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Smokers' Melanosis in a Nigerian Population: A Preliminary Study

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Abstract

Aim: Terms relating to pigmentation of the oral mucosa include physiologic (racial) pigmentation, oral pigmented nevi, oral melanotic maculae, melanoma, and smokers' melanosis. The literature is replete with studies about oral mucosal pigmentation which is thought to result from melanin incontinence. The documented etiological factors are both local and systemic and include hormones, drugs, smoking, and idiopathic causes. This study investigated the prevalence of melanosis among Nigerian smokers and controls who were non-smokers.

Methods and Materials: A total of 1270 sites were examined in 253 subjects consisting of 60 smokers and 193 non-smokers. They were all systemically healthy adults drawn from 12 factories located in different urban and rural settings in the state of Lagos in Nigeria. Five oral mucosal sites were examined per subject. A single examiner performed all examinations and recorded all findings. Pigmentation was scored either as "present" or "absent." Subjects' smoking status, degree, and duration of smoking were ascertained and recorded using an examiner-administered questionnaire.

Results: There were five pigmented sites (0.52%) among non-smokers and 18 (6%) among smokers. The buccal mucosa was the most frequently pigmented site found in smokers while the lingual mucosa was the most common site found for non-smokers. The prevalence of pigmented sites increased directly among smokers with the duration of smoking (years); degree of smoking (cigarettes smoked per day); and

smoking pack-years (degree of smoking divided by 20 and multiplied by duration of smoking, where 20 is the average number of cigarettes in a pack of cigarettes). SPSS version 11.0 was used for data entry and analysis. Frequency distributions were generated for all categorical variables for descriptive aspects of the analysis. Means were determined for quantitative variables such as age and number of cigarettes smoked. For homogenous variances, the student's t test was used for quantitative variables between smokers and non-smokers, while for non-homogenous variances the Mann-Whitney test was adopted. Chi-square statistic was used for comparisons between smokers and non-smokers. In tables with low expected frequencies, Fisher's exact test was adopted. Statistical tests yielding p-values =/<0.5 were considered significant.

Conclusions: Smokers in this study had a significantly higher prevalence of pigmented oral mucosal sites (melanosis) than non-smokers. The number of pigmented sites increased with the degree and duration of smoking. The buccal mucosa was the most frequently pigmented site found among the smokers in this study.

Keywords: Melanosis, pigmentation, smokers, prevalence

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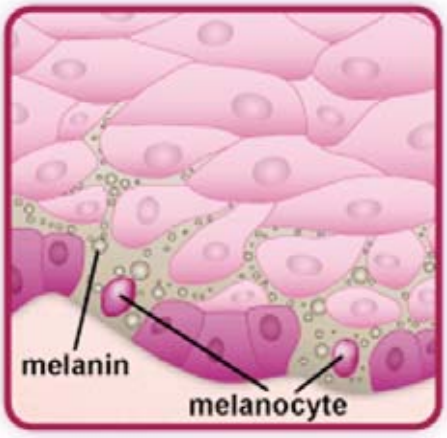
Introduction

Dental and prosthetic stains caused by smoking[1] as well as those from other sources[2,3] are well documented in the dental literature. Pigmented oral mucosal lesions[4,5] have also been well documented and categorized. Recently, pigmentations of the oral mucosa as a direct consequence of smoking have received more emphasis in the literature.

It is known excessive melanin pigmentation results from basilar melanosis. This is a consequence of melanin incontinence resulting from direct stimulation of melanocytes by nicotine which leads to the production of melanosomes by the melanocytes. These melanocytes suffer from various degrees of incontinence, leading to mucosal pigmentation.[6] Researchers have found an association between oral mucosal pigmentation and race,[7] drugs, hormones,[8] and radiation therapy.[9] More recently cigarette smoking, including passive smoking, has been implicated.[10,11,12] Several studies have reported a positive association between smoking and oral mucosal pigmentation. They include studies by Motalebnejad,[13] Sarwathi et al.,[14] Araki et al.,[15] and Hedin and Axell.[16] Oral mucosal pigmentation has also been found in association with heavy drinking,[17] Addison's disease,[18] and cancer.[19,20]

