Republic of Iraq
Ministry Of Higher Education and Scientific Research
University Of Misan
College Of Dentistry

GRADUATION PROJECT

GINGIVAL PIGMENTATION

A Review article submitted in partial fulfillment of the requirements for the degree of Bachelor in Dentistry at University of Misan

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Dedication:

Our study trip has reached its end after exhaustion and hardship, and concluding the research of my graduation with all vigor. I'm grateful to everyone who has been credited with me journey, and help me, even with ease Parents, family, friends, and esteemed teachers. I present to you a study of graduation.And do not forget the greatest credit to doctor and research supervisor (Dr.Heba Abdul Hussein) , by providing me with valuable and useful Information.

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1.1 Abstract:

Gingival pigmentation has intrigued clinicians and researchers alike owing to its numerous etiologies of origin and the difficulties faced in its absolute elimination. The present paper aims to highlight the biochemistry of gingival pigmentation, the common causes and various aspects related to the evaluation of pigmentation. Gingival pigmentation has been defined as the discoloration of the gingiva due to lesions associated with extrinsic and intrinsic factors. Melanin is the most commonly implicated pigment in gingival pigmentation. The biochemistry of melanin pigmentation has been dealt with in detail by several authors and the cells related to the phenomenon i.e., melanocytes, melanophages have been widely studied. Numerous attempts have been made to classify gingival melanin pigmentation. Broadly, lesions have been classified as physiologic and pathologic. Physiologic pigmentation is due to greater melanocyte activity whereas pathologic pigmentation can be due to several causes including endocrine disorders, heavy metal pigmentations, malignancies, so on. Furthermore, for accurate diagnosis and treatment planning, it becomes essential to evaluate the pigmentation in an elaborate and extensive manner. With an increasing demand for esthetics, the diagnosis and treatment of pigmented lesions of the gingiva has gained utmost significance.

Keywords: Gingival pigmentation, Melanin, Melanocytes, Drug induced oral pigmentation.

1.2 Introduction

Health and appearance of gingiva are important parts of a smile [1]. The color of the gingiva is various among different individuals and it is thought to be associated with cutaneous pigmentation [2]. It varies from light to dark brown or black. The skin tone, texture and color differ in various races and regions [3]. The gingival color depends primarily upon the number and size of vasculature, epithelial thickness, degree of keratinization and pigments within the gingival epithelium. Melanin, carotene, reduced hemoglobin and oxy-hemoglobin are the prime pigments contributing to the normal color of the oral mucosa [4].

Gingival pigmentation is presented as a diffuse deep purplish discoloration or as irregularly shaped brown and light brown or black patches, striae or strands. It results from melanin granules, which are produced by melanoblasts. Melanin, a non-hemoglobin–derived brown pigment, is the most common of the endogenous pigments and is produced by melanocytes present in the basal and suprabasal cell layers of the epithelium [5].

Melanin pigmentation appears as early as 3 h after birth in the oral tissues and in some cases is the only sign of pigmentation on the body. It is generally agreed that pigmented areas are present only when melanin granules synthesized by melanocytes are transferred to the keratinocytes. This close relationship is known as the ‘epidermal-melanin unit’ [6].

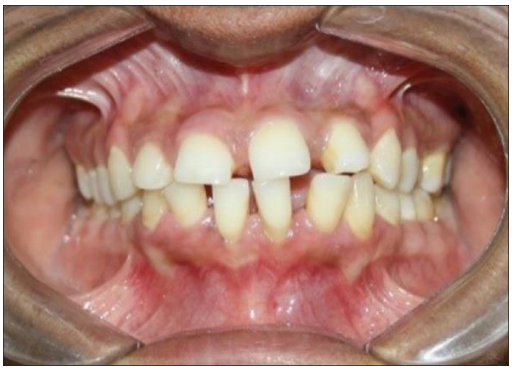
PIGMENTED LESIONS OF ORAL MUCOSA

- Blue / purple vascular lesion e.g. (Kaposi sarcoma)
- Brown melanotic lesions e.g. (Nevocellular and blue nevi)
- Brown heme Associated lesion
- Gray / black pigmentation

