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Review article

The Pathogenesis of Oral Manifestations of COVID-19

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Abstract

The COVID-19 pandemic which causes the SARS-CoV-2 opens the way to more than thousand serious pathological conditions of various organs and systems, including those in the oral cavity.

Objective: To perform a systematic analysis of scientific articles and identify the main pathogenetic factors of COVID-19 affected the oral cavity.

The search was performed on the PubMed and Google Scholar platforms using the following strategy: "COVID-19" + "Oral cavity". All articles presented in the open access, published before 01/04/2022 in the format of Case Reports, Clinical Studies, Clinical Trial Protocols, Clinical Trials, Multicentre Studies were analysed.

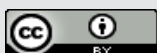
135 publications were included in the study after exclusion, 33.518 cases were analysed. Damage to the teeth, tongue, hard palate and oral mucosa, dysgeusia, xerostomia and ageusia are the most common manifestations of COVID-19 (17.137 reported cases). Suggested mechanisms of dysgeusia in patients with COVID-19 include direct cytotoxic effects of the virus on ACE-2-expressing receptors, angiotensin II imbalance, and peripheral taste and olfactory neurotropism. Salivary glands with increased expression of ACE-2 are also a target for COVID-19, they progress to xerostomia with the development of dysgeusia. The primary lesion of the oral mucosa was manifested in the form of multiple erythema and oedema (29 cases). Ulcers happened due to mucosal bite caused by muscle contraction, irritation by a foreign object during intubation were shown to lead to the development of neoplasms from benign fibroma to an aggressive form of cancer, especially against the background of corticosteroids (3 cases). Vitamin D deficiency lead to a decrease in the density of the maxillofacial bone and serves as a factor for tooth migration and periodontitis. The addition of a secondary infection is observed in connection with the suppression of the immune system, both by the virus itself and by medications. Pseudomembranous candidiasis (3 cases), recurrent herpes simplex (3 cases), saccharomyces cerevisiae (2 cases) and others have been registered.

The analysis demonstrated that damage of the oral cavity can occur both because of the direct action of COVID-19, and indirectly, through psycho-emotional stress, antibacterial drugs, co-infection, neglect of hygiene measures, vitamin D and zinc deficiency.

Keywords: COVID19, oral cavity pathology, pathophysiology, pathogenetic factor.

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a single-chain RNA virus. Coronavirus disease 2019 (COVID-19) known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) became an important problem for healthcare in the worldwide. The common clinical symptoms are fever, headache, sore throat, cough, diarrhoea [1,2].

Until May 2022 there are 462 million cases detected and 6.07 million deaths not maintaining the once not registered. It affected not only immune, respiratory, and nervous systems, but also other organs and systems, including oral cavity [3-7]. Dyspepsia was the first recognized oral symptom of COVID-19, however, other

Search strategy

In the current study the search process was conducted in PubMed and Google Scholar using the following keywords strategy: "COVID-19" or "SARS-CoV-2" and "oral cavity". Case Reports, Clinical Studies, Clinical Trial Protocols, Clinical Trials, Multicentre Studies were reviewed. All articles presented in these domains published before 01.05.2022 were analysed. Different types of oral cavity injury were evaluated.

Based on the search terms in the databases number of articles reviewed consists of 135 from 2019 till May 2022.

The total of 33.518 cases were analysed in these articles, including patients with COVID-19-associated dysgeusia, hypogeusia, xerostomia and ageusia (17.137 reported cases), necrotizing gingivitis and periodontitis (7 cases), masticatory muscle pain (15 reported cases), oral bleeding and bruxism leading to the migration of teeth (6 patients reported), periodontitis calculus and ulcers (27 reported cases), cracked or fissured lip or tongue (18 reported cases), cheilitis (5 reported cases), recurrent herpes simplex (3 reported cases), pseudomembranous candidiasis (3 reported cases), *saccharomyces cerevisiae* (white plaque) (3 reported cases), erythema (29 reported cases), papilla (22 reported cases), vesicles and erosions

Main part

Stress caused several consequences of the COVID-19 as while people on quarantine got affected materially and spiritually it was a psychological pressure that caused several manifestations such as masticatory muscle pain (15 reported cases), oral bleeding and bruxism it even led to migration of teeth (6 patients reported).

Vitamin D deficiency was a prominent factor as people on quarantine had less contact with sun light it led to reduction of maxillofacial bone density as it led again to migration and periodontitis of teeth.

