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Systematic Review

The Role of Vitamins and Trace Elements on Oral Health: A Systematic Review

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Abstract

Introduction: Nutritional guidance is one of the very important components of preventive dentistry today. To prevent oral, dental and craniofacial diseases, one approach is having a suitable diet. Hence, the aim of this review was to provide a concise, didactic update on the role of vitamin and trace elements on various aspects of oral health and diseases.

Methods: Literature search was carried out electronically through Google scholar, Pubmed and Ebsco data base and there was no time frame limitation set for the year of article published.

Results: Out of 38 articles, 14 were Epidemiological studies followed by 11 Narrative reviews, 6 Systematic reviews, 4 Randomised control trail, 2 Systematic reviews with meta-analysis and 1 Meta-analysis.

Conclusion: Diet containing vitamins and trace elements play an important role in normal health of the oral structures and these deficiencies can cause oral diseases such as developmental defects, oral mucosal diseases and periodontal diseases. Dietary recommendations made to aid in the control of oral disease are simultaneously optimal recommendations for improving general health.

Keywords: Vitamins; Trace Elements; Oral Health; Dental Caries; Mouth Neoplasms; Periodontitis

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Introduction

Having a sufficient dietary intake is required to maintain health, as such diet will provide the required nutrients and energy. Furthermore, an appropriate diet is also important for maintaining oral health. Essential food of all the metabolically active cells and tissues is required for maintaining health.[1] Nutritional guidance is one of the very important components of preventive dentistry today. Proper nutrition is important not only for the formation of sound teeth but also for the maintenance of oral health. Dietary recommendations made to aid in the control of oral disease are simultaneously optimal recommendations for improving general health.[2] Oral health is influenced by dietary intake and nutrition via a number of pathways, including craniofacial development, oral mucosal, and dental diseases such as dental caries, enamel defects, and periodontal diseases. Dental diseases alter the quality of life and have a negative impact on self-esteem, anxiety and impaired social function. Tooth loss is a best exemplar which reduces the ability to eat a nutritious diet, the enjoyment of food and confidence to socialize.[3] Micronutrients such as vitamins and trace elements play a key role in a number of metabolic pathways. These compounds can interact in a way that physiological adaptation to a deficiency may influence the metabolism of micronutrients, resulting in multiple deficiencies.[4] Vitamins are catalysts for all metabolic reactions using proteins, fats and carbohydrates for energy, growth and cell maintenance. Because only small amounts of these chemical substances obtained from food facilitate millions of processes, they may be regarded as miracle workers. Vitamins are grouped within two categories according to their level of solubility in fat solvents and water (Figure 1). Vitamins that are soluble in fat are A, D, E and K, while those that are soluble in water include B complex and vitamin C.[5]

Trace elements are compounds that are essential in small amounts for maintaining integrity of physiological and metabolic mechanisms within the body. Deficiency of these elements may lead to a number of clinical outcomes instead of a specific manifestation, as each trace element is related to a number of enzyme systems.[1] According to WHO there are 19 trace elements divided into three groups (Table 1).[6] Frieden in 1981 proposed a biological

classification of trace elements based on their amount in tissues (Table 1).[1]

The deficiency of any of the trace elements may be apparent as a combination of various clinical manifestations rather than a specific presentation as each trace element is related to many enzyme systems.1

Both vitamins and trace elements had a significant effect on oral and general health where its imbalance leads to malnutrition. The available literature on role of vitamins and trace elements toward oral health is minimal. Hence the present systematic review was aimed to find out the role of vitamins and trace elements on oral health.

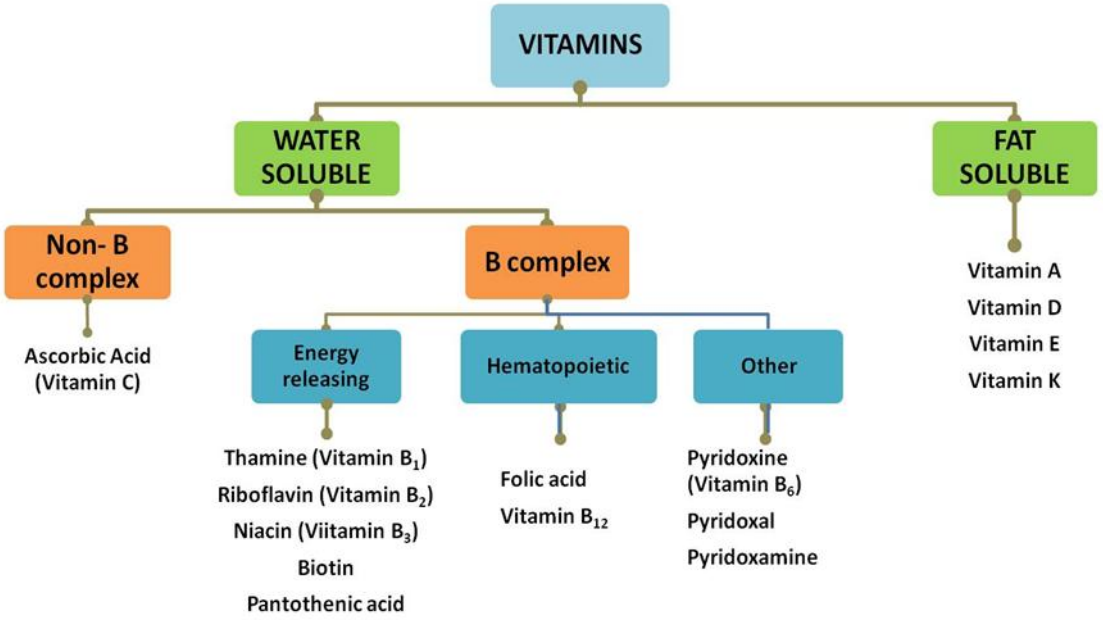

Figure 1. Classification of Vitamins based on Solubility

Table 1. Classification of Trace Elements

According to World Health Organisation	
Essential elements	Chromium, Copper, Selenium, Molybdenum, Iodine and Zinc.
Probably essential elements	Manganese, Silicon, Nickel, Boron and Vanadium.
Potentially toxic elements	Fluoride, Lead, Cadmium, Mercury, & Lithium.
According Frieden's Classification of Elements (1981)	
Essential elements	Boron, Cobalt, Copper, Iodine, Iron, Manganese, Molybdenum, and Zinc.
Probably essential elements	Chromium, Fluorine, Nickel, Selenium, and Vanadium.
Potentially toxic elements	Bromine, Lithium, Silicon, Tin, and Titanium.