Classification of gingival pigmentation

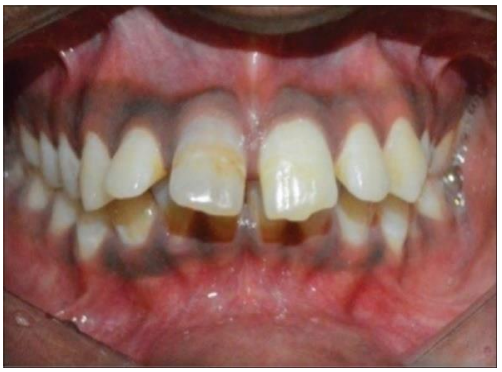
Class I

Pigmentation in the Attached Gingiva only



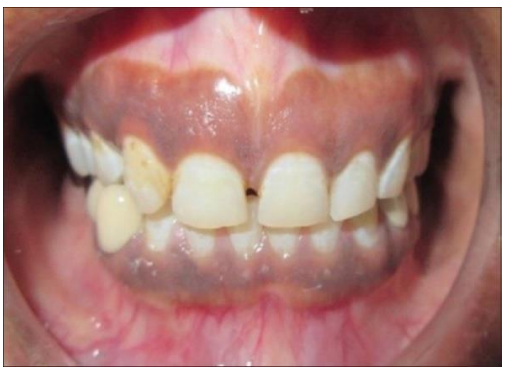
CLASS II

Pigmentation in the Attached Gingiva & Interdental Papilla



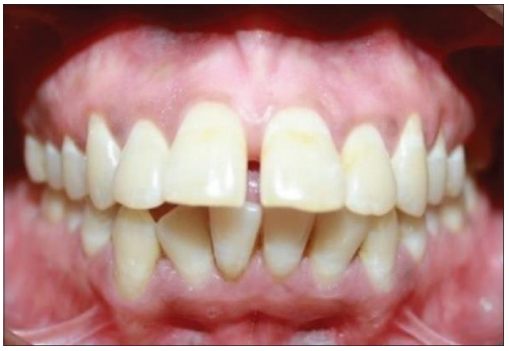
Class III

Diffuse Pigmentation involving all parts of gingiva



Class IV

Pigmentation in Marginal Gingiva only



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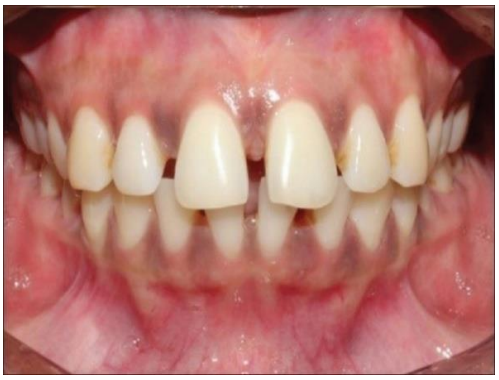
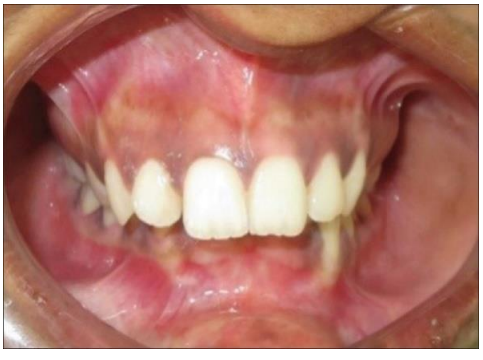
Pigmentation in Interdental Papilla only



Class VI

Pigmentation in Marginal Gingiva & Interdental Papilla



1.3 Causes

The gingiva is considered the most frequently pigmented tissue in the oral cavity [7]. Gingival pigmentation is a discoloration of the gingiva due to a variety of lesions and conditions associated with several endogenous and exogenous etiologic features [8]. It may range from physiologic reasons (e.g., racial pigmentation) to manifestations of systemic illnesses (e.g., Addison's disease) to malignant neoplasms (e.g., melanoma and Kaposi's sarcoma). It is essential to understand the cause of a mucosal pigmentation before planning the treatment of such lesion [9].