Low oral hygiene was registered, as people got are affected mentally and emotionally during and even after COVID-19 quarantine, they didn't pay a lot of attention for teeth brushing, flossing and mouth washing in general. This led to affecting the gum causing periodontitis calculus and even ulcers (27 reported cases). Affected dentition remain untreatable after the virus for a long period especially during quarantine, when the dental offices were closed for casual cases (available only for emergency).

People were even afraid to get out since the virus is new and quarantine measures made them have that feeling of fear. All mentioned above reasons lead to

oral lesions of COVID-19 are known now. Scientists are still exploring and discovering new facts about it every single day.

Until May 2022 more than 3 thousands of clinical trials have being studied, at that same moment 4.317.900 Nucleotide records, 3.293.819 SRA runs and 237.704 studies reported on PubMed. The comprehensive systematic review is needed to summarise these research data [8-10].

This review dedicated to the connection of COVID-19 with dental and oral cavity problems, showing the harmful consequences of virus and medications used for treatment.

(24 reported cases), petechiae with pustules (27 reported case), canker sores (1 reported case), multiple reddish macules (26 reported case), burning sensation (25 reported cases), blisters (1 reported case), erythema and edema (29 reported cases), fibroma on tongue, lips, cheeks or oral and maxillofacial area (2 reported cases), carcinomas (2 reported cases). In most cases the oral lesions were symptomatic (painful) in about 70% of the cases.

COVID-19 affects dentition as it manifested itself in several registered and not registered cases some were as a sequence of the disease as a cross infection, and some were as symptoms and several manifestations on the tongue trough, hard palate and skin of maxillofacial area.

Dysgeusia, hypogeusia, xerostomia and ageusia are the most common symptoms which showed that the patient is with that disease it effected most patient and there were 17.137 reported cases. Necrotizing gingivitis and periodontitis were reported in 7 cases.

postpone of dental treatment and therefore worsening of the diseases.

Cracked or fissured lip or tongue (18 reported case), cheilitis (5 reported cases), recurrent herpes simplex (3 reported cases), pseudomembranous candidiasis (3 reported cases), white plaque (*saccharomyces cerevisiae*) (3 reported cases), erythema (29 reported cases), papilla (22 reported cases), vesicles and erosions (24 reported cases), petechiae with pustules (27 reported case) and canker sores (1 reported case). Those pathological changes occurred from totally different pathogenic factors as its not mainly caused by COVID-19 virus but secondary infections: some are caused by viruses, some by bacteria and others by fungi, as the main factor for all of this is suppression of immune system thus even normal microflora of the oral cavity in this situation turns to aggressive pathogenic.

One of the main factors are medications treating COVID-19, for example corticosteroids have immunosuppressing action nevertheless antibacterial medications causes dysbacteriosis in the oral cavity which is harmful for the oral health.

Hairy tongue is frequently seen in the context of COVID-19 due to the lack of desquamation and the growth and enlargement of the filiform papillae of the tongue, resulting mainly in discoloration of the tongue, halitosis and metallic taste.

Antibiotic intake during this period is relevant, as most COVID-19 patients are treated with azithromycin under treatment protocol.

Recent observations of increased accumulation of inflammatory cells in the endothelium, endothelial inflammation, and enhanced damage/dysfunction via endothelial ACE2 are likely to occur after SARS-CoV-2 infection. As the mucus membrane of the nose and oral cavity is the first portal for COVID-19 virus the inflammatory process manifested by multiple reddish macules (26 reported case), burning sensation (25 reported cases), blisters (1 reported case), erythema and oedema (29 reported cases). They may be treated by antihistamines reducing the inflammation and suppressing the hypersensitive immunological reaction (81 reported cases).

Discussion

The virus pathogenic way of spreading is airborne rote, as the patient will get infected with the virus when infectious particles are inhaled. Risk factors for severe manifestation of COVID-19 include elderly age, pregnancy, underlying medical conditions such as

If a manifestation such as ulcers, continued biting of oral area caused by stressful muscle contraction with wrong bite, irritation with a foreign object causing trauma in oral cavity could be developed to a benign tumour (fibroma on tongue, lips, cheeks or anywhere in oral and maxillofacial area, there are 2 reported cases). It should be also maintained that any kind of fibroma could turn into aggressive cancer especially with corticosteroids on the background (carcinomas reported in 2 cases).

