

Evidence mapping and quality analysis of published dental literature on COVID-19 – A systematic review

ABSTRACT

A large number of scientific articles have been published regarding impact of COVID-19 infection on dental practice, dental professionals, and the mode of spread of infection via dental procedures. The present systematic review was planned with an aim of evidence mapping and quality analysis of published research on the dental aspects of COVID-19 infection. The protocol was registered at <https://share.osf.io/registration/46221-C87-BA8>. The search was performed in Scopus, PubMed, Cochrane, and Embase databases till 15th July 2020. There was no restriction of year of publication and language. All types of published articles related to Dentistry, Dentist, Dental practice, and Oral health education on COVID-19 were included. The Joanna Briggs Institute's (JBI) Critical Appraisal Tools were used for the risk of bias analysis of included studies. A total of 393 articles were short-listed and were checked for eligibility and finally, 380 articles were included. Among the 380 research articles published (till July 15, 2020), the majority of the included articles belonged to the lowermost strata of the evidence pyramid. There were 54 original research articles with no randomized clinical trial, systematic review or, meta-analysis pertaining to the dental perspective of COVID-19 infection. The level of available evidence about dentistry and COVID-19 infection is very low with a lack of researches of highest quality. The guidelines/recommendations for dental professionals, proposed by the different scientific organizations/societies regarding COVID-19 infection are only consensus-based necessitating the need to formulate evidence-based guidelines. There is a need to identify essential research questions and strengthen the study designs in most of the aspects related to the dentistry and COVID-19 pandemic.

Keywords: COVID-19, dental professionals, dentistry, evidence mapping, oral health, quality analysis

INTRODUCTION

An illness similar to common flu with high infectivity and signs similar to pneumonia was reported in Wuhan city of China in December 2019. The condition spread rapidly to different parts of china in January 2020 and later started gripping the globe in February 2020. The investigation to find out the etiology of the infection had led to the characterization and isolation of a virus termed as the novel coronavirus (2019-nCoV).^[1] This is an enveloped RNA virus comprising of strains leading to respiratory syndromes such as SARS and MERS. The 2019-nCoV has found to have wide distribution, genetic recombination, and a higher rate of infection.^[2,3]

The main infective pathways of SARS-CoV-2 are airborne and direct contact.^[4] Coughing, sneezing, exhalation, or speaking are the common routes of the airborne infection


that occurs through the released droplets. As they settle and contaminate the surfaces, any contact subsequent touching to eyes, nose, and mouth leads to COVID-19 infection.^[3-5] The role of saliva has also been implicated in the spread of infection.^[6-9]

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Received: 27 October 2020, **Accepted in Revised Form:** 12 February 2021, **Published:** 15 July 2021

Access this article online	
Website: www.njms.in	Quick Response Code 
DOI: 10.4103/njms.NJMS_237_20	

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How to cite this article: Rahul M, Tewari N, Mathur V, Goel S, Jain G. Evidence mapping and quality analysis of published dental literature on COVID-19 – A systematic review. *Natl J Maxillofac Surg* 2021;12:139-61.

Since the emergence of this pandemic, there has been a panic among the dental fraternity across the world, especially regarding the possible spread of this infection through dental operatories. The cross-sectional studies evaluating the knowledge, attitude, and practice in dental professionals regarding the spread of COVID-19 infection through the dental procedures have also reported a high level of concern in them.^[10,11] There has been a sense of fear, anxiety, and reluctance among dental professionals to continue their dental practice in the pandemic.^[12] Even the World Health Organization had released a series of guidelines (last published on August 3, 2020) advised to delay the routine nonessential oral health services until there has been sufficient reduction in COVID-19 transmission rates.^[13] However, the American Dental Association in their opinion (released on August 13, 2019) strongly disagrees with these recommendations to delay routine dental care.^[14] To an extent this belief is justified, since the oral cavity is in direct communication with the respiratory system which harbors the virus and aerosol generating dental procedures can pose threat to the operators, auxiliaries, and the patients.^[15,16]

After the start of the current pandemic, there are thousands of scientists working on various aspects of Coronavirus origin, epidemiology, demographic distribution, clinical symptoms, diseases progression, after effects, recovery time, prevention, and vaccination. The profession of dentistry is also largely affected by the current pandemic and there are many areas in which research is undergoing with respect to COVID-19 pandemic and dental profession as a whole. However, some of the areas are being investigated more and some are not. The published literature is quite discrete, which makes it difficult to draw any conclusion. This article is aimed at evidence mapping of the available literature, its quality analysis and pointing at areas of gap and future research.

METHODS

This systematic review was carried out according to the PRISMA guidelines and principles of Global Evidence Mapping.^[17,18] The protocol was registered with <https://osf.io/registries> (Registration/46221-C87-BA8).

Information sources

The search was performed in Scopus, PubMed, Cochrane, and Embase databases till July 15, 2020. There was no restriction of year of publication and language. Google Scholar and Open Grey search were performed for grey literature. To identify the additional studies the Cross references of eligible studies were checked. Hand searching was also performed in general and specialty journals of dentistry. Two authors (NT and MR) performed the literature search and study selection

independently as per the predefined search strategy. Any disagreement was resolved after consultation with the senior reviewer (VM).

Search strategy

The four reviewers (NT, VPM, SG, and MR) identified the possible domains and subdomains which could be focused for identifying the available dentistry related literature on COVID-19 infection. They were finalized after a focused group discussion in two stages within the review team.

A broad-based search was implemented using the text words and MeSH terms. The key words were: "Dentistry", "Dentist", "Dental practice", "Saliva", "Aerosol", "Oral Health", "Oral disease", "Periodontics", "Pediatric dentistry", "Prosthodontics", "Endodontics", "Orthodontics", "Oral Surgery", "Oral Pathology", "Community dentistry", "Public Health Dentistry", "Conservative Dentistry", "Oral diagnosis", "Oral Radiology". Partial searches with "AND" and "OR" were done with the above keywords individually with "Covid-19", "Corona virus" and "SARS-COV-2". The strategy used for partial search was (1) Search ((Dentistry OR Dentist) OR Dental practice) (2) Search (((Saliva) OR Aerosol) OR Oral Health) OR Oral disease) OR Periodontics) OR Pediatric dentistry) OR Prosthodontics OR Endodontics OR Orthodontics OR Oral Surgery) OR Oral Pathology) OR Community dentistry) (3) Search (((((((((((Corona virus OR SARS-COV-2 OR Covid-19. The duplicates were removed and titles and abstracts were assessed for their eligibility as per inclusion criteria.

Study selection and eligibility criteria

Inclusion criteria-1

All types of published articles (*In vitro* studies/Background information/Expert opinion/Letter to editor/Case series or Case reports/Cohort studies/Case-control studies/Non-randomized clinical trials/Randomized clinical trials/Critically appraised topics (Evidence synthesis and guidelines)/Systematic reviews/Meta-analysis). (2) Dentistry, Dentist, Dental practice and Oral health education related research articles on SARS-COV-2 with no restriction of language.

Exclusion criteria-1

Researches related to virus other than SARS-COV-2. 2. Researches not relevant to dentistry, dentist, dental practice, and oral health education.

Data collection process

The self-designed sheets, pilot-tested (tested on two included studies) were used for data extraction pertaining to different categories of studies. Two calibrated reviewers (MR and NT) collected the data from the included studies. The inter

reviewer agreement for different variables was found to be high with Cohen's kappa values ranging from 0.68 to 0.82. In case of any disagreement, the third reviewer (GJ) was consulted and it was resolved by consensus.

Assessment of risk of bias

The included studies were assessed for their methodological quality using the JBI Critical Appraisal Tools.^[19] The case reports, case series and all the included research articles (except editorials, expert opinion, letter to editor, narrative reviews) were analyzed for their methodological quality using respective JBI tools and divided into high, moderate, and low risk of bias (ROB). The scores were assigned to each of the included study pertaining the points applicable to methodological quality assessment, and on the basis of the scores, they were categorized into high (score 75% and above), moderate (score 50%–74%), and low ROB (score below 50%).

Statistical analysis

The included studies showed wide variations in the population, aim, objectives, outcome variables, and tools

used for their assessment. Considering the heterogeneity of data, it was only analyzed for the descriptive characteristics without meta-analysis. Cohen's kappa statistics was used to determine inter-reviewer agreement.