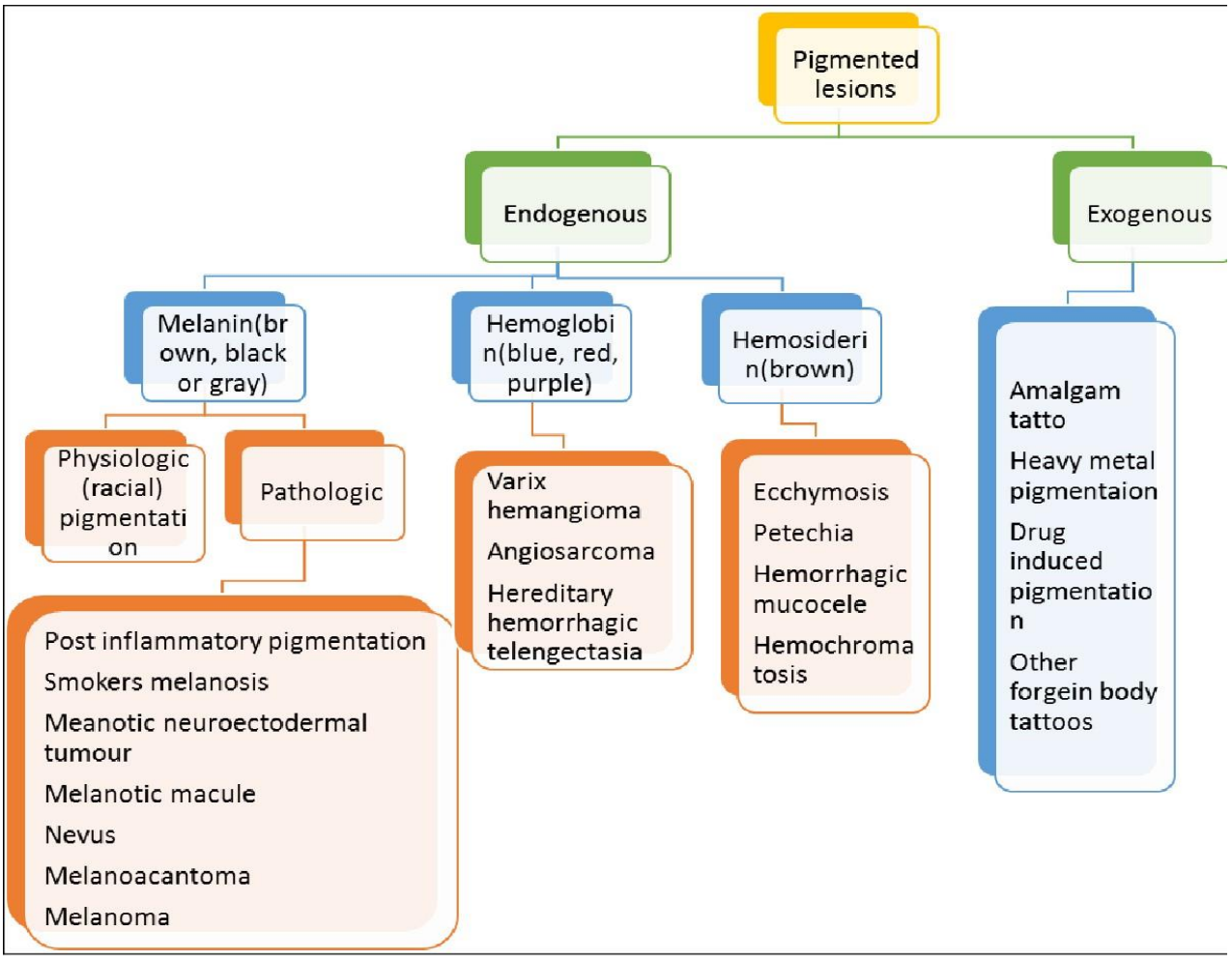


Figure 2: classification of pigmented lesion.

Broadly, gingival pigmentation may be classified as physiologic or pathologic.

1.3.1 Physiologic (ethnic/racial) gingival pigmentation

All patients except albinos have some degree of physiologic melanin distribution throughout epidermis. Physiologic pigmentation develops during the first two decades of life but may not come to the patients notice until later. Pigmentation is asymptomatic and no treatment is required. Moreover, color variation may be uniform, unilateral, bilateral, mottled, macular or blotched and may involve the gingival papillae alone or extend throughout the gingiva and into other oral tissues [10]. Eumelanin is present in large amounts in individuals with dark skin and hair and is the more photoprotective. Physiologic pigmentation clinically manifests as multifocal or diffuse melanin pigmentation with variable prevalence in different ethnic groups. It is common in African, Asian and Mediterranean populations, and it is due to greater melanocyte activity rather than greater number of melanocytes. Attached gingiva is the most common site of such pigmentation [8].

The process of pigmentation consists of three phases [11]:

I) Activation of melanocytes.

II) Synthesis of melanin.

III) Expression of melanin.

I) The activation phase occurs when the melanocytes are stimulatedby factors like stress hormones, sunlight etc. leading to production of chemical messengers like melanocyte stimulating hormone.

II) In synthesis phase, melanocytes make granules called melanosomes. This process occurs when the enzyme tyrosinase converts amino acid tyrosine into a molecule called dehydroxyphenylalanine (DOPA). Tyrosinase then convertsDOPA into secondary chemical dopaquinone. After a series of reactions, dopaquinone is converted into either dark melanin (eumelanin) or light melanin (pheo-melanin).

III) In expression phase, melanosomes are transferred from the melanocytes to the keratinocytes which are the skin cells located

above melanocytes in the epidermis. After this, melanin color eventually becomes visible on the surface of skin.

