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E-CIGARETTES AND ORAL HEALTH: A LITERATURE REVIEW

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ABSTRACT

The epidemic of tobacco use is one of the greatest threats to global health today. Tobacco-induced oral diseases contribute significantly to the global oral disease burden. Smoking has many negative effects on the mouth, including staining of teeth, reduction of the ability to smell and taste, development of oral diseases like smoker's palate, smoker's melanosis, coated tongue, oral candidiasis, dental caries, periodontal disease, implant failure, oral precancer and cancer. E-Cigarettes (Electronic Cigarettes) are battery-powered devices that work by heating a liquid into an aerosol that the user inhales and exhales. It contains nicotine which has plenty of health consequences. Research suggests that E-Cigarettes are bad for heart and lungs. It raises blood pressure and spikes adrenaline that increases heart rate and likelihood of having a heart attack. Similarly, E-Cigarettes has a large effect on overall Oral Health too. It causes death of gum tissues that leads to gum recession. Nicotine from e-cigarettes reduces saliva in mouth. Lack of saliva leads to dry mouth, plaque build-up, tooth decay. Thus, E-Cigarettes have similar adverse effects on Oral health like how traditional cigarettes do have. So, it's always better to quit smoking before their effects rule the overall health.

Keywords: E-Cigarette, Oral Health, Smoking, Oral disease, Oral cancer, Forensic

INTRODUCTION

Tobacco use is one of the biggest global threats and challenges for human health nowadays. Tobacco use is linked with various serious illness on human health, such as cancer, cardiopulmonary diseases, internal organs disorders as well as with many other problems **[1]**. One of the many health problems that is linked with tobacco use is, its deleterious impact on oral health. Orofacial region is the first area to encounter tobacco smoke, which comes in direct contact with soft and hard tissues **[2]**. Tobacco is consumed through mouth in various forms like smoking, smokeless tobacco and is known to have damaging effects in oral cavity like Oral Cancer, Gum disease, Teeth wear, Increased cavities risk etc., Thus, quitting the tobacco products is one of the appreciable preventing measure to prevent oral health problems caused by tobacco usage.

To cease the use of tobacco products is not a facile task. There are a number of measurements which are taken in both internal and external therapeutic sources that guide in tobacco cessation. In reprisal for diminished cigarette utilization, tobacco companies are started producing a new idea with technology like Electronic Cigarettes (e-Cigarettes) **[3]**.

Electronic Nicotine Delivery Systems (ENDS), Electronic - Cigarettes have swiftly attained popularity as they were presumed to be a safer replacement to tobacco combustion, especially among younger individuals, pregnant smokers, which can be used as a tools for smoking cessation **[4]**.

One of the major dilemmas concerning E-cigarettes is how it can play a major role in smoking cessation without any negative outcomes **[5]**. Due to these conditions, different opinions exist as to whether they really act as safe and alternative tool for tobacco cessation without any toxicity and ill effects on oral cavity.

Despite the fact that, Electronic Cigarettes were developed, advanced and merchandised as a healthier substitute to smoking tobacco products, there is a extending body of authentication proving that their aerosols contain numerous toxicants, organic compounds and carcinogens generated through the thermal decomposition of the solvents **[4]**. The objective of this article is to impart an evidence-based literature review for the medical and dental practitioners towards Electronic Cigarettes and to enrich their knowledge on profuse effects of the use of Electronic Cigarettes (E-Cigarettes) on Oral Health.

E-Cigarettes

Electronic Cigarette is abbreviated as e-Cigs. They are known by different names. They are sometimes called “e-hookahs”, “mods”, “vapes”, “vape pens”, “tank systems”, and “electronic nicotine delivery systems (ENDS)” **[6]**. It made its first preamble in 2003 by a

Chinese pharmacist, Hon Lik and has been attainable in United States since 2007 **[5]**.