Mouth rinses and oral antiseptics are the best way for prophylaxis of COVID-19 manifestation in the oral cavity and its pathological consequences (cross infections). It is used for treating almost all the manifestations in the oral and maxillofacial area never minding on the antiviral, antibacterial and antifungal medications. Dentists have a big role either in spreading or reducing the amount of disease by doing all hygienic measure like sanitizing after each patient with antiseptics, using a sanitized with autoclave individual instruments for each patient and wearing a face shield and mask.

cardiovascular disease, diabetes, chronic respiratory disease, cancer, and others. Risk factors may be more susceptible to pulmonary complications from COVID-19 due to aspiration, impaired swallowing function and airway dysfunction (Figure 1) [1,2,3].

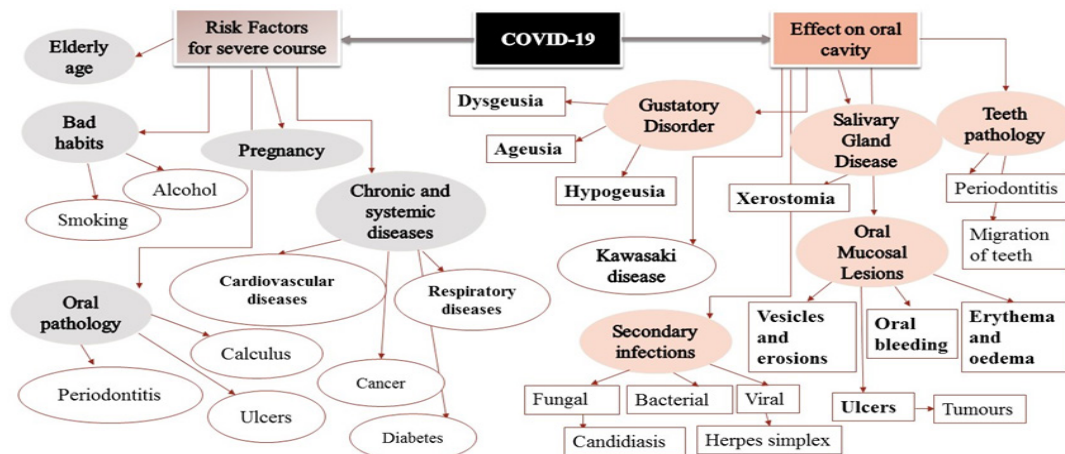


Figure 1 - Risk factors for severe course of COVID-19 and oral cavity manifestations

COVID-19 manifested itself in several registered and not registered cases some were as a sequence of the disease as a cross infection, and some were as symptoms and several manifestations on the tongue trough, hard palate, and skin of maxillofacial area. Taste impairment is one of the most common oral manifestations of the infection, with different degrees varying from dysgeusia, hypogeusia, to ageusia being the most known symptom of COVID-19 as it appeared even in asymptomatic forms of the disease [4,5,6,7]. There are several theories about the mechanism, including:

- Peripheral neurotropism in the gustatory or olfactory nerves, which is more likely than central nervous system invasion.
- Direct taste bud cytotoxicity, as they are rich in ACE2 receptors that support viral fusion and subsequent inflammation.

- Imbalance in angiotensin II might occur in COVID-19, which has an impact on taste sensation.
- Interleukin-6 may be involved in dysgeusia since it could act on the thermo-regulatory centre, which eventually affects the nearby thalamus and both the gustatory and olfactory nerve route.
- Salivary glands with high ACE2 expression could be a target for infection, causing xerostomia with subsequent dysgeusia.
- Defective sialic acid function could accelerate gustatory particles degradation.
- Factors such as hypozincemia, excessive exposure to chemicals and disinfectants, systemic diseases, and certain drugs taken by COVID-19 patients could play a role in the aetiology of dysgeusia [5,8,9,10,65].

During the first quarantine lockdown which was in most of the countries, normal dental procedures and check-ups were suspended. Even after the lockdown ended, going to overcrowded dental clinics was still considered health-threatening and people had fear, especially those who are at high risk of developing complications of COVID-19. Nevertheless, in most cases, temporomandibular disorders (TMD) and bruxism were not included under the definition of emergency cases, leaving many patients without the possibility of consulting their own dentists.