Methods

Search Strategy

Literature search was carried out in Google scholar, Pubmed and Ebsco data base electronically. Manually the analysis was fulfilled through key journals available in the library of the institution. There was no time frame limitation set for the year of article published and only articles published in English were included. The search was made from the articles referenced in the selected articles. The keywords / key phrases used to search databases were vitamins, trace elements, oral health, oral diseases, and vitamins effect on oral health.

Inclusion Criteria

The articles addressing the role of vitamins and trace elements on oral health care were only considered (Table 2).

Table 2: Distribution of the Selected Articles based on the Country Wise Publication

S.no	Country	No of articles published	Year
1	India	18	2001-2016
2	United states of America (USA)	10	2005-2014
3	European union	6	2007-2017
4	Other countries like Japan, Korea, Saudi	4	2003-2016

Exclusion Criteria

Articles which haven't addressed the research objectives were excluded and along the searched articles which full texts were not available have been excluded.

Results

Collected documents included original articles, reviews, editorials, supplements, Continuing dental education articles, interviews, short communication, short reports,

Internet blogs and articles published in various newspapers. Based on inclusion and exclusion criteria a total of 38 articles were gathered (Figure 2) and thoroughly included in the final analysis of which 20 were Pub med indexed and 18 were non pub med indexed articles. Out of 38 articles, 14 were Epidemiological studies followed by 11 Narrative reviews, 6 Systematic reviews, 4 Randomized control trail, 2 Systematic reviews with meta-analysis and 1 Meta-analysis. An attempt was made to check whether the articles complied with the appropriate checklist or not, which resulted in 35 articles following the respective parameters of the checklist. As there is no appropriate checklist for narrative review they are analysed using the parameters given by Ferrari R (2015) [7] (Table 3).

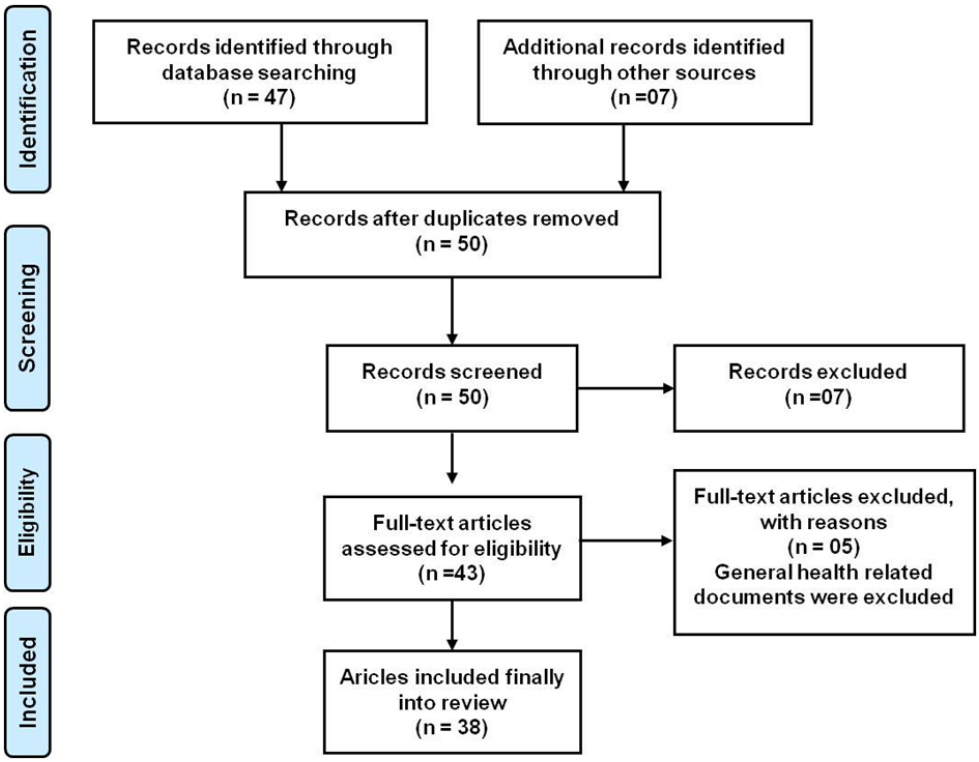

Figure 2. Flow Chart Showing Search Strategy

Table 3. Distribution of Articles based on the Checklist Followed

S.no	Study design	Checklist	No. of articles followed the checklist
1	Cross sectional study; Case control study; Cohort study	STROBE	11
2	Randomised controlled trail	CONSORT	4
3	Systematic review, Meta-analysis	PRISMA	9
4	Narrative review	Ferrari R (2015)103	11

Discussion

Vitamins and trace elements are a group of diverse organic and inorganic compounds which are indispensable for human health and well-being. Most of them directly play a pivotal role in human metabolic pathways which are necessary to maintain health equilibrium. Their deficiencies affect not only general health but also oral health as directly or indirectly associated with the maintenance of oral health status. Hence, this review of literature focuses on the role of vitamins and trace elements on various aspects of oral health and diseases. In developing countries most of the people had been suffering with nutrient deficient diseases as their low socioeconomic status and lack of education levels will not provide sufficient knowledge and importance on nutritional intake and balanced diet. Unavailability of resources had been making them to compromise on daily requirements of diet. Even though some governments of the world are trying to balance this kind of situation through various schemes but lack of sufficient funds and equitable distribution of resources are affecting the success of health schemes.

Role of Vitamins and Trace Elements on Dental Caries

Vitamins and Dental Caries

Vitamins are involved in both the occurrence and prevention of dental caries. In the development of tooth structure, vitamins A, C, and D are required for appropriate deposition and calcification. In contrast, vitamins are also associated with dental caries, in a process involving oral acidogenic microorganisms.[8] Vitamin A: Vitamin A deficiency leads to specific abnormalities in the shape and structure of teeth during

development, in a mechanism involving metaplasia of enamel forming cells and an atrophy of the enamel organ, leading to enamel hypoplasia.[9, 10] According to the study of Bloch,[11] severe vitamin A deficiency during early development did not lead to abnormalities in the form, position, consistency of teeth, and dental caries. Similarly, Shourie [12] did not observe dental caries in Indian children with skin and eye lesions indicating vitamin A deficiency when compared with normal controls. Dietary supplements of vitamin A were also not shown to influence the incidence of caries tendency in children.[13, 14]

Thiamine (Vitamin B_1): Deficiency of cocarboxylase (thiamine pyrophosphate) has been reported by one study to have a major role in dental caries due to accumulation of pyruvic acid in tissue.[15] However, there is very limited evidence for such claims and other studies have reported conflicting results, such as that of Russell from South Vietnam and Thailand and Afonsky from central China.[16, 17] Furthermore, the intake of thiamine was shown to be associated with decreased caries explained by the bacteriostatic potential of thiamine against cariogenic microorganisms.[18, 19]

Riboflavin (Vitamin B_2): Riboflavin deficiency may not lead directly to dental decay.[16, 20-22] Even though this compound is required for some strains of oral lactobacilli, most can remain alive in a riboflavin-free medium.[23, 24]

Nicotinic Acid (Niacin): It was proved to be an irreplaceable nutritional factor for the oral lactic acid-producing bacteria [23, 24] which are necessary for dental caries formation [25].