Major determinant of normal human skin colour is the melanogenic activity within the melanocytes and the quantity and quality of melanin production, but not melanocyte density. The degree of clinical melanin pigmentation in human epidermis and in the epithelium of oral mucosa is related to the amount of melanin i.e., the maturation of melanosomes, the number of keratinocytes containing melanosomes and the distribution of melanin loaded keratinocytes throughout the epithelium [12].

1.3.2 Pathologic gingival pigmentation

a) Endocrine diseases: like Addison's disease, Albright's syndrome, Acromegaly, and Nelson's syndrome [13].

b) Heavy metals: e.g., lead, bismuth, mercury, silver, arsenic, and gold [13]. In children, the possible sources of exposure include lead contaminated water or paint and mercury or silver containing drugs. The pigmentation appears as a blue or black line along the gingival margin and is proportional to the amount of gingival pigmentation. The importance of oral mucosal pigmentation associated with heavy metals lies primarily in the recognition and treatment of the underlying causes to avoid severe systemic toxic effects [8].

c) Kaposi's sarcoma: it is the most common malignancy associated with human immunodeficiency virus infection and it may potentially affect every part of the body. Although, palate is the most common site of AIDS related Kaposi's sarcoma, intraoral lesions may also involve the gingiva and other areas. Gingival lesions may extend into the free gingiva and adjacent mucosa or involve the frena [14].

d) Drug induced: a variety of medications including chloroquine, quinine, minocycline, zidovudine, chlorpromazine, ketoconazole, bleomycin, cyclophosphamide and so on have been known to cause melanin pigmentation. It can involve accumulation of melanin pigments under the influence of drug or deposition of iron after damage to dermis. Minocycline has also been reported to cause pigmentation of the gingiva and lips. Histopathological examination of biopsy specimens from the gingiva and lips showed evidence of increased melanin/melanocytes in the epithelium and melanin/melanophages in the connective tissue [15].

e) Post-inflammatory pigmentation: long standing inflammatory mucosal lesions, mainly lichen planus can cause mucosal pigmentation. These are more frequently seen in the dark-skinned

individuals. Histologically, there is increased production of melanin laden macrophages in the superficial connective tissue [8].

f) Smoking associated melanosis: Brown and Houston dealt with a case of smoker's melanosis involving the anterior facial maxillary gingiva. A localized area of melanin pigmentation was seen in the marginal gingiva of a Caucasian female which was excised and subsequently biopsy was performed. Histological analysis showed the lesion to be benign mucosal melanosis compatible with Smoker's melanosis [12].

g) Hemangioma: vascular lesions presenting as proliferations of vascular channels are tumour like hamartomas when they arise in childhood; in adults benign vascular proliferations are generally varicosities. Depending upon the depth of vascular proliferations, the lesion may have vessels close to the overlying epithelium and may appear reddish, or if a little deeper, blue [8].

h) Amalgam tattoo: accidental displacement of metal particles in oral soft tissues during restorative dental procedures using amalgam may result in amalgam tatoo. The cause may be iatrogenic or traumatic. Metal particles may leach into oral tissues and may cause discoloration overtime. Bortuluzzi presented a case report of a root perforation sealed with gray MTA that resulted in discoloration of marginal gingival [16].

i) Graphite tattoo: tend to occur on the palate and represent traumatic implantation from a lead pencil. The lesions are unusually macular, focal and gray or black. Microscopically, graphite resembles amalgam in tissue although special stains can segregate the two [8].

j) Nevocellular nevus and blue nevus: may be found in any age group and seen commonly on palate and gingiva.

k) Oral melanoacanthoma: the term was first used to describe a benign mixed skin tumor composed of basal and prickle cell keratinocytes and pigment laden dendritic melanocytes. It is considered to be a reactive process unrelated to the neoplastic melanoacanthoma of the skin. It affects mostly black youngsters, develops quickly and has a flat or slightly raised black to brown surface. These features, together with its tendency to affect mucosal sites exposed to trauma, the observed regression following biopsy or removal of offensive irritants, and the histological features of chronic inflammation favor a reactive nature [17]. Bregni et al. depicted four cases each of oral melanoacanthoma and melanotic macule affecting Caucasian and Latin American patients. The authors concluded that these lesions can exhibit a similar clinical presentation and to distinguish among them and other pigmented disorders, the histopathologic analysis is indispensible [18].

l) Mucosal melanomas: extremely rare with a higher prevalence in Japanese people. Tend to occur on the anterior labial gingiva and the anterior aspect of hard palate. In early stages appear

as brown or black plaques and subsequently becomes more diffuse, nodular and tumefactive [19], [20].

m) HIV oral melanosis: such patients undergo hyperpigmentation of skin, nails and mucous membrane. The etiology of such hyper pigmentation remains undetermined though it may be attributed to medication or adrenocortical involvement by opportunistic parasites [21], [22]. Ficarra et al. studied 217 patients seropositive for HIV over 2 years and found that 6.4% developed oral pigmentation. Majority of such patients had multitple macules on the oral mucosa, while labial, palatal and gingival pigmentation were seen in others [23].

