Review Article

EFFECT OF VARIOUS PREDISPOSING FACTORS ON HOST DEFENCE MECHANISMS TRIGGERING ORAL INFECTIONS – A COMPREHENSIVE REVIEW

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ABSTRACT

The oral cavity consists of normal micro-flora which is essential for a healthy mouth. In certain conditions, some of the micro-flora can act as opportunistic pathogens that can breach the host defence and invade deeper tissues to cause infection. Apart from microbial causes, there are many other diverse local and systemic predisposing factors that can also affect host defence mechanisms. In this review, host defence mechanisms have been described briefly and the predisposing factors that can affect an individual's immunity; thus making them more prone towards an infection are also covered. The past 70 years of literature were searched on the "Google Scholar" search engine with the keywords "host defence mechanisms", "immunity", "predisposing factors affecting host defence mechanisms", and "causes of oral infections". Duplicate articles, conference abstracts, and all the articles/books published in languages other than English were excluded. The review concluded that many oral infections are related to predisposing factors and the initiation and progression of infections are dependent on the equilibrium between host defence mechanisms and these factors. Whenever this balance is disturbed, infections can ensue. Maintenance of good oral hygiene and avoidance of predisposing factors is, therefore the key to avoiding many oral infections.

Keywords: Host, defence mechanism, Immunity, Oral, infections. .

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INTRODUCTION

The oral cavity consists of normal micro-flora which is essential for a healthy mouth.[1] There is a wide variety of habitat sites like tongue, teeth, and saliva that permit the micro-flora to exist in a healthy mouth[1]. The normal flora of the oral cavity contains a diverse range of microorganisms including bacteria, fungi, protozoa, and viruses (rarely)[2]. In certain cases, opportunistic pathogens can breach the host defence and invade deeper tissues to cause infection. Apart from microbial causes, there are many other diverse local and systemic predisposing factors that can also affect host defence mechanisms.

In this review, we have briefly described host defence mechanisms and then focus has been stressed on the predisposing factors that can affect an individual's immunity; making them more prone towards an infection. The past 70 years of literature was searched on the "Google Scholar" search engine with the keywords "host defence mechanisms", "immunity", "predisposing factors affecting host defence mechanisms", and "causes of oral infections". Our search revealed more than 500 hits. Duplicate articles, conference abstracts, and all the articles/books published in languages other than English were excluded. A final selection of 64 relevant articles/book chapters was then made and those were then included in this study for review.

Host defence mechanisms: The cells of oral mucosa contribute to the host defences by producing various regulators of immunity like cytokines[3]. Oral mucosa itself provides a physical plus immune barrier and

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prevents its invasion by microorganisms.[4]. Apart from oral mucosa, other host defence mechanisms are also present like salivary mucins, which forms viscoelastic gel for the protection of the oral mucosa[5]. Many specific and non-specific factors (called adaptive & innate immunity respectively) are also part of the hostdefence mechanisms (Fig.1)[6]. Both innate and adaptive immune system work for the body's defence but many differences are present between them like innate immunity is composed of defences that act immediately after exposure to the microorganism but adaptive immunity reacts against the invading organism after sometime[7]. Adaptive immunity has a memory and so it remembers the invading organism and reacts more efficiently on the next exposure but theinnate immune system lacks this property[8].

To date, more than 300-400 microbial species are linked to the oral cavity and it is also suggested that an equal number of species are still uncultured[9]. The composition of micro-flora is diverse at different sites and depends on a lot of factors like the availability of oxygen, salivary flow, and masticatory forces[10]. Normal micro-flora competes with pathogens and protects the host and this is called "Colonization Resistance"[11]. Some of the micro-flora can act as opportunistic pathogens under certain conditions e.g. when the immunity of the host is low, they can give rise to oral infections[12]. These opportunistic pathogens act by first colonizing the host surfaces, then maintain and establish their intracellular life, and finally cross the host barriers to cause infections[12]. Impact of different predisposing factors on host defence mechanisms: The commensal flora and oral defence mechanisms have a pivotal role in preventing oral infections. In healthy individuals, there is a balance between micro-organisms and the host. Disturbance of this balance due to various predisposing factors can lead to oral infections. These predisposing factors can cause temporary or permanent damage. For example, the use of antibiotics for a short period of time causes temporary disturbance but decreased salivary production due to increased age, causes a permanent disturbance in the balance between host and micro-organisms. Various predisposing factors that can trigger oral infections are mentioned in (Fig. 2). These predisposing factors and their effect on oral defence mechanisms are discussed below in detail.

Ageing: Ageing is a normal biological phenomenon but certain oral diseases show an increased incidence in older people as compared with younger people.13With an increase in age, there is a reduction in salivary flow leading to higher plaque deposition that results in gingivitis and ultimately causes periodontal infections[14]. A previous report has suggested that more than 50% of 75 age and older people in the United States show signs of past periodontal destruction[15]. Dental caries is another common problem in the elderly. An earlier study in England has suggested that 20% of 75-84 years old people show signs of root caries[16]. Poor eating habits decreased visual and motor skills, alterations in the salivary gland secretion, and changes in the oral mucous membrane could lead to poor oral hygiene resulting in oral infections[17]. Also, homebound or institutionalized elderly may be predisposed more towards oral infections as they could have limited access to clinical care[18].