Melanin is a non-hemoglobin brown pigment produced by melanocytes residing in the basal layer of the epithelium.[21] Melanocytes in the oral cavity are usually not as active as skin



melanocytes. Oral mucosa pigmentations, though mostly physiological,[22] are usually taken seriously because some could be precursors of severe disease.[15,22]

Only a few researchers have investigated oral mucosal pigmentation in relation to the degree and duration of smoking.[13,19,23] There are no indexed studies on smokers' melanosis in Nigeria and no studies relating smoking with oral cancer. The aims of the present study were as follows:

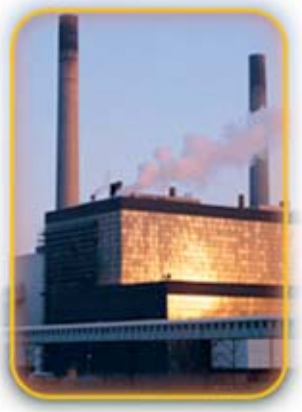
- Assess the level of association between smoking and oral mucosal pigmentation among the study population.
- Describe the distribution pattern of oral mucosal pigmentation among the study population.

- Assess the level of association between duration and degree and duration of smoking on the prevalence of smokers' melanosis.

Methods and Materials

Participant Selection

The present study was carried out with subjects who were likely to use smoking as a method of stress relief. Nigerian factory workers were chosen since they are likely to be under stress as a result of a poor working environment, poor remuneration, and the burden of supporting large families.



The 12 participating factories were scattered around several urban and rural settings in Lagos, Nigeria. There were no significant differences between urban and rural factories for only a thin line exists between rural and urban settings due to massive migration in each direction between rural urban areas.

Inclusive criteria consisted of being a systemically healthy adult factory worker in Lagos with no obvious clinical signs of debilitating disease. Exclusion criteria were the presence of clinical signs suggestive of diabetes mellitus and aggressive periodontitis since the study was part of a general assessment of oral and periodontal status. Subjects suspected to have had radiation therapy or had obvious clinical signs of cancer were excluded. A drug history was not obtained from subjects.

Consent

This study was authorized by the research and ethics of the Lagos University Teaching Hospital in Lagos, Nigeria. Written consent was obtained from the factories participating in the study. The workers were recruited by purposive sampling with written consent. Purposive sampling was adopted to overcome the difficulty of refusal of permission for the study in some factories.

All the factory workers were informed on the purpose and extent of the study. Verbal informed consent was obtained from each subject included in this study. Verbal informed consent was opted for because of the low educational level of most of the factory workers and the anticipated difficulty they would have in comprehending the intricacies of written consent.

Data Collection

A total of 1,270 oral mucosal sites were examined in 253 subjects comprising 193 non-smokers and 60 smokers. The subjects were all systematically healthy black adults primarily from the Yoruba tribe which is one of the three major ethnic groups in Nigeria. Five intraoral sites including the lingual, buccal, gingival, palatal mucosa as well as the floor of the mouth were examined for each subject. The choice of sights was arbitrary but uniform for both subjects and controls. Pigmentation was scored either as "present" or "absent" because to date there is no objective method of scoring such pigmentations.[12]

Smoking status, duration of smoking (number of years), and degree of smoking (number of cigarettes per day) were ascertained and recorded in an examiner-administered questionnaire. Smokers were those who actually engage in the smoking habit while non-smokers were those who did not. Passive smokers were not considered in the study.

Smoking pack years was obtained by multiplying the duration of smoking by degree of smoking divided by 20 (average number of cigarettes in a pack of cigarettes). Smokers were categorized as mild or heavy smokers by a modification of criteria set out by Devorah et al.[24] and adopted by Nwhator.[25] They classified individuals smoking more than ten cigarettes as heavy smokers and smoking ten cigarettes or less as mild smokers. However, the current study classified a person smoking ten cigarettes or more as a heavy smoker considering most of the subjects seen were mild smokers. The classification by Devorah et al.[24] *was* modified and adopted in the current study because no other objective basis for classification was found. The intent is for future researchers to find this categorization useful solely for the purpose of comparison and not as a scientific rule of thumb when referring

to baseline data in the present study. A single examiner who is a specialist with adequate knowledge of oral mucosal pigmentation carried out and recorded all pigmentations.

