# Oral physiological pigmentation in a Western Cape sample


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REQUIREMENTS FOR THE DEGREE M.Ch.D- ORAL MEDICINE AND PERIODONTOLOGY


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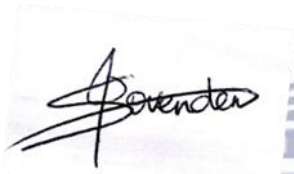
**DECLARATION**

I, Shogan Govender, declare that "*Oral Physiological pigmentation in a Western Cape sample"*, is my own work and that all the sources I have quoted have been acknowledged by references. This thesis has not been submitted for any other degree.



Signed: _____

Shogan Govender

Date: __05 November 2018___



**Conflict of interest:**

The author declares no conflict of interest. No external funding will be obtained for this study.

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- My mum, brothers (Thashlin and Kershion). For all the encouragement, prayers and sacrifices during the past years. Without your support this would not have been possible.

**ABSTRACT:**

Oral physiological pigmentation presents with great variability with respect to sites, forms, patterns and contrasts in colour. Knowledge of the existence of pigmented lesions and their significance remained unclear for both the general public and oral clinicians alike. The possibility of malignant transformation of some pigmented lesions makes them important to monitor and biopsy. The prevalence of physiological pigmentation is unknown for the defined population group in this study. The results will be beneficial as part of a larger multicentre study with South Africa (Feller et al, 2015).

**Methodology:** A cross sectional analytical study of patients that attended the University of the Western Cape Oral Health centres for routine treatment was conducted. After obtaining informed consent, patients were screened and asked a series of questions using a standardized questionnaire. From these completed questionnaires a prevalence relating to oral physiological pigmentation was determined.

Oral physiological pigmentation did not have a male or female predominance in this study population group, but was associated with increased age. Oral pigmentation seemed to be well represented after 18 years of age. Patients were not usually aware of the pigmented gingiva unless being made aware off it.

**Key words:** Oral physiological pigmentation (OPP), melanoma, pigmentations, mucosal, oral pigmented lesion

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## CHAPTER 1: INTRODUCTION

There can be difficulty in distinguishing pathological and physiological oral pigmentation. Causes related to oral pigmentation include increase of melanin production, melanocytosis (increased number of melanocytes) as well as exogenous material accidentally deposited (Sreeja et al, 2015; Mallikarjuna et al, 2013).

Normal oral mucosa colour is related to numerous factors such as, melanogenic activity degree of melanocytes in the basal cell layer, the number of melanocytes in the basal cell layer, melanin production relating to amount and type, epithelium thickness, para-keratinized or ortho- keratinized, lamina propria vascularity and blood haemoglobin content (Masilana et al, 2015). The different types of melanin include, Eumelanin, Pheomelanin, Mixed type melanin, Neuromelanin, Oxymelanin. (Sreeja et al, 2015; Dummet et al, 1960).). Eumelanin being the most common as well as being produced in 'black' and 'brown' subtypes (Dummet et al, 1960).

Oral melanomas are malignant neoplasms of melanocytes and commonly arise de novo, but up to one-third of cases are said to arise from benign melanotic oral lesions (Warszawik-Hendzel et al, 2014; Tlholoe et al, 2015). Initially they may appear asymptomatic, but become very aggressive and fatal due to being diagnosed to late, which is when the melanoma is large and metastasized to regional lymph nodes. Approximately 85% of patients with malignant melanomas in the early stages; are found to metastasize to the liver, lung bone or brain by direct haematogenous dissemination, thus showing the aggressiveness of the pathology. Oral physiological pigmentation is found in a considerable population size. People are exposed to so much more environmental risk factors that more consideration and research needs to go into the prevalence of oral physiological pigmentation to provide evidence for early diagnosis of possible malignant transformation of these oral pigmented lesions (Tlholoe et al, 2015).

## CHAPTER 2: LITERATURE REVIEW

### 2.1.Prevalence

The prevalence of oral physiological pigmentation (OPP) between ethnic groups can range from 0% to 89% possibly due to genetic, secondary and environmental factors (Rosa et al, 2007). The intensity and distribution is variable between ethnic groups as well as between individuals in the same ethnic group and in different areas of the mouth (Mallikarjuna et al, 2013). OPP was reported in 100% of healthy dark skinned individuals of the African population and 30% - 98% Asian population (cited in Sreeja et al, 2015). Scientific studies related to population geography related to OPP, dictated that greater numbers of patients with oral melanin pigmentation hailed from African, East-Asian or Hispanic ethnic backgrounds. (Tamizi et al, 1996; Dummet et al, 1960; Tishkoff et al,2009). South Indians who have darker skin were found to have higher levels of oral pigmentation than North and Northeast Indians (Stokowski et al, 1997). South Indians were found to have more oral pigmentation on keratinised gingiva with the greatest pigmentation in the incisor region. It was also found that there was reciprocation between the degree of gingival pigmentation and skin pigmentation (Poonaiyan et al, 2014). OPP is not uncommon within the HIV infected population (included patients with and without antiretrovirals), however, higher percentages were found in Venezuela (38%) and India (30%) and lower percentages found in Italy (6, 4%) and Sub-Saharan Africa (Tanzania- 4, 7%, Kenya- 6%). South African HIV- OPP prevalence is unknown, however Arendorf et al (1998), in a study reported 1% in a greater Cape Town population but no differentiation was made between the different ethnic groups in South Africa and no other exclusions was made regarding other causes of OPP (cited in Chandran et al, 2014). About 55% of mucosal melanomas were presented in the head and neck area; of which 70% affected the paranasal sinuses and the nasal cavity, and 25% affected the oral mucosa. Of all oral malignancies, 0.26% and 5% account for oral mucosal melanomas (Tlholoe et al, 2015).Oral mucosal melanomas commonly arise de novo, but up to one-third of cases are said to arise from benign melanotic oral lesions (Warszawik-Hendzel et al, 2014; Tlholoe et al, 2015).

