Online ISSN : 2249-4618
Print ISSN : 0975-5888
DOI : 10.17406/GJMRA

Global Journal

of Medical Research: J

Dentistry & Otolaryngology

Highlights

A Retrospective Analytical Study

Prevelance of Patterns of Impactions

Prevalence of Oral Manifestations

Various Forms of Tobacco Consumption

Discovering Thoughts, Inventing Future

VOLUME 23 ISSUE 2 VERSION 1.0

Global Journal of Medical Research: J
Dentistry & Otolaryngology

Global Journal of Medical Research: J
Dentistry & Otolaryngology
Volume 23 Issue 2 (Ver. 1.0)

Open Association of Research Society

This is a special issue published in version 1.0 of "Global Journal of Medical Research." By Global Journals Inc.

Incorporation No.: 0423089
License No.: 42125/022010/1186
Registration No.: 430374
Import-Export Code: 1109007027
Employer Identification Number (EIN):
USA Tax ID: 98-0673427

Global Journals Inc.

*(A Delaware USA Incorporation with "Good Standing"; **Reg. Number: 0423089**)*

Sponsors: Open Association of Research Society
Open Scientific Standards

Publisher's Headquarters office

Global Journals® Headquarters
945th Concord Streets,
Framingham Massachusetts Pin: 01701,
United States of America
USA Toll Free: +001-888-839-7392
USA Toll Free Fax: +001-888-839-7392

Offset Typesetting

Global Journals Incorporated
2nd, Lansdowne, Lansdowne Rd., Croydon-Surrey,
Pin: CR9 2ER, United Kingdom

Packaging & Continental Dispatching

Global Journals Pvt Ltd
E-3130 Sudama Nagar, Near Gopur Square,
Indore, M.P., Pin:452009, India

Find a correspondence nodal officer near you

To find nodal officer of your country, please email us at *local@globaljournals.org*

eContacts

Press Inquiries: *press@globaljournals.org*
Investor Inquiries: *investors@globaljournals.org*
Technical Support: *technology@globaljournals.org*
Media & Releases: *media@globaljournals.org*

Pricing (Excluding Air Parcel Charges):

Yearly Subscription (Personal & Institutional)
250 USD (B/W) & 350 USD (Color)

Editorial Board

Global Journal of Medical Research

Dr. Han-Xiang Deng

MD., Ph.D
Associate Professor and Research Department
Division of Neuromuscular Medicine
Davee Department of Neurology and Clinical Neurosciences
Northwestern University Feinberg School of Medicine
Web: neurology.northwestern.edu/faculty/deng.html

Dr. Pina C. Sanelli

Associate Professor of Radiology
Associate Professor of Public Health
Weill Cornell Medical College
Associate Attending Radiologist
NewYork-Presbyterian Hospital
MRI, MRA, CT, and CTA
Neuroradiology and Diagnostic Radiology
M.D., State University of New York at Buffalo,
School of Medicine and Biomedical Sciences
Web: weillcornell.org/pinasanelli/

Dr. Roberto Sanchez

Associate Professor
Department of Structural and Chemical Biology
Mount Sinai School of Medicine
Ph.D., The Rockefeller University
Web: mountsinai.org/

Dr. Michael R. Rudnick

M.D., FACP
Associate Professor of Medicine
Chief, Renal Electrolyte and Hypertension Division (PMC)
Penn Medicine, University of Pennsylvania
Presbyterian Medical Center, Philadelphia
Nephrology and Internal Medicine
Certified by the American Board of Internal Medicine
Web: uphs.upenn.edu/

Dr. Feng Feng

Boston University
Microbiology
72 East Concord Street R702
Duke University
United States of America

Dr. Seung-Yup Ku

M.D., Ph.D., Seoul National University Medical College,
Seoul, Korea Department of Obstetrics and Gynecology
Seoul National University Hospital, Seoul, Korea

Dr. Hrushikesh Aphale

MDS- Orthodontics and Dentofacial Orthopedics.
Fellow- World Federation of Orthodontist, USA.

Santhosh Kumar

Reader, Department of Periodontology,
Manipal University, Manipal

Gaurav Singhal

Master of Tropical Veterinary Sciences, currently pursuing Ph.D in Medicine

Dr. Aarti Garg

Bachelor of Dental Surgery (B.D.S.) M.D.S. in Pedodontics and Preventive Dentistr Pursuing Phd in Dentistry

Sabreena Safuan

Ph.D (Pathology) MSc (Molecular Pathology and Toxicology) BSc (Biomedicine)

Getahun Asebe

Veterinary medicine, Infectious diseases, Veterinary Public health, Animal Science

Dr. Suraj Agarwal

Bachelor of dental Surgery Master of dental Surgery in Oromaxillofacial Radiology.
Diploma in Forensic Science & Oodntology

Osama Alali

PhD in Orthodontics, Department of Orthodontics, School of Dentistry, University of Damascus. Damascus, Syria. 2013 Masters Degree in Orthodontics.

Prabudh Goel

MCh (Pediatric Surgery, Gold Medalist), FISPU, FICS-IS

Raouf Hajji

MD, Specialty Assistant Professor in Internal Medicine

Surekha Damineni

Ph.D with Post Doctoral in Cancer Genetics

Arundhati Biswas

MBBS, MS (General Surgery), FCPS, MCh, DNB (Neurosurgery)

Rui Pedro Pereira de Almeida

Ph.D Student in Health Sciences program, MSc in Quality Management in Healthcare Facilities

Dr. Sunanda Sharma

B.V.Sc.& AH, M.V.Sc (Animal Reproduction, Obstetrics & gynaecology), Ph.D.(Animal Reproduction, Obstetrics & gynaecology)

Shahanawaz SD

Master of Physiotherapy in Neurology PhD- Pursuing in Neuro Physiotherapy Master of Physiotherapy in Hospital Management

Dr. Shabana Naz Shah

PhD. in Pharmaceutical Chemistry

Vaishnavi V.K Vedam

Master of dental surgery oral pathology

Tariq Aziz

PhD Biotechnology in Progress

Contents of the Issue

Global Journal of Medical Research: J
Dentistry & Otolaryngology
Volume 23 Issue 2 Version 1.0 Year 2023
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Association of Various Forms of Tobacco Consumption with Pre-Malignant and Malignant Conditions of Oral Cavity.- A Retrospective Analytical Study

By Vanshika Saggar, Dr. Megha Bahal, Dr. Amoldeep Kaur, Karanjit Singh, Dr. Seerat Dhillon & Dr. Sartaj Singh Sandhu

Abstract- India faces a twofold burden in the form of smoking and smokeless tobacco and is considered the leading capital of tobacco consumption. Tobacco contains numerous toxins and carcinogens which are extremely harmful to the human body and may cause oral cancers, lung cancers, heart disease, stroke, COPD, emphysema etc. It is the major cause of morbidity and mortality worldwide, and is considered the most significant etiological factor of oral cavity cancers, especially oral squamous cell carcinoma. Tobacco, is even said to have a link with the development of pre malignant conditions of the oral cavity namely leukoplakia, erythroplakia, oral submoucous fibrosis, tobacco pouch keratosis which may progress to developing oral cancers. This is a questionnaire based research study conducted in the community health care centres in Chattisgarh with the aim to study the association of pre malignant lesions with tobacco consumption prevalence, patterns of pre malignant conditions occurring in the oral cavity in response to various forms of tobacco consumption and the relation of premalignant and malignant conditions of oral cavity among tobacco users.

GJMR-J Classification: *NLM: QZ 200-380*

Association of Various Forms of Tobacco Consumption with Pre- Malignant and Malignant Conditions of Oral Cavity.- A Retrospective Analytical Study

Vanshika Saggar [α], Dr. Megha Bahal [σ], Dr. Amoldeep Kaur [ρ], Karanjit Singh [ω], Dr. Seerat Dhillon [¥] & Dr. Sartaj Singh Sandhu [§]

Abstract- India faces a twofold burden in the form of smoking and smokeless tobacco and is considered the leading capital of tobacco consumption. Tobacco contains numerous toxins and carcinogens which are extremely harmful to the human body and may cause oral cancers, lung cancers, heart disease, stroke, COPD, emphysema etc. It is the major cause of morbidity and mortality worldwide, and is considered the most significant etiological factor of oral cavity cancers, especially oral squamous cell carcinoma. Tobacco, is even said to have a link with the development of pre malignant conditions of the oral cavity namely leukoplakia, erythroplakia, oral submoucous fibrosis, tobacco pouch keratosis which may progress to developing oral cancers. This is a questionnaire based research study conducted in the community health care centres in Chattisgarh with the aim to study the association of pre malignant lesions with tobacco consumption prevalence, patterns of pre malignant conditions occurring in the oral cavity in response to various forms of tobacco consumption and the relation of premalignant and malignant conditions of oral cavity among tobacco users.

I. Introduction

India is considered as the global capital for tobacco consumption and tobacco is regarded as the major etiological factor for oral cancer. The various forms of tobacco consumed are smokeless tobacco (the chewing form - gutka, paan, missy, mawa, snuff) and the smoking tobacco (beedi, cigarettes, reverse smoking). Studies have proved that tobacco contains a myriad of toxins and irritants which are potential carcinogens namely, extremely elevated levels of trace elements such as copper, magnesium, zinc found in the chewing tobacco cause fibrosis of oral mucosa, Areca nut causes stimulant and noxious defects. In the smoking form nicotine, is an alkaloid which causes addiction and nitrosation of these alkaloids (polyacrylic hydrocarbons etc) produces nitrates and nitrites which determine the level of carcinogenicity. Oral cavity cancers, account to 3% of all malignancies and the most common oral malignancy is squamous cell carcinoma. As per the World Health Organization report, the most significant risk factor for cancer is tobacco use, which alone is responsible for 22% of oral cancer deaths worldwide. 38% of these oral cancers, arise from premalignant conditions of the oral cavity namely leukoplakia, oral sub mucous fibrosis, Erythroplakia, palatal lesions of reverse cigarette smoking, tobacco pouch keratosis. In this study, we aim to study the association of pre malignant lesions with tobacco consumption prevalence, patterns of pre malignant conditions occurring in the oral cavity in response to various forms of tobacco consumption and the relation of premalignant and malignant conditions of oral cavity among tobacco users.

II. Methods and Materials

This study its a cross - sectional community based design conducted for a span of 6 months from July 2019 to January 2020 in 8-9 community health care centres in Chattisgarh. A dental camp was conducted for Oral Health checkups with a questionnaire survey form made to be filled for the prevalence of Tobacco Consumption among resident population. A total of 200 candidates were included in the study. The inclusion criteria were the general population above the age of 18 years who had tobacco consumption as a habit with diversifying frequency. Exclusion criteria were pregnant women, people having oral ulcers without any specific tobacco consumption history, disabled and handicapped population, the population having medical concerns, people above the age of 80 years, and those who were not willing to participate in the study. The sample size was large enough to provide reliable estimates for the association of various forms of

Author α ω: Intern, Baba Jaswant Singh Dental College, Hospital and Research Institute Ludhiana Punjab.
Author σ: Assistant Professor, Department of Oral Medicine and Radiology, Baba Jaswant Singh Dental College Hospital and Research Institute Ludhiana Punjab. e-mail: meghabahal001@gmail.com
Author ρ: Assistant Professor, Department of Oral and Maxillofacial Surgery, Baba Jaswant Singh Dental College Hospital and Research Institute Ludhiana Punjab.
Author ¥: Post Graduate Student 2nd year, Department of Orthodontics & Dentofacial Orthopaedics, Dasmesh Institute of Research & Dental Sciences, Faridkot, Punjab
Author §: Junior Resident, Government Multiple Speciality Hospital, Chandigarh.

tobacco with pre- malignant and malignant conditions, for different population groups for each of the Community health centres.

III. Data Collection

Patients were encountered in dental camps. Questionarre was made to be filled along with the regular dental checkups.

IV. Ethical Issues

Informed consent was taken from the study participants after fully explaining the study in a language they understood well. No biological sample was taken. Confidentiality was maintained.

a) Data analysis

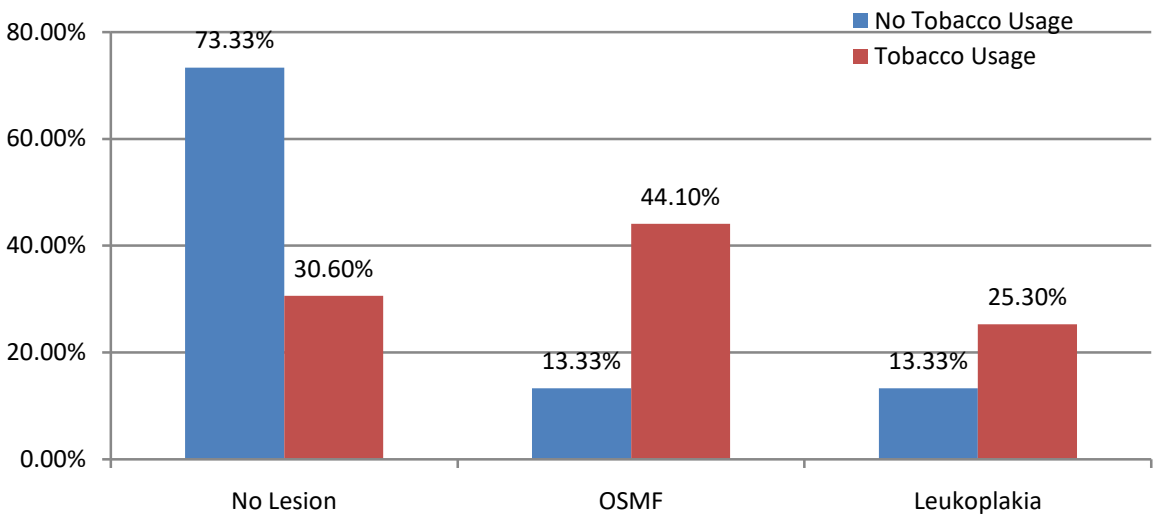
Data were entered in Microsoft Excel 2007. Data analysis was done using SPSS (version 20.0; SPSS Inc. Chicago, IL, USA) software. Statistical significance (P value) was set at a level of 0.023. Data were evaluated and proportions were obtained showing a correlation between various forms of tobacco consumption and the occurrence of pre malignant and malignant conditions. Chi square test was performed to check the statistical significance.

V. Results

a) Association of Pre malignant lesion with Tobacco Consumption Prevalence

Among the subjects who were not using tobacco in any of the form 73.33% were having no lesion whereas 13.33% each were having OSMF and Leukoplakia. Among the subjects with tobacco usage, 44.1% were having OSMF and 25.3% were having Leukoplakia whereas 30.6% were without any lesion. the difference between the groups was statistically significant when analysed using chi square test

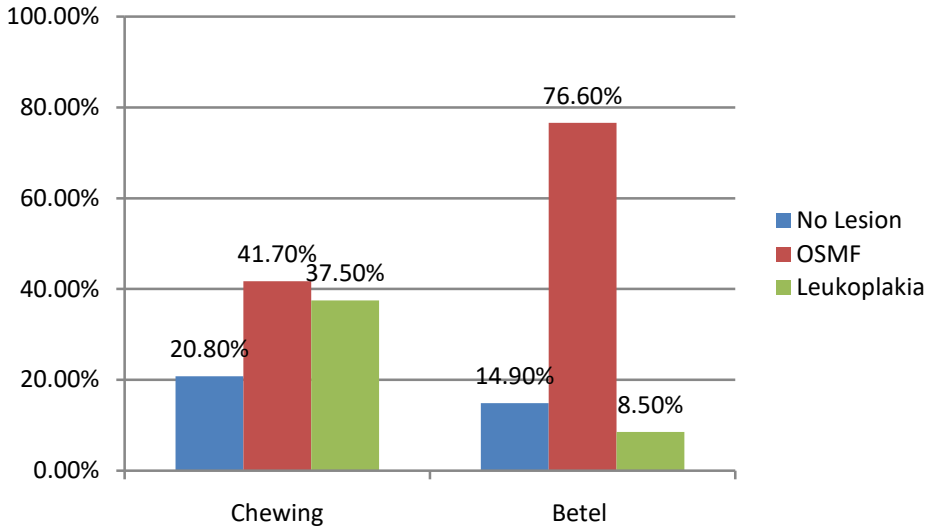
	No Lesion	OSMF	Leukoplakia	Ch Sq	P value
No Tobacco Usage	22	4	04	13.657	0.001 (Sig)
	73.33%	13.33%	13.33%		
Tobacco Usage	52	75	43		
	30.6%	44.1%	25.3%		



b) Association of Pre malignant lesion with Form of Smokeless Tobacco

Among the subjects who were using chewing tobacco 41.70% were having OSMF whereas 37.5% were having Leukoplakia whereas Among the subjects who were using betel 76.60% were having OSMF whereas 8.5% were having Leukoplakia. The difference between the groups was statistically significant when analysed using chi square test

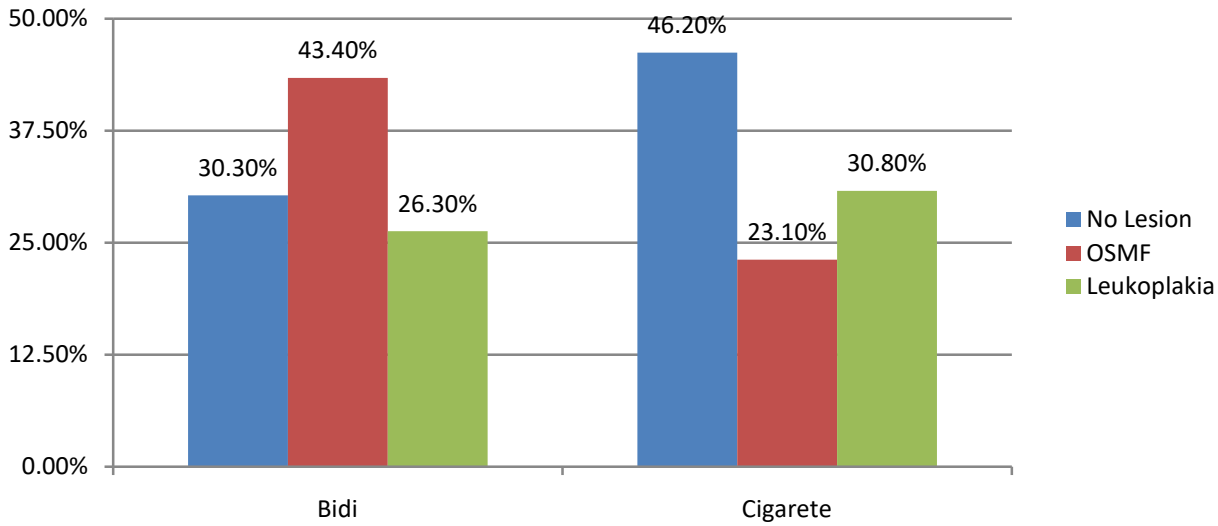
	No Lesion	OSMF	Leukoplakia	Ch Sq	P value
Chewing	10	20	18	13.657	0.001 (Sig)
	20.8%	41.7%	37.5%		
Betel	7	36	4		
	14.9%	76.6%	8.5%		



c) *Association of Pre malignant lesion with Form of Smoking Tobacco*

Among the subjects who were using bidi 43.40% were having OSMF whereas 26.3% were having Leukoplakia whereas Among the subjects who were using cigarette 23.1% were having OSMF whereas 30.8% were having Leukoplakia. The difference between the groups was statistically non-significant when analysed using chi square test. Among the cigarette users 46.2% were lesion free and among the bidi users, 30.3% were lesion free

	No Lesion	OSMF	Leukoplakia	Ch Sq	P value
Bidi	23	33	20	2.078	0.532 (Non-Sig)
	30.3%	43.4%	26.3%		
Cigarette	6	3	4		
	46.2%	23.1%	30.8%		



d) *Association of Precancerous Lesions with Oral Cancer*

Among the subjects who were having OSMF, 23.6% developed oral cancer and among the subjects with Leukoplakia, 17% developed oral cancer. Among the subjects with no precancerous lesion none of the subjects developed oral cancer The chi square association between precancerous lesions and oral cancer was statistically significant when analysed using chi square test with p value of 0.001.