Most studies have indicated adverse effects on patient psycho-emotional status causing (stress, anxiety, depression), which in turn lead to the TMD and bruxism symptoms severity, increased maxillofacial pain and caused several manifestations such as masticatory muscle pain, oral bleeding following by the migration of teeth. This needs various kinds of treatment, like the massage of tense and painful areas, stretching, thermotherapy, drug therapy, use of oral antiseptics, relaxation techniques, meditation that can be administered through the remote mode [11].

COVID-19 ongoing outbreak, along with the associated social restrictions, have impacted the vitamin D status of the general population as it has been associated with developing both type 1 and type 2 diabetes, cognitive decline, malignant neoplasms, autoimmune diseases,

cardiovascular diseases, osteoporosis, risk of fall in the elderly and overall mortality. People in the quarantine had less contact with sun light which led to vitamin D deficiency, following by the reduction of maxillofacial bone density, periodontitis and migration of teeth [12].

Low oral hygiene was also registered, as people did not pay a lot of attention for teeth brushing, flossing and mouth washing in general. This led to affecting the gum causing periodontitis calculus and even ulcers [2,3,11,13,133].

Swelling of oral cavity (including palatal, lingual, and gum) was reported in some patients with COVID-19. Loss of taste and smell and more severe and oral lesions were reported in older patients and in severe COVID-19.

Secondary infections caused by viruses, bacteria and fungi, as the main factor for all of this is suppression of immune system thus even normal microflora of the oral cavity in this situation turns to aggressive pathogenic as one of the main factors are medications treating COVID-19, for example corticosteroids have immunosuppressing action nevertheless antibacterial medications causes dysbacteriosis in the oral cavity [37,48,51,52,53,68,81,111,115,126,135].

Table 1 - Clinical oral manifestation of COVID-19 and treatment experience

COVID-19 oral manifestation	Patients (N)	Area affected	Treatment	Outcomes	References
Necrotizing areas	7	Labial interdental papillae	Metronidazole, Chlorhexidine mouthwash	Signs and symptoms completely regressed after 5-7 days of treatment	35, 90,134
Dysgusia	1290	Tongue	Artificial saliva, Pilocarpine, Zinc supplements, Alterations in drug therapy and Alpha lipoic acid	The symptom persisted for a median of 8-21 days but even so some patients gustatory sense have not been completely recovered	4, 5, 8-10, 14, 25-27, 31, 34, 42, 46, 48, 52, 60, 61, 62, 65, 66, 68, 73, 74, 76, 78, 85, 86, 91, 92, 95, 100, 102,108,135
Xerostomia	225	Tongue, Palate, Gums	Solutions such as artificial saliva and gels to improve dry mouth sensation	Xerostomia and dry mouth sensation were improved after the treatment	8, 49, 64,76, 110
Change in sensation of the tongue (burning sensation)	25	tongue	Antiseptic mouthwash Chlorhexidine 0.12% mouthwashes	Burning sensation disappeared after the treatment	4, 49, 68, 90
Masticatory muscle pain	15	Tongue, Palate, Gums	Analgesics	Pain became mild after taking analgesics	49
Edema an irritation of oral cavity	23	Tongue, Palate, Gums	Anti-inflammatory drugs and mouth washes	Symptoms recovered in 5-7 days	8, 49, 65
Plaque-like changes in the tongue	11	Tongue	Fluconazole, Antiseptic mouthwash	After 14 days the lesion showed almost complete resolution	49, 66
Oral bleeding	6	Tongue, Palate, Gums	Antiseptic mouthwash with Hydrogen peroxide	It all recovered and bleeding stopped in a while after treatment	49
Ulcers	27	Tongue, Hard palate	Solution with Triamcinolone acetonide 0.05%	Lesions completely regressed after treatment	4, 35,36, 37,50, 51,52,58, 65-67,77,79,81
Recurrent herpes	3	Tongue, Hard palate	Intravenous acyclovir, Valaciclovir	Lesions regressed 10 days after the treatment	37, 65
Multiple reddish macules	26	Tongue, Hard palate, Buccal mucosa, Lips	Systemic corticosteroids with antiseptic mouthwash	The lesions completely regressed after 14–21 days of treatment	35,50,53,58,66,126
Tongue depapillation	2	Tongue, Palate, Lips	Triamcinolone acetonide, Neomycin, Nystatin	Tongue depapillation persisted after the treatment	4,68
Candidiasis	3	Tongue, Palate, Lips	Intravenous Fluconazole, Chlorhexidine digluconate 0.12% mouthwash, and 1% Hydrogenperoxide, Solution with Triamcinoloneacetonide 0.05%, Nystatin solution	Lesions regressed after the treatment and patient reported being asymptomatic , Completely regressed after treatment	4, 37,15