## 2.2.Melanin as a determinant of the colour of skin and oral mucosae

Normal colour of the skin and oral mucosa are contributed by four pigments which include melanin, carotenoids, reduced HB and oxygenated HB. Melanin is an endogenous non-hematogenous pigment and is the most important contributor to the colour of skin and oral mucosae (Sreeja et al, 2015).

Melanin is produced by melanosomes which reside within melanocytes in the basal cell layer of the epithelium (Masilana et al, 2015). Melanin is also produced by neural crest products such as the nevus cells and can be found in skin and the oral mucosa. Depending on the quantity of melanin in the tissues and location, pigmentation induced by melanin can be black, grey, blue or brown in colour (Sreeja et al, 2015; Mallikarjuna et al, 2013; Gondak et al, 2012 ).

Melanosomes are transported from the melanocytes cytoplasm to the specialised dendritic protrusions on the melanocytes cell membrane which is then passed through the cell membrane to the adjacent keratinocytes to form a complex called the 'keratinocyte-melanin unit'. Contained by this unit, the melanin provides a protective supra-nuclear function thereby protecting the nuclear DNA from ultraviolet radiation within the skin. It is unknown if the similar happenings regarding the oral keratinocytes and protection against ultra violet light exists (Masilana et al, 2015).



## 2.3.Classification

There are many attempts to classify oral pigmentation (Dumett et al, 1964; Hedin, 1977; Hanioka et al, 2005). Addendum A shows the latest revised classification prescribed by Peeran et al (2014), however its use in daily oral examinations by health care providers are unknown.

## 2.4.Clinical presentation

OPP is evident from childhood and is often multifocal, nevii are usually focal which can be present from birth or grow in the latter period of life (Mallikarjuna et al, 2013). There is a greater probability that most melanoma precursor cells originated from progenitor melanocytes which have acquired cytogenetic alteration of their oncogenes, tumour-suppressor genes and DNA repair genes. As a result the melanoma precursor cells have acquired a malignant phenotype. Alternatively, precursor melanoma cells may originate as mature melanocytes residing in the submucosa, which have undergone cytogenetic alteration culminating in de-differentiation. These melanoma precursor cells have an extended self-renewal capacity, which sustains the growth of the melanoma (Warszawik-Hendzel et al, 2014). Most oral melanomas are pigmented lesions, presenting as elevated brown to bluish-black masses. Presentation of such lesions can originate in pre-existing flat areas of pigmentation in about 30% of cases (Masilana et al, 2015), or could present as a fast growing ulceration with spontaneous bleeding. All benign OPP are suggested to be examined with concern as OPP tend to be potential sites for future melanoma transformation (Mallikarjuna et al, 2013; Masilana et al, 2015).

OPP should be scrutinised when undergoing examination of patients which include a thorough medical and dental history, examinations extra- orally and intra- orally as well as laboratory tests if needed (Mallikarjuna et al, 2013). Adoption of practical assessment tools should be used from a consortium of classification (Addendum A), or the ABCD checklist (Asymmetry, Border irregularities, Colour variegation, and Diameter > 6 mm) which is used often in diagnosis and evaluation of cutaneous melanomas and could potentially be of some use when assessing OPP (Gondak et al, 2012). Other clinical tests do exist such as diascopy, radiography and surgical biopsies which can be used to confirm clinically suspicious lesions to and attain a definitive diagnosis (Mallikaarjuna et al, 2013).

Most of the oral pigmentation are physiological in nature with the potential of some being precursors to severe diseases (Mallikarjuna et al, 2013).

Therefore there needs to be a standard practical way of evaluating and diagnosing potential precursor lesions that may become potentially harmful. As seen in the latest classification by Peeran et al (2014), the possible causes can be quite extensive; therefore it is essential that certain contributing risk factors or parameters be developed in order to narrow the spectrum for clinicians to diagnose potential harmful OPP lesions.

## CHAPTER 3: RESEARCH DESIGN AND METHODOLOGY

### 3.1. Aim:

To determine the prevalence of oral physiological pigmentation (OPP) in a Western Cape sample

### 3.2. Objectives:

a. Describe the presence of OPP by;

1. Age,
2. Gender,
3. Oral distribution in terms of: Focal, diffuse, unilateral or bilateral

b. Compare the presence of OPP with number of cigarettes smoked per day

c. Determine the patient's perception of skin colour in relation to OPP



### 3. 3. Methodology

#### 3.3.1. Study design:

Cross sectional analytical study

#### 3.3.2. Study Site:

The study was conducted at the University of the Western Cape oral health centres situated in Tygerberg and Mitchell's Plain.

#### 3.3.3. Sample size

A convenient sample of 257 participants visiting Tygerberg and Mitchell's plain oral health centres over a period of four weeks were included in the study. The obtained data was thereafter analysed with the aid of a statistician.

### 3.3.4 Ethical considerations

Ethical clearance was obtained by the UWC Biomedical Ethics Research Committee with Project registration number: BM/16/5/13. All aspects of this study were designed in accordance to the UWC research ethics policy.

Due to the voluntary nature of the project, the study was clearly explained to the participants, along with the reassurance of refusal to participate. Written and informed consent was obtained from all participants (Appendix 1). All participants remained anonymous and no identifying features were attached to the questionnaire.

All aspects of the research study were discussed with potential participants and information sheets were provided so that informed consent could be attained. The patient was excluded from the study if he/she was in extreme pain or had a life threatening dental related emergency, whom was also referred appropriately for management. Any pigmentation questionable was sent for biopsy for definitive diagnosis and managed appropriately.

During the screening and questionnaire process, there was no obstruction or delay of daily service delivery. Each patient was referred to the appropriate department for treatment after participation in the study. The screening was performed by one examiner, the primary investigator (Registrar in oral medicine and Periodontics), so as to standardise the protocol.

### 3.3.5. Inclusion and exclusion criteria:

#### 3.3.5.1 Inclusion criteria:

Any patients, who attended the University of the Western Cape Tygerberg and Mitchells Plain oral health centres for routine dental care, were included in the study.