Smoking: Tobacco smoking and periodontal infections are closely related. There is now evidence that the periodontal micro-flora of smokers is different than non-smokers19and also they heal less satisfactorily than people who do not smoke[20]. More alveolar bone loss leading to increased pocket depth measurements is also found in smokers[21].Tobacco smoking is also considered to have a close aetiological relationship with oral cancer[22]. In terms of prevalence, oral cancer is ranked sixth as the most common disease globally with smoking as one of its predisposing factors. It is believed that the presence of nitrosamines, specifically 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) and N-nitrosonornicotine (NNN) in tobacco smoke could be the cause of oral cancer[23]. It has been reported earlier that there is a high prevalence of Candida (30%-70%) in the oral cavity of smokers, as smoking can cause localized alterations in the epithelium and this allows candida colonization, leading to Candidiasis[24].Another probability for smokers to have more prevalence of candidiasis is that the smoke of cigarette may contain nutritional factors that candida species can utilize to nurture[25].

Prolonged antibiotic therapy: Antibiotics have been used as a lifesaving drug worldwide during the past 80 years 26 but with persistent antimicrobial therapy, there is a loss of colonization resistance which can then lead to the development of opportunistic infections.27 Frequent intake of antibiotics can also increase the number of candida in the oral cavity causing oral candidiasis[28].McGoven et al. previously proposed that candida can be isolated in greater numbers from patients who are on Tetracycline therapy[29].In another study, a high amount of candida Albicans was detected from the saliva of the patients who received antibiotic therapy for the treatment of their systemic diseases[30]. Moreover, various animal researches have supported that the broad-spectrum antibiotics leads to the reduction of healthy oral micro-flora and is one of the factors responsible for the initiation and establishment of oral infection[31].

Immunosuppression: Humoral and cell-mediated immunity to act as defence line against infections. Immunosuppression can occur due to many factors ranging from congenital immunodeficiency to more prevalent causes such as drugs-related immunosuppression or as a consequence of human immunodeficiency virus (HIV)[32]. In Candidiasis, there is typically a defect in cell-mediated immune response[33]. In an earlier study, yeast cultures were obtained from sixteen HIV-positive patients and it was concluded that increasing yeast burden in their oral flora could be related to diminished cell-mediated immunity[34]. The frequency of viral infection differs with the nature and degree of immunosuppression and it is evident that reactivation of the latent virus is the most vital determinant of the types of viral infections most commonly found in immunosuppressed patients[35].

Poor oral hygiene: Oral health is regarded as a key characteristic of a healthy lifestyle and poor oral hygiene can not only lead to oral diseases like caries but can also cause systemic infections like osteoporosis, cardiovascular diseases, and bacteremia[36]. Kerstin et al. performed a study to determine the association between oral hygiene, oral lesions, and oral cancers and reported that poor oral hygiene and ill-fitting dentures are noteworthy risk factors for oral squamous cell carcinoma to occur[37]. It has been well reported that tooth decay and periodontium related diseases occur as a consequence of poor oral hygiene[38]. Retained dental plaque on tooth surfaces provides a suitable niche for microbes to grow and cause dental decay and periodontal diseases[39].

Xerostomia: Saliva produced by salivary glands is essential for the integrity of the oral mucosa. Saliva provides nutrients to oral micro-flora and also possesses antibacterial factors[40]. Saliva performs many important functions in the oral cavity like lubrication, buffering, remineralization, and also helps in thedigestion[41]. People with decreased salivary flow experience problems such as difficulty in speech, mastication, swallowing, halitosis, and there is an increased possibility of oral infections in these individuals too[42].

Many factors can lead to xerostomia like dehydration, less water intake, salivary gland pathology, and it can also occur as a side effect of certain medications such as antihypertensive and antidepressant drugs and diseases such as Sjogren's syndrome[43].Decreased salivary flow predisposes the oral cavity to changes and diseases such as candidiasis,[44] dental caries,[45] and periodontitis[46].

Pregnancy: Pregnant women are more prone to oral infections such as periodontal diseases, due to female hormonal influences. The occurrence of periodontal disease in pregnancy has been linked to other serious complications like premature birth and low weight birth[47]. During pregnancy, yeast colonization in females is also reported to be increased that is related to preterm birth[48]. The literature also reports a higher incidence of infection related to Herpes simplex and Epstein bar virus during pregnancy[49]. These infectious agents, if transmitted to the embryo or fetus may cause early embryonic and fetal death, miscarriages, and can induce major congenital anomalies leading to long-term consequences like developmental and growth problems[49].