VI. Discussion

In the present study, among the subjects with tobacco consumption 44.1% were having OSMF and 25.3% were having leukoplakia. Thus we conclude, that there is a strong relation between the consumption of tobacco and the occurrence of premalignant conditions in the oral cavity. Among the subjects who were using chewing tobacco 41.70% were having OSMF whereas 37.5% were having Leukoplakia whereas and among the subjects who were using betel 76.60% were having OSMF whereas 8.5% were having Leukoplakia. Thus reflecting that, chewing tobacco and betel quid consumption, both are highly responsible for the occurrence of OSMF and leukoplakia, with betel quid being the most dangerous one. Thomas et al. in Kerala conducted Case control study considering risk associated with tobacco chewing in multiple OPMLs like leukoplakia, erythroplakia and OSMF. The adjusted Occurrence rate among continuous tobacco chewers was very high (OR = 37.8, 95%). Hashibe et al. investigated the association of other habits with OSMF. This study found ever-tobacco chewing as a strong risk factor for OSMF (41%). Thus results are in accordance to these studies conducted in Kerala.

Oral submucous fibrosis, is basically characterised by abnormal collagen deposition and frequently occurs on buccal mucosa. Clinically OSF patients experience burning sensation after consumption of spicy food, reduced mouth opening, dry mouth, pain, taste disorders, restricted tongue mobility, trismus and Leukoplakia is the adaptive response of the body to the irritants of tobacco, it is a non scrappable white patch or plaque that develops in the oral cavity and is strongly associated with tobacco.

Among the smoking forms, people who were using beedi, 43.40% were having OSMF whereas 26.3% were having Leukoplakia and among the subjects who were using cigarette 23.1% were having OSMF whereas 30.8% were having Leukoplakia. Thus, we can clearly establish an association between the smoking forms of tobacco and the occurrence of pre malignant lesions. However, bidi smoking has a stronger potential of causing OSMF as compared to cigarette smokers. Researches have proved that smoke from bidi contains three to five times the amount of nicotine, tar and carbon monoxide as a regular cigarette and thus placing users at a high risk of addiction. The low prices of bidi's, their easy availability, lack of knowledge, low socio-economic status, addiction -all these factors contribute to increasing use of bidi's.

Among the subjects who were having OSMF, 23.6% developed oral cancer and among the subjects with Leukoplakia, 17% developed oral cancer. Thus we can establish a definite relation between the pre malignant and malignant conditions, which reflects that When pre malignant lesions are neglected not treated treated, it leads of oral cancer- mainly squamous cell carcinoma. A study conducted by Dr Biplab Nath in Tripura stated that 35% oral cancers are preceded by leukoplakia. In our study, the frequency of oral cancers being preceded by leukoplakia (17%) was less than the findings of other studies conducted in Tripura (35%). The early diagnosis of these pre malignant lesions can help reduce the ocurrence of oral cancer. A study done by Subapriya et al. in Tamil Nadu indicated that the chewing of betel nut and tobacco, chewing of tobacco alone, bidi smoking and alcohol consumption (OR = 1.65) were all significant risk factors for oral cancer. On histological examination dysplastic changes, atypical hyperplasia, keratosis with dysplasia indicate malignant transformations. SCC is one of the major reason of premature deaths worldwide. Among the subjects with no precancerous lesion none of the subjects developed oral cancer. Early detection of oral cancer is very crucial because survival rates remarkably increase when timely intervention is done. Among the subjects with no precancerous lesion none of the subjects developed oral cancer.

The first step in the management of these pre malignant conditions is habit cessation which can be achieved via verbal counsellings, announcing incentives, educating the population and having de-addiction centres. The interventions in the treatment of OSMF include a wide spectrum of medications comprising of dietary supplements (vitamins and antioxidants), anti-inflammatory agents (corticosteroids), proteolytic agents (such as hyaluronidase and placental extracts), vasodilators, immunomodulators, and anti-cytokines. For the management of leukoplakia, retinoids and antioxidants should be prescribed. The ideal treatment for a leukoplakia is surgical excision. The commonly used surgical options for the excision are conventional scalpel surgery, carbon dioxide laser ablation, electrocauterization, and cryosurgery. The timely intervention in these premalignant conditions can prevent the progression towards Oral cancer. The treatment modality for oral cancer depends upon the stage at which it is diagnosed - after the biopsy and TNM staging of tumour mass the treatment option is chosen. It may vary from chemotherapy, external radiation therapy to surgical excision of tumour mass.

VII. Conclusion

From the present study we conclude that there is a direst link between various forms of tobacco consumption and premalignant conditions, and These premalignant conditions may progress to oral cancer Tobacco is the leading cause of premature deaths globally. With Timely intervention, habit cessation and antioxidant therapy these premalignant conditions can be controlled. However if not curbed at the right time, these premalignant lesions carry a strong predisposition

to become oral cancer. 23.6% of the oral cancers were preceded by OSMF and 17% were preceded by leukoplakia.

References Références Referencias

1. Saraswathi TR, Ranganathan K, Shanmugam S, Sowmya R, Narasimhan PD, Gunaseelan R. Prevalence of oral lesions in relation to habits: Cross-sectional study in South India. Indian J Dent Res. 2006; 17: 121–5.
2. Krishna Priya M, Srinivas P, Devaki T. Evaluation of the Prevalence of Oral Mucosal Lesions in a Population of Eastern Coast of South India. J Int Soc Prev Community Dent. 2018; 8: 396–401.
3. Hernandez BY, Zhu X, Goodman MT, Gatewood R, Mendiola P, Quinata K, et al. Betel nut chewing, oral premalignant lesions, and the oral microbiome. PLoS One. 2017; 12:e0172196.
4. Warnakulasuriya S, Reibel J, Bouquot J, Dabelsteen E. Oral epithelial dysplasia classification systems: predictive value, utility, weaknesses and scope for improvement. J Oral Pathol Med.
5. Khan Z, Dreger S, Shah SMH, Pohlabeln H, Khan S, Ullah Z, et al. Oral cancer via the bargain bin: The risk of oral cancer associated with a smokeless tobacco product (Naswar).

This page is intentionally left blank

Global Journal of Medical Research: J
Dentistry & Otolaryngology
Volume 23 Issue 2 Version 1.0 Year 2023
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Chronic Otitis Media and Hearing Loss in Nepalese Schoolchildren

By Milan Maharjan, Rosy Bajracharya & Elina Maharjan

Abstract- *Background:* Chronic otitis media is one of the leading causes of avoidable hearing loss in children in developing countries. Early diagnosis and management of chronic otitis media can prevent hearing loss and the consequences that follow. These include delayed language development, poor academic performance and lifelong socioeconomic impacts.

Objectives: To find out the prevalence of chronic otitis media in school-aged Nepalese children and to evaluate associated hearing loss.

Methods: This is a retrospective study conducted by reviewing the screening records of school-based ear health programs conducted by our institute over a five-year period. Medical records of children diagnosed with chronic otitis media were studied and segregated. Data including diagnoses, tympanic membrane findings and pure tone audiogram reports were documented and analyzed.

Keywords: *chronic otitis media, hearing loss, schoolchildren, nepal.*

GJMR-J Classification: *LCC: RF309*

Strictly as per the compliance and regulations of:

Chronic Otitis Media and Hearing Loss in Nepalese Schoolchildren

Milan Maharjan [α], Rosy Bajracharya [σ] & Elina Maharjan [ρ]

Abstract- ***Background:*** Chronic otitis media is one of the leading causes of avoidable hearing loss in children in developing countries. Early diagnosis and management of chronic otitis media can prevent hearing loss and the consequences that follow. These include delayed language development, poor academic performance and lifelong socioeconomic impacts.

Objectives: To find out the prevalence of chronic otitis media in school-aged Nepalese children and to evaluate associated hearing loss.

Methods: This is a retrospective study conducted by reviewing the screening records of school-based ear health programs conducted by our institute over a five-year period. Medical records of children diagnosed with chronic otitis media were studied and segregated. Data including diagnoses, tympanic membrane findings and pure tone audiogram reports were documented and analyzed.

Results: The medical screening records of 79,340 children were studied. Chronic otitis media was seen in 8.04% (n=6382) of children, of which 78.94% (n=5038) were found to be unilateral, and 21.06% (n=1344) with bilateral ears diagnosed. Of the children with chronic otitis media, 41.57% (n=2653) had hearing a loss of 25dB or greater. Hearing loss was conductive in 93.40% (n=2478) of these cases and mixed loss was found to be in 6.6% (n=175) of these. The degree of hearing loss increased with the increasing age of the children.

Conclusions: Chronic otitis media in children is a public health issue in Nepal. This needs to be addressed urgently to reduce disease burden. Early management of chronic otitis media can prevent hearing loss caused by chronic ear infections in Nepalese children.

Keywords: chronic otitis media, hearing loss, schoolchildren, nepal.

I. Introduction

Chronic Otitis media (COM) is a permanent abnormality of the pars tens a or pars flaccida, most likely a result of previous acute otitis media, otitis media with effusion or long-standing negative middle ear pressure.[1] The prevalence of chronic otitis media has been reported to be between less than 1% in high-income countries to up to 46% in disadvantaged ethic groups and low-income countries.[2] A prevalence of 1-2% of COM in children in a definite community is considered low and a prevalence of more than 4% is considered high, which also indicates a public health issue requiring urgent attention.[3]

Author σ ρ: Ear Care Nepal, Jawalakhel, Lalitpur, Nepal.
Corresponding Author α: MBBS, MS., Ear Care Nepal, Jawalakhel, Lalitpur, Nepal. e-mail: earcarenepal@gmail.com

Chronic otitis media is the leading cause of preventable hearing loss in children, especially in developing countries. According to the WHO, about 60% of people with COM have clinically significant hearing loss and 90% of these are in developing countries.[3] This is a matter of serious concern especially in children because of the negative developmental and educational impacts caused by hearing loss. Chronic otitis media contributes most to the global burden of hearing loss; hence, eliminating it can potentially reduce the global burden of hearing loss.

Recent prevalence of chronic otitis media in Nepalese children is not known, and there is lack of accurate data. The little available data are from either hospital-based or of small cohort studies. More recent data on COM prevalence would help to determine if COM management should be prioritized in the national health care program. Therefore, the main objective of our study is to find out the most recent status of chronic otitis media in Nepalese children and to evaluate corresponding hearing loss.

II. Methods

This is a retrospective study based on data from the medical records of Nepalese Schoolchildren who participated in the school-based ear health programs conducted by our institute over a five-year period from January 2015 through January 2020. Permission to conduct the school-based ear health programs was obtained in writing from the educational authorities of the concerned district and from the individual schools. Schools that provided written consent to conduct ear health program were included in the study. The schools that did not consent were excluded.

The medical records contain otoscopic findings of the tympanic membrane, final diagnoses and pure tone audiometry reports of all the children. Detail findings of the tympanic membrane such as the integrity of the membrane, the size and site of perforations, the presence of ear discharge and cholesteatoma were recorded. Demographic details such as age, gender, grade, and ethnicity were also documented. All the confirmed cases of chronic otitis media in children in grades1 through 10along with their pure tone audiometry reports were included in the study. Children diagnosed with acute otitis media, otitis media with effusion, ear diseases other than COM and children with normal findings were excluded from this study. Children

with incomplete medical records or missing data were also not included in this study.

The school-based ear screening programs were conducted and documented by senior Ear Nose Throat surgeons having more than five years experiences in this community screening work. A Heine Mini 3000 otoscope was used for tympanic membrane examinations. Chronic otitis media was diagnosed when there was a permanent abnormality of the pars tensa or pars flaccida with or without active ear discharge. It is divided into chronic otitis media mucosal and chronic otitis media squamous as per Browning et al. classification of COM.[4]

Pure tone audiometry was conducted and documented by an audio-technician using an Arphi Proton SX3 pure tone audiometer. Hearing loss was defined as a pure tone average of four frequencies 0.5, 1, 2, and 4kHz greater than 25dB HL in one or both ears. Data analysis was done using frequency and percentage. The ethical clearance to conduct the study was approved by the Nepal Health Research Council (NHRC) bearing registration number 345/2021 P.

III. Results

Over a period of five years from January 2015 until January 2020, 79,340 children from grades 1 through grade 10 were screened for ear and hearing problems. Out of which, chronic otitis media was diagnosed in 8.04% (n=6,382) children, of which 50.75% (n=3,239) were in boys and 49.25% (n=3,143) in girls. Ages of the children in the study ranged between 4 to 18 years old. The majority of the children with chronic otitis media 60.59% (n=3,867) were aged 11-15 years old with only 3.85% (n=246) of children in the 4 to 5 years age group testing positive for this. Chronic otitis media was seen in 41.84% (n=2,670) of right ears, in 37.10% (n=2,368) of left ears and bilaterally in 21.06% (n=1,344) of the children. Mucosal-COM was seen in 30.68% (n=1,958), and squamous-COM in 6.80% (n=434) children. Different types of COM by age group are shown in Table 1.

Table 1: Age distribution of children with different types of chronic otitis media

Age distribution	Children with chronic otitis media n (%)	Types of chronic otitis media n (%)	
<5 years old	246 (3.85%)	Mucosal	239 (97.15%)
		Squamous	7 (2.84%)
5-10 years old	1,220 (19.12%)	Mucosal	1135 (93.03%)
		Squamous	85 (6.97%)
11-15 years old	3,867 (60.59%)	Mucosal	3580 (92.58%)
		Squamous	287 (7.42%)
>15 years old	1,049 (16.44%)	Mucosal	994 (94.76%)
		Squamous Active	55 (5.24%)
Total	6,382		

Hearing loss was seen in 41.57% (n=2,653) of the children with chronic otitis media, out of which 93.40% (n=2,478) of the cases were conductive hearing loss, which was of mild degree in87.36% (n=2,165), moderate in 9.76% (n=242) and moderately severe in 2.86% (n=71) of the children. Mild conductive hearing loss was the commonest type of hearing loss. This was seen in 81.60% (n=2,165) of the children with COM, whereas, moderately severe mixed hearing loss was the least commonly seen in only 1.31% (n=35) of children with chronic otitis media. 95.60% of children with mucosal-COM had associated hearing loss, whereas only 74.65% of children with squamous-COM had hearing loss. The type and degree of hearing loss associated with different types of COM by age groups are shown in Table 2.

Table 2: Chronic otitis media with type and degree of hearing loss

Age distribution	Children with chronic otitis media n (%)	Children with hearing loss n (%)	Type and degree of hearing loss n (%)		
<5 years old	246 (3.85%)	14 (5.69%)	Conductive hearing loss	Mild	13 (92.86%)
				Moderate	1 (7.14%)
5-10 years old	1,220 (19.12%)	438 (35.90%)	Conductive hearing loss	Mild	372 (84.93%)
				Moderate	28 (6.40%)
				Moderately Severe	11 (2.51%)
			Mixed hearing loss	Moderate	10 (2.28%)
				Moderately Severe	9 (2.05%)
				Severe	8 (1.82%)
11-15 years old	3,867 (60.59%)	1,603	Conductive	Mild	1,372 (85.59%)

		(41.45%)	hearing loss	Moderate	101 (6.30%)
				Moderately severe	42 (2.62%)
			Mixed hearing loss	Moderate	48 (3%)
				Moderately severe	21 (1.31%)
				Severe	19 (1.18%)
>15 years old	1,049 (16.44%)	598 (57.01%)	Conductive hearing loss	Mild	408 (68.22%)
				Moderate	112 (18.73%)
				Moderately severe	18 (3.01%)
			Mixed hearing loss	Moderate	29 (4.85%)
				Moderately severe	5 (0.83%)
				Severe	26 (4.35%)
Total	6,382	2,653 (41.57%)			

IV. Discussions

Despite improvement in public health care in last two decades, there is still a significant burden of chronic otitis media in school-aged children in Nepal. This study shows that the prevalence of chronic otitis media in Nepalese schoolchildren is 8.04%. According to WHO categorization of the countries with disease burden, a prevalence rate of 8.04% places Nepal in the group of the countries with the highest prevalence rates. The high prevalence rate in our study may be caused by increased exposure of the study children to risk factors associated with low socioeconomic strata such as overcrowding, passive smoke and poor nutrition.