#### 3.3.5.2 Exclusion criteria:

(a) Patients with a history of prescription medication with side effects known to cause hyperpigmentation

(b) Patients previously diagnosed with systemic conditions known to cause hyperpigmentation

(c) Patients diagnosed with any immuno- inflammatory mediated disease or condition of the oral mucosa

### 3.3.6. Data collection and procedure:

**Oral examination and questionnaire**

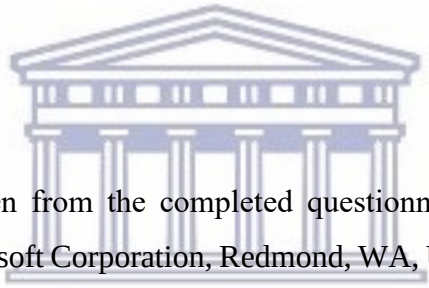
The patients were examined in a dental chair with incandescent (white light) after a verbal explanation of the study and details of their possible voluntary and confidential participation was given. Upon agreeing to participate, he/she was given a consent form to complete as well as an information sheet, thereafter the questionnaire was completed. If the patient declined such participation, the patient was acknowledged for their time and allowed to continue with their dental visit unhindered. All examination sets included a mouth mirror and a square piece of gauze for retraction.

The extra-oral examination included inspection and palpation of the head and neck region, focusing on asymmetry, and swelling or tenderness. Participants were referred to a medical doctor if they presented with fixed, firm, or unexplained lymph nodes or asymmetries.

An intra-oral examination was performed on the soft tissues with careful attention to the site, colour, texture, distribution and pattern of the OPP. A questionnaire of 19 items (Q1 to Q19) was used to determine some medical and behavioural aspects of each patient (Appendix 3). The patients perception of their skin colour was recorded on a visual guide (Appendix 3) numbered 1 (light skin) to 7 (dark skin) for analysis, this guide was meant to stay clear of any racial or ethical prejudice. Due to ethical constraints regarding ethnicity, patients were asked to evaluate their own skin colour and their perception was recorded on the visual guide number line (Appendix 3).

All the information attained was documented on a standardised questionnaire previously formulated. Patients were allowed to opt out of the study without prejudice. All data collected was treated confidentially at all times.

**Data capture and analysis**



All data that was taken from the completed questionnaires' and were captured on Microsoft excel (Microsoft Corporation, Redmond, WA, USA) spreadsheets .Statistical comparisons where done with the statistical software IBM SSP system with the aid of Prof H. W. Kruijsse (Statistician). The data collected was subjected to descriptive analysis and prevalence's were calculated. The significance of the differences of prevalence's were calculated by Catpca, crosstab and frequencies. Statistical significance was set at p- value <0.05.

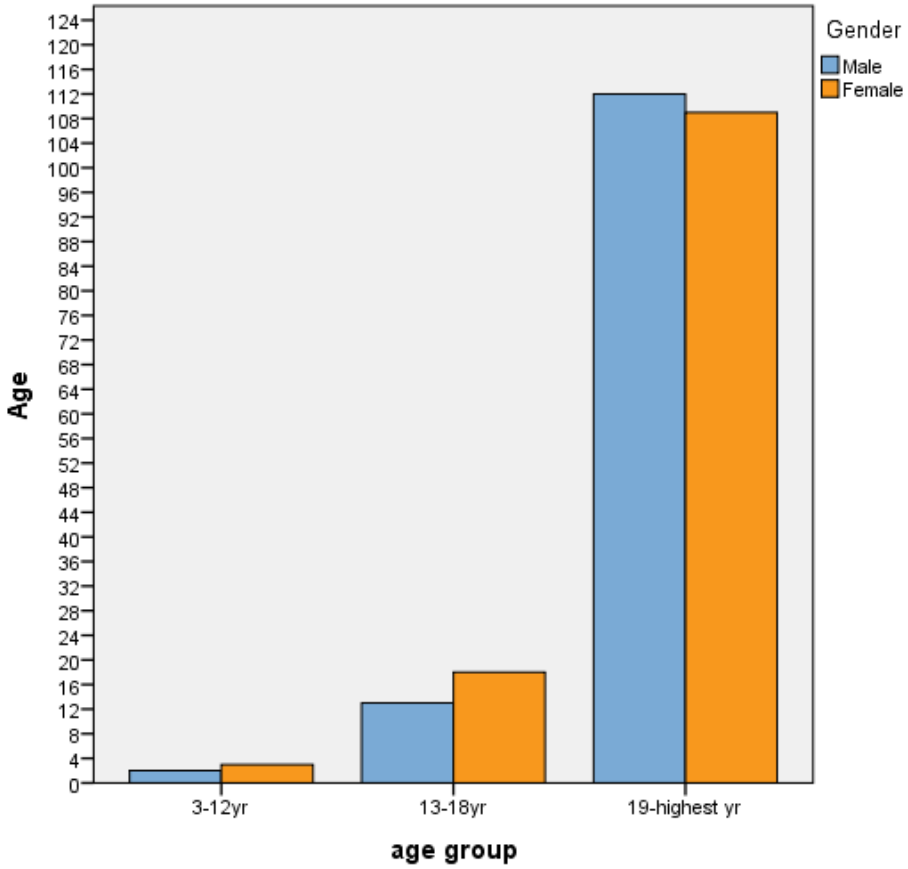
The influence of independent variables such as sex, age etc. on the prevalence of OPP was examined using logistic regression.

## CHAPTER 4: RESULTS

A convenient sample of 257 (127 male and 130 female) patients who visited UWC oral health centres (Tygerberg or Mitchell's plain), over a period of four weeks, were examined for the presence of oral pigmentation under the criteria formulated in the data collection sheet.

The patients' age ranged between 3 and 82 years old. Age was categorised into three age groups: below 12; from 13 to 19 and older than 18. See figure 1 and Table 1.