Pyridoxine (Vitamin B_6): Pyridoxine deficiency leads to increased caries incidence.[26, 27] According to Hill man, Cabaud and Schenone [28] study done on pregnant women described that excess pyridoxine suppresses cariogenicity. Its caries-deterrent action is via changes in oral flora from dominance of homofermentative lactic acid producing type to the heterofermnetative form, which show lower production of lactic acid and greater production of volatile end products. Hetreofermantative forms use up pyridoxine leading to a competitive system, which results in suppression of heavy acid producers.[28]

Other B Vitamins: Other B vitamins that have a role in caries formation are biotin, pantothenic acid, folic acid, and inositol.[23, 24] High saliva folic acid level promotes the development of caries [29] and increased levels of inositol acts as cariostatic,[30]

Vitamin C (Ascorbic Acid): Ott and hanke human study revealed that dietary supplements of ascorbic acid leads to reduction in intensity of dental caries. Structurally ascorbic acid is responsible for enamel hypoplasia.[19, 31] According to Boyle,[31] Teeth of scorbutic adults have a porotic dentin, pulpal hyperemia and edema, and altered secondary dentin

According to Dierks study in children Vitamin C are protective against the secondary decay which forms around margins of fillings but in contrast Grandison, Stott, and Cruikshank reported that there is no significant modification in the caries course while administering Vitamin C daily in children.[15]

Vitamin D: Deficiency of vitamin causes problems in dentin and predentin calcification and mal-formation of dentin. Essential amounts of vitamin D during the development of teeth has a relationship with decreased frequency of caries.[32] Whether supplements of vitamin D can help prevent dental caries still requires more evidence from further research.

Vitamin E: Lack or insufficient amounts of vitamin E results in premature atrophy and papillary layer edema, depigmentation, hypoplasia, bizarre anatomic forms, unnatural eruption rate, and production of cysts.[33] Fat cells and fibrous connective tissue are produced and take the place of the parenchyma of the salivary glands.[33]

Vitamin K: Research has shown that this vitamin can reduce acid formation when added to saliva-glucose mixtures *in vitro*.[34] Previous studies have investigated the usefulness of vitamin K in preventing dental caries by inhibiting the enzymes that have a role in microbial degradation of carbohydrates.[35]

Trace Elements and Dental caries

Navia: has suggested a tentative classification of the trace elements into five groups according to their ability to promote or reduce caries:

Caries-promoting elements: selenium (Se), magnesium (Mg), cadmium (Cd), platinum (Pt), lead (Pb), silicon (Si)

Elements that are mildly cariostatic: molybdenum (Mo), vanadium (V), strontium (Sr), copper (Cu), boron (B), lithium (Li), gold (Au)

Elements with doubtful effect on caries: beryllium (Be), cobalt (Co), manganese (Mn), tin (Sn), zinc (Zn), bromine (Br), iodine (I)

Caries-inert elements: barium (Ba), aluminium (Al), nickel (Ni), iron (Fe), palladium (Pd), titanium (Ti)

Elements that are strongly cariostatic: fluorine (F), phosphorus (P).[36]

Fluoride: Fluoride can modify both tooth quality and caries susceptibility. Exposure to fluoride during the period of tooth development produces morphologic changes in teeth. It influences the size and shape of teeth, rounder cusps and shallower fissures have been noticed in fluoridated areas. Incorporation of appropriate amounts of fluoride into the hydroxyapatite of tooth substance, greatly increasing resistance of the enamel and dentine to the carious process by formation of the larger more insoluble crystals of fluorapatite.[36]

Curzon MEJ et al (1996) stated that Fluoride has been termed an essential trace element on the basis of its role in calcification (which includes effects on teeth).[37]

Jackson D (1974) stated that the inhibitory effect of fluorides in drinking water on dental caries in permanent teeth faded with age, up to about 40 years of age, showed prevention of dental caries of about 30%.[38]

Lemke CW et al (1970) done a study in Antigo in 1960, 1964 and 1966 to show the regression from excellent to poor dental conditions that occurred after the removal of adequate fluorides from the public water supply. Dental examinations made in 1964, four years after fluoridation had stopped, and in 1966, just after fluoridation had been reinstituted, showed that DMF rates had greatly increased and were characteristic of those rates found in nonfluoridated areas in Wisconsin.[39]

Angelillo IF et al (1990) randomly selected three areas of Naples which were supplied with drinking water naturally containing different fluoride concentrations. Prevalence of caries-free children was 40.5% in the area with low fluoride (0.3 ppm) in water supply, 41.9% in the optimal fluoride (1 ppm) area and 71.6% in the high fluoride (4 ppm) area.[40]

Sheiham et al (2001): The findings of more than 800 controlled trials showed that fluoride, either in water or in toothpaste, is the most prophylactic agent against dental caries.[41]

Burt and Pai (2001)[42] and Amid I. Ismail, Hanan Hasson (2008).[43] Authors evident through systematic reviews that fluoride supplements prevents dental caries in permanent teeth but inconsistent evidence for primary teeth.

Role of other Trace Elements on Dental Caries

Trace elements, other than fluoride, have long been thought to play a role in the initiation of dental caries, both favourably and unfavourably. Trace elements having a detrimental effect on caries formation are: Strontium, titanium, Vanadium, Lithium, Iodine, Tin, Silver, Bromine, Sodium, Boron Molybdenum, Aluminium, Chlorine, Magnesium, Silicon, Chromium, Nickel. They acts synergistically with fluoride in reducing enamel dissolution and increases dentine (and possibly enamel) thickness and may affect the rate of caries progression. They enhances uptake and retention of fluorides applied topically and also shows antibacterial effect against cariogenic microorganisms.[44] Trace elements promoting caries formation are Selenium, Zinc, Manganese, Copper, Barium, Lead, Calcium, Cadmium, Arsenic, Iron, Potassium and Zirconium.[44]

Studies done by Glass RL et al.,[45] Anderson RJ,[46] Schamschula RG et al.,[47] Glena R et al.,[48] Gauba K et al.,[49] Bowen WH[44] concluded that Selenium, Copper, Iron, Manganese, Lead, Zinc showed positive association with caries while Fluoride, Calcium, Magnesium, Molybdenum, Vanadium, Strontium, Lithium were associated negatively with caries experience.