Table 1 (Continuation) - Clinical oral manifestation of COVID-19 and treatment experience

COVID-19 oral manifestation	Patients (N)	Area affected	Treatment	Outcomes	References
White plaque (Saccharomyces cerevisiae)	3	Tongue	Fluconazole, Nystatin, Chlorhexidine, and, Hydrogen peroxide 1%	After 14 days the lesion showed almost complete resolution	35,36, 90,115
Erythema	29	Tongue, Tonsils	Fluconazole, Nystatin, Chlorhexidine, and, Hydrogen peroxide 1%	Showing improvement after 10 days	37,65,58, 66,78,79,133
Blisters	1	Hard palate, Labial mucosa	Hyaluronic acid, Chlorhexidine, Prednisolone and Valaciclovir	The patient developed crusts on the external lip mucosa 3 days after	52
Vesicles and erosions	24	Lips, Tongue, Buccal mucosa	Antiseptic mouthwash with Chlorhexidine and oral gel mycoheal	Total recovery after 10 days of treatment	50,79,80,126
Canker sores	1	Tongue, Lips, Gingiva	Hygiene control with a brush and toothpaste was also indicated, rinses with Chlorhexidine	Oral cavity recovery of the lesions after 20 days	36
Gingival hyperpigmentation	Not given	Tongue, Lips, Gingiva	Not given	Not given	4
Petechiae and Pustules	27	Oropharynx, Palate	Prednisolone, Antibiotic therapy (Amoxicillin)	Recovered after treatment	36,53, 65,68,126
Ageusia	3006	Tongue	Oral Paracetamol, Chlorhexidine	The majority of patients completely recovered the taste sensation	5,7,21,22,30,34,42, 48,54,60,65,70, 75,83,87,89,97,100, 101,106,107,109,110,113
Hairy tongue	1	Hard palate, Tongue	Acyclovir, Antiseptic, Nystatin, Panthenol, Local anesthetic	Not given	90
Nodule in the lip (fibroma)	2	Lower lip	Chlorhexidine digluconate alcohol-free mouth rinses, and daily applications of 1% Hydrogen peroxide	Not given	37,114
Periodontitis	N/A	Teeth and gums	Antiseptic mouthwash	Not given	11
Calculus	N/A	Teeth neck	Scaling and good oral hygiene	The patient was recalled after 10 days for oral prophylaxis	2
Bruxism, teeth grinding, and teeth clenching	N/A	Teeth and masticatory muscles	Using teething guard and Botox in the masticatory muscles	Immediate relief after treatment	112
Hypogeusia	851	Tongue	Not given	The symptom persisted for a median of 8-21 days but even so some patient gustatory sense haven't been completely recovered	5, 8, 37, 34, 42, 48, 67, 83, 88, 97, 98, 104, 109, 113, 118
Cracked (fissured)	18	Tongue or lip	Neomycin ointment Nystatin and Triamcinolone acetonide 0.05% and hygiene of the area using gauze with Chlorhexidine	The lesions completely regressed after treatment	4, 37, 55, 56, 57
Cheilitis	5	Lips	Neomycin ointment Nystatin and Triamcinolone acetonide 0.05% and hygiene of the area using gauze with Chlorhexidine	The lesions completely regressed after treatment	4, 79, 111
Gingivitis	1	Gums	Hyaluronic acid and chlorhexidine mouthwash, Prednisolone	Lesions improved within 3 days	52
Papilla	22	Tongue or lip	Not given	After 5 days, the lesion presented complete remission	50, 55, 66, 126
Tongue enlargement	2	Tongue	Not given	After 5 days, the lesion presented complete remission	66, 90
Gustatory dysfunction	11990	Tongue	Not given	The symptom persisted for a median of 8-21 days but even so some patient gustatory sense haven't been completely recovered	6, 8, 11, 15-20, 23, 28-30, 32-34, 38-42, 43-45, 47, 49, 59, 63, 64, 69, 71, 72, 82, 84, 90, 93-95, 99, 103, 105

Hairy tongue is a frequently seen secondary infection in the context of COVID-19 due to the lack of desquamation and the growth and enlargement of the multiform papillae of the tongue, resulting mainly in

discoloration of the tongue, halitosis and metallic taste. Antibiotic intake during this period is relevant, as most COVID-19 patients are treated with azithromycin under the treatment protocol [90].