Fig: 1 – OPP frequency with age



| 10Table 1- OPP frequency with age | | | |
|---|---|---|---|
| | Frequency | Percent | Cumulative Percent |
| 3-12yr | 5 | 1.9 | 1.9 |
| 13-18yr | 31 | 12.1 | 14.0 |
| 19-highest year | 221 | 86.0 | 100.0 |
| Total | 257 | 100.0 | |

A score list of 14 indicators (P1 to P14) was used to determine the occurrence and location of pigmentation at various sites intra-orally including the lips, refer to appendix 3 (Table on Site). Therefore, and irrespective of the location, the total number of detected pigments per patient (the sum of P1 to P14) was used as the dependent variable.



| Table: 2- Gender distribution of OPP | | |
|---|---|---|
| | Frequency | Percentage |
| Male | 127 | 49.4 |
| Female | 130 | 50.6 |
| Total | 257 | 100 |

According to Fig: 1 and Table: 2, no difference in prevalence was shown between male and female.

The occurrence of total pigmentation per patient per age group is presented in Figure 2 and Table 2, also categorised from light skin to dark skin according to patient's perception. Amongst all variables in the questionnaire, all patients presented with the same colour and texture of oral physiological pigmentation. According to Fig: 2, participants who perceived themselves to have medium skin colour, presented with more OPP. There is no agreement with the literature that darker skin people have more total pigmentation than lighter skin people, which could be attributed to the limitation of the study. Also seen in Fig: 2 is that the majority of the participants perceived their skin colour within the medium skin colour range rather than dark or light.

FIG 2: Total OPP with age in perceived skin colour

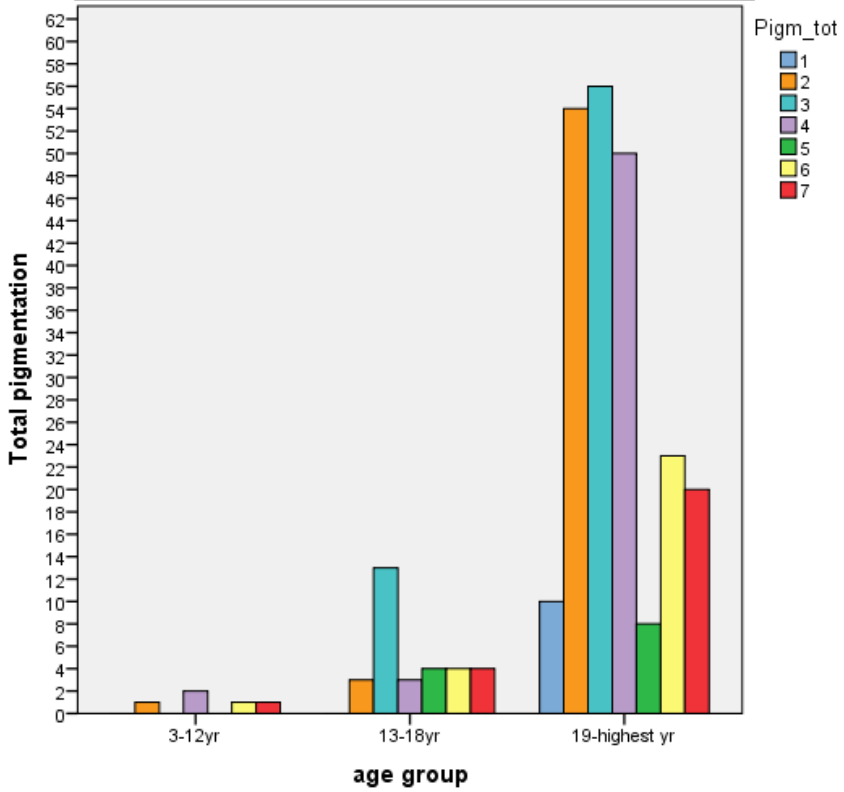
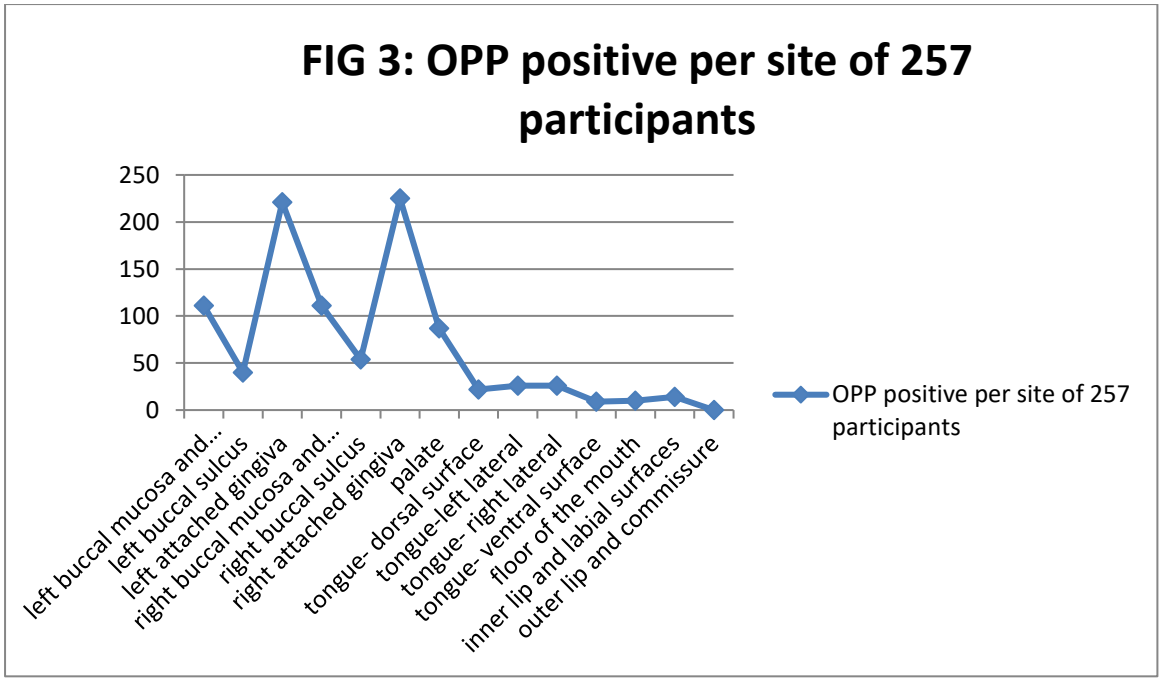