Statistical Analysis

SPSS version 11.0 (SPSS, Chicago, IL, USA) was used for data entry and analysis. For descriptive aspects of the analysis, frequency distributions were generated for all categorical variables. Means were determined for quantitative variables such as age and number of cigarettes smoked. For homogenous variances, the student's t test was used for quantitative variables between smokers and non smokers, while for non-homogenous variances the Mann-Whitney test was adopted. Chi-square statistic was used for comparisons between smokers and non-smokers. In tables with low expected frequencies the Fisher's exact test was utilized. Statistical tests yielding p-values =/<0.5 were considered significant.

Results

A total of 23 (1.8%) pigmented sites were identified among the 1,270 mucosal sites examined in the 253 subjects of which 18 (78.3%) were found in smokers while 5 (21.7%) were found in non-smokers.

Pigmented Sites by Smoking Status

The most frequently pigmented site was the buccal mucosa in smokers and the lingual mucosa in non-smokers. Differences in pigmentation of the lingual mucosa and the floor of mouth were not statistically significant (p=0.15 and 0.23, Fisher's exact test, respectively). However, using Fisher's exact test smokers had a significantly higher prevalence of pigmented sites than non-smokers in all five intraoral sites examined as follows (Table 1):

- Buccal mucosa (p<0.001)
- Gingival mucosa (p=0.01)
- Palatal mucosa (p=0.013)

The prevalence of pigmented sites increased directly with three factors among smokers as follows:

- Duration of smoking (years)
- Degree of smoking (cigarettes smoked per day)
- Smoking pack years (degree of smoking divided by 20 and multiplied by duration of smoking, where 20 is the average number of cigarettes in a pack of cigarettes)

Pigmented Sites by Smoking Duration

The prevalence of pigmented sites was significantly associated (X^2=22.94, df=3, p<0.001) with smoking duration in years as shown in Table 2. (Note: X^2 refers to chi square; df refers to degrees of freedom; while the statistical test used is the chi-square statistic.)

Pigmented Sites by Smoking Degree

The prevalence of pigmented sites was significantly associated (X^2=25.24, df=1, p<0.001) with the degree of smoking (number of cigarettes smoked per day) as shown in Table 3.

Pigmented Sites by Smoking Pack-Years

The prevalence of pigmented sites increased with but was NOT significantly associated (X^2=2.45, df=1, p=0.16) with smoking pack-years (Table 4). Smoking pack-years is defined as the degree of

Table 1. Prevalence of pigmented oral mucosal sites by smoking status.

Pigmented Mucosal Site	Smokers (N=60)		Non-smokers (N=193)		P-Value
	n	%	n	%	
Lingual	3	5.0	3	1.6	0.15 (x^2=2.35,p=0.15)
Buccal	7	11.7	1	0.5	<0.001 (Fisher's exact)
Gingival	4	6.7	1	0.5	0.01 (Fisher's exact)
Palatal	3	5.0	0	0.0	<0.013 (Fisher's exact)
Floor of Mouth	1	1.7	0	0.0	0.23 (Fisher's exact)
Total	18	30.1	5	2.6	

Table 2. Prevalence of pigmented oral mucosal sites by duration of smoking in years.

Duration (Years)	Sites Pigmented		Sites Not Pigmented	Total
	n	%		
<5	2	1.4	143	145
5-9	2	5.0	38	40
10-14	4	6.2	61	65
>14	10	20.0	40	50
Total	18		282	300

X^2=22.94, df=3, p<0.001

Table 3. Prevalence of pigmented mucosal sites by degree of smoking.

Degree (Number of Cigarettes)	Sites Pigmented		Sites Not Pigmented	Total
	n	%		
Mild smokers (< 10cigarettes)	10	3.7	260	270
Heavy smokers (10 cigarettes and above)	8	26.7	22	30
Total	18		282	300

X^2= 25.24, df=1, p<0.001 (Fisher's exact test)

Table 4. Prevalence of pigmented mucosal sites by smoking pack-years.