RESULTS

Study selection

The search conducted in different electronic databases identified 2432 articles. Twenty-five additional records were found through other sources. A total of 393 full-text articles were short-listed after removal of duplicates and evaluation of titles and abstracts. They were further assessed for eligibility and finally 380 articles were included. The details of the search have been presented as PRISMA chart [Figure 1]. The excluded studies and reasons are presented in Appendix Table 1.^[S1-S13] The included studies were arranged in an Evidence-based pyramid according to their levels of evidence [Figure 2].^[20] The ideas, editorials, letter to the editors, opinions, and narrative reviews were mapped in the present SR but not subjected to quality assessment or ROB

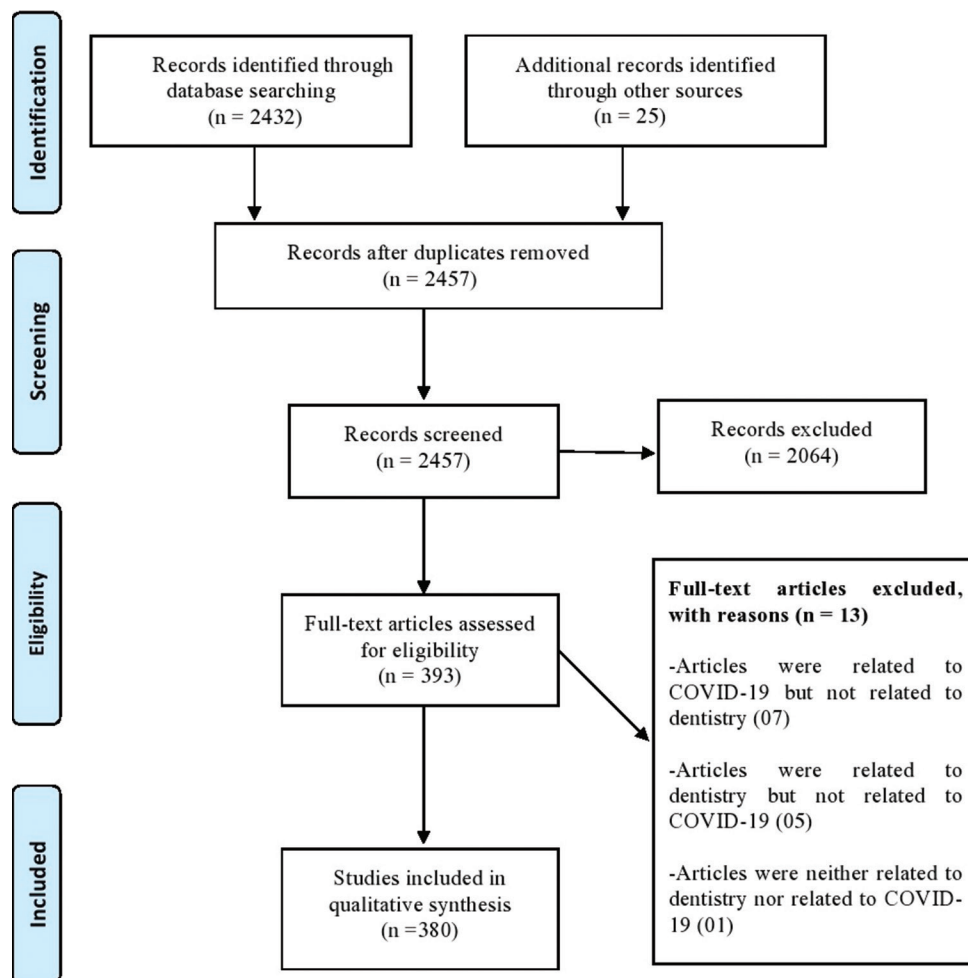


Figure 1: PRISMA flowchart

Table 1: Guidelines issued by various scientific bodies/Organizations/Universities related to dental consideration of coronavirus disease 2019

Scientific body/Organization/University	Month/year	Consensus/evidence based	Dental practitioners	Purpose of guidelines in perspective of SARS-COV-2 infection
Center for Disease Control and Prevention ^[21]	December/2019	Consensus based	General dentists	Infection control and prevention in Dental settings
Polish Dental Association ^[22]	January/2020	Consensus based	General dentists	Infection control and patient management
Chinese Stomatological Association ^[23]	March/2020	Consensus based	General dentists	Infection control in dental practice
American association of Endodontists ^[24]	March/2020	Consensus based	General dentists	Infection control and dental management
American Dental Association ^[25]	March/2020	Consensus based	General dentists	Management of emergency and nonemergency dental procedures
British Dental Association ^[26]	March/2020	Consensus based	General dentists	Management of dental practice
Indian Dental Association ^[27]	March/2020	Consensus based	General dentists	Infection control prevention during dental treatment
University of Washington school of medicine ^[28]	March/2020	Consensus based	Oral maxillofacial surgeons	Preoperative instructions, operator protection, surgery scheduling and training of residents
French Society of Stomatology ^[29]	April/2020	Consensus based	General dentist and Oral and maxillofacial surgeons	Infection control and patient management
Dental Council of India ^[30]	April/2020	Consensus based	General dentists, Dental colleges and students	General and dental treatment consideration
Collaboration of Hadassah School of Dental Medicine (Israel); University of Pennsylvania (USA) and University of Rochester Medical Center (USA) ^[31]	May/2020	Consensus based	Endodontists and Oral maxillofacial surgeons	Operatory and clinical considerations for management
Ministry of Health and Family Welfare, India ^[32]	May/2020	Consensus based	General dentists	Categorization of dental procedures into high, moderate and low risk. Suggested the modifications in dental practice management in preliminary, implementation and follow-up phases

SARS-COV-2: Severe acute respiratory syndrome coronavirus 2


Figure 2: Evidence based pyramid: Dentistry and COVID-19

analysis. However, the remaining articles (*in vitro* studies, case series or case reports, cohort studies, case-control studies, and cross-sectional studies) were included in the quality assessment. The global distribution of studies included in the quality analysis is shown in Figure 3.

Study characteristics

Figure 2 shows the level of evidence of available literature pertaining to the dental perspective of SARS-COV-2. Among the 380 research articles published till July 15, 2020, the

majority of the included articles belonged to the lowermost strata's of the evidence pyramid. There were 54 original articles with no randomized clinical trial, systematic review, or meta-analysis.

It was observed that 12 scientific bodies had issued guidelines/recommendations [Table 1] related to dental perspectives of novel SARS-COV-2 infection.^[21-32] All of them were consensus based and majority had been issued for general dentists with only few targeted for specialists such as oral-maxillofacial surgeons. Majority of them were aimed at infection control and precautions related to dental procedures during SARS-COV-2 pandemic.

The characteristics of questionnaire-based studies are given in Appendix Table 2.^[S14-S38] It was found that nine out of 25 studies had assessed the knowledge, attitude, and behavior of dental professionals regarding COVID-19 infection and reported that majority of the participants were aware of its etiopathogenesis, symptoms, and transmission. Although most of the dental professionals considered it as moderately dangerous and very few were confident of avoiding the infection in their clinics. Six studies which evaluated fear and anxiety among dental professionals and patients

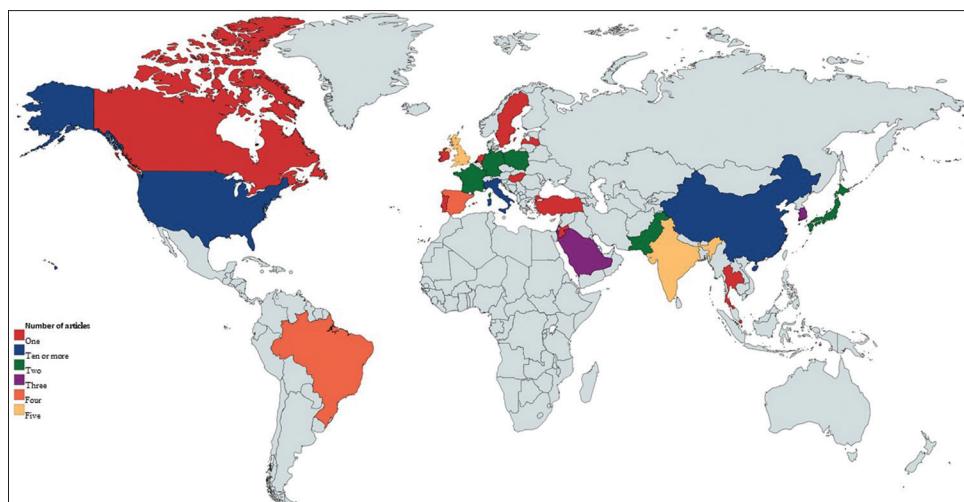


Figure 3: Global distribution of studies included in the quality analysis

undergoing dental treatment reported that the majority of dental professionals were in psychological distress and had changed their patient management protocol. Several of them reported to have performed only the emergency dental procedures in the pandemic. Similarly, patients undergoing treatments in the dental clinics expressed concerns about acquiring SARS-COV-2 infection during their treatments. Majority of them also believed that the dentists belonged to a high-risk category. Appendix Table 2 also described the results of questionnaire-based studies evaluating the impact of COVID-19 pandemic on functioning of dental academic institutions and the knowledge and attitude of the parents of pediatric patients toward dental treatments, appointments, and the oral symptoms associated with the COVID-19 infection.

