379
Duration of the fillings (years)	27 (5-50)	14 (1-50)	15 (1-50)	1.066	0.004

Table 9 shows the condition of amalgam in the oral cavity in patients with and without OMC adjacent to AR. In our study, most patients had AR in good condition and no OMC, scoring the highest percentage (66.3%). However, 11 patients (13.3%) with OMC presented with good condition of amalgam, while only one patient (1.2%) presented with ditching

Table 9: The condition of amalgam in the oral cavity in patients with and without OMC adjacent to AR.

Variable			OMC		Total	p*
			No	Yes		
Condition of amalgam in oral cavity	Good	**n (%)**	55 (66.3)	11 (13.3)	66 (79.5)	0.260
	Others	**n (%)**	16 (19.3)	1 (1.2)	17 (20.5)	
Total		n (%)	71 (85.5)	12 (14.5)	83 (100)	

*Pearson Chi-Square

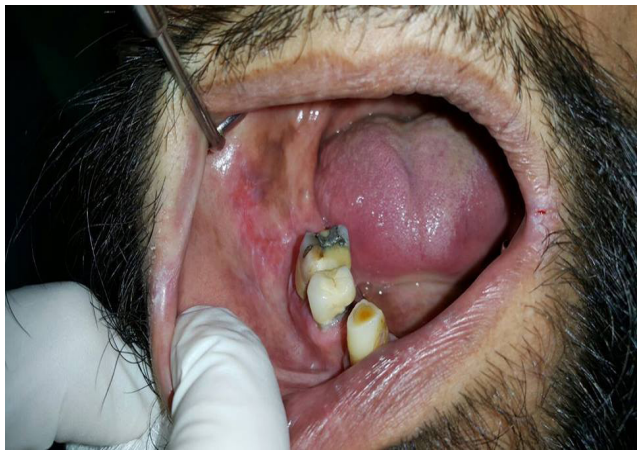

Figure 1. Intraoral view showing an oral lichenoid lesion involving the right buccal mucosa and in close proximity with amalgam restoration on tooth 47. The lesion appears non-homogeneous with mixed white and erythematous area. The pigmentation on the right buccal mucosa may be racial.

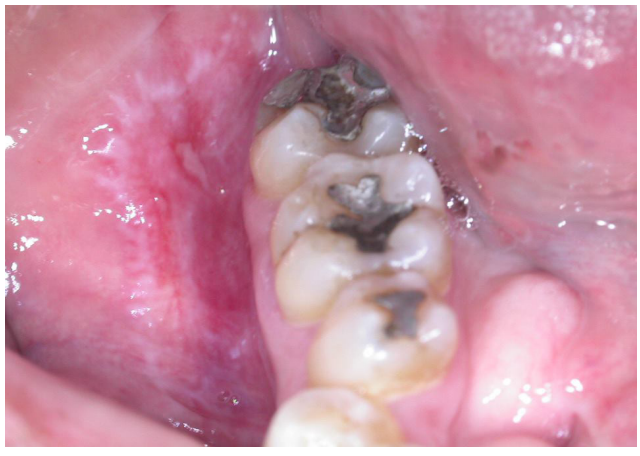

Figure 2. Intraoral view shows an oral lichenoid lesion located on the right buccal mucosa and in close proximity with amalgam restorations on teeth 47, 46 and 45. Clinically the lesion presents as an irregular central area of erythema and atrophy, with peripheral white radiating striae.

DISCUSSION

In this study, OMC adjacent to AR were found to be uncommon among our study cohort. However, it had been stated that amalgam tattoo was one of the common findings (21), but some studies reported that the presence of oral lichenoid reactions was infrequent (20). This might be due to the diminishing use of the amalgam restorations nowadays (23).

From the results, we observed that the ratio of female to male likelihood of having OMC adjacent to AR was 1:1 which was similar to another study that showed that there was no bias towards female with OLLs (22). On the other hand, some reported that the prevalence of female getting OLLs was three times higher than men (24). Others stated that prevalence of amalgam tattoo among women was higher than

men (7). These accumulated findings suggest there is considerable variation in the gender distribution of OMC associated with AR.

In our analysis regarding the ethnic profile of patients with or without OMC adjacent to AR, we were unable to perform a legitimate comparison with other studies due to differences in racial group composition in these other countries. Nonetheless we observed that the highest racial predilection for OMC adjacent to AR occur mostly in Chinese, followed by Malays with none recorded among Indian and other races. This racial prevalence might not be totally accurate as the study was conducted during fasting month of Ramadan. Malay patients tend to abstain from seeking dental treatment during this month. An alternative explanation would be that our results may reflect the urban racial profile of outpatient attendees in our Faculty which largely provides dental healthcare services to the residents in the Klang Valley metropole (25).