The largest population-based survey was conducted in 1991 in the general population and found that 7.4% of all Nepalese had middle ear pathology.[5] Following that, a few studies conducted in small pediatric populations have reported prevalence rates of 3.26% by Thakur et al.[6] 5% by Adhikari et al.[7] and 10% by Maharjan et al.[8] The relatively low prevalence rate reported by Thakur et al. could be due to differences in sampling size and sampling technique followed in the study. Adhikari et al. conducted the study in urban private schools where socioeconomic status and literacy rates of the parents are high, which could explain the lower number of children with COM in their study group. The school where Maharjan et al. conducted their study mostly enrolled children from one particular ethnic group with poor socioeconomic backgrounds where children had the habit of swimming in dirty water along with their cattle during hot and humid weather in the plains of Nepal, which must have acted as a predisposing factor for chronic discharging ear. Swimming in local pools has been considered an associated risk factor in developing COM.[9] Incomparison, the prevalence of COM in children has been reported as 4.79% in India,[10] 5.2% in Bangladesh,[11] 7.26% in Malaysia,[12] 1.74% in Thailand,[13] 2.19% in Korea[14] and 1.65% in Indonesia.[15]

In the African countries, lower prevalence rates of COM have been reported such as 4% in Rwanda,[16] 5.3% in Malawi,[17] 1.4% in Tanzania,[18] and 1.5% in Kenya.[19] Low prevalence rates have been reported in other parts of the globe as well, such as 1.31% in Saudi Arabia[20] and, 0.94% in Brazil.[21] Developed nations such as the US, the UK and most of the European countries have prevalence rates of less than 1%.[3] Contrary to this, high prevalence rates of COM are reported in certain populations and ethnic minorities[22]such as Australian Aborigines,[23] the Inuit[24] and Greenlandic children.[25,26] The wide range in the prevalence rates in these epidemiological studies could be due to differences in exposure to risk factors and access to health care among the study population, population size, ethnic group, sampling technique, and methodology. Differences in the definition and classification of COM used in the study is another important factor for wide variations in the prevalence rates. In our study, the Browning classification of COM was followed because it is the classification of choice used in Nepal. Classifications such as suppurative and non-suppurative COM are now less commonly used because it is the progression of the same pathological process. Similarly, use of tubo-tympanic as safe and attico-antral as unsafe COM is not recommended any longer since marginal perforations of the pars tensa can also develop complications.[27] Many studies classified COM as tubo-tympanic and attico-antral.[7,28,29] Muftah et al.[9] and Hunt et al.[17]only included the cases with active ear discharge lasting more than 2 weeks with perforated tympanic membrane and excluded the cases with dry perforation and healed tympanic membrane in their study. Other factors such as genetic and environmental factors as a possible cause need to be further studied in certain populations and ethnic minorities.

We did not find gender preponderance in our study; COM was almost equal in both boys and girls, which is consistent with other studies.[16,30] Several studies found that older children were more likely to develop COM than the younger children were.[9, 17, 30] We too found that 60.59% of the COM cases were seen in older children aged 11-15 years and least affected were the youngest children aged five years and younger at 3.85%. COM as well as sequelae of COM such as tympanosclerosis and atelectasis climbed steadily with increasing age suggesting chronicity of the disease.[19] The high prevalence of COM in older children could be result of frequent and untreated or poorly treated cases

of acute otitis media and/or otitis media with effusion, which progressed into the chronic phase of the disease. Additionally, traditional practices such as instillation of oil or other liquids to treat ear diseases can lead to continuous otorrhoea progressing the disease into the chronic phase. This trend could explain increasing rates of COM in older children.

Chronic otitis media was unilateral in 78.94% (n=5,038) and bilateral in 21.06% (n=1,344) children. This finding is consistent with other studies.[7, 16, 19, 28,31] Bilateral disease are thought to have poor consequence because of associated bilateral hearing loss and poorer surgical outcome. Eustachian tube dysfunction is considered as the main pathogenesis of bilateral disease whereas, in unilateral cases, more localized causes are assumed. Many studies suggest an increased risk of developing COM in the contralateral ear in later years but to evaluate the status of the contralateral ear, a long-term follow up of the children with unilateral disease would be needed.[32, 33]

In this study, out of 6,382 cases, mucosal-COM was the most commonly observed COM, detected in 30.68% (n=1,958) of the children and the squamous type detected in only 6.80% (n=434). Similar findings were also noted in other studies.[7,10,28,29,31] Contrary to our findings, squamous-COM was more commonly seen in a study conducted by Kumari et al.[34] whereas; Abraham et al.[18] did not find a single case of squamous-COM in their study. Simoes et al.[19]detected squamous-COM in only 0.45% cases whereas 62.51% (n=3,990) of the children had scarring of the tympanic membrane such seen as a thin and healed tympanic membrane, tympanosclerosis, and chalk white patches suggesting previous history of otitis media.

A literature review on childhood hearing loss published by Davidson et al. found that children from developing countries had almost double the chances of developing associated hearing loss in COM than in children from developed countries. In our study, we found that 41.57% (n=2,653) of the children with COM were suffering from hearing loss. Similarly, other studies conducted in developing countries also reported increase possibilities of developing hearing loss due to COM. [9, 31, 34, 35]

The hearing loss in this study was predominantly the conductive type 93.40% (n=2478) and of a mild degree 87.36% (n=2165). Muftah et al. also observed a similar pattern[9] whereas Anggraeni et al. stated that most of the hearing loss associated with COM in their study group was of a moderate degree.[35] In our study mixed hearing loss suggesting involvement of the inner ear was seen in 6.60% (n=175) of children with COM. This finding demonstrates that the inner ear is vulnerable to chronic discharging ears.[36-40] Significant involvement of bone conduction thresholds were noted in cases with COM.[41-44] In this study we observed that hearing loss in children with COM increased steadily with increasing age, from 5.69% in <5 year old's to 57.01% in children >15 years old. Sakagami et al. found hearing deterioration was more in the ear with COM than in the normal ear; 0.61dB/year versus 0.13 dB/year.[45] Long-term follow up of COM and its impact on the bone conduction found significant association between duration of COM and presence of involvement of bone conduction.[41,44]

It was observed that in mucosal-COM, 94.76%% of the hearing loss was of the conductive type and only 5.23% was mixed type, whereas in squamous-COM mixed hearing loss increased to 17.28%. Opposite to our findings, mixed hearing loss was seen more often in mucosal-COM by kumari et al.[34]In general, a healed tympanic membrane is rarely considered a problem therefore hearing tests are only occasionally done, especially in children. In our study, we noticed that 17.22% of the total hearing loss was seen in children with healed tympanic membranes and 4.60% of which was of mixed type. This finding suggests that scarring of the tympanic membrane should not be taken casually, and it should be further investigated for hearing loss. Similarly, atelectasis of the tympanic membrane was also found to be associated with involvement of the inner ear.[44, 46] The size of the tympanic membrane perforation was also found to be related to sensorineural hearing loss.[44, 46] In this study, 75.68% of the children had large sized tympanic membrane perforations, but we did not observe similar findings. We did not find any cases of COM with profound hearing loss. This could be because children with profound hearing loss may be deprived of enrolling into the normal education system and were thus under-represented in our study.

Poor socioeconomic status has been associated with a higher prevalence of COM due to risk factors such as poor hygiene, overcrowded living conditions and malnutrition.[9, 30] This study was conducted in children studying in government schools. The schools run by the state government in Nepal are considered to provide inferior education quality as compared to the more expensive private schools. Therefore, only the most underprivileged children attend government schools. That could explain the higher prevalence rates seen in our study population. Many studies found statistically significant association between COM and socioeconomic status.[11, 30, 47, 48] In school-based studies, prevalence of COM was found more commonly in children studying at rural schools as compare to urban schools; 2.7% versus 0.7%,[15] 5.11% versus 2.32%,[28] 7% versus 1.8%,[30] and 5.7% versus 4.8%.[48] The wide variation was because these studies were conducted in areas where distinct differences in socioeconomic status such as low socioeconomic status in rural areas and higher status in urban schools was obvious. Lack of access to proper health care in rural settings is another reason for the wide variations in prevalence rates. Hence, improvement in access to

affordable health care for children of such communities could decrease the disease burden.

This study has both strengths as well as weaknesses. The strength of our study is that it is the largest study documented in a pediatric population in recent years in Nepal, and it explored the detail classification of chronic otitis media and hearing evaluation of all the children with COM. A limitation of this study is that this is a retrospective school-based study. This study only covered schoolchildren; younger children and those who did not attend schools were not included in the study. Although examinations were carried out using an otoscope in respective schools by senior Ear Nose and Throat surgeons with more than five years of experience, early cases of cholesteatoma could have been misdiagnosed as mucosal-COM. Microscopic examination of the ears of all the children was not feasible for the children in this study.

This study suggests that chronic otitis media is still a public health issue in Nepal that needs to be addressed urgently to reduce the burden of disease. Findings of our study could help in developing a national health care program focusing on ear and hearing care in Nepal. Measures such as conducting school entrance ear screening, raising public awareness about ear and hearing care, and early treatment of chronic otitis media could prevent hearing loss in most children.

V. Conclusions

Chronic otitis media is a public health issue in Nepal. Early diagnosis and proper treatment of chronic otitis media could prevent most of the hearing loss in schoolchildren. Health measures such as school entrance screening, public awareness program and integration of ear and hearing screening in national health care could reduce the burden of disease.

Acknowledgement

The authors would like to thank Alan Goldstein for his help in editing the article.

References Références Referencias

1. Browning GG. Aetiopathology of inflammatory conditions of the external and middle ear. In: Kerr AG, editor. Scott-Brown's Otolaryngology. 6th ed. London: Hodder Arnold, 1997.
2. World Health Organization, Prevention of hearing impairment from chronic otitis media: report of a WHO/CIBA foundation workshop. London, U.K. 1996; 19–21. Available from: https://apps.who.int/iris/handle/10665/63870
3. World Health Organization, Chronic suppurative otitis media; burden of illness and management options. Geneva, Switzerland. 2004; 2-83. Available from: https://apps.who.int/iris/handle/10665/42941
4. Browning GG, Merchant SN, Kelly G, Swan I RC, Canter R, McKerrow WS. Chronic otitis media. In: Gleeson M, editor. Scott-Brown's otolaryngology. 7thed. London: Hodder Arnold; 2008. P.3395-3445.
5. Little P, Bridges A, Guragain R, Friedman D, Prasad R, Weir R. Hearing impairment and ear pathology in Nepal. J Laryngol Otol. 1993; 107: 395-400. https://doi.org/10.1017/S0022215100123278
6. Thakur SK, Singh SK, Mahato B, Singh A, Mahato D. Pattern of otological diseases in school-going children of the Sunsari district of Eastern Nepal. The Internet Journal of Otorhinolaryngology. 2015; 17: 1. http://ispub.com/doi/10.5580/IJORL.25808
7. Adhikari P, Joshi S, Baral D, Kharel B. Chronic suppurative otitis media in urban private school children of Nepal. Braz J Otorhinolaryngol. 2009 Sep-Oct; 75: 669-72. https://doi.org/10.1016/s1808-8694(15)30516-4
8. Maharjan M, Bhandari S, Singh I, Mishra SC. Prevalence of otitis media in school going children in Eastern Nepal. Kathmandu Univ Med J. 2006; 4: 479-82. https://pubmed.ncbi.nlm.nih.gov/18603958/
9. Muftah S, Mackenzie I, Faragher B, Brabin B. Prevalence of chronic suppurative otitis media and associated hearing impairment among school-aged children in Yemen. Oman Med J. 2015 Sep; 30: 358-65. https://doi.org/10.5001/omj.2015.72
10. Chadha SK, Sayal A, Malhotra V, Agarwal AK. Prevalence of preventable ear disorders in over 15000 schoolchildren in northern India. J Laryngol Otol. 2013; 127: 28-32. https://doi.org/10.1017/s0022215112002691
11. Shaheen MM, Raquib A, Ahmad SM. Chronic suppurative otitis media and its association with socio-economic factors among rural primary school children of Bangladesh. Indian J Otolaryngol Head Neck Surg. 2012; 64: 36–41. https://doi.org/10.1007/s12070-011-0150-9
12. Elango S, Purohit GN, Hashim M, Hilmi R. Hearing loss and ear disorders in Malaysian school children. Int J Pediatr Otorhinolaryngol. 1991 Jul; 22: 75-80. https://doi.org/10.1016/0165-5876(91)90098-v
13. Chayarpham S, Stuart J, Chongsuvivatwong V, Chinpairoj S, Lim A. A study of the prevalence of and risk factors for ear diseases and hearing loss in primary school children in Hat Yai, Thailand. J Med Assoc Thai. 1996 Jul; 79: 468-72. https://europepmc.org/article/med/8855627
14. Kim CS, Jung HW, Yoo KY. Prevalence and risk factors of chronic otitis media in Korea: results of a nation-wide survey. Acta Otolaryngol. 1993; 113: 369–75. https://doi.org/10.3109/00016489309135827
15. Anggraeni R, Hartanto WW, Djelantik B, Ghanie A, Utama DS, Setiawan EP et al. Otitis media in Indonesian urban and rural school children. Pediatr

Infect Dis J. 2014 Oct; 33: 1010-15. https://doi.org/10.1097/inf.0000000000000366
16. Mukara KB, Lilford RJ, Tucci DL, Waiswa P. Prevalence of middle ear infections and associated risk factors in children under 5 years in Gasabo district of Kigali city, Rwanda. Int J Pediatr. 2017; Article ID 4280583: 8. https://doi.org/10.1155/2017/4280583
17. Hunt L, Mulwafu W, Knott V, Ndamala CB, Naunje AW, Dewhurst S, et al. Prevalence of paediatric chronic suppurative otitis media and hearing impairment in rural Malawi: A cross-sectional survey. PLoS One. 2017; 12: e0188950. https://doi.org/10.1371/journal.pone.0188950
18. Abraham ZS, Ntunaguzi D, Kahinga AA, Mapondella KB, Massawe ER, Nkuwi EJ et al. Prevalence and etiological agents for chronic suppurative otitis media in a tertiary hospital in Tanzania. BMC Res Notes. 2019; 12: 429. https://doi.org/10.1186/s13104-019-4483-x
19. Simões EA, Kiio F, Carosone-Link PJ, Ndegwa SN, Ayugi J, Macharia IM. Otitis media and its sequelae in Kenyan schoolchildren. J Pediatric Infect Dis Soc. 2016 Dec; 5: 375-384. https://dx.doi.org/10.1093%2Fjpids%2Fpiv038
20. Zakzouk SM, Hajjaj MF. Epidemiology of chronic suppurative otitis media among Saudi children–a comparative study of two decades. Int J Pediatr Otorhinolaryngol. 2002; 62: 215–18. https://doi.org/10.1016/S0165-5876(01)00616-4
21. Godinho RN, Goncalves TML, Nunes FB, Becker CG, Becker HMG, Guimaraes RES. Prevalence and impact of chronic otitis media in school age children in Brazil. First epidemiologic study concerning chronic otitis media in Latin America. Int J Pediatr Otorhinolaryngol. 2001; 61: 223-32. https://doi.org/10.1016/S0165-5876(01)00579-1
22. Davidson J, Hyde ML, Alberti PW. Epidemiologic patterns in childhood hearing loss: a review. Int J Pediatr Otorhinolaryngol. 1989 Jul; 17: 239-66. https://doi.org/10.1016/0165-5876(89)90051-7
23. Gunasekera H, Knox S, Morris P, Britt H, McIntyre P, Craig JC. The spectrum and management of otitis media in Australian indigenous and nonindigenous children: a national study. Pediatr Infect Dis J. 2007 Aug; 26: 689-92. https://doi.org/10.1097/inf.0b013e3180621177
24. Ayukawa H, Bruneau S, Proulx JF, Macarthur J, Baxter J. Otitis media and hearing loss among 12-16-year-old Inuit of Inukjuak, Quebec, Canada. Int J Circumpolar Health. 2004; 63: 312-14. https://doi.org/10.3402/ijch.v63i0.17926
25. Jensen RG, Koch A, Homoe P. The risk of hearing loss in a population with a high prevalence of chronic suppurative otitis media. Int J Pediatr Otorhinolaryngol. 2013; 77: 1530-1535 https://doi.org/10.1016/j.ijporl.2013.06.025
26. Anvstorp MB, Homoe P, Bjerregaard P, Jensen RG. Chronic suppurative otitis media, middle ear pathology and corresponding hearing loss in a cohort of Greenlandic children. Int J Pediar Otorhinolaryngol. 2016; 83: 148-153. https://doi.org/10.1016/j.ijporl.2016.01.017
27. Ibekwe TS, Nwaorgu OGB. Classification and management challenges of otitis media in a resource-poor country. Niger J Clin Pract. 2011 Jul-Sep; 14: 262-9. https://doi.org/10.4103/1119-3077.86764
28. Parmar SM, Sood A, Chakkal HS. Prevalence of chronic suppurative otitis media in schoolgoing children. Indian journalof otolology. 2018; 24: 223-6. https://www.indianjotol.org/text.asp?2018/24/4/223/254227
29. Bellad SA, Kavi A, Mudhol RS. Prevalence of chronic suppurative otitis media among schoolchildren residing in rural area of Belagavi, South India. Indian J Otolaryngol Head Neck Surg. 2019 Nov; 71: 1549-52. https://doi.org/10.1007/s12070-019-01627-9
30. Parvez A, Khan Z, Hashmi SF, Khan MS. A cross sectional study of chronic suppurative otitis media and its associated factors among primary school children in rural and urban areas of Aligarh, India. Int J Community Med Public Health. 2016; 3: 2150-2154. DOI: http://dx.doi.org/10.18203/2394-6040.ijcmph20162561
31. Kamal N, Joarder AH, Chowdhury AA, Khan AW. Prevalence of chronic suppurative otitis media among the children living in two selected slums of Dhaka city. Bangladesh Med Res Counc Bull. 2004 Dec; 30: 95-104. https://pubmed.ncbi.nlm.nih.gov/16240980/
32. Thampi M, Gupta A, Sen K, Jain S. Evaluation of contralateral ear in unilateral chronic otitis media: necessary or not? Indian J Otolaryngol Head Neck Surg. 2020. https://doi.org/10.1007/s12070-020-01824-x
33. Da Costa SS, Rosito LPS, Dornelles C, Sperling N. The contralateral ear in chronic otitis media: a series of 500 patients. Arch Otolaryngol Head Neck Surg. 2008 Mar; 134: 290-3. https://doi.org/10.1001/archoto.2007.38
34. Kumari MS, Madhavi J, Krishna NB, Meghanadh KR, Jyothy A. Prevalence and associated risk factors of otitis media and its subtypes in South Indian population. Egyptian journal of ear nose throat and allied sciences. 2016; 17: 57-62. http://dx.doi.org/10.1016/j.ejenta.2016.04.001
35. Anggraeni R, Carosone-Link P, Djelantik B, Setiawan EP, Hartanto WW, Ghanie A et al. Otitis media related hearing loss in Indonesian school children. Int J Pediatr Otorhinolaryngol. 2019 Oct; 125: 44-50. https://doi.org/10.1016/j.ijporl.2019.06.019