The results of studies elucidating the role of saliva in detection of COVID-19 and its contagion are presented in Appendix Table 3.^[7,8,9, S39-S54] It was observed that the majority of included studies evaluated the role of saliva in COVID-19 diagnosis and found it to be a reliable method of diagnosis. Similarly, there were studies which compared the reliability of saliva with nasopharyngeal and oropharyngeal swabs. They reported it to be equivalent or slightly less sensitive and/or specific but emphasized its utility as an alternative detection method, due to the ease of collection/self-collection, greater acceptance of the patients and lower risks involved during sample collection.

The included studies comprised of four case reports and case series each related to dentistry and SARS-COV-2 [Table 2].^[33-40] They did not report any specific oral manifestation related to SARS-COV-2 infection. It was further stated that the ones present might have developed as a consequence of the treatment regimen administered. In an assessment of the salivary viral loads, it was reported that early morning

samples were of greater diagnostic importance and showed higher titers of viral RNA as compared to the nasopharyngeal and oropharyngeal swabs in early stage of disease.^[33,34]

The other studies included in this systematic review were focused on the application of tele-dentistry for patient management and the web-based teaching methods for dental students during the SARS-COV-2 pandemic [Table 3].^[41-50] Few *in vitro* and human experiments had also been conducted to evaluate the efficacy of mouthwashes for reducing the viral loads, and reported a positive effect.^[49,50]

Quality assessment of individual studies according to the JBI Critical appraisal tools

There was substantial agreement (75%) between the two reviewers (MR and SG) in quality assessment of the studies. Among the 25 questionnaire-based studies, six were found to have high ROB, while 14 had moderate and five had low ROB [Supplementary Figure 1]. Majority of studies had not assessed the validity and reliability of questionnaires used in their study. Similarly, among the 19 studies which had focused on the potential role of saliva in COVID-19 diagnosis, low ROB was observed in 10 studies, moderate risk bias in nine and none of the included studies had high ROB when assessed for methodological quality [Table 1]. Out of the eight case reports/series, only one case series had moderate ROB while all other had a low ROB [Supplementary Figure 2]. Among the 10 miscellaneous studies included, two had high ROB whereas four each had moderate and low ROB [Table 3].

DISCUSSION

The COVID-19 pandemic has affected the livelihood of almost all the human beings across the globe. Many small-scale and large-scale industries including oral health care have

Table 2: Case reports and case series included in the systematic review

Author/year	Country	Type of study case report/ case series	Age in years/ gender	Focus of interest diagnosis/ clinical manifestations/ management	Main findings	Risk of bias
Tajima <i>et al.</i> /2020 ^[33]	Japan	Case report	71 years/male	Early morning salivary specimen for COVID-19 diagnosis	Early morning salivary specimen were tested negative with RT-PCR only after 39 days	Low
Yoon <i>et al.</i> /2020 ^[34]	Korea	Case series	46 years/female 65 years/female	Viral loads in saliva and nasopharyngeal specimens and effect of chlorhexidine mouthwash on viral loads	Saliva samples had high viral load in early stage of disease compared to oropharyngeal samples Chlorhexidine mouthwash was effective in reducing viral load for short term period	Low
Amorim Dos Santos <i>et al.</i> /2020 ^[35]	Brazil	Case report	67 years/male	Oral mucosal lesion as a secondary manifestation of COVID-19	Recurrent herpes simplex, geographic tongue and candidiasis were the nonspecific oral findings	Low
Martín Carreras-Presas <i>et al.</i> /2020 ^[36]	Spain	Case series	56 years/male 58 years/male 65 years/female	Oral lesions associated with COVID-19 infection	Case 1 and case 2 showed multiple yellowish ulcers with erythematous halo. Case 3 presented with multiple blisters on inner side of lower lip	Moderate
Yang <i>et al.</i> /2020 ^[37]	China	Case report	44 yeas/male	Presence of viral RNA during recovery	Viral RNA was present in throat swab, urine, saliva and salivary titers were extremely high	Low
Han <i>et al.</i> /2020 ^[38]	Korea	Case report	Mother and neonate 27 days old	Assessment of viral load of COVID-19 in in different clinical specimens	COVID-19 was detected in the samples from saliva, urine, nasopharynx, oropharynx, and plasma of neonates. The persistence of high viral load was there in stool even when other specimens were tested negative	Low
Azzi <i>et al.</i> /2020 ^[39]	Italy	Case series	71 years/male 64 years/male	Detection of COVID-19 in saliva and respiratory swabs	Persistence of COVID-19 was detected in saliva in spite of being respiratory swabs found negative	Low
Martínez Lamas <i>et al.</i> /2020 ^[40]	Spain	Case series	74 years/male 73 years/male 43 years/ female 54 years/ female	<i>In vivo</i> evaluate the effectiveness of PVP-I mouthwash against COVID-19	Viral RNA was found in all the cases in baseline saliva samples. In 2 out of the 4 patients. A significant drop in viral load was seen with PVP-I that remain low for at least 3 h	Low

RT-PCR: Reverse transcription polymerase chain reaction, PVP-I: Povidone-iodine, COVID-19: Coronavirus disease 2019

suffered a significant loss during this pandemic. Dentistry, dental practice, and dental practitioners have suffered psychological, emotional, and economic impact primarily due to the scare of the spread of infection associated with the dental procedures along with its potential risk to the dental practitioners. There have been several publications, during this pandemic, which aim to evaluate the potential role of saliva in COVID-19 diagnosis and its comparison with the conventional oropharyngeal and nasopharyngeal swab technique. There were other research articles identifying the oral manifestations of COVID-19, evaluating the impact on dental education and the effect of mouth rinse used for disinfection of oral cavity on COVID-19.

An evidence pyramid helps to categorize the quality of evidence of the published literature addressing a research question. In this systematic review, we have included 380 research articles pertaining to the dental perspective of COVID-19. The present SR observed that the majority of the included articles belonged to the lowest strata of the evidence

pyramid. There were 54 original articles (including two *in vitro* trials) with no randomized clinical trial, systematic review, or meta-analysis published pertaining to the dental aspect of COVID-19 infection. This exhibited significant paucity in the highest level of evidence. This further highlights the avenues for the primary and secondary researches for future.

The review identified 12 different guidelines/recommendations given by various scientific organizations/societies. However, it was observed that all the guidelines were consensus based without any quality evidence supporting them, especially from the literature which already existed before the emergence of COVID-19 infection as a pandemic. Although this is a novel virus, with less available literature/research, these guidelines/recommendations should have been based on the scientific literature related to similar kinds of viruses or the general principles of infection control. This necessitates the need to analyze the researches related to COVID-19 infection and formulate an evidence-based guideline pertaining to dental perspectives of this infection.

Table 3: Other studies conducted on dental/oral perspective of coronavirus disease 2019

Author	Year	Country	Study design	Aim	Results	Risk of Bias
Raja and Shaheed ^[41]	2020	Pakistan	Cross-sectional	Assessment of online available information and its accuracy	4.54% websites had health on the net foundation code of conduct seal, and 10.6% did not fulfill any of the requirements	Moderate
Yang et al. ^[42]	2020	China	Cross sectional	Evaluation of health care services provided by a public tertiary dental hospital	Nonemergency dental services were suspended by all public tertiary dental hospitals and were only performing emergency treatments	Moderate
Guo et al. ^[43]	2020	China	Cross sectional	To evaluate the oral health care management	Dental treatment has not led to infection of COVID-19 among any oral health care worker or patient	High
Xu et al. ^[44]	2020	China	Cross sectional	Assessment of potential route of infection on oral mucosa	Presence of ACE2 receptors on oral mucosa explain SARS-COV-2 infection susceptibility	Low
Carter et al. ^[45]	2020	UK	Cross sectional	Monitoring the patient load and outcomes at a dental care center	Symptomatic irreversible pulpitis/apical periodontitis were the most common diagnoses. About 65% of consultations resulted in extractions and very few require aerosol generating procedures	Low
Liu et al. ^[46]	2020	China	Cross sectional	Assessment of online continuing dental education during epidemic	The offline courses were stopped by all the dental institutions. Total number of online courses before epidemic was 33 which increased to 119 during the epidemic	Moderate
Saccomanno et al. ^[47]	2020	Italy	Cross sectional	Role of tele-orthodontics for patient management during COVID-19 pandemic	Tele-orthodontics require lesser time, decreases risk of infection, minimize the missed appointments and allow more follow-ups	Moderate
Giudice et al. ^[48]	2020	Italy	Cross sectional	Advantages of telemedicine in dental practice during COVID-19	Telemedicine is found to be an effective approach for the management of oral and maxillofacial pathologies, dental fractures, and their follow-up	Low
Bidra et al. ^[49]	2020	USA	In vitro	Effectiveness of H ₂ O ₂ and PVP-I oral rinses for in-vitro inactivation of COVID-19 virus	PVP-I was better than H ₂ O ₂ after 15 s and 30 s contact times at various concentration for virus inactivation	High
Yu et al. ^[50]	2020	China	Cross sectional	Analysis of characteristics of endodontic emergencies	In 53.10% cases symptomatic irreversible pulpitis was the endodontic emergency	Low

PVP-I: Povidone-iodine, SARS-COV-2: Severe acute respiratory syndrome coronavirus 2, COVID-19: Coronavirus disease 2019

The results of questionnaire-based studies have shown that the dental professionals and the patients seeking oral health care are in significant psychological distress in this pandemic. Since the majority of these studies suffered from moderate to high ROB and lacked essential details regarding the development of questionnaires and their validity and/or reliability, it necessitates using caution before drawing any conclusion from these studies. Another interesting observation was that the fear, anxiety, and lack of confidence among dental professionals, even after having good scores of knowledge and attitude related to COVID-19 infection, this can be attributed to the lack of consensus about signs and symptoms of COVID-19 infection, lack of a proper protocol for infection control in dental operatory, and limited belief on the recommendations issued by the scientific associations. It is further warranted that there is a need to perform quality studies to address the concerns of dentists as well as patients coming to the dental operatory to reduce their fear of getting infection in the dental clinics.