In this study, the mean age of patient presenting with OMC adjacent to AR is 61 years old which was higher compared to previous studies that reported a mean age of 50 years and above. (17, 24). These findings indicate that overall OMC presenting as contact lesions of AR are largely found in late adult life. An earlier study on tongue lesions revealed that a sizeable number of outpatients attending the Primary Dental Care Unit belongs to the older age group (25).

Nothing is known about the role of social habits in AR-related OMC. In our study, less than 5% patients presenting with AR-related OMC had social habits. This suggests that social habit is not an aetiologic factor contributing to the development of AR-dependent OMC. However, other study did report that smoking contributed to 25-31% of smoker's melanosis due to increased melanin production (26).

Majority of the patients with OMC in our study had more than one disease with many having systemic diseases like hypertension, hypercholesterolaemia and cardiovascular diseases. A study revealed that lichenoid lesions might be due to drugs consumption mainly oral hypoglycaemic drugs and non-steroidal anti-inflammatory drugs (NSAIDS) (27, 28). Our results do not show that consumption of drugs like antihypertensives, anticholesterolaemia and antidiabetics are more prevalent in patients with OMC. However, this could be due to the low incidence of OLL in our study population. Amalgam tattoo may mimic other pigmented oral lesions such as post-inflammatory hyper-pigmentation, (29, 30). Underlying systemic diseases such as Peutz-Jeghers syndrome, Addison's disease and Crohn disease may results in oral pigmentations, (31-33) and systemic lupus erythematous may cause OLLs (28).

Previous studies that investigated the characteristics of AR including the duration of the amalgam, have shown that it is an important factor in the development of these OMC adjacent to AR (17). A similar finding was made in this study which further lend support that the duration of AR is significant factor predisposing to the development of OMC. In our study, the duration of amalgam for OLL to develop was 40 years which was longer than another study which reported 27 years (22). The average age of amalgam in patient present with lesion was very high, as the more corrosive damages may have been produced over the time frame (22).

As suggested by some authors, patients with OLLs had an average of 5 teeth restored with amalgam (22) which was quite similar with our study where the average number of teeth restored with amalgam was six. There was definitely a corresponding increase in the total number of surfaces of teeth with amalgam when the number of teeth involved increased. Our findings compared favorably with another study where the mean number of surfaces with amalgam was 5 (22) with some difference in this study which was an average of ten surfaces. OLLs occurred due to high levels of mercury content in the saliva which may have leaked through the teeth to the surrounding oral mucosa (20, 36, 4).

Finally, the condition of the existing AR was also evaluated here. We subdivided AR condition into two categories: good (shiny, smooth and well-sealed amalgam) and defective amalgam (rough, sharp edges and leakage). In this study, most of the amalgam were in good condition and in patient present with OLL, the amalgam showed some minor defect. This contrasted markedly with another study (20) where most of the OLLs cases occurred in association with rough AR. There was regression of OLL after the removal of rough surfaces and sharp edges of the amalgam, (35). In contrast, the condition of amalgam in our study did not really influence the occurrence of these lesions.

There were a few limitations in this study, mainly the unachievable number of target patients due to the low patient attendance in outpatient clinic during fasting month. Besides that, patients presented with OLLs had incomplete data in their records, resulting in omission of many cases which could lead to a slight bias towards patients with amalgam tattoos. Therefore, it was difficult to study the prevalence of OLLs among our study population. Due to incomplete data about the amalgam tattoo patients, we were unable to identify the most common site of the lesion in the oral cavity in 16 cases retrieved from the Oral Medicine archives.

CONCLUSION

In summary, the study conducted showed low prevalence of OMC adjacent to AR in our study population. Female and male had the same prevalence. Chinese patients were more commonly affected followed by Malays and then Indians. Mean age onset for these changes was 61 years old and social habits were not closely related to these OMC. Seven diseases namely cardiovascular diseases, hypertension, hypercholesterolaemia, diabetes mellitus, endocrine disorders, respiratory diseases and infectious diseases showed significant correlation with OMC. Characteristic of amalgam might have contributed to these changes due to the intimate contact, the longer the AR, the higher the risk of getting OMC. Rough and corroded surfaces may cause irritation and contribute to OLL over time even if it was shown to be insignificant in our study.

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DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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