Table 3- Presence of total OPP in different age groups compared to perceived skin colour

| | | Age groups | | | Total |
|---|---|---|---|---|---|
| | | 3-12 year | 13-18 year | 19-highest year | |
| Pigmentation_total | 1 | 0 | 0 | 10 | 10 |
| | 2 | 1 | 3 | 54 | 58 |
| | 3 | 0 | 13 | 56 | 69 |
| | 4 | 2 | 3 | 50 | 55 |
| | 5 | 0 | 4 | 8 | 12 |
| | 6 | 1 | 4 | 23 | 28 |
| | 7 | 1 | 4 | 20 | 25 |
| Total | | 5 | 31 | 221 | 257 |

The above shows that pigmentation was detected with all patients, with a higher degree of total pigmentation attributed with increase in age.

| Table 4- OPP in specific sites of the oral cavity | | | |
|---|---|---|---|
| **SITE** | | **Present in specific site of the 257 participants** | **Percentage per area/site** |
| Left | Buccal mucosa and cheek | 111 | 43.2 |
| | Buccal sulcus | 40 | 15.6 |
| | Attached gingiva | 221 | 86 |
| Right | Buccal mucosa and cheek | 111 | 43.2 |
| | Right buccal sulcus | 54 | 21 |
| | Right attached gingiva | 225 | 87.5 |
| Palate | | 87 | 33.9 |
| Tongue | Dorsal surface | 22 | 8.6 |
| | Left lateral | 26 | 10.1 |
| | Right lateral | 26 | 10.1 |
| | Ventral surface | 9 | 3.5 |
| Floor of the mouth | | 10 | 3.9 |
| Inner lip and labial surfaces | | 14 | 5.4 |
| Outer lip and commissure | | 0 | 0 |






| Table 5- distribution and pattern of OPP | | | |
|---|---|---|---|
| **Distribution** | | **Per 257 participants** | **Percentage** |
| | **Localised** | **30** | **11.7** |
| | **Generalised** | **227** | **88.3** |
| **Pattern** | | | |
| | **Diffuse** | **194** | **75.5** |
| | **Spotted** | **63** | **24.5** |

A three dimensional CATPCA with HIV, smoking, alcohol, awareness and pigmentation totals showed that the first three variables are weakly related to the occurrence of pigmentation. As expected awareness and pigmentation defined a dimension and suggested some communality (Table 3).

Table 6- Awareness of OPP in light and dark skinned individuals

| | | Awareness | | Total |
|---|---|---|---|---|
| | | Yes | No | |
| Pigmentation_ total from light to dark skinned individuals | 1 | 0 | 10 | 10 |
| | 2 | 13 | 41 | 54 |
| | 3 | 0 | 56 | 56 |
| | 4 | 13 | 37 | 50 |
| | 5 | 0 | 8 | 8 |
| | 6 | 0 | 23 | 23 |
| | 7 | 0 | 20 | 20 |
| Total | | 26 | 195 | 221 |

## Chapter 5: Discussion

Oral pigmentation was positive in all patients examined with the distribution being the difference. According to previous studies, (Tamizi et al, 1996; Dummet et al, 1960; Tishkoff et al, 2009). , Africa was one of the geographical areas which had a higher presentation of oral physiological pigmentation. OPP was shown to be more pronounced with increase in age. There was a variation of patients aged above 18 years who presented with greater pigmentation per area of gingiva or it was more pronounced.

There was slight evidence which showed variability amongst gender regarding oral physiological pigmentation. The sample examined had an almost equal distribution of male (49.4%) versus female (50.6%) patients (Table 2).

According to the literature OPP most commonly affected the gingiva, hard palate and buccal mucosa, which was also shown with this study. Described in Table 7, is the presentation of OPP from areas of most frequent occurrence to least frequent occurrence.



| **Table 7: Descending order- most frequent site to less frequent site of occurrence** |
|---|
| Right attached gingiva |
| Left attached gingiva |
| Bilateral buccal mucosa and cheek |
| Palate |
| Right buccal sulcus |
| Left buccal sulcus |
| Left and right lateral tongue |
| Dorsal tongue |
| Inner lip and labial surface |
| Floor of the mouth |
| Ventral tongue surface |
| Outer lip and commissure |

The results also highlight that when OPP presented on the buccal mucosa, lateral tongue and attached gingiva, the appearance was usually bilateral. In this study the distribution of OPP was found to be generalised in 227 subjects and (88.3%) localised in 30 subjects (11.7%). However none of the localised OPP were characteristic of any pathology. For future studies it would be of some importance to record the localised OPP and follow up with age to assess if localised OPP becomes generalised as one gets older or to identify any pathological changes.

The pattern of occurrence was found to be diffuse in 194 candidates and spotted in 63 candidates. However no long term follow up has been made for any of these patterns or distributions. The general texture of the OPP was smooth as any other texture was excluded from the study for pathological testing and investigation. In the current sample chosen, there were not a large number of participants that where HIV positive. There was also low number of patients, who smoked cigarettes possibly due to non-disclosure, possibly from fear of prejudice. Which did not allow a comparison to OPP, as any patient attending the faculty where voluntarily allowed to participate. It is possible to do other studies with the main focus being smoking and HIV seropositive being the inclusion criteria for the specific study.

The sample size in this study was 295 patients of which 195 individuals were not aware of the presence of OPP, however when made aware it did raise concerns. After reassurance and education regarding OPP, the patients where no longer concerned. Awareness and early detection of pathology may be an important relationship to consider regarding OPP. It was also noted in this study that the lighter skinned individuals were more aware of the OPP than darker skinned individuals.

According to the literature oral physiological pigmentation is directly associated with skin colour intensity (Rosa et al, 2007; Masilana et al, 2016) , however in my study there was a limitation to attain ethical clearance to identify patients according to ethnicity or for the primary investigator to decide who is dark or light skin using visual colour guides. Therefore in this study we compared the patient's perception of skin colour with oral physiological pigmentation and thus could not get an accurate comparison.