According to the results of majority of studies included in this SR, saliva can be recommended as an alternative for the detection of COVID-19 to the nasopharyngeal and oropharyngeal swabs with good sensitivity and specificity. Although 10/19 studies showed low ROB, the sample size

in majority of them was less. Similarly, it was observed that in early period of infection (first week) the saliva has more diagnostic potential as compared to the late stages. The use of the samples from the confirmed patients of COVID-19 can be regarded as a confounding factor, making it a less reliable alternative. Among the other studies, there was variability in research questions, scarcity of numbers and a moderate ROB. These areas must also be addressed in future researches for improving the understanding and management protocols of this infection.

CONCLUSION

1. The level of available evidence pertaining to the dentistry and COVID-19 infection is very low with lack of researches of highest quality
2. The guidelines/recommendations for dental professionals, proposed by the different scientific organizations/societies regarding COVID-19 infection are only consensus-based necessitating the need to formulate evidence-based guidelines
3. The various surveys explain the good knowledge, attitude, and practices among dental professionals and patients; however, they also report significant fear and anxiety in several aspects

4. Saliva can serve as an alternative for diagnostic test of COVID-19 infection, however, there is need to specify indications and appropriate phase of infection for its accuracy
5. There is a need to identify essential research questions and strengthen the study designs in most of the aspects related to the dentistry and COVID-19 pandemic.

LIMITATIONS

1. Inclusion criteria could have been more specific in order to fulfill a single-study objective rather than evaluating the all the published literature
2. As the majority of published literature had low level of evidence and high/moderate ROB making the results of this SR less reliable
3. Like all the evidence mappings, the present SR suffers from the limitation of the date of the last literature search. Since the SARS-CoV-2-related medical and dental literature have been constantly increasing, there would have been some researches which could not be included in the present evidence mapping.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Appendix Table 1: List of excluded studies and reasons for exclusion

List of excluded studies	Reasons for exclusion
Current practice and potential strategy in diagnosing COVID ^[S1]	Articles were related to COVID-19 but not related to dentistry
Integrated sample inactivation, amplification, and Cas13-based detection of SARS-CoV-2 ^[S2]	
Bioinformatics studies on a function of the SARS-CoV-2 spike glycoprotein as the binding of host sialic acid glycans ^[S3]	
Identification of nsp1 gene as the target of SARS-CoV-2 real-time RT-PCR using nanopore whole-genome sequencing ^[S4]	
The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2 ^[S5]	Articles were related to dentistry but not related to COVID-19
Mesenchymal stromal cells and their secreted extracellular vesicles as therapeutic Tools for COVID-19 pneumonia? ^[S6]	
COVID-19 awareness among healthcare students and professionals in Mumbai metropolitan region: A questionnaire-based survey ^[S7]	
Interventions to reduce aerosolized microbes in dental practice: A Systematic review with network meta-analysis of randomized controlled trials ^[S8]	
Evaluation of the spatter-reduction effectiveness and aerosol containment of eight dry-field isolation techniques ^[S9]	Articles were neither related to dentistry nor related to COVID-19
Knowledge and apprehension of dental patients about MERS-A questionnaire survey ^[S10]	
Awareness of droplet and airborne isolation precautions among dental health professionals during the outbreak of corona virus infection in Riyadh city, Saudi Arabia ^[S11]	
Evaluation of preparedness of healthcare student volunteers against MERS-CoV in Makkah, Saudi Arabia: A cross-sectional study ^[S12]	
Aerosol Filtration Efficiency of Common Fabrics Used in Respiratory Cloth Masks ^[S13]	

MERS-CoV: Middle East respiratory syndrome coronavirus, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RT-PCR: Reverse transcription polymerase chain reaction, COVID-19: Coronavirus disease 2019

- S1. Wan DY, Luo XY, Dong W, Zhang ZW. Current practice and potential strategy in diagnosing COVID-19. *Eur Rev Med Pharmacol Sci* 2020;24:4548-53.
- S2. Arizti-Sanz J, Freije CA, Stanton AC, Boehm CK, Petros BA, Siddiqui S, *et al.* Integrated sample inactivation, amplification, and Cas13-based detection of SARS-CoV-2. *Nat Commun* 2020;11:5921.
- S3. Robson B. Bioinformatics studies on a function of the SARS-CoV-2 spike glycoprotein as the binding of host sialic acid glycans. *Comput Biol Med* 2020;122:103849.
- S4. Chan WM, Ip JD, Chu AW, Yip CC, Lo LS, Chan KH, *et al.* Identification of nsp1 gene as the target of SARS-CoV-2 real-time RT-PCR using nanopore whole-genome sequencing. *J Med Virol* 2020;92:2725-34.
- S5. Cheng VC, Wong SC, Chuang VW, So SY, Chen JH, Sridhar S, *et al.* The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2. *J Infect* 2020;81:107-14.
- S6. Muraca M, Pessina A, Pozzobon M, Dominici M, Galderisi U, Lazzari L, *et al.* Mesenchymal stromal cells and their secreted extracellular vesicles as therapeutic tools for COVID-19 pneumonia? *J Control Release* 2020;325:135-40.
- S7. Modi PD, Nair G, Uppe A, Modi J, Tuppekar B, Gharpure AS, *et al.* COVID-19 awareness among healthcare students and professionals in mumbai metropolitan region: a questionnaire-based Survey. *Cureus* 2020;12:e7514.
- S8. Koletsi D, Belibasakis GN, Eliades T. Interventions to reduce aerosolized microbes in dental practice: a systematic review with network meta-analysis of randomized controlled trials. *J Dent Res* 2020;99:1228-38.
- S9. Ravenel TD, Kessler R, Comisi JC, Kelly A, Renne WG, Teich ST. Evaluation of the spatter-reduction effectiveness and aerosol containment of eight dry-field isolation techniques. *Quintessence Int* 2020;51:660-70.
- S10. Ashok N, Rodrigues JC, Azouni K, Darwish S, Abuderman A, Alkaabba AA, *et al.* Knowledge and apprehension of dental patients about MERS-A questionnaire survey. *J Clin Diagn Res* 2016;10:ZC58-62.
- S11. Baseer MA, Ansari SH, AlShamrani SS, Alakras AR, Mahrous R, Alenazi AM. Awareness of droplet and airborne isolation precautions among dental health professionals during the outbreak of corona virus infection in Riyadh city, Saudi Arabia. *J Clin Exp Dent* 2016;8:e379-87.
- S12. Elrggal ME, Karami NA, Rafea B, Alahmadi L, Al Shehri A, Alamoudi R, *et al.* Evaluation of preparedness of healthcare student volunteers against Middle East respiratory syndrome coronavirus (MERS-CoV) in Makkah, Saudi Arabia: A cross-sectional study. *Z Gesundh Wiss* 2018;26:607-12.
- S13. Konda A, Prakash A, Moss GA, Schmoldt M, Grant GD, Guha S. Aerosol filtration efficiency of common fabrics used in respiratory cloth masks. *ACS Nano* 2020;14:6339-47.