n) Haemochromatosis: patients with haemochromatosis frequently display bluish gray pigmentation of the hard palate, gingiva and buccal mucosa. The pigmentation is caused by deposition of iron containing pigments ferritin and haemosiderin within the skin and mucous membranes [14], [17].

o) Oral melanocytic pigmentations have been reported in patients with Laughier–Hunziker syndrome and with Carney complex [24], [25].

p) Gingival tattoo: Rawal et al. reported four cases of cultural practice of gingival tattoo in West African females of three different ethnic groups. Four black females presented with diffuse pigmentation of the maxillary attached gingiva and without any radiographic abnormalities. It was revealed that the women had had one or more sessions of traditional gingival tattooing. Biopsy exhibited dense fibrous connective tissue containing aggregates of foreign material consistent with a foreign body tattoo [26].

q) Unusual pigmentations of the gingiva: Ashri and Gazi reported three cases of unusual pigmentations of gingiva associated with habitual chewing of plants. The first was a brown pigmentation caused by the use of bark of Juglans regia for cleaning of teeth. The second was a bright yellow pigmentation due to chewing of seeds of Cola nitida. The third case reported a mousy brown pigmentation associated with chewing of leaves of Catha edulis [27].

1.4 Gingival depigmentation techniques

Different procedures have been proposed for gingival depigmentation.

1.4.1 Scalpel surgical technique

In this technique, the pigmented gingival epithelium along with a layer of the underlying connective tissue is surgically removed by splitting the epithelium with blade. Care should be taken not to leave any pigmented remnants over the denuded area [29].

The scalpel method is one of the most economic techniques and also does not require extensive armamentarium [6]. It is highly recommended in consideration of the equipment constraints that may not be frequently available in clinics. Moreover, it is known that the healing period for scalpel wounds is faster than other techniques [30].

However, scalpel surgery causes bleeding during and after the procedure and it is necessary to cover the surgical site with periodontal dressing for 7–10 days. Though the initial results of depigmentation procedure are highly encouraging, repigmentation is a possibility. This process may be attributed to the fact that active melanocytes from the adjacent pigmented tissues migrate to the treated areas [6].

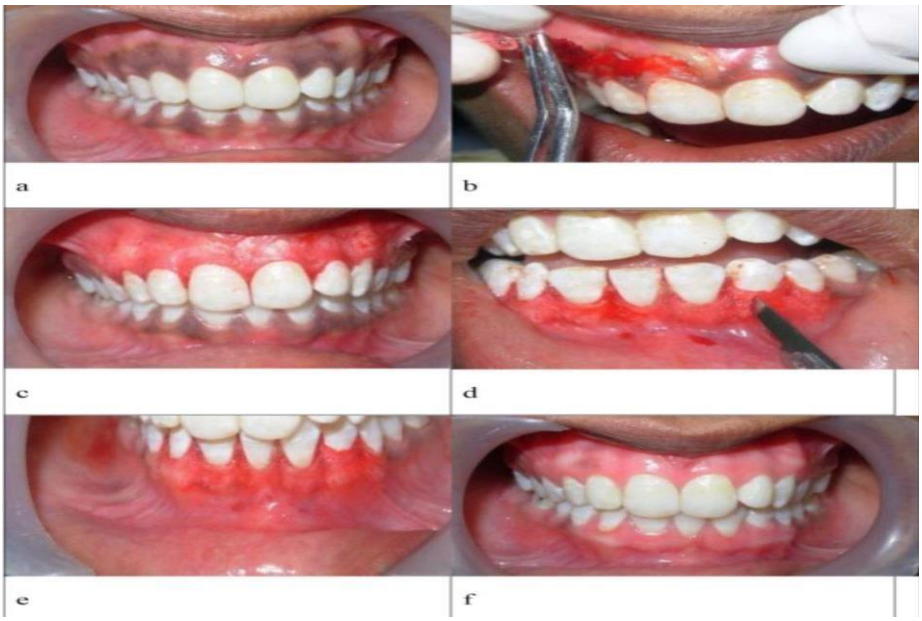


Figure. 1. a. pre-operative view, b. Maxillary pigmentation removal using scalpel surgical technique, c. Immediately after depigmentation, d. Mandibular pigmentation removal, e. Immediately after depigmentation, f. After 3 months