Evolution of e-Cigarettes

The first generation devices were designed in such a way that they bear a resemblance to cigarettes in appearance ("cigalikes") **[7]** and can be recharged as well as scrapped after use **[8]**. They substantially produce aerosol at a fixed puff duration or frequency. It is a bit massive when compared to the traditional cigarettes. This type of e-cigarettes is easily accessible, easy to use and cheap. They are also the most frequently used devices in media to depict everything related to electronic cigarettes **[7]**.

In the second generation, these devices often comprehend refillable e-liquid cartridges, more powerful batteries that permit the user to modify the length and frequency of puff and operate the heating coil at the press of a button **[8]**. They are very commonly referred to as Mid-Size Electronic Cigarettes. They are substantially larger than first generation e-cigarettes (Cigalikes). In addition, these vaporizers also possess batteries of significantly higher capacity (usually 3-7 times higher) than cigalikes **[7]**.

Advanced Personal Vaporisers (APV) were developed in third generation and became more habitual. These devices traditionally attribute high capacity batteries, greater ability for user control and customization such as adjustable voltage or power and refillable cartridges that have an impact on the potential toxin of nicotine content of aerosol produced **[8]**. The fundamental component of a third generation e-cigarette, in majority of the cases, is a mod - the "brain" and the power source **[7]**.

The most recent, influential, powerful, advanced and innovative devices in the market are the fourth-generation electronic cigarettes. They are the innovative regulated mods. These mods come along with automatic temperature control and the potentiality to operate very low electric resistance builds in addition to clearomizers (or rebuildable tanks) themselves, highlighting adjustable and dual airflow slots **[7]**.

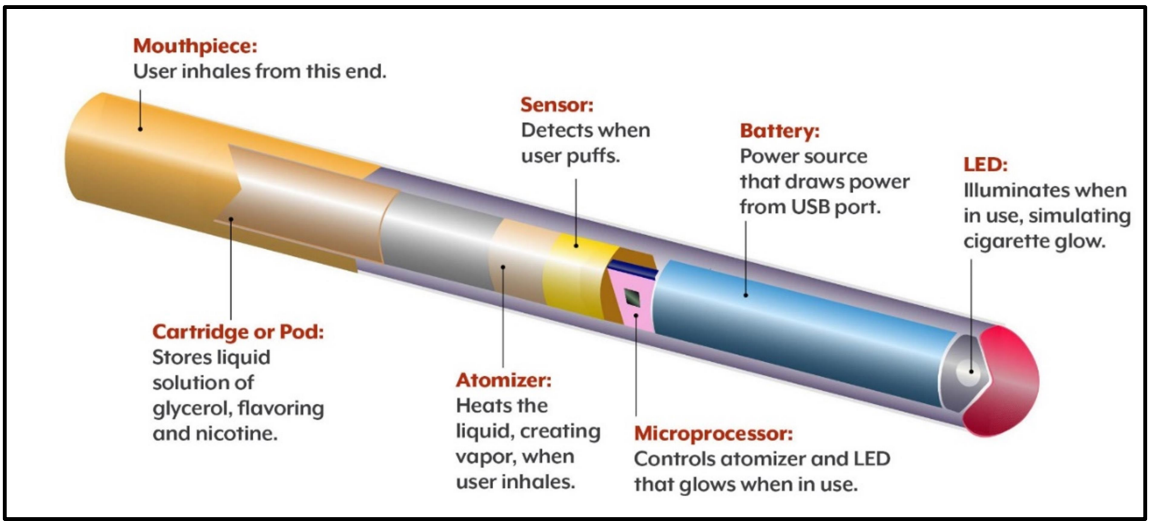
The Anatomy of an e-Cigarette

In spite of disparate names for e-cigs, such as Electronic Nicotine Delivery Systems (ENDS), electronic vaporizers, vape pens, box mods etc, the fundamental physical components of these devices are identical **[3]**. Devices can be battery – powered or rechargeable; disposable or refillable. E-cigarette components includes mouthpiece, cartridge, heating element / atomiser, vaporising chamber, microprocessor, battery, LED.