36. Papp Z, Rezes S, Jókay I, Sziklai I. Sensorineural hearing loss in chronic otitis media. Otol Neurotol. 2003 Mar; 24: 141-4. https://doi.org/10.1097/00129492-200303000-00003
37. Shetty KC, Jayaramaiah SK, Kolathingal B, Alva S. Sensorineural hearing loss in chronic otitis media: analysis of an overlooked entity. Int J Otorhinolaryngol Head Neck Surg. 2019 Sep; 5: 1355-59. http://dx.doi.org/10.18203/issn.2454-5929.ijohns20193883
38. Cusimano F, Cocita V, D'Amico A. Sensorineural hearing loss in chronic otitis media. JLaryngolOtol. 2007; 103: 158-163. https://doi.org/10.1017/S0022215100108333
39. Levine BA, Shelton C, Berliner KI, Sheehy JL. Sensorineural loss in chronic otitis media: Is it clinically significant? Arch Otolaryngol Head Neck Surg. 1989; 115: 814-16. https://doi.org/10.1001/archotol.1989.01860310052021
40. MacAndie C, O'Reilly BF. Sensorineural hearing loss in chronic otitis media. Clin Otolaryngol Allied Sci. 2001; 24: 220-22. https://doi.org/10.1046/j.1365-2273.1999.00237.x
41. Rajput MS, Rajput MSA, Arain AA, Zaidi SS, Hatem A, Akram S. Mucosal type of chronic suppurative otitis media and the long-term impact on hearing loss. Cureus. 2020 Sep; 12: e10176. https://doi.org/10.7759/cureus.10176
42. Feng H, Chen Y. Analysis of sensorineural hearing loss in chronic suppurative otitis media. Lin Chuang Er Bi Yan Hou Ke Za Zhi. 2004 Oct; 18: 579-81. https://pubmed.ncbi.nlm.nih.gov/15620131/
43. Amali A, Hosseinzadeh N, Samadi S, Nasiri S, Zebardast J. Sensorineural hearing loss in patients with chronic suppurative otitis media: Is there a significant correlation? Electron Physician. 2017 Feb; 9: 3823-27. https://doi.org/10.19082/3823
44. Singer AEA, Awad A-NOG, El-Kader RMA, Mohamed AR. Risk factors of sensorineural hearing loss in patients with unilateral safe chronic suppurative otitis media. Am J Otolaryngol. 2018 Mar-Apr; 39: 88-93. https://doi.org/10.1016/j.amjoto.2018.01.002
45. Sakagami M, Maeda A, Node M, Sone M, Mishiro Y. Long-term observation on hearing change in patients with chronic otitis media. Auris Nasus Larynx. 2000; 27: 117-20. https://doi.org/10.1016/s0385-8146(99)00065-6
46. Jesic SD, Jotic AD, Babic BB. Predictors for sensorineural hearing loss in patients with tubotympanic otitis, cholesteatoma, and tympanic membrane retractions. Otol Neurotol. 2012; 33: 934-40. https://doi.org/10.1097/mao.0b013e318259b885
47. Chadha SK, Agarwal AK, Gulati A, Garg A. A comparative evaluation of ear diseases in children of higher versus lower socioeconomic status. J Laryngol Otol. 2005; 120: 16-19. https://doi.org/10.1017/S0022215105001520
48. Adhikari P. Chronic suppurative otitis media in school children of Kathmandu Valley. Int Arch Otorhinolaryngol. 2007; 11: 175-178. http://arquivosdeorl.org.br/additional/acervo_eng.asp?id=421

This page is intentionally left blank

Global Journal of Medical Research: J
Dentistry & Otolaryngology
Volume 23 Issue 2 Version 1.0 Year 2023
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Prevelance of Patterns of Impactions in the State of Punjab- A Retrospective Research Analysis

By Rashi Bahl, Amoldeep Kaur, Megha Bahal, Siddharth Bahl, Vanshika Saggar & Simrat Singh Johal

Abstract- An impacted tooth is the one that has lost its ability to erupt fully in the oral cavity. If a tooth which is impacted at the age of 18 years has high chances of 30-50% of erupting in the oral cavity by the age of 25 years. Studies show that if it does not erupt by the age of 25 years it will not change its position and will remain impacted for the rest of the lifetime. There is need of surgical removal of the tooth. It requires extensive skills and experience to handle such cases with minimum trauma to the oral tissues. With evolution it is seen that there is constant reduction in the jaw size which seems to be the reason for increased chances of impaction. Apart from evolution, the changes in the dietary pattern with industrial revolution, for raw food to its soft texture food which doesn't require much of muscle efforts, hinder the proper jaw development leading to increased chances of impaction. It is seen that the teeth to erupt first in the oral cavity has rare chances of impaction and vice versa.(1)

Keywords: *impaction, third molar, dentoalveolar, surgical, extraction, congenital, embedded.*

GJMR-J Classification: *NLM: WU 113*

Strictly as per the compliance and regulations of:

Prevelance of Patterns of Impactions in the State of Punjab- A Retrospective Research Analysis

Rashi Bahl [α], Amoldeep Kaur [σ], Megha Bahal [ρ], Siddharth Bahl [ω], Vanshika Saggar [¥] & Simrat Singh Johal [§]

Abstract- An impacted tooth is the one that has lost its ability to erupt fully in the oral cavity. If a tooth which is impacted at the age of 18 years has high chances of 30-50% of erupting in the oral cavity by the age of 25 years. Studies show that if it does not erupt by the age of 25 years it will not change its position and will remain impacted for the rest of the lifetime. There is need of surgical removal of the tooth. It requires extensive skills and experience to handle such cases with minimum trauma to the oral tissues. With evolution it is seen that there is constant reduction in the jaw size which seems to be the reason for increased chances of impaction. Apart from evolution, the changes in the dietary pattern with industrial revolution, for raw food to its soft texture food which doesn't require much of muscle efforts, hinder the proper jaw development leading to increased chances of impaction. It is seen that the teeth to erupt first in the oral cavity has rare chances of impaction and vice versa.[1] Initially there is enough space in the oral cavity for the teeth to erupt, hence the first molar and incisors are rare impacted while third molars are commonly impacted. The aim of the present study is to evaluate the prevalence of impacted teeth in the state of Punjab.

Keywords: impaction, third molar, dentoalveolar, surgical, extraction, congenital, embedded.

I. Introduction

The mandibular third, molars are the most frequently impacted teeth in the human and surgical extractions have become one of the commonest dentoalveolar surgery (Gbotolorun et al,2007).[2]The most often congenitally missing as well as impacted teeth are the third molars, which are present in 90% of the population with 33% having at least one impacted third molar. They account for 98% of all the impacted teeth. The incidence varies from 9.5% to 68% in different populations.[2.3]

Author α: Professor and Head, Department of Oral and Maxillofacial Surgery, Baba Jaswant Singh Dental College, Hospital and Research Institute, Ludhiana, Punjab.
Author σ: Senior Lecturer, Department of Oral and Maxillofacial Surgery, Baba Jaswant Singh Dental College, Hospital and Research Institute, Ludhiana, Punjab.
Author ρ: Senior Lecturer, Department of Oral Medicine and Radiology, Baba Jaswant Singh Dental College, Hospital and Research Institute, Ludhiana, Punjab. e-mail: meghabahal001@gmail.com
Author ω §: Intern, Shaheed Kartar Singh Sarabha Dental College and Hospital, Sarabha, Ludhiana, Punjab.
Author ¥: Intern, Baba Jaswant Singh Dental College, Hospital and Research Institute, Ludhiana.

According to Garn the mandibular third molar is an unusual tooth characterized by considerable variability in formation, timing, variation in crown and root morphology and not infrequentiy, by agenesis. Impaction is defined as completely or partially unerupted and positioned against another tooth, bone or soft tissue, so that its further eruption would be unlikely.[3.4] Third molars are the most frequently impacted teeth because of their particular topography, phylogeny and ontogeny. They are directly or indirectly associated with numerous disorders in the mouth, jaw and facial regions.[5] Development of mandibular third molars starts in the ramus of mandible at about the age of seven years. The third molars are the last teeth to erupt in all races despite racial variations in the eruption sequence. Racial variation in facial growth, jaw and teeth size, nature of diet, extent of generalised tooth attrition, degree of use of masticatory apparatus and genetic inheritance are the crucial factors which determines the eruption pattern, impaction status and incidence of agenesis of third molars. Impacted teeth were seldom a problem for Neolithic man.[6] Their highly abrasive diet caused attrition of teeth resulting in reduction of mesiodistal distance of dentition. This allows medial migration of teeth and adequate space was available for the eruption of third molars .But with the arrival of refined food and consequential reduction in the masticatory functional load, today, the rate of impaction of third molar shows a significant increase (John Hunter theory of nature and nurture).[7] Mead believed that delay in eruption causes impaction of teeth. Radiographs like I.O.P.A.R and orthopantomograms (OPG) are used to evaluate the type of impaction, any anatomical impediments that are preventing its eruption; whether it is completely or partially embedded in bone, marginal bone height, condition of adjacent second molars and relation of third molars to inferior alveolar canal; so that a proper management can be planned.[8] So our study is aimed to evaluate the prevalence of, Impaction of mandibular third molar and angulation of impaction radiographically.

II. Methods and Materials

The study was conducted in Department of Oral surgery, BJS Dental College Ludhiana. Study represents retrospective analysis of panoramic radiographs (orthopantomograms) of patients referred to Department

of oral surgery from January 2019 to August 2021 with indication for surgical removal of impacted third molars. Four hundred and fifty radiographs were reviewed and related data were selected from their dental records.

Inclusion criteria of the study group was complete root formation of mandibular third molar. Exclusion criteria were: patients younger than seventeen years, poor quality of OPG, incomplete records, presence of dentoalveolar trauma or other pathological dentoalveolar condition, presence of any systemic or craniofacial anomaly or syndrome (such as Down Syndrome, Cleidocranialdysplasia) and absence of mandibular second molar. To eliminate the inter-examination errors, the radiographs were analysed by a single examiner in a dark room using an appropriate X-ray viewer and magnifying lenses. The angulation and class and type pattern of impaction were established via visual impression.

Orthopantomograms were taken for all subjects in order to assess the level of eruption, angulation, third molar space, mesiodistal length of impacted 3rd molar and relation of inferior alveolar nerve to impacted third molar. It was also used for evaluating agenesis of third molar and angulations of impaction.

Impacted third molar can also be classified according to their angular relationship to the adjacent second molar. Angulation of the impacted third molar can be determined by evaluating the angle formed between the intersected longitudinal axes of the impacted third molar and the adjacent second molar, as described by Winter, either usually or by using an orthodontic protractor.

Depth or level of maxillary and mandibular third molar can be classified using Pell and Gregory classification system, where the impacted teeth are assessed according to their relationship to the occlusal surface of adjacent second molar. If the third molar is at the same level or above the occlusal surface of the adjacent second molar then it is classified as A. If it is between the Occlusal surface and cervical line of second molar then it is classified as B.C level is when the third molar is below the cervical line of the adjacent second molar.

Third molar can also be classified according to the relationship between Cemento enamel Junction (CEJ) of impacted tooth and the associated bone level. Level A is assigned to any impacted third molar that is not buried in bone. Level B is assigned to any impacted third molar that is partially buried in bone, when any part of the CEJ is lower than the bone level. Level C is assigned to impacted third molars that are completely buried in bone.

III. Results

There were 450 patients consisting 288 males and 162 females age between 14 to 25 years with mean age of 19.62 years (SD =2.575). Table 1 illustrates type of impaction. In the mandibular arch (left), Mesioangular impaction was the most frequently seen (38.4%) followed by horizontal (38%), vertical (8.9%) and distoangular impaction (3.3%). In the mandibular arch (right), Mesioangular impaction was most frequently seen (37.1%), followed by horizontal impaction (28.2%), vertical (10%) and distoangular impaction (12%) as shown in Table 2. Table 3 shows type of impaction in the maxillary arch (right), the most frequently impacted third molar was found to be in horizontal angulation (49.1%) which is followed by distoangular impaction (27.1%), mesioangular impaction (5.8%) and (0.2%) vertical impaction. In the maxillary arch (left), the most frequently impacted third molar was found to be in horizontal angulation (46.2%), which is followed by distoangular impaction (26.4%), mesioangular (8.9%) and vertical impaction (0.2%) as shown in table 4.

Table 1: Angulation of impaction of mandibular third molar on the left side (1) mesioangular, (2) distoangular, (3) horizontal, (4) vertical

MAND LEFT ANGULATION			
		Frequency	Percent
Valid	0	50	11.1
	1	173	38.4
	2	15	3.3
	3	171	38.0
	4	40	8.9
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

Table 2: Angulation of impaction of mandibular third molar on the right side (1) mesioangular, (2) distoangular, (3) horizontal, (4) vertical

MAND RIGHT ANGULATION			
		Frequency	Percent
Valid	0	56	12.4
	1	167	37.1
	2	54	12.0
	3	127	28.2
	4	45	10.0
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

Table 3: Angulation of impaction of maxillary third molar on the left side (1) mesioangular, (2) distoangular, (3) horizontal, (4) vertical

MAX LEFT ANGULATION			
		Frequency	Percent
Valid	0	81	18.0
	1	40	8.9
	2	119	26.4
	3	208	46.2
	4	1	.2
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

Table 4: Angulation of impaction of maxillary third molar on the right side (1) mesioangular, (2) distoangular, (3) horizontal, (4) vertical

MAX RIGHT ANGULATION			
		Frequency	Percent
Valid	0	79	17.6
	1	26	5.8
	2	122	27.1
	3	221	49.1
	4	1	.2
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

According to level/depth of impaction (Pell and Gregory), in the maxillary arch (left) level3 was most abundant (33.1%), followed by level 1 (31.6%) and then level 2(17.6) as shown in table 5. According to level/depth of impaction (Pell and Gregory), in the maxillary arch (right), level 3 was most abundant (33.6%), followed by level 1(32%) and then level 2 (16.4%) (table 6). According to level/depth of impaction (Pell and Gregory), in the mandibular arch (left), level 2 was most abundant (34.2%), followed by level 1(28.4%) and then level 3 (25.8%) as shown in table 7. According to level /depth of impaction (Pell and Gregory) for mandibular arch (right), level 2 is most abundant (45.8%), followed by level 3 (21.1%) and then level 1 (20.9%) (table 8).

Table 5: Occlusal relation of the maxillary left third molar (1) Level1, (2) level 2, (3) level 3

MAX LEFT P AND G OCC			
		Frequency	Percent
Valid	0	79	17.6
	1	142	31.6
	2	79	17.6
	3	149	33.1
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

Table 6: Occlusal relation of the maxillary right third molar (1) Level1, (2) level 2, (3) level 3

MAX RIGHT P AND G OCC			
		Frequency	Percent
Valid	0	80	17.8
	1	144	32.0
	2	74	16.4
	3	151	33.6
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

Table 7: Occlusal relation of the mandibular left third molar (1) Level1, (2) level 2, (3) level 3

MAND LEFT P AND G OCC			
		Frequency	Percent
Valid	0	50	11.1
	1	128	28.4
	2	154	34.2
	3	116	25.8
	4	1	.2
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

Table 8: Occlusal relation of the mandibular right third molar (1) Level1, (2) level 2, (3) level 3

MAND RIGHT P AND G OCC			
		Frequency	Percent
Valid	0	54	12.0
	1	94	20.9
	2	206	45.8
	3	95	21.1
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

According to the ramus relationship to the third molar (Pell and Gregory) in the maxillary arch (left), most abundant is Class III (32.9%), followed by Class I(29.1%) and then class II (20.2%) as shown in table 9. According to the ramus relationship to the third molar (Pell and Gregory) in the maxillary arch (right), most abundant is Class III (33.3%), followed by Class I(32%) and then Class II (16.7%) as shown in table 10. According to ramus relationship to the third molar (Pell and Gregory) in the mandibular arch (left), the most abundant is Class II (41.3%) , followed by Class III (24.2%) and then Class I (23.1%) as shown in table 11. According to ramus relationship to the third molar (Pell and Gregory) in the mandibular arch (right), the most abundant is Class II (49.1%), followed by Class III (19.8%) and then Class I (18.9%) as shown in table 12.

Table 9: Ramus relationship of impacted maxillary left third molar, (1) class 1, (2) class 2, (3) class 3

MAX LEFT P AND G RAMUS			
		Frequency	Percent
Valid	0	79	17.6
	1	131	29.1
	2	91	20.2
	3	148	32.9
	Total	449	99.8
Missing	System	1	.2

Table 10: Ramus relationship of impacted maxillary right third molar, (1) class 1, (2) class 2, (3) class 3

IMPACTED MAX RIGHT P AND			
		Frequency	Percent
Valid	0	80	17.8
	1	144	32.0
	2	75	16.7
	3	150	33.3
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

Table 11: Ramus relationship of impacted mandibular left third molar, (1) class 1, (2) class 2, (3) class 3

MAND LEFT P AND G RAMUS			
		Frequency	Percent
Valid	0	50	11.1
	1	104	23.1
	2	186	41.3
	3	109	24.2
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

Table 12: Ramus relationship of impacted mandibular left third molar, (1) class 1, (2) class 2, (3) class 3

MAND RIGHT P AND G RAMUS			
		Frequency	Percent
Valid	0	54	12.0
	1	85	18.9
	2	221	49.1
	3	89	19.8
	Total	449	99.8
Missing	System	1	.2
Total		450	100.0

IV. Discussion

A large population of individuals may have one or more impactions. The prevalence and types of impactions vary in different racial and ethnic groups. These may be due to racial genetic characteristics, inbreeding as well as epigeneric factors such as food habits. It is therefore important to understand the pattern of impactions in various communities and population sub-groups.[9]

This study was undertaken to study the prevalence and pattern of impactions in the Punjab population. Orthopantomographs were taken of 450 subjects from Ludhiana district who consented to participate in our study. Only those subjects who confirmed to the inclusion and exclusion criteria outlined previously were selected for the study.

The parameters sought were prevalence of impacted third molars, angulation, level of eruptions, mesiodistal width of impacted third molars and retromandibular space available. The OPGs were also used for evaluating the agenesis of third molars.

In our study, the frequency of missing third molars showed a predilection for maxilla over mandible which was consistent with the study of hattab [18] and sandhu [19] and nanda [20].