Role of Vitamins and Trace elements on Oral Structures

Role of Vitamins on Oral Structures

Vitamin A: Vitamin A is indispensable to the proper growth and development of periodontium, teeth, salivary gland, and oral epithelium. Teeth are less sensitive to vitamin A deficiency, although some studies suggest that it can exacerbate existing periodontitis.[50] Previous studies have been unsuccessful in proving an association between vitamin A and periodontal disease.

Vitamin B_1: The possible oral manifestations of a deficiency of this vitamin are hyper sensitivity of the oral mucosa, glossitis and loss or diminution of taste, minute vesicles (simulating herpes) on the buccal mucosa, below tongue or on the palate and erosion of oral mucosa.[51]

Vitamin B_2: Lack or insufficient amounts of riboflavin (ariboflavinosis) leads to glossitis, angular cheilitis, seborrheic dermatitis, and a superficial vascularizing keratitis. Glossitis involves magenta discoloration and atrophy of the papillae. In non-severe cases, the dorsum has been observed to with a patchy atrophy of the lingual papillae and engorged fungiform papillae. In extereme deficiency, the whole dorsum becomes flat, with a dry and commonly fissured surface. Angular cheilitis is initiated with inflammation of the commissure of the lips, with following erosion and ulceration.[52]

Vitamin B_3: Pellagra is a niacin deficiency disease caused by a primary inadequate dietary intake. Pellagra is characterized by dermatitis, diarrhea, dementia, glossitis, gingivitis, and generalized stomatitis.[50] Lack of insufficient amounts of vitamin B-complex and niacin in animals led to a black tongue and gingival inflammation, and destruction of the gingiva, periodontal ligament, and alveolar bone.

Vitamin B_9: Folic acid deficiency is probably the most common vitamin deficiency in humans because body's stores of folate are relatively low which can last for upto 4 months only. Folic acid deficiency may cause Megaloblastic anemia. Folic acid-deficient animals demonstrate necrosis of the gingiva, periodontal ligament, and alveolar bone without inflammation. Angularcheilosis and gingivitis are also present. Folic acid deficient animals have shown to be vulnerable to ulcerations and infections of lips, tongue, gingiva, periodontium and oropharynx. Folic acid supplementation may increase resistance to the development of periodontal inflammation in humans.[52]

Vitamin B_{12}: Its deficiency leads to pernicious anemia resulting in Oral structural symptoms like bright red, smooth, sore, and burning tongue resulting from an atrophic glossitis.[52]

Vitamin C: Severe vitamin C deficiency results in scurvy, characterized by hemorrhagic diathesis and retardation of wound healing. Bleeding, swollen gingiva and mobile teeth are also common features of scurvy.[53] Insufficient amounts of this vitamin also causes mal-formation of collagen and osteoid structures, and problems in osteoblastic function. In addition, other problems include elevation of capillary permeability, traumatic haemorrhages, increased activity of the contractile elements of the peripheral blood vessels, and sluggishness of blood flow.[53] Gingival changes include redness, swelling, tendency towards bleeding upon minimal stimulation and an alteration towards consistency.[54, 55]

Vitamin D: Its deficiency characterized by delayed eruption of permanent teeth and there may be enamel defects ranging from pitting to complete absence of enamel.[56] Vitamin D and calcium deficiency have been found to result in generalized jaw bone resorption and loss of PDL.[50] Novel findings have indicated a relationship between periodontal health and consumption of vitamin D and calcium, with better periodontal health with intake of these supplements, including greater mineral density of mandibular bones and inhibition of alveolar bone resorption.[57] For instance a study by Garcia et al. [58] indicated that these supplementation improved health in periodontal disease at doses higher than 800-1,000 IU daily. Also, vitamin D has anti-inflammatory properties as it inhibits immune cell cytokine expression and leads to the secretion of molecules with antibiotic effects from monocytes and macrophages. The 1,25(OH) $_2D_3$-VDR is important in maintaining oral homeostasis and its dysfunction results in periodontal disease.[57]

Vitamin E: Vitamin E deficiency is rare in human beings. There is no association between insufficient amounts of this vitamin and oral complications, however systemic forms increase gingival wound healing in a rat model.[52]

Role of Trace Elements on Oral Structures

Fluorine: The excessive concentrations of fluoride during calcification stage of the teeth can result in a kind of enamel hypoplasia termed dental fluorosis.[59] Fluorine, in the form of fluorapatite crystals, is an important part of the organized matrix of hard tissues like bone and teeth. It is also believed that fluoride, in combination with calcium, stimulates osteoblastic activity resulting in strong teeth and bone.[60]

Copper: Lack or insufficient amounts of Cu, in particular during development, results in anemia and defective keratinisation in the oral cavity.[61] Its deficiency leads to lowered immunity can result in various infections of the oral cavity due to accompanied neutropenia.[62] Deficiency prevents normal response of reticulo-endothelial system to infection. Therefore, copper may have a role in influencing periodontal disease and alveolar bone resorption.[63]

Lead: It has deleterious effects on the periodontium. Lead line is caused in the gingiva if there is an excessive intake. Periodontal disease is also more prevalent in those with a high intake of lead; gingival ischemia and "black-livid" rough calculus are other findings.[63]

Iodine: Its anti-bacterial and anti-plaque effect is helpful to treat various forms of periodontal disease. Its bactericidal effectiveness is not time-dependent; its ability to kill micro-organisms is immediate once it gets contacted with organisms.[64]

Beryllium: It inhibits calculus formation by preventing calcification of the organic precursor that forms the nidus for initiation of calculus.[63]

Iron: Deficiency impairs the bactericidal ability of phagocytes, impairs lymphocyte response to mitogen stimulation and decreases T-cells. Higher amounts of iron than required may lead to greater bacterial virulence, changes in polymorphonuclear cell function, and greater susceptibility to infection.[65]