Appendix Table 2: Questionnaire-based surveys pertaining to dentistry and severe acute respiratory syndrome coronavirus 2

Author/year/Country	Aim	Sample population	Sample size	Distribution	Type of questions	Number of questions	Validity of questionnaire	Reliability of questionnaire	Results	Risk of bias
Biadsee <i>et al.</i> /2020/ Israel ^[S14]	To assess the early manifestations of COVID-19, with an emphasis on olfactory and oral disorders	COVID-19 patients	128	Online	Objective	31	Yes	Yes	25.8% patients had olfactory and taste dysfunctions as only symptom and 38.3% of cases reported initial symptom as an olfactory dysfunction. In overall, 56% of patients reported with xerostomia	Low
Kamate <i>et al.</i> /2020/ India ^[S15]	To assess the KAP of dental practitioners regarding COVID-2019 pandemic	Dental practitioners (multiple countries)	860	Online	Objective	24	Yes	Yes	Good knowledge and practice scores were observed among 92.7% and 79.5% of dentists, respectively. Good knowledge scores were significantly associated with qualifications and years of practice. Good practice scores were associated with qualifications only	Low
Duruk <i>et al.</i> /2020/ Turkey ^[S16]	To investigate kind of precautions Turkish dentists, take in dental clinics during the COVID-19 pandemic	Dentists	1958	Online	Objective	23	Yes	Yes	Dentists' self-assessed COVID-19 knowledge scores from 1 to 5 were 59.2%, 15.3%, 8.8%, 9.9%, and 6.8%, respectively. Only 26.65% of dentists attended an informational meeting on COVID-19 and 15.39% had informed their patients about COVID-19	Moderate
Sun <i>et al.</i> /2020/ China ^[S17]	To evaluate knowledge of and attitudes toward COVID-19 among parents of child dental patients	Parents of children undergoing dental treatment	148	Telephone interview	Objective	10	Not mentioned	Not mentioned	About 66.22% parents were of opinion that environment of dental department is more dangerous compared to public places. However, 83.78% would take their children to dental treatment in case of severe toothache	Moderate
Peloso <i>et al.</i> /2020/ Brazil ^[S18]	To evaluate impact of quarantine resulting from the COVID-19 pandemic on dental appointments and patients' positions and concerns regarding their ongoing dental treatment	Patients requiring dental treatment	595	Online	Objective	12	Not mentioned	Yes	38.3% patients said they would attend their scheduled dental appointment. Those have concern were worried about risk of getting infected and/or contaminating their family members (18.5%). Only 5% were of opinion that dentists belongs to a group having high risk of contamination	Moderate

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Appendix Table 2: Contd...

Author/year/Country	Aim	Sample population	Sample size	Distribution	Type of questions	Number of questions	Validity of questionnaire	Reliability of questionnaire	Results	Risk of bias
Putrino et al./2020/ Italy ^(S19)	To assess the Knowledge, management of patients and clinical experience of Italian dentists during COVID-19	Dentists	535	Online	objective	24	Yes	Yes	50% of dentists not noticed any decrease in number of patients visiting in the outbreak. According to clinician's majority of would not be worried about getting coronavirus infection during dental treatment. Regarding definition, 73% correctly answered about the coronavirus. 63.2 about nCoV and 44.1% about SARS-CoV-2	Low
Quinn et al./2020/ Europe ^(S20)	To carry out an investigation to assess the immediate response of the European Academic Dental Institutions	Dental institutions	69	Online	Single answer and objective	Not mentioned	Yes	Not mentioned	90% of schools used the online pedagogical software tools further using live or streamed videos (72%), links to online materials (48%), and virtual meetings (65%) and less frequently small-scale working groups, journal club or social media groups	High
Ahmed et al./2020/ Multiple Countries ^(S21)	To evaluate Fear and Practice Modifications among Dentists to Combat n-COV Outbreak	Dentists	650	Online	Objective	22	Yes	Not mentioned	78% general dentists from 30 countries were anxious and scared by effects of COVID-19. 90% dentists were aware about the changes in treatment protocols. Dental practices have either modified their services according to the emergency treatment recommended guidelines or closed down their practices	Low
Shacham et al./2020/ Israel ^(S22)	To assess the COVID-19 and Psychological Factors Associated with Elevated Distress among Dentists and Dental Hygienists	Dentists and Dental Hygienists	338	Online	Objective	20	Not mentioned	Yes	Risk of elevated psychological distress was found in 11.5% and was found among those who have background illness, fear of contracting COVID-19 from a patient and higher subjective overload	Moderate

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Appendix Table 2: Contd...

Author/year/Country	Aim	Sample population	Sample size	Distribution	Type of questions	Number of questions	Validity of questionnaire	Reliability of questionnaire	Results	Risk of bias
Cagetti <i>et al.</i> /2020/ Italy ^[S23]	To assess the symptoms/signs, protective measures, awareness, and perception levels regarding COVID-19 among dentists	Dentists	3599	Online	Objective	12	Yes	Yes	502 dentists suffered one or more symptoms related to COVID-19 and 31 were positive for virus SARS-CoV-2 and 16 had developed the disease. Only 2% of dentists were confident about avoiding infection	Moderate
De Stefani <i>et al.</i> /2020/ Italy ^[S24]	To evaluate dentists' knowledge regarding COVID-19 and perception of risks, their attitude in resuming their activities	Dentists	1500	Online	Objective	29	Not mentioned	Not mentioned	64.3% dentists were been trained for prevention of infection but not specifically for COVID-19. About 57.2% said they were trained insufficiently to restart their work after lockdown	Moderate
Tysiac-Mista <i>et al.</i> 2020/Poland ^[S25]	To evaluate attitudes and professional approaches of Dental Practitioners during the COVID-19 Outbreak	Dental practitioner	875	Online	Objective	Not mentioned	Not mentioned	Yes	71.2% dentists responded decided to suspend the clinical practice during outbreak. Factors responsible were the shortage of PPE. There was significant decrease in patients number admitted weekly in pandemic compared to before	Moderate
Costa <i>et al.</i> /2020/ Brazil ^[S26]	To evaluate the knowledge of OMFS professionals about the pandemic status of the COVID-19	Oral and maxillofacial surgeons	142	Online	Not mentioned	Not mentioned	Not mentioned	Not mentioned	About transmission most known were droplet inhalation (98.6%) oral mucous membrane (89.4%), cough (85.6%), and mucous membrane of eyes (33.8%). About symptom awareness, fever (98.6%) followed by dry cough (88.7%). Majority of the OMFS were of opinion that COVID-19 not associated with any oral manifestations	High
Van Doren <i>et al.</i> /2020/USA ^[S27]	To evaluate how the pandemic has affected dental education and how students regard these changes	Dental students	63	Online	Objective	Not mentioned	Not mentioned	Not mentioned	Majority opine that didactic learning had not changed, however, there was worsening of preclinical learning. Respondents believe that lacked hands-on, clinical experience do give patient clinical experience although many said that virtual case discussions teaching was critical	High

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Appendix Table 2: Contd...

Author/year/Country	Aim	Sample population	Sample size	Distribution	Type of questions	Number of questions	Validity of questionnaire	Reliability of questionnaire	Results	Risk of bias
Schwendicke <i>et al.</i> /2020/ ^[S28] Germany	To assess the economic impact of such policies on dental practices in Germany using a modeling approach	Dentists	146	Telephonic interview	Both Objective and nonobjective	Not mentioned	Not Mentioned	Not mentioned	The results found that within base-case, the mean revenue reductions were 18.7%/15.7% from the public insurance, it was 18.7/18.6% from the private insurers and was 19%/19% for out-of-pocket expenses in the low/high volume practices respectively	Moderate
Blackhall <i>et al.</i> /2020/ ^[S29] United Kingdom	To analyze the pattern of presentation and management of maxillofacial emergencies during the lockdown	OMFS patients during pandemic	529 patients	Smartphone based database	Objective	Not mentioned	Not mentioned	Not mentioned	Among 529, 395 patients attended the physical and 134 received online remote consultations with telephone or video link. Among patients 255 were trauma related, 221 were infection and 48 were postoperative complications. Among those had physical consultations, according to clinicians 17% could have managed with remote consultation	Moderate
Quadri <i>et al.</i> /2020/ ^[S30] Saudi Arabia	To investigate current knowledge on COVID-19 among dental health-care workers and conduct quasi-experiment among who were unaware of information	Dental interns, auxiliaries, and specialists	706	Online and via Email	Objective	17	Yes	Yes	The knowledge was related to the qualification levels (interns vs. auxiliaries vs. specialists). After intervention the number of participants with correct responses to knowledge questions had increased significantly	Moderate
Cotrin <i>et al.</i> /2020/ ^[S31] Brazil	To evaluate the impact of coronavirus pandemic and quarantine in orthodontic appointments, and patients' anxiety	Patients undergoing orthodontic treatment	354	Online	Objective	11	Not mentioned	Not mentioned	78.2% were going out only when needed, 13.0% were not leaving home and 8.8% were going outside home as usual without respecting quarantine.	Moderate

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Appendix Table 2: Contd...