Prosthesis and faulty dental restorations: The increased prevalence of Candida Albicansis found in denture wearers as compared to the dentate individuals[50]. Denture stomatitis (DS) is a common infection caused by candida species affecting up to 60% of individuals wearing dentures[51]. Patients with DS commonly present with inflammation of palatal mucosa which is in contact with the denture's acrylic surface[51]. The inflammation and infection in DS patients occur as a result of inferior oral hygiene coupled with bad denture hygiene[52]. Apart from candida, elevated count of lactobacilli species have also been reportedin denture wearing patients[53].

It has been proposed earlier that nearly half of dental restorations are performed to replace a faulty or failed restorations and the leading cause of failure of tooth restorations is afracture[54]. With faulty dental restorations, lactobacilli count increases and these species are closely associated with dental caries[55]. Defective dental restorations can affect oral hygiene and have been reported to be involved with increased prevalence of recurrent caries and periodontal diseases[56].

Nutritional deficiencies: A deficiency of essential nutritional factors like vitamins, iron, and folic acid are considered predisposing factors of oral infections[57]. Jenkins et al. previously reported that iron or folic acid deficiency may help the hyphae of Candida Albicans to invade the epithelium in susceptible individuals.58These alterations can make the epithelial surface more favourable for adhesion of candida, which can then cause candidiasis[58].

The practice of prescribing vitamins is a common practice in complementary or alternative medicine[59]. Previous statistical data has shown that in the United States, people are now choosing vitamins over prescription medications due to their benefits .Vitamin D plays an important role in tooth development and its deficiency can cause dental caries[60]. A study was performed in Canada to assess the relationship between vitamin D and dental caries in more than 1,000 (six to eleven-

year-old) children and it was concluded that there was a strong relationship between low serum levels of vitamin D and dental caries[61]. It was also proposed in that study that improving vitamin D of these children could be considered as a preventive measure, which can lower the risk of dental caries[61].

Trauma: Trauma can be caused by many factors notably ill-fitting prosthesis[62]. O'Grady and Peter studied the effect of trauma in the aetiology of candidiasis.63This study involved the induction of trauma and experimental candidiasis to the tongue of rats. On histological examination, it was observed that the hyphae invaded the trauma site much quicker than the control animals and it was concluded that trauma can help Candida Albicans to establish oral infections[63]. Dental trauma is common in toddlers due to poor motor skills and it has been reported earlier that by 14 years of age, approximately 30% children have suffered a dental trauma[64]. These injuries can give rise to oral infections

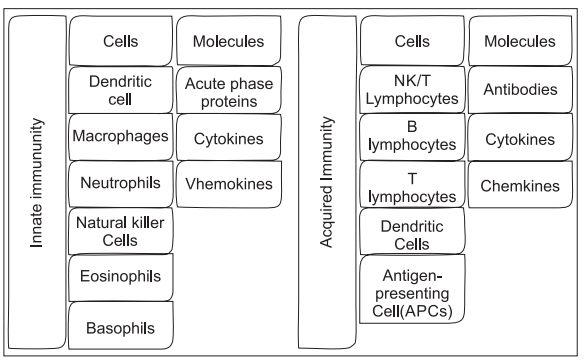

Fig 1: Cells and molecules of Innate and Acquired Immunity

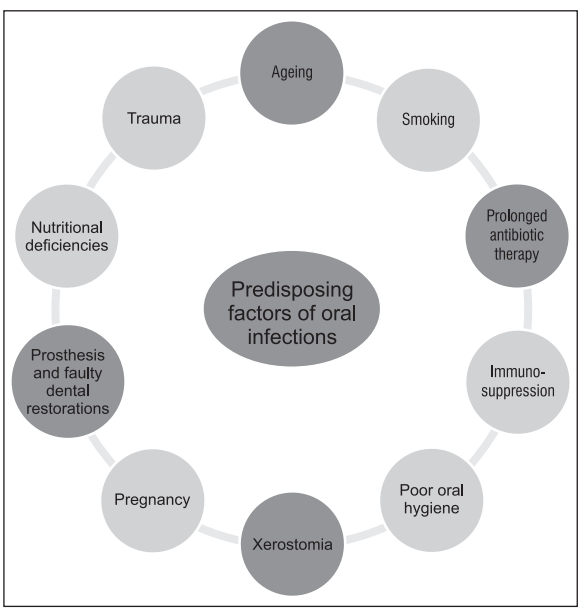

Fig. 2: Showing common predisposing factors of oral infections

which are usually a consequence of pulpal necrosis.

CONCLUSIONS

Many oral infections are related to predisposing factors and the initiation and progression of infections are dependent on the equilibrium between host defence mechanisms and these factors. Whenever this balance is disturbed, infections can ensue. Maintenance ofgood oral hygiene and avoidance of predisposing factors is, therefore, the key to avoiding many oral infections.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Farooq I: Main Idea, literature review, article writing, overall supervision.

Khabeer A: Data analysis article writing and formatting.

Ali S: Literature Review, final draft, proof Reading, bibliography.

Jandan BA: Data compilation, Proof Reading.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.