Zinc: It is required in cellular proliferation, for wound healing and in restoring a missing sense of taste.[66, 67] Impaired taste sensation can arise from a lack of the zinc-containing protein, gustin, in saliva.[67] It modifies the defense mechanisms of the periodontium, regulates the inflammatory process, has a membrane stabilizing effect and regulates function in inflammation by inhibiting release of lysosomal enzymes from PMNs and histamine from mast cells.[2, 68] Even mild zinc deficiency have a negatively impact on immune system, leading to an increased susceptibility to oral infections. Excessive intake causes specific defects in the function of T-lymphocytes, granulocytes and inhibits collagen formation where an inverse relationship has been found between serum zinc levels and tooth-supporting alveolar bone loss.[69]

Selenium: Lack or insufficient amounts may cause problems for the production of antibodies and the bactericidal activity of neutrophils. On the other hand, small amounts above what is required might decrease susceptibility to infection and increase antibody production.[65]

Tin: Leverett DH et al (1984) evaluated plaque and gingivitis reducing abilities of oral rinses containing 0.1% aqueous solution of stannous fluoride and 0.05% aqueous solution of sodium fluoride in children. The stannous fluoride group had lower Plaque Index and Gingival Index scores.[70]

Role of Vitamins and Trace Elements in Oral Lesions

Vitamins and Oral Lesions

Based on epidemiological evidence, vitamin C intake may be associated with a lower risk of gastric and esophageal cancer.[71] Antioxidant supplementation (vitamins C and E) may have a role in oral cancer patients where decrease in supplements results in increase of oxidative stress. Whole saliva may contain simply measured indicators of oxidative processes and may provide an important tool for monitoring and treating oral cancer.[72] Vitamin A exerts a protective effect against the development of oral leukoplakias, and induced the regression of established leukoplakias by decreasing number of layers of spinous cells, reducing the loss of polarity of basal cells and by disappearance of nuclei with condensed chromatin from the epidermal layer.[73] Some studies evident the importance of vitamins in oral mucosal lesions (Table 4).

Trace Elements and Oral Lesions

Trace Metals and Oral Lichen Planus and Oral Lichenoid Reactions

Lichen planus, contact allergy and hypersensitivity OLR's could have a relation with exposure to metal alloys often used in dentistry. There is a hypothesis on a

potential link of (OLR's) with exposure to Cr, Co, and Ni and amalgam alloys as released into the oral cavity.[74] Among them, the most common metal is nickel. These trace metals when come into contact with oral mucosa induce sensitivity reactions in response to the immune-mediated damage of the basal epithelial keratinocytes. Some studies state that OLR due to amalgamation may have a risk of malignant transformation.[75]

Table 4. Studies Showing the Relation between Vitamins and Oral Lesions

Author	Recommended vitamin	Oral condition	Note
Chandra Mouli PE et al [76] (2012)	Vitamin- E	Oral lesions	Vitamin- E can inhabit reactions of tobacco specific nitrosamine (carcinogens) which undergo specific activation and detoxification process.
Balwant Rai et al [77] (2008)	Vitamin- E and Vitamin C	Oral Lichen planus	Counteract free radical mediated cell disturbances
T.N.Uma Maheswari [78] (2013)	Vitamin- E	Leukoplakia	Antioxidant combination [Vitamin A, E and C] had proved to be most effective with maximum clinical resolution (90%) recorded [79] and regression of dysplasia recorded as 97.5% [80]
U.Raghushwanshi et al. [81] (2012)	α-tocopherol	Oral carcinoma	The low levels of α-tocopherol in patients could be a cause or effect for oral carcinoma.
Vikas Fotedar et al [82] (2013)	Vitamin- E	Oral cancer and chemo-prevention	The antioxidant vitamin E (α-TF) prevents development of cancers in oral cavities
Rai Balwant [83] (2008)	Vitamin- E and Vitamin C	Oral cancer	A weak antioxidant defence system makes the mucosal cells more vulnerable to the cytotoxic effect of reactive oxygen species which intracellular environment more favourable for DNA damage and disease progression.
Sumit Bhatja [84] (2012)	B-carotene and Vitamin- E	Oral mucosal lesions	Chemo-preventive.
S Chitra and C S SHyamala Devi [85](2008)	Vitamin- E	Oral squamous cell carcinoma	The levels of glycol-conjugates were significantly decreased in radiation treated oral squamous cell carcinoma patients having Vitamin- E supplementation. This measurement may be useful in assessing disease progression and identifying patients resistant to therapy and the role of Vitamin- E on reduction in glycol-conjugate levels.
Soma Gupta et al [86] (2004)	Vitamin- E	Oral submucous fibrosis (OSMF)	Plasma Vitamin- E level was found to be decreased in grade II and III OSMF cases but not in grade I cases. However, mean Vitamin- E level was found to be decreased (9.3 ± 0.3 mg/L) as compared to healthy controls (mean = 10.1 ± 1.2 mg/L).
Maher et al [87] (1997)	Vitamin A, D, E and B complex	Oral submucous fibrosis	A beneficial clinical response in subjects with OSF to multiple micronutrient intervention

Trace Elements and Oral Submucous Fibrosis

Trace elements have been extensively studied in recent years to assess if they have any modulating effects in the predisposition of oral malignant conditions. Relatively less scientific literature has been documented in the area of oral premalignant conditions, keeping the scientific premises, that the zinc levels in the tissue and serum of pre malignancies may be used in understanding the pathogenesis, and in establishing treatment.[88]

Trace Elements and Oral Pre Cancer and Cancer

Trace elements are known to act as anti-cancer agents through control of a number of biological mechanisms. A number of studies have claimed that there is a relationship between trace elements and cancer mortality. Reduction in the contents of Copper (Cu) and Zinc (Zn) was found in the blood tests of cases with head and neck cancer. The copper to zinc ratio can be considered as a suitable biomarker for carcinogenesis during development and progression.[89-91] Trace elements, such as copper and zinc, are reported to be involved in anticarcinogenic defense mechanisms of the human body. A number of studies have reported that serum copper levels were significantly higher in the sera of patients with oral premalignant and malignant lesions.[88] In the previous literature, higher levels of serum copper in the oral leukoplakia and oral squamous cell carcinoma (OSCC) was indicated. In a recent study, serum copper was elevated in patients with OSMF and increased further with progression of OSMF. Other studies indicate that lower zinc serum levels are found in those with premalignant disorders, such as oral leukoplakia, which be the result of Zn intake and counter reaction to oxidants from tobacco or high copper of areca quid metabolism.[92] Regardless of significant differences between serum Zn levels in oral leukoplakia and OSMF, it has been suggested that zinc inhibits the invasive potential of malignant prostate cells. Decrease iron in patients with OSMF patients could result from the uptake of iron in collagen synthesis. It has been suggested that reduced iron results in decreased epithelial vascularity leading to elevation of penetration of arecoline, and ending in fibrosis.[92] Nutrition deficiency as a result of burning sensation and erosions in patients with OSMF and increased tumor burden in patients with OSCC are major factors for iron depletion.