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1.4.2 Bur abrasion method

In this technique a medium grit football shaped diamond bur is used at high speeds to denude the epithelium. The procedure requires 45 min to1hour for completion [32].
It is relatively simple, safe, non-aggressive method and easy to perform. Above all, it causes less discomfort and is esthetically acceptable to the patients [33]. Also, this technique does not require any sophisticated equipment and is hence, economical[34] (see Figure. 1).
On the other hand, bur abrasion method was found to be difficult in controlling the depth of de-epithelialization. Moreover, bleeding and post-operative pain are anticipated [5] (Figure. 2)

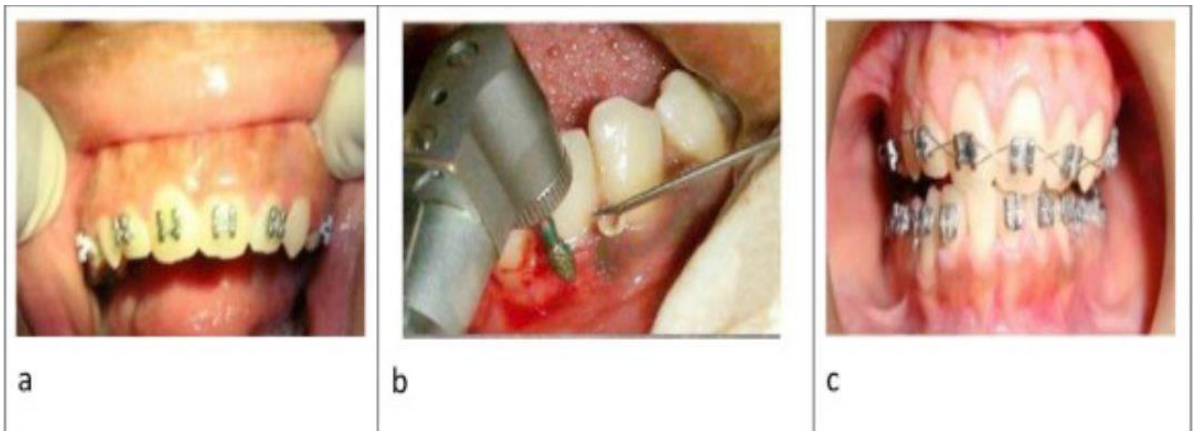

Figure. 2. a. Pre-operative, b. Gingiva depigmentation by bur abrasion, c.3 Months post-operative view [31].

1.4.3 Electro-surgery

Electro-surgery is the use of high frequency electrical energy in the radio transmission frequency band, which is applied directly to tissue to induce histological effects. As the current passes, the impedance to the passage of current though the tissue generates heat, which boils the tissue water, creating steam, resulting in either cutting or coagulation of tissue [29].
It was found that this method controls hemorrhage, permits adequate contouring of tissues, causes less discomfort to patient, less scar formation and lesser chair time [35].
Electro-surgery requires more expertise than scalpel surgery. Prolonged or repeated application of current to tissue induces heat accumulation and undesired tissue destruction. Contact with periosteum or alveolar bone and vital teeth should be avoided [30] (Figure. 3).

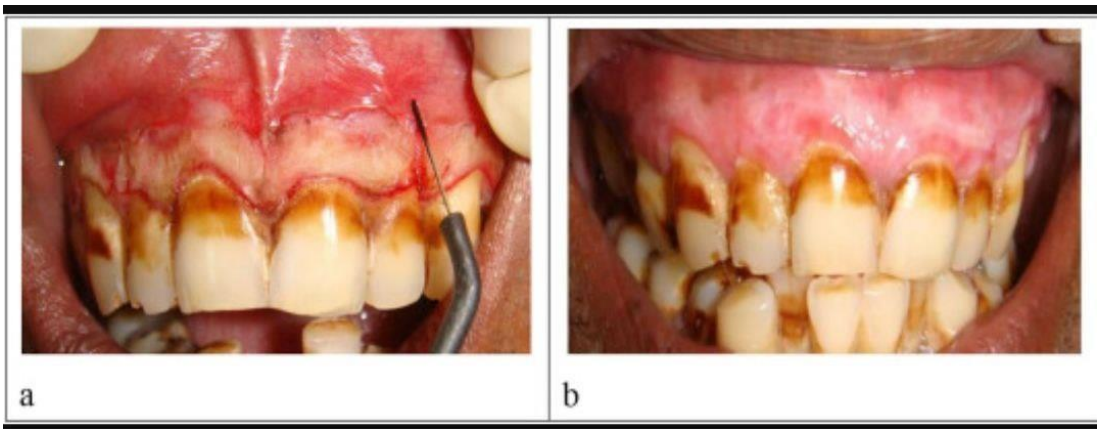

Figure. 3. a. Depigmentation by electrosurgical technique, b. Complete healingafter 1 month.