Patients' perception of skin colour varied and was biased. Based on the results (Fig:2) on skin colour, it was determined that the visual guide used was a weak tool, as patients perceived their skin colours differently and there was no baseline of colour to compare to of light skin and dark skin, and this made it difficult to form an accurate comparison to OPP.

## Chapter 6: Conclusion

In a general population in the Western Cape it can be established that OPP occurred frequently compared to other geographical areas in the world. Ethnicity may have a more specific variability however ethically this comparison seemed not to be appropriate. An ethical comparison between skin colour and oral physiological pigmentation of oral gingiva deemed to be difficult. Therefore the study relied on the patient's perception for this comparison. The subjectivity of skin colour varied amongst patients, due to their personal perception of skin colour being unique and biased as to what the individual considered light skin versus dark skin. There is a need to obtain a standardised way of detecting skin colour in individuals other than relying on patients perceptions and maintaining ethical considerations.

The most common sites of occurrence were in line with other studies showing commonality. The attached gingiva, buccal mucosa and palate were most frequently affected by OPP. The pattern and distribution of OPP in a Western Cape sample mostly appeared to be generalised and diffused rather than localised and spotted, this again may have coincided with the geographical setting. Patients were not aware of the presence of OPP which may impact negatively on identifying pathogenic risk.

## Chapter 7: Recommendations

Future studies comparing intensity of colour and a more ethical approach in comparing this with ethnicity in South Africa.

Possible long term monitoring of localised and spotted OPP with increase of age to assess possible change to generalised or diffuse pattern or even pathological change.

Patient awareness of OPP compared to education given by oral practitioners regarding OPP.

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## CHAPTER 9: APPENDICES

### Appendix 1

### Information Sheet for Oral Soft tissue examination

The following document serves to provide the relevant information regarding the proposed study. Details of the principle investigator are provided should you have any further queries. If you wish, the presence of a translator can be made available to assist in understanding the information contained within this document.

Title: Oral physiological pigmentation in a Western Cape sample

Principle Investigator: Dr Shogan Govender

Position: Postgraduate student within the Department of Oral Medicine and Periodontology

Contact details

Project registration number: BM/16/5/13

Office number: (021) 937-3167 Cell Number: 0732603317

Email address: 2440461@myuwc.ac.za



BIOMEDICAL RESEARCH ETHICS ADMINISTRATION

Research Office

New Arts Building,

C-Block, Top Floor, Room 28

I, Dr Shogan Govender, hereby invite you to participate in a research study. Please take the time to read the following information regarding the research and what would be required of you as a participant. Feel free to ask questions if you require any further information or clarify any concerns you may have.

**What is the purpose of this research?**

To examine intra –oral soft tissue with oral physiological pigmentation and compare the prevalence with a few risk factors. Examples of risk factors i.e: age, gender, smoking etc. As well as recording the distribution of the OPP according to location, pattern, colour, distribution, and texture. All information required will be on the standardised questionnaire that has been formulated.

**What would be required from you?**

An oral examination so I can assess the oral physiological pigmentation. And to ask a few questions formulated in my questionnaire.

**Why have you been invited?**

You are invited to participate as you meet all the necessary criteria which are:

1. You are visiting UWC oral health centre for routine dental care



Kindly inform Dr Shogan Govender of any specific medical conditions and medications you are currently taking if you are interested in participating.

**Your decision to participate:**

The decision to participate is voluntary and will in no way affect the quality of treatment that you have been scheduled for. If you decide to participate, you would be asked to sign a consent form in order to record that you have chosen to take part. You will still be free to withdraw at any time at no consequence to you. There is no binding agreement to your participation.

**Are there any disadvantages to your participation?**

None

**Are there any benefits to you taking part?**

The information obtained from this research will not benefit you; however it will increase our understanding of the prevalence of oral physiological pigmentation.

Confidentiality:

All personal and medical information obtained from you during the course of this research will be kept strictly confidential and protected. All samples taken and data collected will have no information pertaining to your identity. However, your personal information may be given out if required by law.

**How will your data be collected?**

All information acquired from you during the clinical examination and questionnaire will be written on the questionnaire itself. No name or personal information will be attached to the form to trace it back to the participant. Only a generic record number will be attached randomly to the questionnaire for record purposes. All data will then be transferred onto an electronic database which will be held on a password protected computer with restricted access. Hard paper will be stored in a secure location accessed only by the researcher. Your data will be accessible only to authorized persons such as researchers within the team, supervisors, and regulatory authorities. Your data will be retained for a period of 3 years before it will be disposed of securely.



**What will happen on completion of this research study?**

The results of this research will be submitted as a thesis for a specialist degree in Periodontics and Oral Medicine. If approved by the university senate, the research will be submitted for publication within a medical/dental scientific journal. The outcome of the study will be made available to you if you request.

**Appendix 2**

**Informed consent**

I, (Name…….) have been informed about the study entitled Oral physiological pigmentation in a Western Cape sample, by Dr. S. Govender.

I understand the purpose and procedures of the study as explained by Dr. S Govender.

I have been given an opportunity to ask questions about the study and have been answered to my satisfaction.

I declare that my participation in this study is entirely voluntary and that all information acquired will be destroyed appropriately at the end of the study.