Kawasaki Syndrome is a vascular inflammatory disease of unknown cause but associated with viral diseases, mainly affects children under 5 years of age and rarely affects adults, its symptoms are fever of more than 5 days above 39°C, mainly skin rashes on the body or genital area, swollen lymph nodes in the neck, the initial and most obvious symptoms of this syndrome is in the oral cavity, as the patient will develop cracked lips and a very red swollen tongue, increased accumulation of inflammatory cells in the endothelium inflammation and enhanced damage or dysfunction via endothelial ACE2 are likely to occur after COVID-19 infection. A systemic inflammatory response to pneumonia can enhance the inflammatory response within coronary artery lesions, causing endothelial dysfunction and thus promoting the development of Kawasaki. Therefore, COVID-19 hyperinflammation may act as a priming trigger that can lead to Kawasaki syndrome [55,56,57,67,76].

Ulcerations, continued biting of oral area caused by stressful muscle contraction with wrong bite, irritation with a foreign object causing trauma in oral cavity, increased excretion of ACE2, TMPRSS2 and FURIN proteins which developed the appearance of benign tumours

Conclusions

Dental and oral cavity injury may happened as a direct result of COVID-19 but also due to other causes such as side reactions of medications, stress, coinfection, neglect of hygiene measures, vitamin D deficiency and others. SARS-CoV-2 opens a route to more than thousands of serious conditions, where even treating symptoms and consequences with medications increase the risk for a totally new disease, elevated the amount of cross infections.

Conflict of interest. Authors declare the absence of a conflict of interest.

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such as fibroma on tongue, lips, cheeks or anywhere in oral and maxillofacial area. Furthermore, benign tumours might easily turn into malignant tumours as aggressive corticosteroids took while treating the COVID-19 are cancerogenic factors that play a big role for developing tumours especially carcinomas [37,114,119,135].

Mouth rinses and oral antiseptics are the best way for prophylaxis of COVID-19 manifestation in the oral cavity and its pathological consequences (cross infections). It is used for treating almost all the manifestations in the oral and maxillofacial area never minding on the antiviral, antibacterial and antifungal medications. Dentists have a big role either in spreading or reducing the amount of disease by doing all hygienic measure like sanitizing after each patient with antiseptics, using a sanitised with autoclave individual instruments for each patient and wearing a face shield and mask [122,129,132,134].

There are some limitations to this study, such as subjects were not taken from a single cohort of patients and included different gender, age, variants of COVID-19 pathology as well as different comorbidity.

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All authors have read, agreed to the final version of the manuscript, and signed the copyright transfer form.

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COVID-19 кезіндегі ауыз қуысы зақымдалуының патофизиологиялық аспектілері

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Түйіндеме

SARS-CoV-2 коронавирусынан туындаған COVID-19 пандемиясы әртүрлі ағзалар мен жүйелерде, мыңдаған ауыр патологиялардың дамуына ықпал етті, соның ішінде ауыз қуысының дерті де бар.

Шолудың мақсаты: COVID-19 кезіндегі ауыз қуысы зақымдануының негізгі патогенездік факторларын анықтау және осы бағыттағы ғылыми мақалаларға жүйелі талдау жүргізу.

Ағымдағы зерттеу «COVID-19» + «Oral cavity» стратегиялары бойынша, PubMed және Google Scholar платформаларында жүргізілді. Көптеген клиникалық жағдайлар мен зерттеулердің нәтижелері сипатталған және 04.01.2022 жылға дейін жарияланған барлық ашық қолжетімді мақалалар талданды.