Author/year/Country	Aim	Sample population	Sample size	Distribution	Type of questions	Number of questions	Validity of questionnaire	Reliability of questionnaire	Results	Risk of bias
	and concerns about their ongoing orthodontic treatment								44.7% were calm, 23.4% were afraid (fear), 22.9% are anxious, 5.6% were indifferent and 3.4% were panic when asked about anxiety and feeling about coronavirus pandemic	
Khader <i>et al.</i> /2020/ Jordan ^[S32]	To assess the level of awareness, perception, and attitude regarding the COVID-19 and infection control	Dentists	368	Online	objective	Not mentioned	Not mentioned	Not mentioned	Majority reported to have fever and cough as symptoms. About 1/3rd of dentists said that patients with COVID-19 and may present with no symptoms. 316 (85.9%) aware of symptoms of respiratory infection, 94.3% aware of history of travel to areas of transmission, and 93.8% mentioned history of contact with the infected patients. 17.7% of 368 dentists see COVID-19 as very dangerous, 71.7% as moderately dangerous, and 35 (9.5%) as not dangerous	Moderate
Abbasi <i>et al.</i> /2020/ Pakistan ^[S33]	To determine the perceptions of students towards e-learning during the lock down	MBBS and BDS students	382	Email	Objective	22	Yes	Yes	Among 382 participants, 76% were using mobile for e-learning whereas 75.7% of participants had negative attitude towards e-learning	Moderate
Gambhir <i>et al.</i> /2020/ India ^[S34]	To assess the knowledge, awareness and hygiene practices regarding COVID-19 among private dental practitioners in India	Dentists (Chandigarh, Panchkula and Mohali)	215	Email and WhatsApp	Objective	15	Yes	Yes	87% and 82.5% subjects respectively answered correctly about the main symptoms of COVID-19 and primary mechanism of transmission. 1/3rd of dentists were unaware about use of PPE during dental treatment	Low
Consolo <i>et al.</i> /2020/ Italy ^[S35]	To investigate dentist behavior and analyze their reactions in relation to SARS-CoV-2 pandemic restrictive measures introduced by national administration	Dental practitioner	356	Online	Objective	40	Not mentioned	Not mentioned	63.5% dentists were working for 30-40 h or more per week whereas other were working <30 h per week. Almost all of the respondents closed or reduced their activity to urgent procedures only. About 92.7% patients had cancelled their appointments	High

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Appendix Table 2: Contd...

Author/year/Country	Aim	Sample population	Sample size	Distribution	Type of questions	Number of questions	Validity of questionnaire	Reliability of questionnaire	Results	Risk of bias
Martina <i>et al.</i> /2020/ Italy ^[536]	To assess dentist's anxiety about returning to their daily activities, and what perception of the risk is for dentists and orthodontists	Dentists	349	online	Objective	31	Not mentioned	Not mentioned	112 dentists reported no distress, 160 had slight distress, 58 had moderate distress, and 19 had severe distress. Returning to the daily clinical activity was a source of anxiety for 192 which was associated with level of their distress	High
González-Olmo <i>et al.</i> /2020/Spain ^[537]	To identify impact of COVID-19 on self-perceived vulnerability, infectiousness, aversion to germs, and other behaviors regarding dental practice	Normal population	1008	Personal interview	Objective	13	Yes	Not mentioned	A significant difference was seen by gender on the germ aversion subscale and in risk of waiting in the waiting area tooth extraction, endodontics and fillings. Women consider risk to be higher compared to men. Those above 60 years and with systemic disease had significant differences on subscales of infectivity and germ aversion	Moderate
Huntley <i>et al.</i> /2020/ USA ^[538]	To understand effect of the COVID-19 pandemic on OMFS residency	Oral maxillofacial surgery residents and post docs	174	Email	Open and closed ended	51	Not mentioned	Not mentioned	96.5% reported modifications in their training program. N95 respirator mask plus standard PPE precautions while aerosol-generating procedures get varied by procedure locations and 36.8% reporting limited access to the respirators. Residents scheduled to graduate in 2022 were most concerned with completion of graduation and decreased operative experience	High

KAP: Knowledge, Attitudes, and Practices, COVID-19: Coronavirus disease 2019, OMFS: Oral and maxillofacial surgery, PPE: Personal protective equipment, SARS-COV-2: Severe acute respiratory syndrome coronavirus 2

- S14. Biadsee A, Biadsee A, Kassem F, Dagan O, Masarwa S, Ormianer Z. Olfactory and oral manifestations of COVID-19: Sex-related symptoms-a potential pathway to early diagnosis. *Otolaryngol Head Neck Surg* 2020;163:722-8.
- S15. Kamate SK, Sharma S, Thakar S, Srivastava D, Sengupta K, Hadi AJ, *et al.* Assessing knowledge, attitudes and practices of dental practitioners regarding the COVID-19 pandemic: A multinational study. *Dent Med Probl* 2020;57:11-7.
- S16. Duruk G, Gümüşboğa ZŞ, Çolak C. Investigation of Turkish dentists' clinical attitudes and behaviors towards the COVID-19 pandemic: A survey study. *Braz Oral Res* 2020;34:e054.
- S17. Sun J, Xu Y, Qu Q, Luo W. Knowledge of and attitudes toward COVID-19 among parents of child dental patients during the outbreak. *Braz Oral Res* 2020;34:e066.
- S18. Peloso RM, Pini NIP, Sundfeld Neto D, Mori AA, Oliveira RCG, Valarelli FP, *et al.* How does the quarantine resulting from COVID-19 impact dental appointments and patient anxiety levels? *Braz Oral Res* 2020;34:e84.
- S19. Putrino A, Raso M, Magazzino C, Galluccio G. Coronavirus (COVID-19) in Italy: Knowledge, management of patients and clinical experience of Italian dentists during the spread of contagion. *BMC Oral Health* 2020;20:200.
- S20. Quinn B, Field J, Gorter R, Akota I, Manzanares MC, Paganelli C, *et al.* COVID-19: The immediate response of european academic dental institutions and future implications for dental education. *Eur J Dent Educ* 2020;24:811-4.
- S21. Ahmed MA, Jouhar R, Ahmed N, Aber H, Khawaja S, El Abed R, *et al.* Fear and practice modifications among dentists to combat novel coronavirus disease (COVID-19) outbreak. *Int J Environ Res Public Health* 2020;17:2821.
- S22. Shacham M, Hamama-Raz Y, Kolerman R, Mijiritsky O, Ben-Ezra M, Mijiritsky E. COVID-19 factors and psychological factors associated with elevated psychological distress among dentists and dental hygienists in Israel. *Int J Environ Res Public Health* 2020;17:2900.
- S23. Cagetti MG, Cairoli JL, Senna A, Campus G. COVID-19 outbreak in north Italy: an overview on dentistry: A questionnaire Survey. *Int J Environ Res Public Health* 2020;17:3835.
- S24. De Stefani A, Bruno G, Mutinelli S, Gracco A. COVID-19 Outbreak Perception in Italian Dentists. *Int J Environ Res Public Health* 2020;17:3867.
- S25. Tysiąc-Miśta M, Dziedzic A. The Attitudes and Professional Approaches of Dental Practitioners during the COVID-19 Outbreak in Poland: A Cross-Sectional Survey. *Int J Environ Res Public Health* 2020;17:4703.
- S26. Costa SM, Lacerda GT, Villafort RN, Silveira RL, Amaral MBF. What do we know about COVID-19?: Maxillofacial surgeons survey. *J Craniofac Surg* 2020;31:e661-3.
- S27. Van Doren EJ, Lee JE, Breitman LS, Chutinan S, Ohyama H. Students' perceptions on dental education in the wake of the COVID 19 pandemic. *J Dent Educ*. 2020 Jul 5;10.1002/jdd.12300. doi: 10.1002/jdd.12300.
- S28. Schwendicke F, Krois J, Gomez J. Impact of SARS-CoV2 (Covid-19) on dental practices: Economic analysis. *J Dent* 2020;99:103387.
- S29. Blackhall KK, Downie IP, Ramchandani P, Kusanale A, Walsh S, Srinivasan B, *et al.* Provision of emergency maxillofacial service during the COVID-19 pandemic: A collaborative five centre UK study. *Br J Oral Maxillofac Surg* 2020;58:698-703.
- S30. Quadri MF, Jafer MA, Alqahtani AS, Al Mutahar SA, Odabi NI, Daghriri AA, *et al.* Novel corona virus disease (COVID-19) awareness among the dental interns, dental auxiliaries and dental specialists in Saudi Arabia: A nationwide study. *J Infect Public Health* 2020;13:856-64.
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Appendix Table 3: Salivary implications in the diagnosis of SARS-CoV-2 infection