Conclusions

Diet containing Vitamins and Trace elements play an important role in normal health of the oral structures. Deficiencies cause oral diseases such as developmental defects, oral mucosal diseases and periodontal diseases. The commonly affected oral structures as a result of vitamin deficiency are soft tissues like tongue, gingiva and lining mucosa. However, fat soluble vitamin deficiency affects hard tissues, by impaired development of teeth and bony support. Signs and symptoms of vitamin toxicity have not been reported clearly for both water and fat soluble vitamins for oral health due to lack of research on long term and excessive use of vitamins as compared to vitamin deficiency.[6] So thorough knowledge on dietary management of vitamins and trace elements are essential for healthy living.

Authors' Contributions

PSS and SP contributed equally to this study.

Conflict of Interest Disclosures

Author declares that he has no competing interests.

Ethical Approval

Not applicable.

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References

1. Lussier G, Loew FM. Case report. Natural Hymenolepis nana infection in mongolian gerbils (Meriones unguiculatus). Can Vet J. 1970;11(5):105-7. pmid: 5464373.
2. McDonald J. Dietary and nutritional influences on dental caries. Nutrition in oral health and disease. Philadelphia: Leaand Febiger; 1985. p. 151-60.
3. Petersen PE, Bourgeois D, Ogawa H, Estupinan-Day S, Ndiaye C. The global burden of oral diseases and risks to oral health. Bull World Health Organ. 2005;83(9):661-9. pmid: 16211157.
4. Neha Bansal ND. Impact of micronutrients on oral health. Excel Int J Educ Res. 2014;2(1):89-102.
5. Thomas AG. Vitamins and trace elements. Curr Paediatr 1992;2(3):172-4. doi: 10.1016/0957-5839(92)90259-t.
6. Kathariya R, Kulkarni N, Kulkarni M, Kalele K. Trace elements in oral health and disease: An updated review. J Dent Res Rev. 2014;1(2):100. doi: 10.4103/2348-2915.133959.
7. Ghosh A. Role of Vitamins in Oral Health & Disease: an Overview. Indian J Appl Res. 2015;5(12):292-5.
8. Harris R. Dietary Chemicals vs. Dental Caries. Am Chem Soc. 1970;94:33-45.
9. Boyle PE. Manifestations of Vitamin-A Deficiency in a Human Tooth-Germ. J Dent Res. 2016;13(1):39-50. doi: 10.1177/00220345330130010301.
10. Dinnerman M. Vitamin A deficiency in unerupted teeth of infants. Oral Surg Oral Med Oral Pathol. 1951;4(8):1024-38. pmid: 14863873.
11. Bloch C. Effects of Deficiency in Vitamins in Infancy: Caries of the Teeth and Vitamins. Am J Dis Child. 1931;42(2):263-78.
12. Shourie K. Dental Garies in Children in Madras City in Relation to Economic and Nutritional Status. Indian J Med Res. 1942;30(4):561-73.
13. Day CDM, Sedwick HJ. The Fat-Soluble Vitamins and Dental Caries in Children. J Nutr. 1934;8(3):309-28. doi: 10.1093/jn/8.3.309.
14. Mellanby M, Pattison CL. The Action of Vitamin D in Preventing the Spread and Promoting the Arrest of Caries in Children. Br Med J. 1928;2(3545):1079-82. pmid: 20774325.
15. Sharpenak AE, Stomatol H. Dietary Chemicals vs. Dental Caries. Am Chem Soc. 1958;3(3).
16. Russell AL. International nutrition surveys: a summary of preliminary dental findings. J Dent Res. 1963;42(1)Pt 2:233-44. doi: 10.1177/00220345630420012401. pmid: 13975634.
17. Afonsky D. Some observations on dental caries in central China. J Dent Res. 1951;30(1):53-61. doi: 10.1177/00220345510300011401. pmid: 14824329.
18. Balogh K, Petrucz K, Angyal J. Inhibition of bacterial growth in human saliva by vitamins B1, B2, and B6. J Dent Res. 1960;39:886-91. doi: 10.1177/00220345600390052201. pmid: 14448449.
19. Boyle P, Wolbach S, Bessey O. Histopathology of teeth of guinea pigs in acute and chronic vitamin C deficiency. J Dent Res. 1936;15:331.
20. Mann AW, Dreizen S, et al. A comparison of dental caries activity in malnourished and well-nourished patients. J Am Dent Assoc. 1947;34(4):244-52. pmid: 20282522.
21. Hurtarte A, Scrimshaw NS. Dental findings in a nutritional study of school children in five Guatemalan highland villages. J Dent Res. 1955;34(3):390-6. doi: 10.1177/00220345550340031401. pmid: 14381576.
22. Tabrah FL. Absence of dental caries in a Nigerian bush village. Science. 1962;138(3536):38-9. pmid: 13918843.
23. Dreizen S, Spies TD. Observations on the relationship between selected B vitamins and acid production by microorganisms associated with human dental caries. J Dent Res. 1953;32(1):65-73. doi: 10.1177/00220345530320012001. pmid: 13052755.
24. Koser SA, Fisher BJ. Vitamin requirements of oral lactobacilli. J Dent Res. 1950;29(6):760-73. doi: 10.1177/00220345500290060801. pmid: 14803595.
25. Orland FJ, Hemmens ES, Harrison RW. The effect of partly synthetic diets on the dental caries incidence in Syrian hamsters. J Dent Res. 1950;29(4):512-28. doi: 10.1177/00220345500290041501. pmid: 15436924.
26. Strean L, Bell F, Gilfillan E, Emerson G, Howe E. The importance of pyridoxine in the suppression of dental caries in school children and hamsters. New York State Dent J. 1958;24:133.
27. Strean L, Gilfillan E, Emerson G. Suppressive effect of pyridoxine as dietary supplement on dental caries in Syrian hamster. New York Dent J. 1956;22:325-7.
28. Strean L. Vitamin B 6 und Zahnkaries. Schweiz Mschr Zahnheihi. 1957;67:981-8.
29. Makila E. Salivary folic acid activity in various conditions of the human mouth. Arch Oral Biol. 1966;11(8):839-44. pmid: 5226778.
30. McClure FJ. The cariostatic effect in white rats of phosphorus and calcium supplements added to the flour of bread formulas and to bread diets. J Nutr. 1960;72:131-6. pmid: 13773798.
31. Boyle PE. The tooth germ in acute scurvy. J Dent Res. 1934;14:172.
32. Mellanby M. Nutrition and disease. London, UK: 1934.
33. Nelson MA, Jr., Chaudhry AP. Effects of tocopherol (vitamin E)-deficient diet on some oral, para-oral, and hematopoietic tissues of the rat. J Dent Res. 1966;45(4):1072-7. doi: 10.1177/00220345660450040901. pmid: 5224075.
34. Calandra J, Fancher O, Fosdick L. The effect of synthetic vitamin K and related compounds on the rate of acid formation in saliva. J Dent Res. 1944;23(1):31-7.
35. Burrill DY, Caladra JC, et al. The effect of 2-methyl-1,4-naphthoquinone on the incidence of dental caries. J Dent Res. 1945;24:273-82. doi: 10.1177/00220345450240060101. pmid: 21011806.