- Mouthpiece: It is this part from where the user inhales the vapor produced by the usage of e-cigarettes.
- Cartridge: A cartridge is a storage device in which the liquid solutions like glycol, nicotine or e-liquids are stored in an e-cigarette. It serves as a reservoir for an e-cigarette **[2]**. E-liquids or e-juices is the liquid solution that is commonly found in the devices. It can comprise the fundamental ingredients are generally propylene / ethylene glycol, flavouring agent and vegetable glycerine. Cartridge is habitually located where the filter of a traditional cigarette is found. In some devices, the cartridge is refillable.
- Atomiser: An atomiser is the heating constituent of the electronic device. Together with e-liquid and battery, the atomizer is the chief constituent of every e-cigarette. It heats the liquid, creating vapour when the user inhales. This vaporisation occurs at several temperature ranges. It has been approximated that the theoretical vaporisation temperature of the heating component may amount up to 350^0 **[9]**. It is usually located in the in the place where the filter of a traditional cigarette is found. This component normally contains a heating coil **[9]**. The materials that comprehend the heating coils of the atomiser vary remarkably among the diverse device types depending upon the manufacturers **[3]**.
- Sensor: The sensor is a part of device which detects when the user puffs.
- Microprocessor: The microprocessor of an e-Cigarette controls the atomiser and the heating element of the device will get glow during use.
- Battery: A battery is needed to operate an e-cigarette device. It acts as the power source that draws power from the USB port. The power source is generally the biggest component of an electronic cigarette. It is conventionally located at the end of the vaping device where the tobacco is placed in a traditional cigarette. A wide range of different sizes of batteries are available and they can either be disposable or rechargeable **[10]**. They are habitually cylindrical but can also be rectangular. Nickel - metal - hydride (NiMh), Nickel - cadmium (NiCad), Lithium ion (Li-ion), Lithium manganese (LiMn), and Alkaline and lithium polymer (Li-poly) batteries

have been used for the e-cigarettes power source **[2]**.

- LED: The LED present in an electronic cigarette illuminates when in use, giving the appearance of a cigarette glow.



Composition of an e-Cigarette

The e-cigarette is considered as aerosol device in which an individual drawing from the device and puff out can consist of many harmful or possibly harmful substances, which include nicotine, other volatile organic compounds like ethylene glycol, formaldehyde, xylene etc., toxic metals like nickel, mercury, tin, lead, flavouring agents such as diacetyl (a chemical which is known to linked with a serious lung disease) and various cancer causing chemicals **[11]**. Elements which might contribute to the inhalation sequels of e-cigarette include atmospheric conditions, the flow of air, the size of room, number of people present in the vicinity, puff length, interspace between two puffs and user characteristics like age, gender, occupation, health status **[12]**. Since e-cigarettes are not well regulated in many countries, the make-up of e-liquids can change very often.

Nicotine: Nicotine is a naturally derived potent parasympathomimetic alkaloid produced from the nightshade family of plants (Solanaceae) **[3]**. Nicotine is a vital bioactive ingredient of tobacco-derived products comprising of conventional cigarettes, e-cigarettes, cigarillos, and waterpipes **[13]**. The extent of nicotine exposure of e-cigarettes is tremendously variable and its liquids accommodate almost 14.8 to 87.2 mg/ml of nicotine **[14]**. Nicotine is a threatening and highly addictive chemical. When person consumes the nicotine, it may change heart and blood vessels in ways that escalate the risk of cardiovascular diseases. It can elevate the levels of adrenaline thus causing an increase in blood pressure, heart rate, flow of blood to the heart **[15]**. It might also lead to coronary artery disease i.e.,

narrowing of the arteries (vessels that carry blood). Nicotine may also contribute to the hardening of the arterial walls, which in turn, may lead to a heart attack. This chemical can stay in human body for six to eight hours depending on how often inhalation done **[15]**.