Pack-Years	Sites Pigmented		Sites Not Pigmented	Total
	n	%		
0.01 – 0.50	2	1.54	128	130
0.51 – 3.50	11	8.80	114	125
3.51 – 20.00	5	11.11	40	45
Total	18		282	300

X^2= 2.45, df=1, p=0.16 (Fisher's exact test)
Note: Due to small numbers, groups 0.01-0.50 and 0.51-3.50 were combined for the purpose of analysis.

smoking divided by 20 and multiplied by duration of smoking, where 20 is the average number of cigarettes in a pack of cigarettes.

Discussion

This study examined 1270 oral mucosal sites and found only 23 pigmented sites; this indicates oral mucosal pigmentations are rare. Considering obvious limitations of this field cross-sectional study, these pigmented sites could in theory be either melanotic macules equivalent to skin freckles,[26] pigmented nevi occurring at the vermillion border,[27] cancerous melanocytes (melanoma),[15,16] Addison's disease,[14] or racial (physiologic) pigmentation.[7] It is difficult to distinguish racial pigmentation from smoking-related pigmentation in a field survey. However, these pigmented sites are not likely to be either physiological or racial since both subjects and controls belong to the same black race. This view appears to be corroborated by Dummet et al.[28] who observed even with genetic predetermination of pigmentation among individuals of the same race, the actual pigmentation observed is partially influenced by mechanical, chemical (in this case smoking) and physical stimulation. Clinical examination of the subjects revealed none of the smokers had skin freckles or lesions on the vermillion border ruling out pigmented nevi. Furthermore, five (2.6%) pigmented sites were found among 193 non-smokers compared with 18 (30.1%) sites among 60 smokers. In addition, five of a total of 23 (21.7%) pigmented sites were found in non-smokers while 18 (78.3%) were found in smokers; this seems to suggest an association between smoking and these pigmented sites. These sites are, therefore, most likely to be smokers' melanosis.

In the current study the relative prevalence of palatal pigmentation is at variance with a previous report[29] suggesting palatal pigmentations were rare in smokers.

The directly proportional relationship between smoker's melanosis and the duration of smoking in the current study ($p<0.001$) corroborates previous research.[19,23] The differences observed between smokers melanosis in mild and heavy smokers also corroborates an earlier study.[13] Smoker's melanosis seen in the present study increased directly with smoking pack-years which also corroborates previous studies.[13,19,23,28,29] In fact, a study reported the disappearance of smoker's melanosis on the reduction of smoking30 while other studies reported a dose response relationship between smoking and melanosis.[19,31]

Finally, the pathogenesis of smoker's melanosis has been previously linked to the direct stimulation of melanocytes by nicotine.[6] However, it is surprising to find such an etiological agent was also effective as a therapeutic agent when used as 2 mg sublingual nicotine tablets as reported in a another study.[32] This is in contrast to cases treated with an argon laser[33] or just left untreated and disappeared upon reduction or cessation of smoking.[30] It should be noted the reported cases of cure using nicotine were part of a smoking cessation program. Therefore, it is possible it was the cessation of smoking rather than the sublingual nicotine that "cured" those cases. This current theory on the pathogenesis of smokers melanosis seems further questioned by the observation smoker's melanosis is rare in the palate except in individuals who practice reverse smoking.[29] Reverse smoking refers to smoking with the burning end of the cigarette in the oral cavity. A question remains as to whether heat can be the cause of smoker's melanosis or whether it could be acting as a catalyst/co-factor in its pathogenesis. The current theory on pathogenesis of smoker's melanosis as it stands is therefore either incorrect or at best incomplete. It is clear more research is needed to understand the full picture of this disease.

Conclusion

Smokers in this study had significantly more oral mucosal pigmentation (smokers' melanosis) than non-smokers in the buccal ($p<0.001$), gingival ($p=0.01$), and palatal ($p=0.013$) mucosa. The degree and duration of smoking showed a direct significant relationship with mucosal pigmentation. The pathogenesis of smoker's melanosis needs further investigation.

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