Higher prevalence of impacted teeth was found in study of morris and jerman in a study conducted in USA on 5000 subjects (65%)[17,21] ,probably as a result of different age groups included in study. Since our study represents all age groups; and also in study of Quek et al. on 1000 subjects of Chinese population (68%) due to higher jaw teeth size discrepancy, wider teeth and smaller dental arch length of Chinese population

compared with Caucasians.[6, 16, 18, 21]. The frequency of normally erupted third molars in our study is 42%, which is lower than findings of other studies conducted on African american population (58%)[15, 22]. And Indian population (65%)[23,11] which suggests racial and ethnic factors contributing to impaction of third molars. The most common angulation of impaction is mesioangular (6, 24, 21, 23, 25, and 26).

V. Conclusion

An impacted tooth is one that neglects to emit into the dental curve inside the normal formative window. Since affected teeth don't eject, they are held all through the person's lifetime except if separated or uncovered precisely. Teeth may become affected in view of adjoining teeth, thick overlying bone, extreme delicate tissue or a hereditary irregularity.[12] Frequently, the reason for impaction is deficient curve length and space in which to emit. That is the all out length of the alveolar curve is littler than the tooth curve (the consolidated mesiodistal width of every tooth). The knowledge teeth (third molars) are oftentimes affected in light of the fact that they are the last teeth to eject in the oral pit. The most common types of lower wisdom tooth impaction are as follows: in Winter's classification, mesial-angular impaction; in Tetsch and Wagner's classification, oblique medial-angular impaction; in Pell and Gregory's classification, distance from the anterior edge of the mandibular ramus, impaction depth A, and impaction grade 2A; and in Asanami and Kasazaki's classification, distance of the mandibular ramus from the distal surface of the second lower molar, impaction depth A, and anterior inclination. In most cases of surgical removal of an impacted tooth, the anticipated difficulty of the procedure was rated as very difficult.

Conflicts of interest

No conflicts of interest present.

Funding

No fundings granted.

Consent for publication

Written Consent was taken from our patient regarding incorporating his panoramic radiograph in this study.

Competing interests

The authors declare that they have no competing interests.

References Références Referencias

1. Ryalat S, AlRyalat SA, Kassob Z, Hassona Y, Al-Shayyab MH, Sawair F. Impaction of lower third molars and their association with age: radiological perspectives. BMC Oral Health. 2018 Apr 4; 18(1): 58.
2. Jaroń A, Trybek G. The Pattern of Mandibular Third Molar Impaction and Assessment of Surgery Difficulty: A Retrospective Study of Radiographs in East Baltic Population. *International Journal of Environmental Research and Public Health*. 2021; 18(11): 6016.
3. Lima CJ et al. Evaluation of the agreement by examiners according to classification of third molars. Med Oral Patol Oral Cir Bucal. 2012; 17: 281-216.
4. Hattab FN et al. Impaction status of third molars in Jordanian students. Oral Surg Oral MedOral PatholRadiolEndod. 1995; 79(1): 24-29.
5. HaidarZet al. The incidence of impacted wisdom teeth in a Saudi community. Int J Oral Maxillofacial Surg.1986; 15(5): 569-571.
6. QuekSLet al. Pattern of third molar impaction in a Singapore china population: a retrospective radiographic survey. Int J Oral MaxillofacSurg. 2003; 32(5): 548-57.
7. Goax PW, White SC. Oral radiology: Principles and interpretation (2nd Ed). St Louis: CV Mosby Company 1992: 97-112,174-77.)
8. Gann SM, Lewis AB, Bonne B. Third molar formation and its development course. Angle Ortho 1962; 32: 271-79.
9. Goax PW, White SC. Oral radiology: Principles and interpretation (2nd Ed). St Louis: CV Mosby Company 1994: 83-85,126-30, 242-45, 249-53.
10. Kapoor V. Textbook of oral and maxillofacial surgery (15 Ed). New Delhi: Arya (Medi Publishing House 1996: 45-71.
11. Margaret E.R. Lower third mandibular space. Angle Orthod. 1987 April: 155-161. (PubMed]
12. Odusanya S.A., Abayomi I.O. Third molar eruption among rural Nigerians. Oral Surg Oral MED Oral Pathol.1991; 71: 151-154.[PubMed]
13. Robert M.K., Arthur C.W. The incidence of impacted teeth. A survey of Harlem Hospital. Oral Surg. February 1970; 71:151-154. (PubMed]
14. Molander Bet al. Agreement between panoramic and intra oral radiography in the assessment of marginal bone height. DentomaxillofacRadiol. 1991; 20: 155-160.
15. Pell GJ, Gregory BT. Impacted mandibular third molars: classification and modified techniques for removal. Dent Digest. 1933; 39: 330-338.
16. Winter GB. The Principles of Exodontia as Applied to the Impacted Third Molar. St. Louis, MO: American Medical Book Co; 1926.
17. Quek SL, Tay CK, Tay KH, Toh SL, Lim KC. Pattern of third molar impaction in a Singapore Chinese population: a retrospective radiographic survey. Int J Oral MaxillafacSurg. 2003; 32(5): 548-552. [PubMed]
18. HattabFaiez N., Rawashdeh Ma'amon A., Fahmy Mourad S. Impaction status of third molars in Jordanian students. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 1995; 79: 24-29. [PubMed]

19. Sandhu Sumeet, Kaur Tejinder. Radiographic evaluation of the status of third molars in the Asian-Indian students. J MaxillofacSurg. 2005; 63:640-645. [PubMed]
20. Nanda R.S., Chawla T.N. Status of third molar teeth. J Dent Assoc. February 1959; 31(2): 19-29.
21. Morris CR, Jerman AC. Panoramic radiographic survey: a study of embedded third molars. J Oral Surg1971: 29: 122-125.
22. Kramer RM, Williams AC. The incidence of impacted teeth. Oral Surg Oral Med Oral Pathol. 1970; 29(2): 237-241.
23. Ramamurthy A, Pradha J, Jeeva S, Jeddy N, Sunitha J, Kumar S. Prevalence of mandibular third molar impaction and agenesis: a radiographic south Indian study. J Indian Aca Oral Med Radiol2012; 24(3): 173-176.
24. Hassan AH. Pattern of third molar impactions in a Saudi population. Clinical, Cosmetic and Investigational Dentistry 2010; 2: 109-113.
25. Byahatti S, Ingafou MSH. Prevalence of eruption status of third molars in Libyan students. Dental Research Journal, 2012.9; 2: 152-157.
26. Jaffar RO, Mon Mon TO. Impacted mandibular third molars among patients attending Hospital UniversitiSains Malaysia. Archives of Orofacial Sciences (2009), 4(1): 7-12.

This page is intentionally left blank

Global Journal of Medical Research: J
Dentistry & Otolaryngology
Volume 23 Issue 2 Version 1.0 Year 2023
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Estimating the Prevalence of Oral Manifestations in Covid-19 Patients: A Systematic Review

By Dr. Ankita Gupta

Abstract- *Background:* The patients affected with COVID-19 present with a variety of oral manifestations. In this context, our systematic review was conducted to summarize the findings regarding oral manifestations of COVID-19.

Methods: An extensive literature search of several electronic bibliographic databases (PubMed, Scopus, Science direct, Litcovid) was done to retrieve all articles published in the English language from January 1, 2020, to June 30, 2022, reporting the prevalence of oral manifestations among COVID-19 individuals.

Keywords: *COVID-19, COVID tongue, oral ulcers, oral lesions, SARS-CoV-2.*

GJMR-J Classification: *DDC Code: 312.23 LCC Code: RJ59*

Strictly as per the compliance and regulations of:

Estimating the Prevalence of Oral Manifestations in Covid-19 Patients: A Systematic Review

Dr. Ankita Gupta

Abstract- ***Background:*** **The patients affected with COVID-19 present with a variety of oral manifestations. In this context, our systematic review was conducted to summarize the findings regarding oral manifestations of COVID-19.**

Methods: **An extensive literature search of several electronic bibliographic databases (PubMed, Scopus, Science direct, Litcovid) was done to retrieve all articles published in the English language from January 1, 2020, to June 30, 2022, reporting the prevalence of oral manifestations among COVID-19 individuals.**

Results: **Based on their eligibility, a total of 75studies comprising 11,321 patients were included. Most of the articles were published in the year 2020 (n=33) and were from Italy (n=13). Among the patients affected, most of them were in the range of more than 50 years and females (58.1%). Taste alteration (n=43; 57.3%) was found in most people followed by vesiculobullous lesions (n=41; 54.6%) and tongue manifestations (n=26; 34.6%). The most common sites of involvement in descending order were tongue (n=62), oral mucosa (n=27), lips (n=19), and others. In most of the studies, oral symptoms followed the general symptoms.**

Conclusion: **COVID-19 patients show various oral manifestations that may help clinicians for early identification of the disease. Recognition of signs and symptoms of COVID-19 is critical for early diagnosis and better prognosis.**

Keywords: COVID-19, COVID tongue, oral ulcers, oral lesions, SARS-CoV-2.

I. Introduction

The novel Coronavirus 2019 disease (COVID-19) has become a global crisis and a challenge to public health owing to its fast rate of dissemination and increased mortality rate. Although the disease was first observed in December 2019 in the Hubei Province of China, soon it circulated hastily around the world. On March 2020, the disease has been declared as a 'pandemic emergency' by the World Health Organization. The outbreak is responsible for more than 608,328,548 confirmed cases and 6,501,469 deaths worldwide till September 2022 [1].

The incubation period of disease ranges from 1-14 days with fever, cough, shortness of breath or difficulty in breathing, or fatigue as the most common presenting symptoms. Less common features, such as headache, loss of taste or smell, sore throat, diarrhea, and nausea or vomiting, may also be present [2]. The severity of symptoms varies from person to person as it depends upon the time of exposure to the virus, the patient's age and gender as well as the coexisting diseases.

It was found that the coronavirus invades human cells with the help of receptors known as Angiotensin-converting enzyme 2 (ACE 2) and transmembrane protease serine 2 (also called transmembrane serine protease or TMPRSS2) [3]. Among these two, the ACE 2 receptor is found mainly in the cells of the lung, liver, kidney, gastrointestinal (GI) and even on the salivary glands and dorsum of the tongue of the oral cavity [4]. These cells with the receptors act as host cells for the virus through which, the virus invades these cells of the body and starts an inflammatory response in these organs.

Previously, it was assumed that COVID-19 lacks oral manifestations unlike other viral exanthema but after some years, SARS-CoV-2 was detected from the saliva of the patients suggesting a possibility that oral manifestations could be clinical characteristics of COVID-19. Also, the presence of the ACE 2 receptor in some specific organs of the oral cavity such as the tongue and salivary glands confirms the possibility of the involvement of the oral cavity in coronavirus infection. The frequency of oral manifestations among COVID-19 patients is unknown but some previous studies have tried to provide the incidence and prevalence of these manifestations. A huge study conducted by Nuno-Gonzalez on 666 patients suggests that oral cavity findings are present in 25.65% of cases [5]. The commonly occurring oral manifestations found in a case series conducted by Sinadinos and Shelswell were blisters, ulcerations, and desquamative gingivitis [6]. In the oral cavity, the most commonly involved sites in COVID-19 disease are the palate and tongue followed by the gums and the lips [7]. In the tongue, the ulcerations are quite common specifically on the dorsum surface or sides of the tongue. Rarely, only in 15% of patients, the ulcerations develop on the ventral surface [8]. Additionally, multiple pinpoint yellowish ulcers and white plaque can also be present on the tongue [3]. The occurrence of white plaque on the dorsal surface of the tongue is due to the occurrence of fungal infections which is also one of the common oral manifestations of SARS-CoV-2, probably caused by lower immunity. Dima et al reported a case of a neonate with COVID-19 having oral cavity candidiasis [9]. These oral manifestations are accompanied with pain in 75% of

Author: e-mail: ankitag@lnctrishiraj.ac

cases [7]. In another study, 25% of patients reported impaired taste, 15% had burning sensations, and 20% had difficulty in swallowing. Ageusia was observed in 24% of patients, hypogeusia in 35%, and dysgeusia in 38% of the COVID-19 patients. Taste disorders are more common in women than men [10].

A proper understanding of the dentist regarding oral manifestations of COVID-19 is very important as it helps in the early diagnosis of the disease and hence prevents transmission. The present systematic review aims to summarize the findings of the available past literature regarding oral manifestations of COVID-19 to highlight the role of the dentist in intervening the severity of this deadly pandemic disease.

II. Methods

a) Outcome

The primary outcome of this study was the systematic evaluation and characterization of currently reported cases and studies of oral manifestations associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [11].

b) Eligibility criteria

The clinical evidence was searched in the form of original peer-reviewed journal articles which include observational and cross-sectional studies investigating the prevalence of oral disorders in patients with COVID-19. Apart from these, case reports and case series were also included in the systematic review. The range of data publication was limited fromJanuary 1, 2020, to June 30, 2022. Conference papers, book reviews, book chapters, letters to the editor and replies, newspaper and newsletter articles, expert opinions, and theses or dissertations were not used. Articles that are not published in English were also excluded.

c) Data sources and search strategy

We conducted an extensive literature search in several electronic bibliographic databases (PubMed, Scopus, Science direct, Litcovid) and retrieved all articles published from January 1, 2020, to June 30, 2022. Observational cross-sectional, case-control and cohort studies, case reports/ series reporting MIS-C, and letters to the editor were screened. The surveillance studies were also included.

PUBMED [search until 30.06.2022]

((((((((((((((((((((((((oral manifestations) OR (oral involvement)) OR (oral lesions)) AND (gingival lesions)) OR (gingival bleeding)) OR (gingival ulcer)) AND (buccal mucosa involvement)) OR (buccal ulcer)) AND (lip ulcer)) OR (lip mucosa involvement)) AND (tongue lesions)) OR (tongue ulcer)) OR (tongue involvement)) OR (ageusia)) OR (hypogeusia)) OR (dysgeusia)) OR (loss of taste)) OR (altered taste)) OR (gustatory impairment)) AND (burning sensation)) AND (aphthous stomatitis)) AND (ulcers on palate)) AND (COVID-19)) OR (coronavirus)) OR (corona pandemic)) OR ((SARS-CoV-2)

LITCOVID [search until 30.06.2022]

"Oral manifestations in COVID-19" OR "tongue lesions in coronavirus" OR "gingival involvement in coronavirus pandemic" OR " buccal mucosa involvement in COVID-19"

SCOPUS [search until 30.06.2022]

(tongue lesions OR mucosal lesions OR oral lesions AND COVID-19 OR coronavirus)

SCIENCE DIRECT [search until 30.06.2022]

Oral manifestations in COVID-19 OR oral involvement in coronavirus

d) Data collection

The inclusion of studies was done in two phases. In phase I, the titles of all the studies were screened first, followed by the screening of abstracts, based on the inclusion and exclusion criteria. Articles eligible based on the title and abstract would then be read in full and judged for their eligibility. Duplicates were eliminated and irrelevant articles were excluded from the systematic review. The full-text articles of all potential studies were obtained and evaluated for inclusion. In phase II, the references of all the included studies, case reports, and case series were again screened to search for any new potentially eligible studies.

All studies that reported orofacial manifestations in patients with laboratory-confirmed COVID-19 were included. Studies with suspected COVID-19 cases were excluded. To provide a systematic overview of these studies, we evaluated the included studies in terms of their demographic details such as author, year, country, study type, sample size, gender, age, study duration, medical history, admission in the ICU, and severity of the disease. Apart from this, the details related to the oral manifestations such as the site affected, onset of the orofacial manifestations, general symptoms, any special investigations performed, treatment of oral lesions, and outcome of the disease were also recorded. In the end, a total of 75 articles were included in this systematic review. The article inclusion flow diagram is shown in figure 1

e) Outcome measures

The primary outcome was estimating the prevalence of oral manifestations among COVID-19 patients. The secondary outcome was the most common type of oral manifestation and site affected in the oral cavity.

f) Statistical analysis

Qualitative data were resynthesized by grouping and comparing information reported in newly included

studies. Oral and mucosal conditions were summarized in schematic representations.

III. Results

A lot of studies along with the literature reviews have evaluated the oral mucosa involvement in COVID-19. We got 268 articles on the preliminary search, out of them, 75 articles were included in the final analysis [5,6,9,10,12-82].

The demographic characteristics of the included studies (n=75) are shown in table 1. We retrieved the data from 75 studies [5,6,9,10,12-82] including 11,321 patients with individual sample sizes of studies ranging from 14 [47] to 1172 [35]. All the articles (n=75) were published in year 2020 [6,9,12-27,56-69], 2021 [5,28-43,70-79], and 2022[44-55,80-82] but most of the articles (n=33) were from 2020 followed by the year 2021 (n=31) and 2022 (n=15).

The 75 articles included data from 27 countries around the globe. Most of the studies were conducted in Italy (n=13) [16,19,20,22,23,28,29,36,37,58,66,72,81], followed by Brazil (n=7) [10,47,49,52,56,75,77], India (n=7) [17,33,44,45,50,55,80], Egypt (n=5) [34,38,41,68,71], Turkey (n=5) [26,39,42,48,64], Iran (n=4) [25,54,62,79], Spain (n=4) [5,53,59,60], USA (n=4) [27,57,65,67], Saudi Arabia (n=3) [40,46,51], New York (n=2) [30,31], China (n=2) [15,35], Iraq (n=2) [12,43], Israel (n=2) [13,74], Europe (n=2) 18,70], Copenhagen (n=1) [14], California (n=1) [21], France (n=1) [24], Qatar (n=1) [32], Romania (n=1) [9], United Kingdom (n=1) [6], Colombia (n=1) [61], Norway (n=1) [63], Indonesia (n=1) [69], Afghanistan (n=1) [73], Czech Republic (n=1) [76], Ukraine (n=1) [78], and Poland (n=1) [82].

Among 75 studies, most of them were cross-sectional studies (n=36) [5,12-26,29,30,33,34,37-42,44-46,48-51,53-55] followed by case report (n=20) [10,61-75,78-81], case series (n=10) [6,9,56-60,76,77,82], retrospective studies (n=6) [27,28,35,36,47,52], prospective study (n=2) [31,43], and case-control study (n=1) [32].

A total of 11,321 patients were evaluated in the systematic review, of which 6581 (58.1%) were females. Three studies did not report the gender of the patients in their studies [5,22,35]. The age group of most of the studies (n=39) was in the range of more than 50 years followed by less than 30 years (n=12). Three studies did not report the age group of the patients [5,34,35] and one study was conducted among newborns [9]. The detailed age distribution is shown in figure 2.