Propylene / Ethylene Glycol: Glycols are substantially used in the aviation emergency training and in the theatre industry (to create artificial smoke) and are generally known to be upper airway irritants **[12]**. The humectant property that is the ability to attract and retain moisture via absorption of glycol bestows the user with a "throat hit" as comparable to that of conventional cigarettes **[3]**. Studies have revealed that when an individual is exposed for a longer duration to propylene / ethylene glycol, the individual might experience an increase in acute cough and dry throat **[3]**. Perhaps, exposure to glycol may also result in dehydration of mucous membranes and eyes **[12]**. Chronic exposures to glycol aerosols may produce impaired lung functions **[3]**. When propylene glycol is heated it may alter the chemical composition and fabricate propylene oxide in a small proportion which is known as carcinogen **[15]**.

Carbon Monoxide: Carbon monoxide is a harmful gas which exits from during smoking. This gas enters the blood stream through lungs which decreases the amount of oxygen that is carried in the red blood cells. It also increases the amount of cholesterol that is deposited into the inner lining of the arteries which can cause the atherosclerosis leads to heart attack or myocardial infarction **[15]**.

Formaldehyde: Another substance in e-Cigarette is formaldehyde which is categorised as a carcinogen. Formaldehyde is known as a result of the degradation products of propylene glycol and glycerol during the process of evaporation and incomplete combustion **[15]**.

Vegetable Glycerine: Vegetable Glycerine along with propylene glycol constitutes the considerable majority of e-liquid volume, intensify the absorption of the wicking material, and when heated to adequate temperature, they generate fumes of aerosolized particles **[3]**.

Flavouring Agents: A major differentiation between the manufacture of electronic cigarettes and conventional cigarettes is the extensive use of flavouring agents like Benzaldehyde, Eugenol, Cinnamaldehyde to create uniquely flavoured electronic cigarette refill liquids **[3]**. Flavouring is the foremost important reason given by young people most frequently for beginning and continuing the use of Electronic Cigarettes **[2]**.

Benzaldehyde is a low molecular weight, highly reactive aldehyde which is used as a flavouring agent to fabricate fruit- or cherry-flavoured e – liquids **[3]**. Eugenol is a phenylpropene compound which is the vital component of clove oil **[3]**. It has been detected as the potent skin sensitizers in humans. Cinnamaldehyde is a α, β – unsaturated aldehyde that provides cinnamon

its characteristic odour and taste **[3]**. Reports of contact dermatitis from cinnamon exposure have been well – chronicled in the past recent years **[3]**. Diacetyl may be added to cigarette tobacco to impart a buttery sweet taste and a buttery smooth odour.

Pathogenesis of an e-Cigarette

There are numerous changes happening in the cellular level which will be understandable through molecular studies. Electronic Cigarettes can change gene expression in an identical way as tobacco smoking **[16]**. DNA is the cells "instruction manual" that controls a cell normal growth and function **[6]**. DNA damage is an alteration in the basic structure of DNA that is not itself replicated when the DNA undergoes replication **[17]**. Thus when a DNA is damaged, a cell can begin growing out of control and create a cancer **[6]**. There will be cellular mutation which is an alteration in the nucleotide sequence of the genome of an organism, virus, or an extra chromosomal DNA[18]. DNA repair is limited which is a collection of processes by which a cell identifies and corrects damage to the DNA molecule that encodes its genome **[19]**.

Nicotine can decline coronary blood flow by acting on vascular smooth muscle α1-adrenergic receptors to constrict coronary arteries, but can also increase coronary blood flow by increasing cardiac output, causing ensuing flow-mediated dilation (FMD), and directly stimulating coronary artery β2-receptor for coronary vasodilation **[20]**. It also causes blood vessels to constrict or narrow, that limits the amount of blood that flows to organs due to deposition of lipid as plaque which decrease the amount of oxygen and nutrients supply to the other organs **[21]**.