Author	Country	Aim	Comparison (method of assessment)	Results	Conclusion	Study design	Risk of Bias
Wei et al. ^[7]	USA	Evaluation of Field deployable, rapid diagnostic testing of saliva samples for SARS-CoV-2	None (HP-LAMP)	Authors developed HP-LAMP, which enables rapid detection of SARS-CoV-2 directly from saliva in 30 min. This is a simple one-step protocol with a LoD of 2 viral copies per μ L of saliva. The sensitivity was 97% whereas specificity was 100%	This simple method can be easily scaled and deployed to points-of-care, laboratories and locations where testing is greatly needed	Cross sectional (<i>in vitro</i>)	Moderate
Wong et al. ^[8]	Hong Kong	To evaluate POPS for SARS-CoV 2 detection among patients with confirmed or suspected COVID-19	POPS versus nasopharyngeal specimen (rRT-PCR)	A total of 13,772 specimens were identified during study period, including 2130 POPS for severe acute and 8438 NPsp. The 229 same-day POPS-NPsp paired were identified with POPS and NPsp positivity of 61.5% and 53.3%. Negative and positive percent agreement were 76.0%, 65.4%, and 85.2%. Positive agreement was seen in POPS-NPsp tested within 7 days (96.6%) compared to those after 7 days of symptom onset (75.0%) and the overall higher Cp values were seen in NPsp. No significant variation was noted between two types of specimen	POPS is an acceptable alternative specimen to nasopharyngeal specimen for the detection of SARS-CoV-2.	Cross sectional retrospective	Low
Jamal et al. ^[9]	Canada	To compare sensitivity of NPS and saliva for SARS-CoV-2 detection in hospitalized patients	Saliva versus NPSs (RT-PCR)	Out of 91 patients tested positive using NP, mid-turbinate, or nasal swab tested, on admission, 66 (73%) had fever and 68 (75%) had cough. The median time from illness onset to hospital admission was 6 days and 27 (30%) required intensive care. The median time from illness onset to collection of the tested specimens was 12 days. The 3% remained hospitalized, 90% were discharged, and 7% had died	NP swabs were more sensitive than saliva for SARS-CoV-2 detection, particularly among patients beyond the first week of illness	Cross sectional	Low
Chen et al. ^[33]	China	To assess use of POPS as specimens for the detection of SARS-CoV-2 in automated point of care molecular assay.	POPS versus NPS (RT-PCR and Xpert Xpress SARS-CoV-2 assay)	SARS-CoV-2 was detected in either NPS or saliva specimens of all patients. Among them, 84.5% tested positive in both NPS and saliva, 10.3% tested positive in NPS only, and 5.2% tested positive in saliva only. No significant difference was seen in the detection rate between NPS and saliva. The rate of detection was slightly higher for N2 (NPS 94.8% and saliva 93.1%) than that of the E gene target (Saliva: 89.7% vs. 82.8%) on both specimen types	The POPS and NPS were found to have similar detection rates in the point-of-care test for SARS-CoV-2 detection	Cross sectional	Low
Wong et al. ^[34]	China	To assess comparability of DTS samples to NPS samples as an alternative for the detection of SARS-CoV-2 by RT-PCR	DTS versus NPS (RT-PCR)	In the study matched paired DTS and NPS specimens from 62 patients were analyzed. The rates of detection for DTS (53.7%) and NPS (47.4%) samples were comparable	SARS-CoV-2 detection by RT-PCR was equivalent in DTS and NPS specimens	Cross sectional retrospective	Moderate

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Appendix Table 3: Contd...

Author	Country	Aim	Comparison (method of assessment)	Results	Conclusion	Study design	Risk of Bias
Pasomsub <i>et al.</i> [541]	Thailand	To investigate the potential use of saliva samples as a noninvasive tool for the diagnosis of COVID-19	Saliva versus NP and throat swabs (RT-PCR)	The prevalence of COVID-19 diagnosed by NPS and throat swab using RT-PCR was 9.5%. Sensitivity and specificity of the saliva by RT-PCR was 84.2% and 98.9% respectively. An analysis of the agreement of 97.5% was observed between the two specimens	Saliva might be an alternative specimen for the diagnosis of COVID-19. The collection is noninvasive, and nonaerosol generating	Cross sectional	Low
Azzi <i>et al.</i> [542]	Italy	To analyze saliva collected from patients already diagnosed with COVID-19 and compare results with their clinical data and laboratory data	Saliva versus clinical data and laboratory data (RT-PCR, CRP and LDH levels)	Twenty-five subjects were recruited in this study. All the samples tested positive for presence of SARS-CoV-2, while there was an inverse association between LDH and Ct values	Saliva is a reliable tool to detect SARS-CoV-2	Cross sectional	Low
Chu <i>et al.</i> [543]	China	To compare the results of SARS-CoV-2 RT-PCR using different simple nucleic acid extraction methods on nasopharyngeal and saliva specimens	Saliva versus NPS (RT-PCR and pretreatment with proteinase K and heat)	PKH had significantly higher positive detection rate in (80%) than those of heat only (58%) or direct (56%). The median Ct value was significantly earlier for PKH compared to that of heat only and direct	PKH preprocessing resulted in the highest detection rate of SARS-CoV-2 by RT-PCR, and represents an alternative method for nucleic acid extraction	Cross sectional	Low
To <i>et al.</i> [544]	China	To ascertain the serial respiratory viral load of SARS-CoV-2 in POPS samples from patients with COVID-19, and serum antibody responses	Blood versus urine versus POPS versus Rectal swabs (RT-qPCR and EIA)	Salivary viral load was high during the first week of symptoms onset and subsequently declined. Older age was correlated with higher viral load. For 16 cases with serum samples available, 14 days or longer after symptom onset, rates of seropositivity was 94% for anti-NP IgG ($n=15$), 88% for anti-NP IgM ($n=14$) whereas it was 100% for anti-RBD IgG ($n=16$), and 94% for anti-RBD IgM ($n=15$)	POPS samples are a noninvasive specimen more acceptable to patients and health-care workers	Cross sectional	Low
Azzi <i>et al.</i> [545]	Italy	Diagnostic accuracy study to validate the use of a RST as a point-of-need antigen test suitable for a mass screening program	RST versus salivary (rRT-PCR, LFA)	Sensitivity of RST was 0.93, while its specificity 0.42. There were not differences among the asymptomatic and symptomatic individuals. The two subjects who were classified as false negatives tested also negative by salivary rRT-PCR, thus the viral RNA was not detected in the saliva. The 57% of false positive cases had their saliva positive also when observed with rRT-PCR	The RST based on LFA to detect the presence of SARS-CoV-2 may represent an innovative step in the diagnosis of the infection	Cross sectional	Moderate
Zhu <i>et al.</i> [546]	China	Evaluation of clinical performance of saliva in comparison with paired respiratory tract specimens in a larger cohort of patients with COVID-19, and analyzed the temporal change	Saliva versus respiratory tract sample (rRT-PCR)	Among, 442 cases diagnosed with RT-PCR with respiratory tract sample, 382 were SARS CoV-2 positive in both saliva and respiratory tract specimens. 60 patients tested positive with respiratory tract samples. When compared with respiratory tract samples, the sensitivity and specificity of saliva was 86.4% and 97.0% respectively. Analysis of the concordance revealed	Saliva might serve as a substitutable choice for diagnosis by using respiratory tract specimens with comparable performance. Salivary viral load peaked	Cross sectional	Moderate

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Appendix Table 3: Contd...

Author	Country	Aim	Comparison (method of assessment)	Results	Conclusion	Study design	Risk of Bias
Iwasaki <i>et al.</i> ^[547]	Japan	in viral loads and its correlation with severity of illness in saliva To confirm saliva is a noninvasive and reliable alternative to NPSs and facilitate widespread PCR testing in the face of shortages of swabs and protective equipment without posing a risk to health-care workers	Saliva versus NPS (RT-qPCR)	a 92.1% virus detection accuracy and a firm agreement (Cohen's kappa coefficient 0.84) of diagnosis between the respiratory tract and saliva sample SARS-CoV-2 was detected in 8 out of 10 patients in both nasopharyngeal and saliva samples. The overall concordance rate of the virus detection was 97.4%. The viral loads were nearly similar in two samples with mean 5.4 ± 2.4 and 4.1 ± 1.4 log 10 gene copies/ml in NPS and saliva, respectively. CT values were not significantly different with mean 26.5 ± 8.1 and 30.6 ± 4.6 . The viral loads were equivalent between the two samples initially but declined in saliva later	during the 1st week of symptoms and gradually declined over time The study results support the use of saliva as a noninvasive alternative to NPSs to greatly facilitate widespread PCR testing in the face of shortages of swabs and protective equipment	Observational cohort	Moderate
Randad <i>et al.</i> ^[548]	USA	Evaluation of correlation of results of saliva versus serum and to determine the sensitivity and specificity for each diagnostic media, stratified by antibody isotype, for detection of SARS-CoV-2 infection based on COVID-19 case designation for all specimens	Saliva versus serum (multiplex SARS-CoV-2 antibody immunoassay, RT-PCR)	Matched serum and saliva SARS-CoV-2 antigen-specific IgG responses were significantly correlated. The salivary anti-nucleocapsid (N) protein IgG response resulted in the highest sensitivity for detecting prior SARS-CoV-2 infection (100% sensitivity at ≥ 10 days symptom onset). The salivary anti-receptor binding domain IgG response resulted in 100% specificity. Among individuals with SARS-CoV-2 infection confirmed with RT-PCR, the temporal kinetics of IgG, IgA, and IgM in saliva were consistent with those observed in serum. SARS-CoV-2 appears to trigger a humoral immune response resulting in the almost simultaneous rise of IgG, IgM and IgA levels both in serum and in saliva	SARS-CoV-2 antibody testing in saliva can play a critically important role in large-scale serosurveillance to address key public health priorities and guide policy and decision-making for COVID-19	Cross sectional	Moderate
Valentine-Graves <i>et al.</i> ^[549]	USA	To assess the participant-reported acceptability of self-specimen collection and participant suggestions to improve the self-collection and shipping process	Self-collected Saliva versus OPS versus DBS (samples for PCR, antibody testing)	>84% participants reported collecting, packing and shipping of saliva, OPS, and DBS specimens were acceptable. There were no differences in acceptability for any specimen type, packing and shipping, or confidence in samples by gender, age, race/ethnicity, or educational level	Self-collection of specimens for testing, preparing and shipping for analysis were acceptable in the diverse group of US adults	Cross sectional	Low
Faustini <i>et al.</i> ^[550]	United Kingdom	To detect the antibodies to the SARS-CoV-2 spike glycoprotein in both serum and saliva enhances detection of infection	Saliva versus serum (RT-PCR, ELISA)	The IgG1 and IgG3 predominate to both antigens, but more anti-spike IgG1 than IgG3 were detectable. All antigens response was helpful for detecting responses in hospitalized subjects. The Anti-spike, but not nucleocapsid, IgG, IgA and IgM antibody responses were readily detectable in saliva from nonhospitalized symptomatic and asymptomatics. Antibody responses in saliva and serum were independent of symptoms and each other	Detection of antibody response in both saliva and serum is optimal for determining virus exposure. It also helps to understand and understands the immune responses after infection	Cross sectional	Low