36. PShenoy R, Shenai KP. Trace elements and oral health. J Indian Assoc Public Health Dent. 2011;9(18):607.
37. O'Sullivan EA, Williams SA, Curzon ME. Dental caries in relation to nutritional stress in early English child populations. Pediatr Dent. 1992;14(1):26-9. pmid: 1502111.
38. Jackson D. Dental caries: the distinction between delay and prevention. Br Dent J. 1974;137(9):347-51. doi: 10.1038/sj.bdj.4803316. pmid: 4155315.
39. Lemke CW, Doherty JM, Arra MC. Controlled fluoridation: the dental effects of discontinuation in Antigo, Wisconsin. J Am Dent Assoc. 1970;80(4):782-6. pmid: 4392098.
40. Angelillo IF, Romano F, Fortunato L, Montanaro D. Prevalence of dental caries and enamel defects in children living in areas with different water fluoride concentrations. Community Dent Health. 1990;7(3):229-36. pmid: 2076499.
41. Sheiham A. Dietary effects on dental diseases. Public Health Nutr. 2001;4(2B):569-91. pmid: 11683551.
42. Burt BA, Pai S. Sugar consumption and caries risk: a systematic review. J Dent Educ. 2001;65(10):1017-23. pmid: 11699972.
43. Ismail AI, Hasson H. Fluoride supplements, dental caries and fluorosis: a systematic review. J Am Dent Assoc. 2008;139(11):1457-68. pmid: 18978383.
44. Bowen WH. Exposure to metal ions and susceptibility to dental caries. J Dent Educ. 2001;65(10):1046-53. pmid: 11699976.
45. Glass RL, Rothman KJ, Espinal F, Velez H, Smith NJ. The prevalence of human dental caries and water-borne trace metals. Arch Oral Biol. 1973;18(9):1099-104. pmid: 4517686.
46. Anderson RJ. Dental caries prevalence in relation to trace elements. Br Dent J. 1966;120(6):271-5. pmid: 4379482.
47. Schamschula RG, Bunzel M, Agus HM, Adkins BL, Barmes DE, Charlton G. Plaque minerals and caries experience: associations and interrelationships. J Dent Res. 1978;57(3):427-32. doi: 10.1177/00220345780570030101. pmid: 277544.
48. Glena R, Shields C, Featherstone J, Cowles E. Reactivity of carbonated-apatite in the presence of Fluoride and/or Selenium. J Dent Res. 1984;63:184.
49. Gauba K, Tewari A, Chawla HS. Role of trace elements Se and Li in drinking water on dental caries experience. J Indian Soc Pedod Prev Dent. 1993;11(1):15-9. pmid: 8040693.
50. Dorsky R. Nutrition and oral health. Gen Dent. 2001;49(6):576-82. pmid: 12024745.
51. Newman MG, Takei H, Klokkevold PR, Carranza FA. Carranza's clinical periodontology: Elsevier health sciences; 2011.
52. Najeeb S, Zafar MS, Khurshid Z, Zohaib S, Almas K. The Role of Nutrition in Periodontal Health: An Update. Nutrients. 2016;8(9). doi: 10.3390/nu8090530. pmid: 27589794.
53. Nishida M, Grossi SG, Dunford RG, Ho AW, Trevisan M, Genco RJ. Dietary vitamin C and the risk for periodontal disease. J Periodontol. 2000;71(8):1215-23. doi: 10.1902/jop.2000.71.8.1215. pmid: 10972636.
54. Hodges RE, Hood J, Canham JE, Sauberlich HE, Baker EM. Clinical manifestations of ascorbic acid deficiency in man1,2. Am J Clin Nutr. 1971;24(4):432-43. doi: 10.1093/ajcn/24.4.432.
55. Woolfe SN, Hume WR, Kenney EB. Ascorbic acid and periodontal disease: a review of the literature. J West Soc Periodontol Periodontal Abstr. 1980;28(2):44-56. pmid: 6448982.
56. Miley DD, Garcia MN, Hildebolt CF, Shannon WD, Couture RA, Anderson Spearie CL, et al. Cross-sectional study of vitamin D and calcium supplementation effects on chronic periodontitis. J Periodontol. 2009;80(9):1433-9. doi: 10.1902/jop.2009.090077. pmid: 19722793.
57. Anand N, Chandrasekaran SC, Rajput NS. Vitamin D and periodontal health: Current concepts. J Indian Soc Periodontol. 2013;17(3):302-8. doi: 10.4103/0972-124X.115645. pmid: 24049329.
58. Garcia MN, Hildebolt CF, Miley DD, Dixon DA, Couture RA, Spearie CL, et al. One-year effects of vitamin D and calcium supplementation on chronic periodontitis. J Periodontol. 2011;82(1):25-32. doi: 10.1902/jop.2010.100207. pmid: 20809866.
59. Shafer WG, Hine MK, Levy BM. A textbook of oral pathology: Elsevier India; 2004.
60. Organization WH. Trace elements in human nutrition and health. Geneva, Switzerland: World Health Organization; 1996.
61. O'Dell B. Biochemical basis of the clinical effects of copper deficiency. New York, NY: Alan R Liss Inc; 1982.
62. Harless W, Crowell E, Abraham J. Anemia and neutropenia associated with copper deficiency of unclear etiology. Am J Hematol. 2006;81(7):546-9. doi: 10.1002/ajh.20647. pmid: 16755565.
63. Curzon M. Introduction. In: Curzon M, Cutress T, editors. Trace elements and dental disease. 9. Boston: John Wright; 1983. p. 1-10.
64. Menaker L. Nutrition in Dental Caries. The biologic basis of dental caries: an oral biology textbook. Hagerstown: Harper and Row; 1980. p. 343-64.
65. Enwonwu CO. Cellular and molecular effects of malnutrition and their relevance to periodontal diseases. J Clin Periodontol. 1994;21(10):643-57. pmid: 7531721.
66. Nizel A, Papas A. Trace minerals other than fluorides. Nutrition in clinical dentistry. Philadelphia: WB Saunders Company; 1989.
67. Speirs RL, Beeley JA. Food and oral health: 2. Periodontium and oral mucosa. Dent Update. 1992;19(4):161-2, 4-7. pmid: 1289156.
68. Palmer CA. Important Relationships Between Diet, Nutrition, and Oral Health. Nutr Clin Care. 2001;4(1):4-14. doi: 10.1046/j.1523-5408.2001.00101.x.
69. Boyd LD, Madden TE. Nutrition, infection, and periodontal disease. Dent Clin North Am. 2003;47(2):337-54. pmid: 12699235.
70. Leverett DH, McHugh WD, Jensen OE. Effect of daily rinsing with stannous fluoride on plaque and gingivitis: final report. J Dent Res. 1984;63(8):1083-6. doi: 10.1177/00220345840630081601. pmid: 6589269.
71. WHO. Diet, Nutrition, and the Prevention of chronic diseases. Report of a WHO Study Group. Geneva, Switzerland: World Health Organization, 1990 Contract No.: 797.
72. Rai B, Kharb S, Jain R, Anand SC. Salivary vitamins E and C in oral cancer. Redox Rep. 2007;12(3):163-4. doi: 10.1179/135100007X200245. pmid: 17623524.
73. Stich HF, Hornby AP, Mathew B, Sankaranarayanan R, Nair MK. Response of oral leukoplakias to the administration of vitamin A. Cancer Lett. 1988;40(1):93-101. pmid: 3370632.
74. Hughes MF, Beck BD, Chen Y, Lewis AS, Thomas DJ. Arsenic exposure and toxicology: a historical perspective. Toxicol Sci. 2011;123(2):305-32. doi: 10.1093/toxsci/kfr184. pmid: 21750349.
75. Tadakamadla J, Kumar S, Gp M. Evaluation of serum copper and iron levels among oral submucous fibrosis patients. Med Oral Patol Oral Cir Bucal. 2011;16(7):e870-3. pmid: 21196848.
76. Chandra Mouli P, Senthil B, Parthiban S, Malarvizhi A, Priya R, Subha R. Antioxidants and its role in Oral Cancer-a review. Indian J Sci. 2012;1:113-15.
77. Rai B, Kharb S, Jain R, Anand S. Salivary vitamin E and C in lichen planus. Gomal J Med Sci. 2004;6(2).
78. Maheswari U. Treatment of oral leukoplakia with antioxidants-a systematic review. Int J Pharm Biol Sci. 2013;4:33-41.
79. Kaugars GE, Silverman S, Jr., Lovas JG, Brandt RB, Riley WT, Dao Q, et al. A clinical trial of antioxidant supplements in