Only 33 studies have reported the medical history of the patient. Among those studies, most patients were having hypertension (n=25), diabetes (n=19), respiratory disease and asthma (n=7), cardiovascular disease (n=6), allergy (n=4), and others. Regarding hospitalization, 21 studies reported that COVID-19 patients were admitted to the hospital, 11 studies reported hospitalization in ICU, and 5 of the studies also showed that the patients were ventilated (Table 1).

The oral manifestations were divided into 12 categories: taste alteration, tongue manifestation, xerostomia, red and white lesions, vesiculobullous lesions, periodontal changes, burning sensation, bleeding disorders, lip lesions, TMJ disorders, salivary gland disorders, and fungal infections. Most of the patients were having multiple signs and symptoms. Hence, we have calculated the oral manifestation individually. Taste alteration (n=43; 57.3%) was found in most people followed by vesiculobullous lesions (n=41; 54.6%) and tongue manifestations (n=26;34.6%). The detailed results of the type of oral manifestation is shown in figure 3.The most common sites of involvement in descending order were the tongue (n=62) followed by oral mucosa (n=27) and lips (n=19) (Figure 4). Descriptive characteristics of the oral lesions are shown in Table 2.

Taste Disorders and tongue manifestation: The prevalence of taste disorders and tongue manifestation was assessed with data from 43 (57.3%) and 26 (34.6%) studies respectively. Loss of taste or ageusia and was reported by 21 studies [12,14,20,23,35,40-42,44,49, 53,55,56,58,63,65,67,70,72,74]. Taste alteration or dysfunction was reported by [5,13,16-19,21,22,29, 36,38,46,51,54,66,78], Amblygeustia [15], dysgeusia [24,28,37,50,54,59,60]

Three studies [29,36,51] reported geographic tongue and one study [30] reported strawberry tongue among the COVID-19 patients. Other tongue manifestations are shown in table 2.

Vesiculobullous lesions: Forty one (54.6%) included studies and case reports or case series were having the vesiculobullous lesions [5,6,10,26,27,29,31,33,34,37-44,46-51,53,55,56,57,59-62,64,69,70,75-77,79,81,82].

Xerostomia: Xerostomia was noted in 18cross-sectional studies [13,15,28,34,37,38,40,42,44,45,46,48,50-55] and 2 case reports[60,78] constituting 26.6% of the included studies.

Red and white lesions: Eighteen studies(24%) reported red and white lesions in COVID-19 positive patients [9,24-26,29,33,36,37,39,43,49,51,53,57,61,68,80,82].

Periodontal involvement: Twelve studies (16%) were found having the involvement of gingiva and periodontium among the patients of COVID-19 of the present systematic review [6,26,29,32,38,39,42,44, 51,55,59,78].

Burning sensation: Eleven studies (14.6%) reported the complaint of burning sensation [5,33,38,42-44,53,55, 57,60,78].

Bleeding disorders: A total of six studies (8%) reported the incidence of bleeding disorders in COVID-19-positive patients [29,51-53,64,82].

Other findings: Salivary gland disorders (4%) [37,38,52], fungal infection (2.6%) [43,82], and dental pain (2.6%) [34,42] was found in three, two, and two studies respectively.

The latency time between the appearance of systemic symptoms and oral lesions was between 2 weeks before to 10 days after the onset of systemic symptoms. In most of the studies (n=14), general symptoms followed the oral symptoms (Table 2).

General treatment, as well as the treatment for the oral lesions among COVID-19 patients, is given in supplementary table 1. Oral lesions healed between 7 and 21 days after appearance. Different types of therapies including chlorhexidine mouthwash, nystatin, oral fluconazole, topical or systemic corticosteroids, systemic antibiotics, systemic acyclovir, artificial saliva, and photobiomodulation therapy (PBMT) were prescribed for oral lesions depending on the severity and etiology.

IV. Discussion

COVID-19 has become a public health problem around the world. Initially, it was thought that the lack of involvement of the oral mucosa is a differentiating feature of COVID-19 as compared to other viral infections but in April 2020, a case report published by Chaux-Bodard et al have shown the association of COVID-19 with the oral mucosa in a 45-year-old female having painful inflammation of the papilla of the tongue, which ultimately healed as an asymptomatic ulcer in 10 days without a scar along with a skin lesion in the toe and was tested positive on Day 8 [83]. Since then, many observational studies and case reports were published in the literature depicting the involvement of oral mucosa among COVID-19 patients. The present systematic review was conducted with the same intent to elaborate the association between COVID-19 and the oral cavity with the help of previously published studies.

SARS-CoV-2 invades human cells of the lower respiratory system with the help of receptors known as ACE 2 and transmembrane protease serine 2 [3]. Among these two, the ACE 2 receptor is found mainly in the cells of the lung, liver, kidney, gastrointestinal (GI) and even on the cells of nasal epithelium and oral mucosa [4]. These cells act as host cells for the virus through which, the virus invades these cells of the body and starts an inflammatory response in these organs which, in turn, causes the smell and taste dysfunctions early in the course of the disease [15]. Hence, the mechanism of development of oral lesions can be directly through the effects of the replicating virus in these cells (lesions will be SARS-CoV-2-specific) and indirectly as a sequel of possible drug reactions that may develop during the latency period, viral exanthem, through physical and psychological stress of the COVID-19 or its treatment, or co-infection with other bacterial infections enhancing the severity of COVID-19[59]. According to Amorim dos Santos et al [4], the deterioration of the general health of COVID-19 patients along with the longer period of hospitalization and several treatment procedures also predispose the occurrence of oral lesions. Chaux-Bodard et al. hypothesized that oral lesions may arise as a sequel of various inflammatory reactions that induce vascular inflammation [83]. Previously published reports of the Italy and United Kingdom stated the temporary association of pediatric inflammatory multisystem syndrome with SARS-COV-2 cases [84]. Various diseases like Kawasaki disease and erythema multiforme can itself predispose to oral manifestations. Hence, we have excluded such conditions from our systematic review.

Talking about the oral lesions, the most common sites of involvement in descending order were the tongue (n=62), oral mucosa (n=27), lips (n=19), entire oral cavity (palate (n=12), gingiva and periodontium (n=12), and salivary gland (n=3). Sousa et al found the palate and tongue followed by the gums and the lips as the most commonly involved sites in COVID-19 patients [7]. Description of the oral manifestations among COVID-19 patients are as follows:

a) Taste disorders

According to the various published studies, smell and taste changes are the early indicators of the COVID-19 pandemic which are effective in early diagnosis and decision making. Though these symptoms are not life-threatening, they may hamper the quality of life of the patient. Prof C. Hopkins, President of the British Rhinological Society has stated that loss of smell/taste can be the only symptom of COVID-19 [85]. Several public health surveillance organizations such as the European Centre for Disease Prevention and Control, Centre for Disease Control and Prevention (CDC), WHO [86], and Public Health England included the sudden onset of anosmia, ageusia, or dysgeusia in the list of main clinical criteria for the case definition of COVID-19 [87]. In our systematic review also, general symptoms followed the oral symptoms, especially loss of taste. The possible explanation for the taste disturbances in COVID-19 patients is the higher expression of ACE 2 receptor in the tongue as compared to the buccal and gingival tissues resulting in the damage to mucosal epithelial cells of the oral cavity [88].

In the present systematic review, the incidence of taste disorders and tongue manifestation was assessed with data from 43 (57.3%) and 26(34.6%) studies respectively. Al-Zaidi et al in their cross-sectional study found the overall prevalence of taste dysfunction

in 83.08% of COVID-19 patients. The taste recovers at one week for 50% of the participants followed by less than a week (25%), within 2 weeks (18.75%), and within 3 weeks (6.25%) [12]. Amorim dos Santos et al in their living systematic review (LSR) found taste disorder as the most prevalent oral symptom in this population with a prevalence of 45% [4] but in their second LSR, the prevalence decreased to 38%. They stated that the prevalence of taste disorders among COVID-19 patients varies from 14% in Africa to 49% in Europe [89]. Yan CH et al found taste loss in 71% of COVID-19–positive subjects and the association was strongly associated with COVID-19 positivity (OR 10.2; 95% CI, 4.74-22.1) [21]. A total of 52% reported changes in taste sensation in Biadsee A et al study with 52 patients reporting a change in spicy taste perception, 54 in salty taste, 53 in sour taste, and 61 patients in sweet taste [13]. Bodnia NC et al reported a total loss of taste in 70% of patients which resolved within 1-3 weeks for 78% and 3-6 weeks for 22% [14]. A meta-analysis conducted by Tong JY et al have shown that gustatory changes are noted in 43.93% of these individuals [90]. The prevalence of taste alterations was estimated to be around 54.73% [95% CI: 46.28–63.04%] in another meta-analysis conducted by Nijakowski K et al [91].

Three studies conducted by Favia G et al [29], Bardellini E et al [36], and Binmadi NO et al [51] reported geographic tongue in our systematic review. Bardellini E et al conducted a pediatric retrospective cohort study and reported oral pseudomembranous candidiasis (n=2), coated tongue (n=2), taste alteration (n=3), and geographic tongue (n=1) as the most common oral lesions of which, geographic tongue appeared concurrently with the high fever according to the patient's mother [36]. The etiopathogenesis of the geographic tongue is still unclear but some authors reported the association of several non-genetic multifactorial factors, including viral infections [92]. A study conducted by Halepas S et al [30] reported strawberry tongue among COVID-19 patients. Other tongue manifestations are plaque-like changes in the tongue [13,52,61], macroglossia [24,32], ulcerations on tongue [10,24,26,56,73,76,80,81], fissured tongue [29,44,73], lingual papillitis, white tongue and glossitis with patchy depapillation [5], burning sensation in tongue [42,68,78], white coat, numbness, and black discoloration of tongue [43], depapillation of tongue [45,60], hairy tongue [46], Greasy tongue coat [71], and smooth tongue and mycosis of the tongue [82].

b) Vesiculobullous lesions

Forty one included studies and case reports/case series (54.6%) have mentioned the incidence of vesiculobullous lesions [5,6,10,26,27, 29,31,33,34,37-44,46-51,53,55,56,57,59-62,64,69,70,75-77,79,81,82]. Favia G et al widely describes the histological aspect of oral SARS-CoV-2-related lesions and found ulcers (52.8%) as the most detected oral manifestation [29]. Presas CMC et al reported three cases with ulcers, of which one was infected by the SARS-CoV-2 virus and two were suspected patients infected by the SARS-CoV-2 virus. The lesions resemble herpes simplex infection but were not confirmed by biopsies [59]. Painful oral ulcers were the most common orofacial manifestations in patients with COVID-19 in a review conducted by Halboub E et al [93]. Tapia ROC et al [57] and Dalipi ZS et al [70] found bullous and lesions on the palate and oral mucosa respectively. Riad A et al found multiple ulcers (1 and 7 ulcers per patient) with their size ranging between 1 and 5 mm, of which the majority (92.3%) were not bleeding, and all of them (100%) were manifested on the dorsum or side of the tongue. They found a statistically significant association between the number of ulcers and gender, onset, duration, Ct value, and pain score [8]. A systematic review conducted by Orilisi G stated that oral ulcers, cheilitis, and tongue lesions were more common in patients before hospitalization, while perioral pressure ulcers, macroglossia, blisters, and oral candidiasis were more recurrent in patients during hospitalization [94].

Regarding the mechanism of the formation of the ulcer, it was proposed that an increased level of tumor necrosis factor (TNF)-α in COVID-19 patients can lead to chemotaxis of neutrophils to oral mucosa and the development of aphthous-like lesions. Stress and immunosuppression secondary to COVID-19 infection could be other possible reasons for the appearance of such lesions in COVID-19 patients [10].

Red and white lesions: Eighteen studies (24%) reported red and white lesions in COVID-19 positive patients [9,24-26,29,33,36,37,39,43,49,51,53,57,61,68,80,82].

The various types of red and white lesions reported in the included studies are cheilitis and oral lichenoid reaction [24], white plaques on the intraoral mucous layer [25,37,43,68,80], rash and erythema [26], candidiasis [9,29,36,49,51,53], reddish-white spots on the palate [33,57], erythema and lichen planus [39], angular cheilitis [53,82], and reddish plaques on the lower lip [61].

Xerostomia Xerostomia was noted in 18 cross-sectional studies [13,15,28,34,37,38,40,42,44,45,46,48,50-55] and 2 case reports [60,78] with 26.6% of studies reporting the complaint of dry mouth. In a study conducted by Biadsee et al, 56% of patients reported xerostomia which was assessed by the question ''Do you feel the need to drink more (dry mouth)?'' [13]. In the updated version of the LSR performed by dos Santos et al [89], xerostomia was the most prevalent oral symptom identified in patients with COVID-19, whereas, taste disturbances were the predominant feature in the original LSR [4]. In a meta-analysis conducted Nijakowski K et al, xerostomia was prevalent

among 37.58% [95% CI: 26.35–49.53%] of the COVID-19 patients [91].

Periodontal involvement: Twelve studies (16%) [6,26,29,32,38,39,42,44,51,55,59,78] have shown the prevalence of gingivitis and periodontitis. The gingival manifestations found among the COVID-19 patients of our systematic review were the gingivitis [29], desquamative gingivitis [6,59], ulceronecrotic gingivitis [29], and gingival bleeding [6,38,42,44,55,78]. Periodontitis [32] and necrotizing periodontal disease [51] were reported in two studies.

Other findings: Red and/or swollen lips was observed by Halepas S et al in 48.9% of patients [30]. Pale lips [33], reddish plaques on the lower lip [61], nodule in the lower lip [10], and reddish macules [42] were the findings related to lip involvement in COVID-19 patients. Reddish-white spots on the palate [33], ulcerations on the palate [6,39,56,59,60,81,82], white coat of the palate [43,68], bulla on the left and right palatal mucosa [57], an erythematous surface on the hard palate [64], and angioma type lesion on the right side of the palate [82] were the palatal findings among COVID-19 patients. Eleven studies (14.6%) included in the systematic review found the complaint of burning sensation also [5,33,38,42-44,53,55,57,60,78]. Biadsee A et al found a statistically significant strong association between burning mouth and taste change ($p=0.002$, $p=0.009$, respectively) [13].

Although we have tried to summarize the findings of the studies reporting oral manifestations among COVIOD-19 patients, one of the biggest limitations of this systematic review was the lack of temporal dimension. We were not able to say that these oral manifestations are directly connected to COVID-19, or due to indirect manifestations of other factors such as stress, immunosuppression, and/or medications. Another shortcoming was the lack of definitive diagnosis as most of the included cases have not undergone biopsy for confirmation of the diagnosis.

V. Conclusion

Our systematic review shows a higher prevalence of oral manifestation, specifically taste alteration (57.3%) followed by vesiculobullous lesions (54.6%), and tongue manifestations (34.6%). COVID-19 patients show various oral manifestations that may help clinicians with early identification of the disease. Recognition of signs and symptoms of COVID-19 is critical for early diagnosis and better prognosis. Dental practitioners can play an important role not only in the prevention of COVID-19 transmission but also in breaking the chain of COVID-19 disease. Raising awareness of these symptoms is important to initiate early diagnosis and treatment of this deadly COVID-19 disease.

Declarations

Ethics approval and consent to participate-Not required.

Availability of data and material-Can be made available whenever required.

Competing interests- None

Funding- None

Authors' contributions- All authors contributed equally for the article.

Acknowledgements- None

References Références Referencias

1. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. Available from https://covid19.who.int/. Accessed on 3rd September 2022.
2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in china. N Engl J Med. 2020 Apr; 382(18): 1708-20. https://doi.org/10.1056/NEJMoa2002032
3. Kipshidze N, Dangas G, White CJ, Kipshidze N, Siddiqui F, Lattimer CR, et al. Viral coagulopathy in patients with COVID-19: Treatment and care. Clin Appl Thromb Hemost.2020; 26:1076029620936776. doi:10.1177/1076029620936776
4. Amorim Dos Santos J, Normando AGC, Carvalho da Silva RL, Acevedo AC, De Luca Canto G, Sugaya N, et al. Oral manifestations in patients with COVID-19: A living systematic review. J Dent Res. 2021; 100(2): 141–154. doi:10.1177/0022034520957289
5. Nuno-Gonzalez A, Martin-Carrillo P, Magaletsky K, Rios MDM, Mañas CH, Almazan JA, et al. Prevalence of mucocutaneous manifestations in 666 patients with COVID-19 in a field hospital in Spain: Oral and palmoplantar findings. Br J Dermatol. 2021; 184(1): 184–185. doi:10.1111/bjd.19564
6. Sinadinos A, Shelswell J. Oral ulceration and blistering in patients with COVID-19. Evid Based Dent. 2020; 21(2):49. doi:10.1038/s41432-020-0100-z
7. Garcia de Sousa FAC, Paradella TC. Considerations on oral manifestations of COVID-19. J Med Virol. 2021; 93(2): 667–668. doi:10.1002/jmv.26451
8. Riad A, Kassem I, Hockova B, Badrah M, Klugar M. Tongue ulcers associated with SARS-CoV-2 infection: A case series. Oral Dis. 2020. doi:10.1111/odi.13635
9. Dima M, Enatescu I, Craina M, Petre I, Iacob ER, Iacob D. First neonates with severe acute respiratory syndrome coronavirus 2 infection in Romania: Three case reports. Medicine (Baltimore). 2020; 99(33): e21284. doi:10.1097/MD.0000000000021284
10. Amorim dos santos J, Costa Normando AG, Carvalho da Silva RL, et al. Oral mucosal lesions in