If I have any further questions/concerns or queries related to the study I understand that I may contact the researcher at the phone number (021) 937-3167 or via e-mail 2440461@myuwc.ac.za

If you have any questions or concerns about your rights as a study participant, or if you are concerned about an aspect of the study or the researchers then you may contact:

UWC BIOMEDICAL RESEARCH ETHICS ADMINISTRATION

Research Office

New Arts Building,

C-Block, Top Floor, Room 28



_____ _____

Signature of Participant Date References

**Appendix 3- Questionnaire**

Previous medical history:

_____

_____

Medication:

_____

_____

| | |
|---|---|
| Drug or systemic conditions known to cause hyperpigmentation<br>Immune mediated diseases of the mouth | |

Gender:

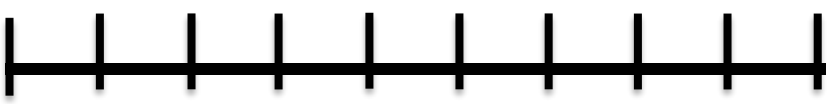
| | |
|---|---|
| male | female |

Age: _____



How would you rate the colour of your skin from very light to very dark using this scale?

very light very dark



The following questions may be confidential in nature; you therefore have the option of answering.

| | | | |
|---|---|---|---|
| Do you take oral contraceptives (Females only) | Yes | No | Choose not to answer |
| How often do you take oral contraceptives? | | | |
| What is the name of the type you take? | | | |

| | | | |
|---|---|---|---|
| Do you know your HIV status? | Yes | No | Choose not to answer |
| Are you HIV positive? | Yes | No | Choose not to answer |
| What is your latest CD4 count? | | | Choose not to answer |
| Are you on antiretroviral drug therapy? | Yes | No | Choose not to answer |
| What is the name of the type you take? | | | |

| | | | |
|---|---|---|---|
| Do you Smoke? | Yes | No | Choose not to answer |
| How many years are you smoking? | | | |
| How many cigarettes per day do you smoke? | | | |



| | | | |
|---|---|---|---|
| Do you use snuff? | Yes | No | Choose not to answer |
| How many years are you using snuff? | | | |
| How many times per day do you use snuff? | | | |

| | | | |
|---|---|---|---|
| Do you consume alcohol? | Yes | No | Choose not to answer |
| How many years do you consume alcohol? | | | |
| How frequent do you consume per week? | | | |

Do you know if you have pigmentation in your mouth?

| Yes | No | Comment: |
|---|---|---|

Do you think having oral pigmentation is something to be worried about?

| Yes | No | Comment: |
|---|---|---|

The following tables will be used to exam oral pigmentation

| **SITE** | | **Tick** | **Colour** | **Texture** |
|---|---|---|---|---|
| Left | Buccal mucosa and cheek | | | |
| | Buccal sulcus | | | |
| | Attached gingiva | | | |
| Right | Right buccal mucosa and cheek | | | |
| | Right buccal sulcus | | | |
| | Right attached gingiva | | | |
| Palate | | | | |
| Tongue | Dorsal surface | | | |
| | Left lateral | | | |
| | Right lateral | | | |
| | Ventral surface | | | |
| Floor of the mouth | | | | |
| Inner lip and labial surfaces | | | | |
| Outer lip and commissure | | | | |

| | | | |
|---|---|---|---|
| **DISTRIBUTION** | Localised | Generalised | Other: |

| | | | |
|---|---|---|---|
| **PATTERN** | Diffuse | Spotted | Other: |

| | |
|---|---|
| Any intra oral pathology noted<br>Fordyces granules and vascularities ( lingual varex) noted intra orally | |

**Appendix 4- Classification systems of Oral pigmentation**

Oral pigmentation index (DOPI):

This index of oral pigmentation is the commonly used index due to its simplicity and ease of use.

*The scores are as follows:*

- No clinical pigmentation (pink-colored gingiva)
- Mild clinical pigmentation (mild light brown color)
- Moderate clinical pigmentation (medium brown or mixed pink and brown color)
- Heavy clinical pigmentation (deep brown or bluish black color)

(Dumett et al,1964)



*Melanin index:*

This index has classified pigmentation as follows:

- No pigmentation
- One or two solitary unit(s) of pigmentation in papillary gingiva without the formation of a continuous ribbon between solitary units
- More than three units of pigmentation in papillary gingiva without the formation of a continuous ribbon
- One or more short continuous ribbons of pigmentation
- One continuous ribbon including the entire area between canines (Hedin, 1977)

*Melanin pigmentation index:*

Takashi et al. have proposed another index to measure gingival melanin pigmentation. The index is as follows:

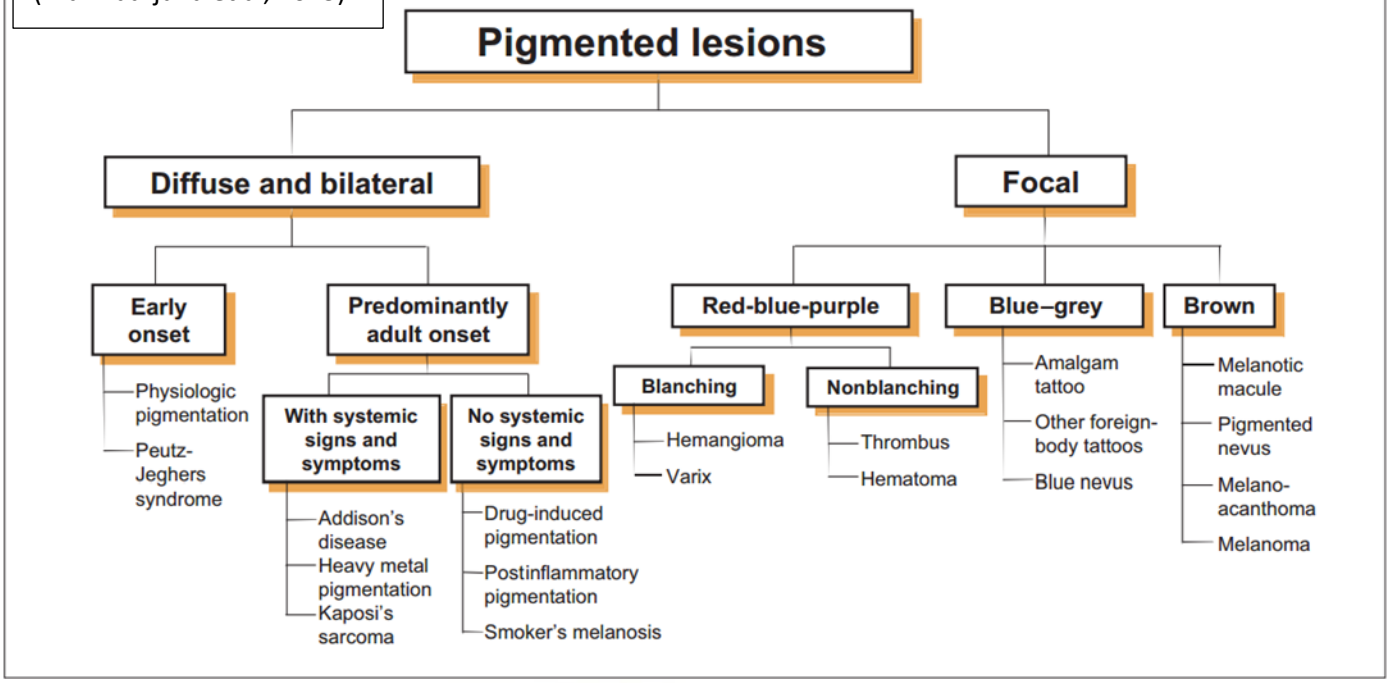
| | |
|---|---|
| Score 0 | No pigmentation |
| Score 1 | Solitary unit(s) of pigmentation in papillary gingiva without extension between neighbouring solitary units |
| Score 2 | Formation of continuous ribbon extending from neighbouring solitary units |