the treatment of oral leukoplakia. Oral Surg Oral Med Oral Pathol. 1994;78(4):462-8. pmid: 7800378.
80. Barth TJ, Zoller J, Kubler A, Born IA, Osswald H. Redifferentiation of oral dysplastic mucosa by the application of the antioxidants beta-carotene, alpha-tocopherol and vitamin C. Int J Vitam Nutr Res. 1997;67(5):368-76. pmid: 9350480.
81. Raghuwanshi U, Choudhari S. Serum alpha-Tocopherol Levels Including Status of Oral Carcinoma Patients. Int J Health Sci Res. 2012;2:60-4.
82. Vikas F, Shailee F, Rajeev K S, Manoj K G. Oral Cancer and Prevention. Int J Pharm Sci Invent. 2013;2:16-20.
83. Rai B. Salivary Levels Vitamin E and C in Different Histological Grading of Oral Cancer. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2008;8(1):123-5. doi: 10.4034/1519.0501.2008.0081.0022.
84. Bhateja S. Role of antioxidants in oral medicine. Int J Pharm Sci Res. 2012;3(7):1971.
85. Chitra S, Shyamala Devi CS. Effect of vitamin E on protein bound carbhohydrate complexes in radiation treated oral squamous cell carcinoma patients. Indian J Clin Biochem. 2008;23(1):92-4. doi: 10.1007/s12291-008-0022-6. pmid: 23105730.
86. Gupta S, Reddy MV, Harinath BC. Role of oxidative stress and antioxidants in aetiopathogenesis and management of oral submucous fibrosis. Indian J Clin Biochem. 2004;19(1):138-41. doi: 10.1007/BF02872409. pmid: 23105446.
87. Maher R, Aga P, Johnson NW, Sankaranarayanan R, Warnakulasuriya S. Evaluation of multiple micronutrient supplementation in the management of oral submucous fibrosis in Karachi, Pakistan. Nutr Cancer. 1997;27(1):41-7. doi: 10.1080/01635589709514499. pmid: 8970180.
88. Nayak AG, Chatra L, Shenai P. Analysis of copper and zinc levels in the mucosal tissue and serum of oral submucous fibrosis patients. World J Dent. 2010;1(2):75-8.
89. Shetty SR, Babu S, Kumari S, Shetty P, Hegde S, Karikal A. Role of serum trace elements in oral precancer and oral cancer-a biochemical study. J Cancer Res Treat. 2013;1:1-3.
90. Swain N, Ray JG. Altered trace element level and antioxidant activity in whole blood of oral leukoplakia and cancer patients in comparison with healthy controls. Int J Oral Maxillofac Pathol. 2011;2(2):2-6.
91. Jayadeep A, Raveendran Pillai K, Kannan S, Nalinakumari KR, Mathew B, Krishnan Nair M, et al. Serum levels of copper, zinc, iron and ceruplasmin in oral leukoplakia and squamous cell carcinoma. J Exp Clin Cancer Res. 1997;16(3):295-300. pmid: 9387904.
92. Bonda PLF, Porrini R, Rizzio E, Pietra R, Fortaner S, Sabbioni E. Trace metals in oral mucosa in relation to the lichen ruberplanus pathology. A preliminary study carried out by neutron activation analysis. J Trace Elem Med Biol. 2001;15(2-3):79-83. pmid: 11787991.