Барлығы 33 518 жарияланымдар қарастырылып, оның ішіндегі бір-біріне ұқсас материалдарды алып тастағаннан кейін, қалған 135 мақалаға зерттеулер жүргізілді. Тістердің, тілдің, қатты таңдайдың және ауыз қуысының сілемейлі қабығының зақымдануы, дисгевзия, ксеростомия және аевезия COVID-19-дың ең жиі кездесетін көрінісі болып табылатыны анықталды (17137 жағдай). COVID-19 шалдыққан науқастарда дамыған дисгевзиялардың болжамды механизмдеріне: вирустың ангиотензинге айналдырушы ферментті (ААФ-2) экспрессиялайтын дәм сезетін рецепторларға тікелей цитоуытты әсерін, ангиотензин II дисбалансын, перифериялық дәм мен иіс сезу нервтеріне нейротропизмін жатқызуға болады. ААФ-2-ні жоғары деңгейде экспрессиялайтын сілекей бездері де COVID-19 үшін нысана болып табылады, олардың зақымдануы дисгевзиямен ксеростомияны тудырады. Ауыз қуысының сілемейлі қабатының біріншілікті зақымдануы көптеген эритема және ісіну түрінде көрінген (29 жағдай). Бұлшықет жиырылуынан, интубация кезінде тітіркенуден туындаған ауыз қуысының сілемейлі қабығының зақымданулары, ойық жаралардың, қатерсіз фибромалардың, обырдың агрессивті түрінің дамуына ықпал етуі мүмкін, бұл әсіресе кортикостероидтарды қабылдау аясында (3 жағдай) байқалады. Витамин D тапшылығы жақ-бет сүйегінің тығыздығының төмендеуіне ықпал етеді және периодонтиттің даму факторы ретінде қарастырылады. Екіншілікті инфекциялардың қосылуы вирустың, дәрі-дәрмектердің әсерінен, иммундық жүйенің әлсіздігінен байқалады. Науқастардың псевдомембранозды кандидозға (3 жағдай), қайталанатын қарапайым герпеске (3 жағдай), *saccharomyces cerevisiae* (2 жағдай) және т.б., шалдығатыны тіркелген.

Жүргізілген зерттеулерде ауыз қуысының зақымдануы, COVID-19-дың тікелей әсерінен және кейбір жанама ықпалдардың: психозмоциялық стресстің, бактерияға қарсы препараттардың, коинфекциялардың, гигиеналық шараларды елемейді, D дәрумені мен мырыш тапшылығының салдарынан дамуының көрсетілді.

Түйін сөздер: COVID-19, ауыз қуысының патологиясы, патофизиология, патогенездік фактор.

Патофизиологические аспекты поражения ротовой полости при COVID-19

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Резюме

Пандемия COVID-19, вызванная коронавирусом SARS-CoV-2 открывает путь к более чем тысячи серьезных патологий различных органов и систем, в том числе и ротовой полости.

Цель обзора: систематический анализ научных статей и выявление основных патогенетических факторов поражения ротовой полости при COVID-19.

В данном исследовании проводился поиск на платформах PubMed и Google Scholar с использованием следующей стратегии: «COVID-19» + «Oral cavity». Были проанализированы все статьи, находящиеся в открытом доступе, опубликованные до 01.03.2022 в формате описания случая, клинических и многоцентровых исследований.

Всего 135 публикаций были включены в исследование после исключения повторов, проанализировано 33 518 случаев. Поражения зубов, языка, твердого неба и слизистой полости рта, дисгевзия, ксеростомия и агевзия - наиболее частые проявления COVID-19 (17137 случаев). Предполагаемые механизмы дисгевзии у пациентов с COVID-19 включают прямое цитотоксичное действие вируса на вкусовые рецепторы, экспрессирующие АПФ-2, дисбаланс ангиотензина II, периферический нейротропизм вкусовых и обонятельных нервов. Слюнные железы с высокой экспрессией АПФ-2 также являются мишенью для COVID-19, их поражение вызывает ксеростомию с последующей дисгевзией. Первичное поражение слизистой полости рта проявлялось в виде множественных эритем и отека (29 случаев). Язвы вследствие прикуса слизистой, вызванного сокращением мышц, раздражения посторонним предметом во время интубации способствуют травматизации полости рта и могут вести к развитию новообразований от доброкачественной фибромы до агрессивной формы рака, особенно на фоне приема кортикостероидов (3 случая). Дефицит витамина D способствует снижению плотности челюстно-лицевой кости, и служит фактором миграции зубов и периодонтита. Присоединение вторичной инфекции наблюдается в связи с подавлением иммунной системы, как самим вирусом, так и медикаментами. Зарегистрированы псевдомембранозный кандидоз (3 случая), рецидивирующий простой герпес (3 случая), *saccharomyces cerevisiae* (2 случая) и прочее.

Проведенный анализ показывает, что поражение ротовой полости может возникнуть как следствие прямого действия COVID-19, так и опосредованно, через психоэмоциональный стресс, прием антибактериальных препаратов, коинфекцию, пренебрежение мерами гигиены, дефицит витамина D и цинка.

Ключевые слова: COVID19, патология ротовой полости, патофизиология, патогенетический фактор.