Effects of an E-cigarate on systemic organs

One e-cigarate (Filled cartridge) equals to the smoking of 2-3 packs of regular cigarettes. Nicotine found in e-cigarettes is quickly absorbed through the skin, mucous membranes, respiratory airway and gastrointestinal tract[14]. Scientific literature has also revealed that nicotine adversely affects both the mother and the developing foetus by affecting the foetus' nervous system **[14]**.

E-cigarette will affect in various stages of human development i.e intermediate with brainstem autonomic nuclei development will be influenced during the prenatal period, the neocortex, hippocampus and cerebellum are altered during early postnatal period and the limbic system and late maturation is influenced during the adolescence period [14]. Youth and young adults are at risks of nicotine addiction, mood disorders, permanent lowering of impulse control. Neuroplastic changes in brain can be distinguished in individuals who have been exposed to nicotine **[14]**.

An apparent increase was perceived in the levels of immotile sperms and semen leukocytes in smokers whereas a decrease was perceived in semen volumes and sperm

viability **[14]**. Thus e-cigarette smoking drastically diminishes the sperm plasma membrane integrity and correspondingly sperm motility **[22]**.

Smoking imputed diseases include cancer of lungs, bronchus, lip, trachea, mouth, pharynx, ischemic heart disease, hypertension, emphysema, COPD, asthma etc. **[1]**. Chemicals released during e-cigarette use, principally, nicotine, particulates could influence cardiovascular health risks **[8]**. Studies have related e-cigarettes with increased heart rate **[23]**, endothelial cell toxicity **[24]** and impaired flow mediated dilatation **[25]**. Smoking can increase the build-up of plaque (cholesterol, fat, calcium) in blood vessels **[26]**. It also known that nicotine causes mobilization of blood sugar **[9]**.

It may induce dizziness, toxicity, vomiting. Children and adults have been poisoned by swallowing, breathing, or captivating e-cigarette liquid through their eyes or skin. The e-cigarette smoke, vapours, mist are very risky and known to induce damage to eye by precipitating redness, dryness, irritation of the eyes **[14]**. E-cigarettes put forward increased liability of nicotine toxicity due to the obtainability of high nicotine concentrations in the cartridge **[12]**.

With the inhalation of Propylene Glycol / Vegetable Glycerine for over a period of long time, increased cough, mucosal secretions and chest tightness could be observed **[3]**. Human exposure to acute e-cigarette use may provoke oxidative stress and increased airflow resistance **[8]**. Nicotine intensifies mucus production in human bronchial epithelial cells which are major triggers of asthma exacerbation **[3]**. Nicotine in e-cigarettes can weaken the body's immune system, thereby making it more strenuous to kill cancer cells **[6]**. The presence of diacetyl in e-cigarettes as a flavouring agent is known to cause a lung disease called Bronchiolitis obliterans, which is more commonly referred to as popcorn lung. It's a condition in which the lungs smallest airways of an individual are damaged and makes the individual to cough and feel short of breath.

Effects of an e-cigarate on Oral cavity

Chewing or smokeless tobacco products are known to be detrimental etiological factor for oral diseases. Although E-Cigarettes has always been interpreted as a safer alternative when compared to Cigarette, but now, it is considered as one of etiologic factor for the oral cancer and its use has always been associated to many adverse effects intra-orally when correlated with any other organ systems in human body.

Smoking e-cigarettes induces elevated melanin pigmentation in the oral mucosa that may be an effect due to the effect of nicotine on melanocytes located along basal cells, that results in basilar melanosis with differing amounts of melanin incontinence **[27]**. There is a potentiality that the number of Langerhans

Cells in the oral mucosa of smokers might be increased **[28]**. The wound healing of oral mucosa is compromised in these smokers due to local vasoconstriction and poor neutrophil function **[1]**.

The use of e-cigarettes causes tooth discolouration or commonly known as tooth staining. Due to the buffering power and the ability to lower salivary pH, it is known to induce increased risk of dental caries. As nicotine reduces body's ability to produce saliva, it makes mouth more vulnerable to harmful bacteria. Thus, dry mouth and increased bacteria in mouth leads to halitosis (bad breath) as well as dental caries. High levels of nicotine have been shown to be antiproliferative and toxic effects on osteoblast and effect on bone metabolism **[29]**. Nicotine has been acquainted with impaired leukocyte activity and healing by inhibiting neovascularization and osteoblastic differentiation **[30]**.