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Appendix Table 3: Contd...

Author	Country	Aim	Comparison (method of assessment)	Results	Conclusion	Study design	Risk of Bias
Hung <i>et al.</i> ^[521]	China	To evaluate Early-Morning and Spot POPS for Diagnosis of SARS-CoV-2 Infection	Early-morning versus spot POPS (RT-PCR, Ct value)	There was an overall trend of lower Ct values from specimens collected in the early morning, with a gradual decrease of viral load towards night time, but reaching statistical significance only when compared with the specimens collected at bedtime. The 8 of 13 subjects had a higher viral load in early morning than rest of the 4 time points	A diurnal variation of viral shedding from upper respiratory tract with a trend showing higher viral load in early morning	Cross sectional	Moderate
Lamb <i>et al.</i> ^[522]	USA	To develop a rapid screening diagnostic test that could be completed in 30-45 min	Serum versus urine versus saliva versus OPSS versus NPSs (RT-LAMP, qRT-PCR)	RT-LAMP specifically detected SARS-CoV-2 in both clinical specimens and simulated patient samples. RT-LAMP could be successfully completed using human serum, urine, saliva, OPSS, and NPSs. The samples that were positive by RT-LAMP all had a high level of viremia, as indicated by the cycle threshold values <24 Ct by qRT-PCR whereas all samples negative by RT-LAMP had a Ct value > 24 Ct by qRT-PCR	This simple assay could be used outside of a central laboratory on various types of biological samples. This assay can be completed by individuals without specialty training or equipment	Cross sectional	Moderate
Kam <i>et al.</i> ^[523]	Singapore	To evaluate the presence of SARS-CoV-2 in buccal specimens in COVID-19-infected children	Buccal swab versus NPSs (rRT-PCR, Ct values)	Out of 11 children, six were asymptomatic, and 5 symptomatic children had a mild course of illness. SARS-CoV-2 was detected from at least 1 buccal specimen in 9 of 11 children (81.8%). One asymptomatic child with nasopharyngeal Ct values of 33.0 and 30.0 on days 1 and 2 of diagnosis, respectively, had undetectable buccal SARS-CoV-2. Another symptomatic child with nasopharyngeal Ct values of 26.9 and 32.6 on days 2 and 3 of illness, respectively, had undetectable buccal SARS-CoV-2. In the 9 infected children with detectable SARS-CoV-2 in buccal specimens, the mean difference of Ct values between buccal and nasopharyngeal specimens for all infected patients was 10.7 and this was statistically significant. There was a general trend for buccal specimens to contain lower SARS-CoV-2 viral loads (higher Ct values) compared with nasopharyngeal specimens. During the first week of illness/diagnosis, sensitivity of buccal swabs compared with NPS was from 25% to 71.4% on different days of collection	Buccal specimens yielded substantially lower viral loads and had poor sensitivity compared with NPS	Cross sectional	Low

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Appendix Table 3: Contd...

Author	Country	Aim	Comparison (method of assessment)	Results	Conclusion	Study design	Risk of Bias
Han et al. ^[554]	South Korea	To evaluate RNA Load in Symptomatic and Asymptomatic Children with COVID-19	Saliva versus NPSs Feces (RNA detection Allplex 2019-nCoV Assay kit)	Symptomatic children had higher initial RNA load in NPS specimens than asymptomatic. Viral RNA was detectable at high concentration for >3 weeks in fecal samples from 12 (92%) mildly symptomatic and asymptomatic children with COVID-19. In saliva, SARS-CoV-2 RNA was detected during the early phase of the infection for a short period of time	Feces is a promising and reliable source for detecting both current and recent SARS-CoV-2 infection because the viral RNA is present in high loads for a prolonged time	Observational cohort	Moderate

NPSs: Nasopharyngeal swabs, OPSs: Oropharyngeal swabs, RST: Rapid salivary test, DBS: Dried blood sample, DTS: Deep throat saliva, RT-PCR: Reverse transcription polymerase chain reaction, rRT-PCR: Real-time RT-PCR, RT-qPCR: Reverse transcription quantitative polymerase chain reaction, RT-LAMP: Reverse transcriptase loop-mediated isothermal amplification technique, Ct value: Cycle threshold value, HP-LAMP: High performance loop-mediated isothermal amplification, POPS: Posterior oropharyngeal saliva, NPSP: Nasopharyngeal specimen, PKH: Proteinase K Heat, LFA: Lateral flow assay, EIA: Enzyme immunoassay, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, COVID-19: Coronavirus disease 2019, LoD: Limit of detection, LDH: Lactate Dehydrogenase

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Author	Year	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	Score	Risk of bias
Biadsee et al.	2020									100	Low
Kamate et al.	2020									87.5	Low
Duruk et al.	2020									50	Moderate
Sun et al.	2020									62.5	Moderate
Peloso et al.	2020									62.5	Moderate
Putrino et al.	2020									75	Low
Quinn et al.	2020									12.5	High
Ahmed et al.	2020									87.5	Low
Shacham et al.	2020									50	Moderate
Cagetti et al.	2020									62.5	Moderate
Stefani et al.	2020									62.5	Moderate
Tysiac-Mista et al.	2020									50	Moderate
Costa et al.	2020									0	High
Van Doren et al.	2020									0	High
Schwendicke et al.	2020									62.5	Moderate
Quadri et al.	2020									50	Moderate
Cotrin et al.	2020									50	Moderate
Gambhir et al.	2020									75	Low
Consolo et al.	2020									37.5	High
Martina et al.	2020									37.5	High
Olmo et al.	2020									62.5	Moderate
Huntley et al.	2020									25	High
Abbasi et al.	2020									62.5	Moderate
Khader et al.	2020									62.5	Moderate

Supplementary Figure 1: Risk of bias analysis of included questionnaire-based surveys

Questions	Tajima et al./2020	Santos et al./2020	JR Yang et al./ 2020	MS Han et al./ 2020
Were patient's demographic characteristics clearly described?				
Was the patient's history clearly described and presented as a timeline?				
Was the current clinical condition of the patient on presentation clearly described?				
Were diagnostic tests or methods and the results clearly described?				
Was the intervention(s) or treatment procedure(s) clearly described?	Not applicable			Not applicable
Was the post-intervention clinical condition clearly described?				Not applicable
Were adverse events (harms) or unanticipated events identified and described?				
Does the case report provide takeaway lessons?				
Score (%)	100	87.5	87.5	83.33
Risk of bias	Low	Low	Low	Low
a				
Questions	JG Yoon et al. /2020	Carreras-Presas et al. /2020	Lorenzo Azzi et al. / 2020	Martínez Lamas L et al. /2020
Were there clear criteria for inclusion in the case series?				
Was the condition measured in a standard, reliable way for all participants included in the case series?				
Were valid methods used for identification of the condition for all participants included in the case series?				
Did the case series have consecutive inclusion of participants?				
Did the case series have complete inclusion of participants?				
Was there clear reporting of the demographics of the participants in the study?				
Was there clear reporting of clinical information of the participants?				
Were the outcomes or follow-up results of cases clearly reported?				
Was there clear reporting of the presenting site(s)/clinic(s) demographic information?				
Was statistical analysis appropriate?	Not applicable	Not applicable	Not applicable	Not applicable
Score (%)	88.9	55.5	77.8	77.8
Risk of bias	Low	Moderate	Low	Low
b				

Supplementary Figure 2: Risk of bias analysis of included case reports and case series. Risk of bias for cases report graph (a). Risk of bias for case series graph (b). The graphs A and B show the authors' judgments about each item of risk of bias established as percentages in all included studies. This risk of bias analysis was carried out using the Joanna Briggs Institute's critical assessment tools