1.4.4 Cryosurgery

In cryosurgery, the gingiva is freezed with different materials such as liquid nitrogen. This technique is based on rapid freezing of water and slow melting repeatedly, leading to tissue deterioration. The cryotherapy has some direct effects including cell dehydration, enzyme inhibition, protein denaturation, and cell death due to thermal shock. It has also some indirect effects such as changes in vasculature and immune response of the tissue, which leads to cell death [37].

Regarding the advantages of this method, this technique is easy and rapid to apply, does not require anesthesia or suturing, and finally it does not cause any bleeding or scars [38].

However, cryosurgery is followed by considerable swelling, and it is also accompanied by increased soft tissue destruction. Depth control is difficult, and optimal duration of freezing is not known, but prolonged freezing increases tissue destruction [30]

(Figure. 4).

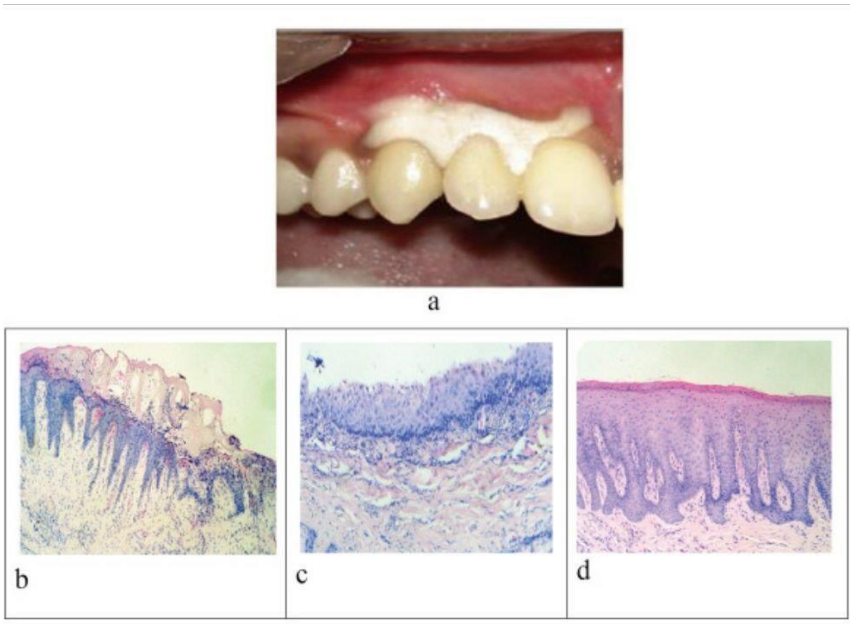

Figure. 4. a. Depigmentation by cryosurgical technique [39]. b. Eight hours following freezing showing epithelial degeneration [39]. c. Specimen after 24 h showing loss of rete pegs [39]. d. Clinical resemblance after a week of application of cryogen [39].

1.4.5. Lasere

Laser ablation of gingival depigmentation has been recognized as one of the effective, pleasant and reliable techniques [2]. It is usually sufficient to eliminate the pigmented areas and do not require any periodontal dressing [5]. It also shows reduced pain and discomfort due to formation of protein coagulum. Meanwhile, it allows clean and dry operating field and stable results [40]. Laser light may also seal free nerve endings [41]. But it also has its own disadvantages of delayed wound healing, thermal damage, deep penetration and the comparably high costs of the procedure [3].

Different lasers have been used for gingival depigmentation including carbon dioxide (10.600 nm), diode (810 nm), Neodymium:Yttrium Aluminium garnet (1.064 nm) and Erbium: YAG (2.940 nm) lasers [2].

The diode laser has been introduced in dentistry few years back. It is a solid-state semiconductor laser that typically uses a combination of elements to change electrical energy into light energy. It also can be delivered through a flexible quartz fiber optic hand piece. This energy level is absorbed by pigmentation in the soft tissues and makes the diode laser an excellent hemostatic agent [2]. It also allows good visibility at the surgical site. The post-operative patient comfort is better at the surgical sites treated with diode laser than surgical scrapping method [4].

The CO2 laser causes minimal damage to the periosteum and bone under the gingiva being treated, and it has the unique characteristic of being able to remove a thin layer of epithelium cleanly [29]. YAG laser has demonstrated the best application of laser use, leaving the least thermal damage

(Figure. 5).