This index is not equipped to describe the degree of melanin pigmentation. (Hanioka et al, 2005)

*Gingival pigmentation index: (Kumar et al, 2012).*

| | |
|---|---|
| Score 0 | Absence of pigmentation |
| Score 1 | Spots of brown to black color or pigments. |
| Score 2 | Brown to black patches but not diffuse pigmentation |
| Score 3 | Diffuse brown to black pigmentation, marginal, and attached |

(Mallikaarjuna et al, 2013).




**Proposed new classification of gingival pigmentation** (Peeran et al, 2014)

| Class | Criteria of classification (Peeran et al, 2014) |
|---|---|
| I | Coral pink/salmon pink coloured gingival |
| II | Localized/Isolated spots/areas of gingival melanin pigmentation which does not involve all the three parts of gingiva, that is, attached, free, and papillary gingiva<br>Mild to moderate pigmentation<br>Severe/intense pigmentation |
| III | Localized/Isolated unit/s of melanin pigmentation which involve all the three parts of gingiva, that is, attached, free, and papillary gingiva<br>Mild to moderate pigmentation<br>Severe/intense pigmentation |
| IV | Generalized diffuse pigmentation which involve all the three parts of gingiva that is, attached, free, and papillary gingiva<br>Mild to moderate pigmentation<br>Severe/intense pigmentation |
| V | Tobacco associated pigmentation like smoker's melanosis and chewing tobacco |

| | |
|---|---|
| VI | Gingival pigmentation due to exogenous pigments<br>Amalgam tattoos<br>Cultural gingival tattooing<br>Drinks<br>Food colours<br>Habitual betelnut/khat chewing<br>Lead-Burtonian line<br>Mercury<br>Silver<br>Arsenic<br>Bismuth<br>Graphite<br>Otherforeign bodies<br>Topical medications<br>Idiopathic |
| VII | Gingival pigmentation due to endogenous pigments<br>Bilirubin<br>Blood breakdown products: Ecchymosis, Petechiae<br>Hemochromatosis<br>Hemosiderin |
| VIII | Drug-induced gingival pigmentation<br>ACTH<br>Antimalarial drugs<br>Chemotherapeutic agent-busulfan and doxorubicin<br>Minocycline<br>Oral contraceptives<br>Phenothiazines |
| IX | Gingival pigmentation associated with systemic diseases and syndromes<br>Addison's disease<br>Albright's syndrome<br>Basilar melanosis with incontinence |

| | |
|---|---|
| | Beta thalassemia<br>Healed muco-cutaneous lesions-Lichen planus, Pemphigus, Pemphigoid<br>Hereditary hemorrhagic telangiectasia<br>HIV-associated melanosis<br>Neurofibromatosis<br>Peutz-Jeghers and other familial hamartoma syndromes<br>Pyogenic granuloma/Granulomatous epulis |
| X | Pigmented benign and malignant lesions involving the gingiva<br>Angiosarcoma<br>Hemangioma<br>Kaposi's sarcoma<br>Malignant melanoma<br>Melanocytic nevus<br>Pigmented macule |



Proposed gingival melanin pigmentation and pigmented lesions index (Peeran et al, 2014)

| | |
|---|---|
| Score 0 | Coronal pink- colored gingiva, no gingival pigmentation, and/ or pigmented lesions |
| Score 1 | Mild, solitary/diffuse, gingival melanin pigmentation involving anterior gingiva, with or without the involvement of posterior gingiva |
| Score 2 | Moderate to severe, solitary or diffuse, gingival melanin pigmentation involving anterior gingiva with or without the involvement of posterior gingiva |
| Score 3 | Gingival melanin pigmentation only in posterior gingiva |
| Score 4 | Tobacco- associated pigmentation : smokers melanosis, chewing tobacco |
| Score 5 | Gingival pigmentation due to exogenous pigments-Amalgam tattoos arsenic, bismuth, chewing betel nut, cultural gingival tattooing, drinks, food colors, lead-burtonian line, mercury, silver, topical medications, idiopathic etc |

| | |
|---|---|
| Score 6 | Gingival pigmentation due to other endogenous pigments: Bilirubin, blood breakdown products, ecchymosis, hemochromatosis, hemosiderin, petechiae etc |
| Score 7 | Drug-associated gingival pigmentation: Antimalarial drugs, minocycline, oral contraceptives etc |
| Score 8 | Gingival pigmentation associated with other causes:<br>Addison's disease, albright's syndrome, basilar melanosis with incontinence, hereditary hemorrhagic telangiectasia, HIV patients, lichen planus, neurofi bromatosis, Peutz-Jeghers syndrome, pyogenic granuloma/granulomatous epulis etc |
| Score 9 | Pigmented benign lesions: Hemangioma, melanocytic nevus, pigmented macule |
| Score 10 | Pigmented malignant lesions: Angiosarcoma, Kaposi's sarcoma, malignant melanoma |