a COVID-19 patient: New signs or secondary manifestations? Int J Infect Dis. 2020; 97: 326–328. doi:10.1016/j.ijid.2020.06.012
11. Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009; 6(7): e1000097.
12. Al-Zaidi HMH, Badr HM. Incidence and recovery of smell and taste dysfunction in COVID-19 positive patients. The Egyptian Journal of Otolaryngology. 2020; 36:47. https://doi.org/10.1186/s43163-020-00050-0
13. 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. Otolaryngology–Head and Neck Surgery. 2020; 163(4): 722–728. DOI: 10.1177/0194599820934380
14. Bodnia NC, Katzenstein TL. Acute loss of smell and taste among patients with symptoms compatible with COVID-19. Dan Med J. 2020;67(9):A05200370
15. Chen L, Zhao J, Peng J, Li X, Deng X, Geng Z, et al. Detection of 2019-ncov in saliva and characterization of oral symptoms in covid-19 patients. SSRN. 2020 Mar 19. https://doi.org/10.2139/ssrn.3557140
16. Dell'Era V, Farri F, Garzaro G, Gatto M, Valletti PA, Garzaro M. Smell and taste disorders during COVID-19 outbreak: Cross-sectional study on 355 patients. Head & Neck. 2020; 42: 1591–1596.
17. Kumar L, Kahlon N, Jain A, Kaur J, Singh M, Pandey AK. Loss of smell and taste in COVID-19 infection in adolescents. International Journal of Pediatric Otorhinolaryngology. 2021; 142: 110626
18. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur Arch Otorhinolaryngol. 2020 Aug; 277(8): 2251-2261. doi: 10.1007/s00405-020-05965-1.
19. Paderno A, Schreiber A, Grammatica A, Raffetti E, Tomasoni M, Gualtieri T, et al. Smell and taste alterations in covid-19: a cross-sectional analysis of different cohorts. Int Forum Allergy Rhinol. 2020 Aug; 10(8): 955-962. doi: 10.1002/alr.22610.
20. Rizzo PB, Borsetto D, Fabbris C, Spinato G, Frezza D, Menegaldo A, et al. Evolution of Altered Sense of Smell or Taste in Patients With Mildly Symptomatic COVID-19. JAMA Otolaryngol Head Neck Surg. 2020; 146(8): 1-5. doi: 10.1001/jamaoto.2020.1379
21. Yan CH, Faraji F, Prajapati DP, Boone CE, DeConde AS. Association of chemosensory dysfunction and COVID-19 in patients presenting with influenza-like symptoms. Int Forum Allergy Rhinol. 2020; 10: 806–813.
22. Sinjari B, D'Ardes D, Santilli M, Rexhepi I, D'Addazio G, Di Carlo P, et al. SARS-CoV-2 and Oral Manifestation: An Observational, Human Study. J. Clin. Med. 2020, 9, 3218; doi:10.3390/jcm9103218
23. Giacomelli A, Pezzati L, Conti F, Bernacchia D, Siano M, Oreni L, et al. Self-reported Olfactory and Taste Disorders in Patients With Severe Acute Respiratory Coronavirus 2 Infection: A Cross-sectional Study. Clin Infect Dis 2020; 71: 889–890.
24. Mascitti H, Bonsang B, Dinh A, Assan F, Perronne V, Leblanc T, et al. Clinical Cutaneous Features of Patients Infected With SARS-CoV-2 Hospitalized for Pneumonia: A Cross-Sectional Study. Open Forum Infect. Dis. 2020; 7: 34-39.
25. Salehi M, Ahmadikia K, Mahmoudi S, Kalantari S, Jamalimoghadamsiahkali S, Izadi A, et al. Oropharyngeal Candidiasis in Hospitalised COVID-19 Patients from Iran: Species Identification and Antifungal Susceptibility Pattern. Mycoses 2020; 63: 771–778.
26. Askin O, Altunkalem R.N, Altinisik D.D, Uzuncakmak T.K, Tursen U, Kutlubay Z. Cutaneous Manifestations in Hospitalized Patients Diagnosed as COVID-19. Dermatol. Ther. 2020; 33: e13896.
27. Katz J, Yue S. Increased odds ratio for COVID-19 in patients with recurrent aphthous stomatitis. J. Oral Pathol. Med. 2020; 50: 114–117
28. Fantozzi P.J, Pampena E, Di Vanna D, Pellegrino E, Corbi D, Mammucari S, et al. Xerostomia, Gustatory and Olfactory Dysfunctions in Patients with COVID-19. Am. J. Otolaryngol. 2020; 41: 102721.
29. Favia G, Tempesta A, Barile G, Brienza N, Capodiferro S, Vestito MC, et al. Covid-19 Symptomatic Patients with Oral Lesions: Clinical and Histopathological Study on 123 Cases of the University Hospital Policlinic of Bari with a Purpose of a New Classification. J. Clin. Med. 2021; 10: 757. https://doi.org/10.3390/jcm10040757
30. Halepas S, Lee KC, Myers A, Yoon RK, Chung W, Peters SM. Oral manifestations of COVID-19 related multi-system inflammatory syndrome in children: a review of 47 pediatric patients. The Journal of the American Dental Association. 2021; 152(3): 202-208, doi: https://doi.org/10.1016/j.adaj.2020.11.014.
31. Rekhtman S, Tannenbaum R, Strunk A, Birabaharan M, Wright S, Grbic N, et al. Eruptions and Related Clinical Course among 296 Hospitalized Adults with Confirmed COVID-19. J. Am. Acad. Dermatol. 2021; 84: 946–952.
32. Marouf N, Cai W, Said K.N, Daas H, Diab H, Chinta V.R, et al. Association between Periodontitis and Severity of COVID-19 Infection: A Case-Control Study. J. Clin. Periodontol. 2021; 48: 483–491.
33. Subramaniam T, Nikalje MR, Jadhav S. Oral manifestations among COVID-19: An observational

study of 713 patients. Dent Res J (Isfahan). 2021; 18: 67.
34. Abubakr N, Salem ZA, Kamel AHM. Oral manifestations in mild-to-moderate cases of COVID-19 viral infection in the adult population. Dent Med Probl. 2021; 58(1):7-15. doi: 10.17219/dmp/130814.
35. Song J, Deng YK, Wang H, Wang ZC, Liao B, Ma J, et al. Self-reported Taste and Smell Disorders in Patients with COVID-19: Distinct Features in China. Current Medical Science. 2021; 41(1): 14-23. DOI https://doi.org/10.1007/s11596-021-2312-7
36. Bardellini E, Bondioni MP, Amadori F, Veneri f, Lougaris V, Meini A, et al. Non-specific oral and cutaneous manifestations of Coronavirus Disease 2019 in children. Med Oral Patol Oral Cir Bucal. 2021 Sep; 26(5): e549–e553.
37. Gherlone EF, Polizzi E, Tetè G, De Lorenzo R, Magnaghi C, Querini RP, et al. Frequent and Persistent Salivary Gland Ectasia and Oral Disease After COVID-19. Journal of Dental Research.2021; 100(5): 464–47.
38. El Kady DM, Gomaa EA, Abdella WS, Hussien RA, Abd ElAziz RH, Khater AGA. Oral manifestations of COVID-19 patients: An online survey ofthe Egyptian population. Clin Exp Dent Res.2021; 7: 852–860.
39. Fidan V, Koyuncu H, Akin O. Oral Lesions in COVID-19 Positive Patients. Am. J. Otolaryngol. 2021; 42: 102905.
40. Natto Z.S, Afeef M, Khalil D, Kutubaldin D, Dehaithem M, Alzahrani A, et al. Characteristics of Oral Manifestations in Symptomatic Non-Hospitalized COVID-19 Patients: A Cross-Sectional Study on a Sample of the Saudi Population. Int. J. Gen. Med. 2021; 14: 9547–9553.
41. Elamrousy W.A.H, Nassar M, Issa D.R. Prevalence of Oral Lesions in COVID-19 Egyptian Patients. J. Int. Soc. Prev. Community. Dent. 2021; 11: 712–720.
42. Bulut D.G, Turker N, Serin S, Ustaoglu G. The Effect of Severe Acute Respiratory Syndrome Coronavirus 2 on the Health of Oral Tissue: A Survey-Based Study. J. Oral Health Oral Epidemiol. 2021; 10: 43–49.
43. Naser Al, Al-Sarraj MN & Deleme ZH. Oral and Maxillofacial Lesions in COVID 19 Infection from Mosul Hospital in Iraq: Epidemiological Study and Approach to Classification and Treatment. J Oral Res 2021; 10(6): 1-14.
44. Muthyam AK, Padma RM, Suhas K, Adepu S, Kommuri S, Dantala S. Oral manifestations in COVID-19 patients. An observational study. Journal of Family Medicine and Primary Care: March 2022; 11(3): 1000-1005. doi: 10.4103/jfmpc.jfmpc_1264_21
45. Ganesan A, Kumar S, Kaur A. Oral Manifestations of COVID-19 Infection: An Analytical Cross-Sectional Study. J. Maxillofac. Oral Surg. 2022. https://doi.org/10.1007/s12663-021-01679-x
46. El Tantawi M, Sabbagh HJ, AlKhateeb NA, Quritum M, Abourdan J, Qureshi N, et al. Oral manifestations in young adults infected with COVID-19 and impact of smoking: a multi-country cross-sectional study. Peer J. 2022; 10:e13555 DOI 10.7717/peerj.13555
47. Soares CD, Souza LL, de Carvalho MGF, Pontes HAR, DDS, Mosqueda-Taylor A, Hernandez-Guerrero JC, et al. Oral Manifestations of Coronavirus Disease 2019 (COVID-19) A Comprehensive Clinicopathologic and Immunohistochemical Study. Am J Surg Pathol 2022; 46: 528–536.
48. Tuter G, Yerebakan M, Celik B, Kara G. Oral manifestations in SARSCoV-2 infection. Med Oral Patol Oral Cir Bucal. 2022; 1;27 (4):e330-9.
49. Schwabhttp G, Palmierib M, Zerbinatia RM, Sarmento DJS, Reisb T, Ortega KL. Lack of direct association between oral mucosal lesions and SARS-CoV- 2 in a cohort of patients hospitalised with COVID-19. Journal of Oral Microbiology. 2022; 14(1): 1-7. https://doi.org/10.1080/20002297.2022.2047491
50. Chawla J, Navaneeth Y, Bakshi SS, Kalidoss VK, Yadav S, Polineni S, et al. Oral manifestations associated with COVID-19 disease: An observational cross sectional study. Journal of Oral Biology and Craniofacial Research. 2022; 12: 279–283.
51. Binmadi NO, Aljohani SR, Alsharif MT, Almazrooa SA, Sindi AM. Oral Manifestations of COVID-19: A Cross-Sectional Study of Their Prevalence and Association with Disease Severity. J. Clin. Med. 2022; 11(15): 4461; https://doi.org/10.3390/jcm11154461
52. de Paula Eduardo F, Bezinelli LM, Gobbi MF, Bergamin LG, de Carvalho DLC, Corrêa L. Oral lesions and saliva alterations of COVID-19 patients in an intensive care unit: A retrospective study. Spec Care Dentist.2022; 1–9.
53. Villarroel-Dorrego M, Chacón L, Rosas R, Barrios V, Pernía Y, Vélez H. Hallazgos bucales en pacientes COVID-19. Actas Dermosifiliogr. 2022;113:183-186
54. Manifar S, Koopaie M, Karimi Farani A, Davoudi M, Kolahdouz S. Assessment of Oral Manifestations and Oral Health in Hospitalized Patients with COVID-19: Machine Learning and Statistical Analysis. Ann Mil Health Sci Res.2022; 20(1):e121764. doi: 10.5812/amh-121764.
55. Bhuyan R, Bhuyan SK, Mohanty JN, Panda NR, Bhuyan V, Ojha P, Priyadarshini P, Sahoo G. A Preliminary Survey on the Oral Manifestation of COVID-19 in the First and Second Waves in Bhubaneswar, City of Odisha, India. Natl J Community Med 2022; 13(5): 294-297. DOI: 10.55489/njcm.130520221617
56. Brandao TB, Gueiros LA, Melo TS, Prado-Ribeiro AC, Nesrallah ACF, Prado GVB, et al. Oral lesions in

patients with SARS-CoV-2 infection: could the oral cavity be a target organ?.Oral Surg Oral Med Oral Pathol Oral Radiol. 2020;000:e1-e7
57. Tapia ROC, Labrador AJP, Guimaraes DM, Valdez LHM. Oral mucosal lesions in patients with SARS-CoV-2 infection. Report of four cases. Are they a true sign of COVID-19 disease? Spec Care Dentist. 2020; 1–6.
58. Vaira LA, Deiana G, Fois AG, Pirina P, Madeddu G, De Vito A, et al. Objective evaluation of anosmia and ageusia in COVID-19 patients: Single-center experience on 72 cases. Head & Neck. 2020; 42: 1252–1258.
59. Presas CMC, Amaro Sánchez J, López-Sánchez AF, Jané-Salas E, Somacarrera Pérez ML. Oral vesiculobullous lesions associated with SARS-CoV-2 infection. Oral Dis. 2020. https://doi.org/10.1111/odi.13382
60. Rodríguez MD, Romera JR, Villarroel M. Oral manifestations associated with COVID-19. Oral Dis. 2020 Aug 17: 10.1111/odi.13555.
61. Corchuelo J, Ulloac FC. Oral manifestations in a patient with a history of asymptomatic COVID-19: Case report. International Journal of Infectious Diseases. 2020; 100 (2020):XXX-XXXs
62. Zarch RE, Hosseinzadeh P. COVID-19 from the perspective of dentists: A case report and brief review of more than 170 cases. Dermatologic Therapy. 2021; 34:e14717.
63. Hjelmeseth J. Loss of smell or taste as the only symptom of COVID-19. Tidsskr Nor Laegeforen. 2020 Apr 3; 140(7). doi: 10.4045/tidsskr.20.0287.
64. Kahraman FC, Çaşkurlu H. Mucosal involvement in a COVID-19-positive patient: a case report. Dermatol Ther. 2020 Jul;33(4):e13797. doi: 10.1111/dth.13797.
65. Smith AC, Hodges J, Pratt M, Porter IM. COVID-19 Patient With Chief Complaint of Anosmia and Ageusia; a Unique Perspective on Atypical Symptomatology and Management in the Military. Military Medicine. 2020; 185: 11/12: 2176
66. Maniaci A, Iannella G, Vicini C, Pavone P, Nunnari G, Falsaperla R, et al. A Case of COVID-19 with Late-Onset Rash and Transient Loss of Taste and Smell in a 15-Year-Old Boy. Am J Case Rep. 2020; 21: e925813
67. Melley LE, Bress E, Polan E. Hypogeusia as the initial presenting symptom of COVID-19. BMJ Case Rep 2020; 13:e236080. doi: 10.1136/bcr-2020-236080
68. Riad A, Gad A, Hockova B, Klugar M. Oral Candidiasis in Non-Severe COVID-19 Patients: Call for Antibiotic Stewardship. Oral Surg. 2020 Sep 21;10.1111/ors.12561. doi: 10.1111/ors.12561.
69. Putraa BE, Adiartoa S, Dewayantib SR, Juzara DA. Viral exanthem with "Spins and needles sensation" on extremities of a COVID-19 patient: A self-reported case from an Indonesian medical frontliner. International Journal of Infectious Diseases. 2020; 96: 355–358.
70. Dalipi ZS, Dragidella F, Dragidella DK. Oral Manifestations of Exudative Erythema Multiforme in a Patient with COVID-19. Case Reports in dentistry. 2021. Article ID 1148945. https://doi.org/10.1155/2021/1148945
71. Eita AAB. Parosmia, Dysgeusia, and Tongue Features Changes in a Patient with Post-Acute COVID-19 Syndrome. Case Rep Dent. 2021; 2021: 3788727.
72. Cirillo N, Colella G. Self-reported smell and taste alteration as the sole clinical manifestation of SARS-CoV-2 infection. Oral Surg Oral Med Oral Pathol Oral Radiol. 2021 Apr; 131(4):e95-e99.
73. Nejabi MB, Noor NAS, Raufi N, Essar MY, Ehsan E, Shah J. et al. Tongue ulcer in a patient with COVID-19: a case presentation. BMC Oral Health. 2021; 21: 273.
74. Klein H, Karni N, Israel S, Gross M, Muszkat M, Niv MY. Reversible Taste Loss in a COVID-19 Patient With Preexisting Chronic Smell Impairment. Journal of Investigative Medicine High Impact Case Reports. 2021; 9: 1–3.
75. Ramires M.C.C.H, Mattia M.B, Tateno R.Y, Palma L.F, Campos L. A Combination of Phototherapy Modalities for Extensive Lip Lesions in a Patient with SARS-CoV-2 Infection. Photodiagnosis Photodyn. Ther. 2021; 33: 102196.
76. Hocková B, Riad A, Valky J, Šulajová Z, Stebel A, Slávik R, et al. Oral Complications of ICU Patients with COVID-19: Case-Series and Review of Two Hundred Ten Cases. J Clin Med. 2021 Feb; 10(4): 581.
77. Teixeira I.S, Leal F.S, Tateno R.Y, Palma L.F, Campos L. Photobiomodulation Therapy and Antimicrobial Photodynamic Therapy for Orofacial Lesions in Patients with COVID-19: A Case Series. Photodiagnosis Photodyn. Ther. 2021; 34: 102281.
78. Emelyanova N, Isayeva G, Komir I, Shalimova A, Buriakovska O, Vovchenko M. Changes in the Oral Cavity of a Patient after Suffering from Coronavirus Infection COVID-19: A Clinical Case. Acta Med. Mediterr. 2021; 37: 827–831.
79. Fathi Y, Hoseini E.G, Mottaghi R. Erythema Multiform-like Lesions in a Patient Infected with SARS-CoV-2: A Case Report. Future Virol. 2021; 16: 157–160.
80. Shenoy P, Archana P, Chatra L, Veena KM, Prabhu R. Tongue Ulcer as an Oral Manifestation of COVID-19: A Case Report. International Journal of Research and Reports in Dentistry. 2022; 5(1): 8-11. Article no.IJRRD.81119
81. Palaia G, Pernice E, Pergolini D, Impellizzeri A, Migliau G, Gambarini G, et al. Erythema Multiforme as Early Manifestation of COVID-19: A Case Report.