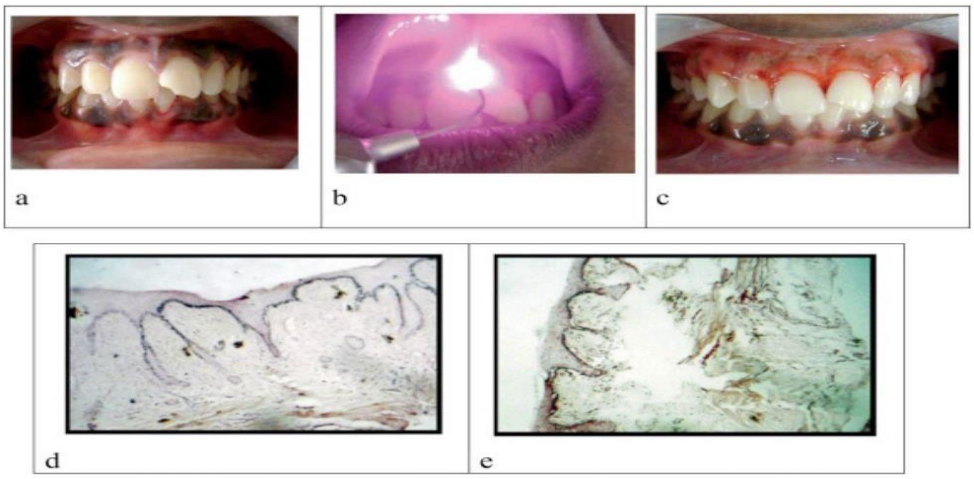

Figure. 5. a. Pre-operative situation, b. Use of the FOX diode laser to treat gingival pigmentation, c. Immediate post-operative view. d: Postoperative biopsy specimen form Er:YAG treated site showed basal cells with moderate staining positivity (50–75%), whereas (Figure. 5e) showed biopsy from CO2 treated sites showed mild to moderate staining (<50%) positivity .

1.4.6. Radiosurgery

Radiosurgery describes the most advanced form of electro-surgery. It is the removal of soft tissue with the aid of radio frequency energy. This electromagnetic energy operates between the frequencies of 3.0 MHz (MHz) to 4.0 MHz, with 4.0 MHz being the optimal frequency [44].The main advantage of radiosurgery can be found in its ability to produce coagulation in the operative area which would often have extensive bleeding [45]. Also, some studies reported less thermal damage and faster healing with the 4 MHz radio wave technology over the scalpel and lasers [44]. On the other hand, the main disadvantage of this method is that it requires at least two sittings for completion within 2 weeks of treatment [46]
(Figure. 6).

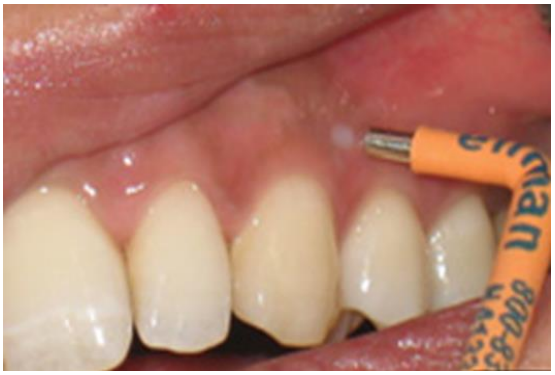

Figure. 6. Depigmentation by radio surgical technique.

1.4.7 Chemical methods

Chemical agents such as 90% phenol in combination with 95% alcohol have been found to be quite harmful to soft oral tissues leading to tissue necrosis and pain. This mixture was found to burn out the pigmented gingiva by destroying tissue down to and slightly below the basal layer of the mucous membranes [47].

1.4.8 Free gingival graft

Free Gingival Grafts are used to create a widened zone of attached gingiva and in root coverage procedures [29] .

It was described by Kumar et al., 2012 [32] for treating severe physiologic melanin pigmentation requiring replacement with an unpigmented free gingival autograft. The result of this procedure showed no evidence of repigmentation even after 4.5 years. Of the 10 treated patients only 1 patient showed repigmentation after 1 year.

Unfortunately, this technique is quite an invasive and an extensive procedure and has the disadvantage of a second surgical site (donor site), , additional discomfort and poor tissue color matching at the recipient site [5].

1.4.9 Acellular dermal matrix allograft

After local anesthesia administration, two vertical incisions are performed on the non-pigmented tissue both mesial and distal to the pigmented area using a #15 scalpel blade. A horizontal sulcular incision is needed to reflect a partial thickness flap containing pigmented area and the reflected flap should be excised. The graft should be prepared and trimmed to fit the recipient site and secured to adjacent attached gingiva with sutures [29].

This method is successfully used in the elimination or greater reduction of gingival melanin pigmentations, and is more efficient than epithelium abrasion after 12 months [47].

1.5 Conclusion

Gingival pigmentation though not a major complication, yet it greatly affects the facial appearance. The patient's medical history is important in determining its cause whether physiological or pathological, but the histopathological examination is conclusive. Accordingly, treatment of the pigmentation is determined either surgically or chemically. Accordingly, our review has lighted the causes and methods of treatment of gingival pigmentation in relation to its histological background.

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