The periodontium is the specialized tissues that both surround and support the teeth, maintaining them in the maxillary and mandibular bones **[31]**. It consists of four principal components, namely Gingiva, Periodontal Ligament, Cementum, Alveolar bone proper. Periodontal diseases are multifactorial infections that are instigated by the interaction between the bacteria found in the dental plaque and the reaction of host immune response to this bacterial infection in the structures around the teeth **[29]**. Bacterial infections cause swollen and bleeding gums, resulting in gingivitis (earliest stage) and in loosening of teeth (advanced stage), the sign of severe periodontitis **[32]**. There is a direct exposure to e-cigarettes has been shown to produce deleterious effects in periodontal ligament cells and gingival fibroblasts **[33]**. There is an interrelation between smoking and the loss of gingival attachment, the increase of gingival regression, tooth loss, deeper periodontal pockets, more extensive alveolar bone loss along with the destruction of connective tissue and matrix **[34]**. Root surface caries amongst individuals with periodontal recession is more abundance in smokers than non – smokers **[35]**. A strong positive interconnection has been illustrated between the use of tobacco products and the severity of periodontal disease. Quitting smoking entails a decreased exposure to the risk of development of periodontal diseases.

- **Oral Cancer**

Oral Cancer includes the cancer of lips, tongue, cheeks, floor of mouth, palate (includes both hard and soft palate). About 90% - 95% of oral cancers are squamous cell carcinoma which are thin irregular white patches, non-healing ulcers or exophytic growths that substantially appear as a growth or sore in oral cavity.

The pathognomonic signs of oral malignancies comprise of stubborn ulceration with rolled margins and fixation to underlying tissues **[1]**. Nicotine, a major component of E-Cigarettes

is responsible for more or less 40% of oral cancers. Nicotine may advance the progression of squamous carcinoma cells by activating the Wnt/β-catenin and Wnt/PCP signaling pathways **[36]**. Nicotine can generate epigenetic alteration of epithelial cells, inhibit multiple systemic functions of host and by way of its toxic metabolites, can produce oxidative stress on tissues to induce Oral Squamous Cell Carcinoma **[37]**.

- **Oral Submucous Fibrosis**

Oral Submucous Fibrosis (OSF) is a chronic, progressive, potentially malignant disorder that is usually characterized by intensifying submucosal fibrosis of the oral cavity and oropharynx **[13]**. Sometimes the fibrosis spreads to the pharynx, and down to the piriform fossae **[38]**. It has been indicated that nicotine and arecoline might induce the over – expression of human telomerase reverse transcriptase (hTERT) mRNA in oral keratocytes, that may have as result to premalignant of Oral Submucous Fibrosis **[39]**. With the progressing fibrosis, the stiffening of certain areas of the mucosa occurs, leading to difficulty in opening the mouth, incapability to whistle or blow out and in swallowing **[38]**.

- **Oral Leukoplakia**

Oral Leukoplakia is the most common potentially malignant lesion of the oral mucosa that cannot be characterized as any other definable lesion **[40]**. Leukoplakia occurs more frequently in smokers who use E-Cigarettes than in non-smokers. The site of the oral cavity affected by Leukoplakia is often correlated with the type of the tobacco habit practiced **[1]**; lateral tongue and floor of mouth in cigarette smokers, palate in pipe smokers and reverse smokers, commissures in bidi smokers, buccal groves in tobacco chewers and lower or upper labial mucosa in snuff dippers **[41]**.

Cigarette smoking is also one of the foremost known contributors to the development of Oral Leukoplakia **[4]**. There is a dose - response - relationship between nicotine usage and occurrence of oral leukoplakia. Intervention studies have demonstrated that reducing or cessation of smoking may result in reversion or disappearance of Oral Leukoplakia **[38]**.

- **Smoker's Palate**

One of the most commonly seen lesions among conventional E-Cigarette smokers is the smoker's palate. It is caused due to chemically or thermally induced keratosis. Smoker's palate is a greyish white discolouration of palate with small nodular excrescences having small central red spots corresponding to the inflamed orifices of the minor salivary glands **[38]**. Smoker's palate is also known by various other names such as Nicotina Stomatitis Palatina, Leukokeratosis Nicotina Palati, Stomatitis Nicotina.

- **Reverse smoker's keratosis**

This is a solemn potentially malignant lesion confronted in people where the lit end of the cigar is held in the mouth, another form of

smoking associated with high levels of heat in the mouth **[42]**. This condition is associated with an increased risk of malignant transformation to oral squamous cell carcinoma. The clinical appearance is often a mixture of red and white patches **[1]**.

- **Erythroplakia**

Erythroplakia is defined as "A fiery red velvety patches of oral mucosa that cannot be characterized clinically or pathologically as any other definable disease" **[43]**. E-Cigarettes may stand as an important aetiological factor of Erythroplakia.

- **Trauma**

Besides oral health implications of e-cigarettes under deliberate conditions, there are cases of oral and facial trauma caused provoked by the explosion and fires from e-cigarette devices malfunction [8]. The dental practitioner may come across cases with burns, alveolar fractures, stemming, tooth evulsions from e-cigarettes explosion near the mouth **[44]**. This potentiality for facial injury is a harm distinctive to e-cigarettes.

Exposure risks for non - users

Aerosolization of e-cigarette liquids (more typically nicotine, propylene glycol, glycerine) produces the smoke that is generally inhaled by the user as well as the non – users **[12]**. Certain studies have disclosed the exposure risks for non - users. Passive smoking sometimes, also referred to as Second hand smoke (SHS) or Environmental tobacco smoke (ETS), is the inhalation of smoke, by persons apart from the intended active smoker **[45]**. It is believed that second hand smoke is more dangerous than first hand smoke as second hand smoke contains both smoke from burning cigarettes and additionally the smoke exhaled by the active smoker.

Passive smoking is a cause of additional episodes and increased severity of various symptoms in children. Breathing second hand smoke obstructs with the standard functioning of the heart, blood and vascular systems in routes that increases the chance of causing a lethal heart attack [US dept]. Investigations reported that the nicotine content in the exhaled breath of active smokers is higher when compared with that of vapers **[5]**. Constant nicotine exposure on surfaces of indoor can lead to third hand exposure through inhalation, dermal contact, ingestion eventually when the aerosol has cleared the room **[12]**. Besides that, on nicotine level in saliva of passive smokers, e-cigarettes do have an influence.

CONCLUSION

Various contemporary documents have reviewed and documented the scientific confirmation relating to the oral disease burden linked with the usage of tobacco. The dental professional is in a strong position to educate the people about tobacco usage and its toxic effect on human during their clinical practice. New and developing tobacco products, shifting use patterns, policy and regulatory changes all confront the

practitioners to look aside from cigarettes when conversing about tobacco use with patients.

The innovation of the new technology and the diverse flavouring options as an alternative to tobacco product for the break of the individual habit but vapours or biproduct from e-cigs involve toxic and carcinogenic carbonyl compounds. The usage of Electronic Cigarettes has been drastically increasing in the past few years and seem to be very fascinating to young users. There is a huge discrepancy in the constituents of e-cigarette products. An imprecise lack of maintaining standards in synthesizing and marketing of e-cig liquids have been disclosed.

Despite the possibly that, e-cigarettes are not recognised as a safer product due to the presence of fewer chemicals and carcinogens, e-cigarette usage can pose adverse effects on health, precisely to the oral cavity. E-Cigarettes are beyond belief to make quitting tobacco easy. Nevertheless, e-cigarettes are not harm free and are not proven to be as cessation aids.

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