Pathogens 2022; 11: 654. https://doi.org/10.3390/pathogens11060654
82. Rafałowicz B, Wagner L, Rafałowicz J. Long COVID Oral Cavity Symptoms Based on Selected Clinical Cases. Eur J Dent. 2022 May; 16(2): 458–463.
83. Chaux-Bodard AG, Deneuve S, Desoutter A. Oral manifestation of covid-19 as an inaugural symptom? J Oral Med Oral Surg. 2020; 26(2): 18. https://doi.org/10.1051/mbcb/2020011
84. Viner RM, Whittaker E. Kawasaki-like disease: emerging complication during the COVID-19 pandemic. The Lancet. 2020; 395(10239): 1741–1743. https://doi.org/10.1016/s0140-6736(20)31129-6
85. Hopkins C, Kumar N. Loss of sense of smell as marker of COVID-19 infection. www.entuk.org/sites/default/files/files/Loss%20of%20sense%20of%20smell%20as%20marker%20of%20COVID.pdf. Accessed on 24th July 2022.
86. Cirillo N. Taste alteration in COVID-19: a rapid review with data synthesis reveals significant geographical differences. medRxiv. 2020. https://doi.org/10.1101/2020.09.11.20192831. Accessed on 28th July 2022.
87. Public Health England. COVID-19: investigation and initial clinical management of possible cases. Updated October 2, 2020. Available at: https://www.gov.uk/government/publications/wuhan-novel-coronavirus-initial-investigation-of-possiblecases/investigation-and-initial-clinical-management-of-possiblecases-of-wuhan-novel-coronavirus-wn-cov-infection#criteria. Accessed on 2nd August 2022.
88. Jafek BW, Murrow B, Michaels R et al. Biopsies of human olfactory epithelium. Chem Senses 2002;27:623-631
89. Amorim Dos Santos J, Normando AGC, Carvalho da Silva RL, et al. Oral Manifestations in Patients with COVID-19: A 6-Month Update. J Dent Res. 2021: 1-9. https://doi.org/10.1177/00220345211029637
90. Tong JY, Wong A, Zhu D, Fastenberg JH, Tham T. The prevalence of olfactory and gustatory dysfunction in COVID-19 patients: a systematic review and meta-analysis. Otolaryngol Head Neck Surg. 2020; 163: 3-11.
91. Nijakowski K, Wyzga S, Singh N, Podgórski F, Surdacka A. Oral Manifestations in SARS-CoV-2 Positive Patients: A Systematic Review. J. Clin. Med. 2022; 11: 2202. https://doi.org/10.3390/jcm11082202
92. Majorana A, Bardellini E, Flocchini P, Amadori F, Conti G, Campus G. Oral mucosal lesions in children from 0 to 12 years old: ten years' experience. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010; 110:e13-8.
93. Halboub E, Ali Al-Maweri S, Alanazi Rh, Qaid Nm, Abdulrab S. Orofacial Manifestations Of Covid-19: A Brief Review Of The Published Literature. Braz. Oral Res. 2020; 34: E124.
94. Orilisi G, Mascitti M, Togni L, Monterubbianesi R, Tosco V, Vitiello F, et al. Oral Manifestations of COVID-19 in Hospitalized Patients: A Systematic Review. Int. J. Environ. Res. Public Health. 2021; 18: 12511. https://doi.org/10.3390/ijerph182312511

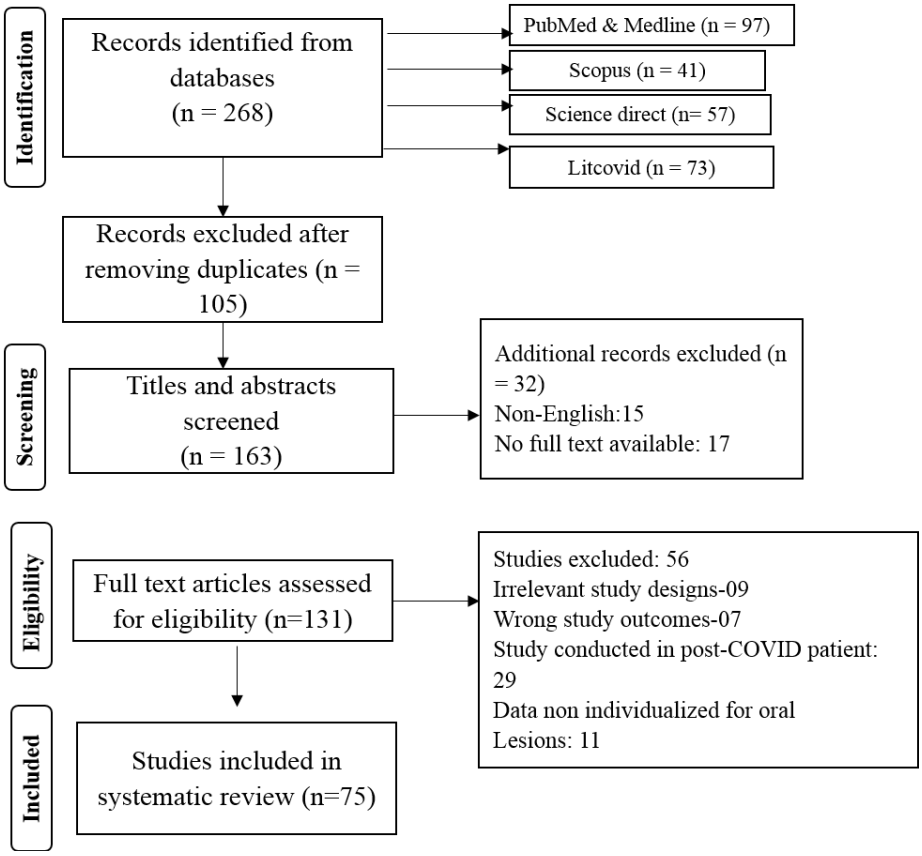


Figure 1: Flow diagram of literature search and selection criteria of the included studies (n=75)

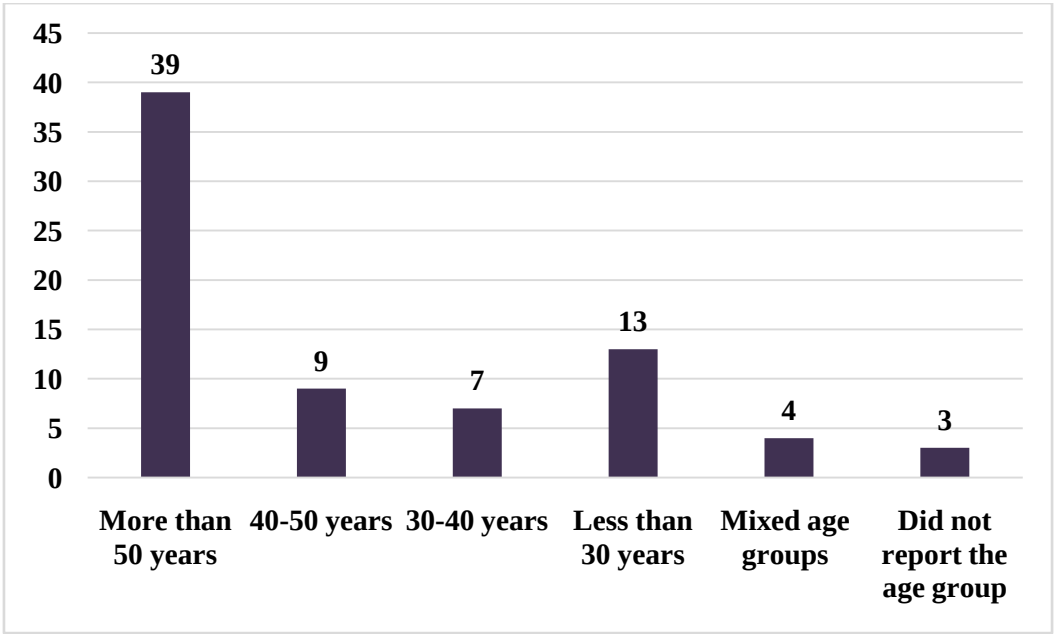


Figure 2: Age distribution of the patients included in the systematic review (n=75)

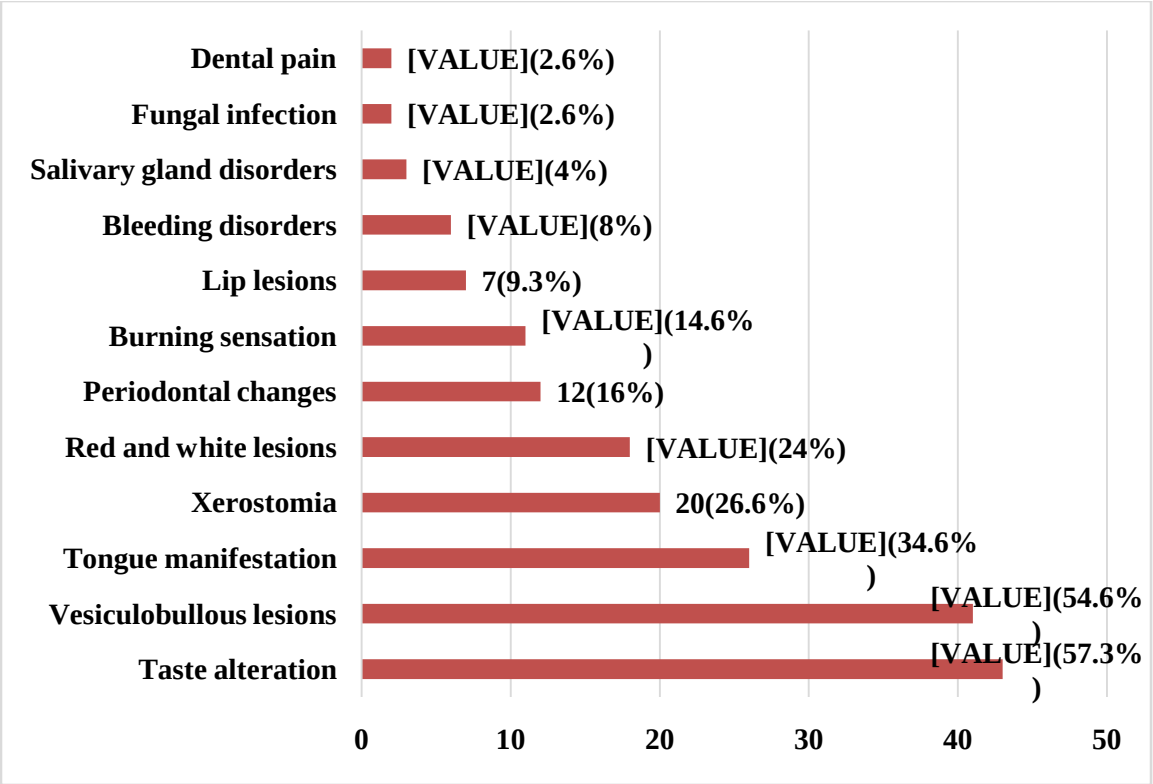


Figure 3: Categories of oral manifestation among the patients with COVID-19

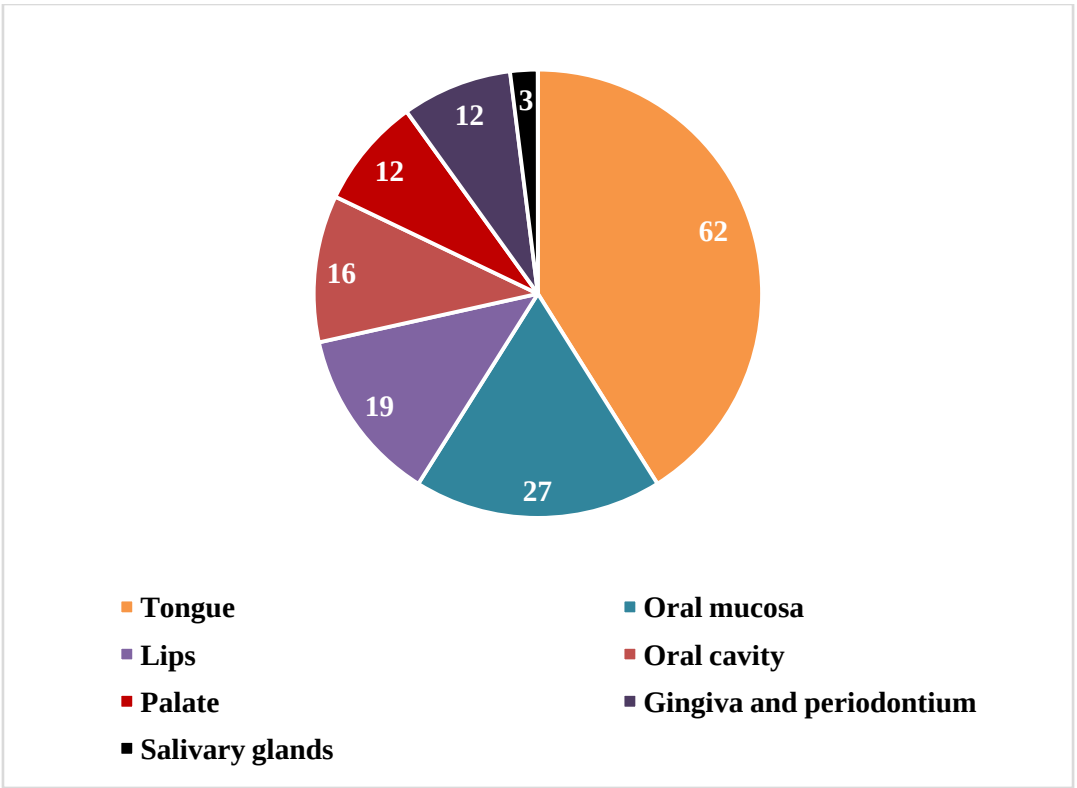


Figure 4: Intraoral sites of involvement among COVID-19 patients

Table 1: Demographic characteristics of the included studies (n=75)

S. No.	Author & Year	Study location	Study design	Sample size	Gender	Age	Study duration	Medical history	Admission in the ICU	Severity of the disease
1.	Al-Zaidi and Badr (2020) [12]	Iraq	Cross-sectional	65	M- 41.6% F- 58.4%	41.2 yrs	5 April 2020 - 17 May 2020	-	-	Moderate
2.	Biadsee et al (2020) [13]	Israel	Cross-sectional	140	M-58; F-70	36.5 yrs	March 25, 2020, and April 15, 2020.	-	-	Mild
3.	Bodnia and Katzenstein (2020) [14]	Copenhagen	Cross-sectional	65	F-22; M-28	45 yrs	March 2020	-	-	Mild
4.	Chen L et al (2020) [15]	China	Cross-sectional	31	M-15 F-16	60.6 yrs	28 February 2020 to 4 March 2020	-	-	-
5.	Dell V et al (2020) [16]	Italy	Cross-sectional	355	M-54%	50 yrs	March10 to 30, 2020	Cardiovascular disease, allergic (Sinusitis)	-	Mild to Moderate
6.	Kumar L et al (2020) [17]	India	Cross-sectional	141	M-58.9%; F-41.1%.	15.2 yrs	May to August 2020	-	-	Mild to Moderate
7.	Lechien JR et al (2020) [18]	Europe(Multi Centre)	Cross-sectional	417	F-263; M-154	36.9 ± 11.4 yrs	-	Allergic Rhinitis Asthma Hypertension Hypothyroidism	Hospitalisation of severe cases	Mild Moderate Severe
8.	Paderno A et al (2020) [19]	Italy	Cross-sectional	508	M-56% F-44% (55±15 years)	55±15 years	March 27 to April 1, 2020	-	Hospitalisation of severe cases	Mild Moderate Severe
9.	Rizzo PB et al (2020) [20]	Italy	Cross-sectional	202	F-55.1% M-44.9%	56 yrs	March 19 and March 22, 2020	-	-	Mild
10.	Yan CH et al (2020) [21]	California	Cross-sectional	59 and 203 (Covid +ve and –ve)	M&F-49.2% (Covid +ve); M-34%, F-65% (covid –ve)	54 yrs	March 3, 2020, and March 29, 2020	Allergic Rhinitis, immunocompromised state, hypertension, DM, Cardiac Disorders, Cancer CLD, History of Head Trauma, Neurological disease	Hospitalisation of severe cases	Mild Moderate Severe

11.	Sinjari B et al (2020) [22]	Italy	Cross-sectional	20	-	-	May 2020 to June 2020)	DM, Cardiovascular conditions	-	Mild to Moderate
12.	Giacomelli A et al (2020) [23]	Italy	Cross-sectional	59	M-40% F-60%	60 yrs	March 19,2020	-	-	Mild
13.	Mascitti H et al (2020) [24]	France	Cross-sectional	59	M:F-3:1	Median age (IQR) was 57.6 (49.4–69.1) years.	March 31, 2020	-	-	Mild
14.	Salehi M et al (2020) [25]	Iran	Cross-sectional	53	M-43.4%; F-56.6%	<50 yrs-20.7%; ≥50 yrs-79.3%	1 March 2020 to 30 April 2020	Cardiovascular diseases (52.83) and DM (37.7%; Chronic kidney disease-20.7%	-	Mild to Moderate
15.	Askin O et al (2020) [26]	Turkey	Cross-sectional	210	M-58.6%; F-41.4%	7.44 ± 17.259 yrs	April 2020.	Comorbidties	29 in ICU 129 in wards	Moderate and Severe
16.	Katz J et al (2020) [27]	USA	Retrospective study	889	F-509 M-386	18-34 yrs-66%	Registry Study	-	-	-
17.	Fantozzi PJ et al (2021) [28]	Italy	Retrospective study	326	M-52.3% F-47.7%	Median age- 57 (48–67) days	6 March to 30 April 2020	Hypertension (n = 29), chronic pulmonary disease (n = 11), DM (n = 10), cardiovascular disease (n = 9), cancer (n = 5)	Hospitalized (median no of days-12.5 days)	Moderate and severe
18.	Favia G et al (2021) [29]	Bari, Italy	Cross-sectional	123	M:F ratio 1.3:1	Median age 72 yrs	October 2020 to December 2020	-	History of Hospitalization and ICU	Moderate and severe
19.	Halepas S et al (2021) [30]	New York	Cross-sectional	47	M-51.1%; F-48.9%	9.0 ± 5.0 yrs	March 15 through June 1, 2020	-	History of Hospitalization, ICU	Mild Moderate Severe

20.	Rekhtman S et al (2021) [31]	New York	Prospective cohort study	296	M-71% F-29%	Median age- 64 (57-77)	May 11, 2020 and June 15, 2020	CAD-23%; Congestive heart failure-14%; Asthma 9%; COPD-14%; DM-34%; Hypertension-71%	History of Hospitalization	Moderate and Severe
21.	Maraouf N et al (2021) [32]	Qatar	Case control	Cases-40; Control-528	Cases-M-50%; F-50% Controls-M-54.9%; F-45.1%	Cases-53.6 yrs Controls-41.5 yrs	February and July 2020	DM-Cases-42.5% Controls-27.8%	Hospitalization and ICU admission	Mild Moderate Severe
22.	Nuno-Gonzalez A et al [5] (2021)	Spain	Cross-sectional	666	-	55.7yrs	10 and 25 April 2020	-	History of Hospitalisation	Mild Moderate
23.	Subramaniam T et al (2021) [33]	India	Cross-sectional	713	M:F-6:3	69 yrs	May 2020 and June 2020	DM Hypertension	-	Mild Moderate
24.	Abubakr N et al (2021) [34]	Egypt	Cross-sectional	573	408 females and 165 males.	36.19 ±9.11 years	May 1, 2020 to July 1, 2020	-	-	Mild Moderate
25.	Song J et al (2021) [35]	China	Retrospective	1172	-	-	December 2019	-	History of Hospitalization	Mild
26.	Bardellini E et al (2021) [36]	Italy	Retrospective	27	M;F-19:8	4.2 yrs	March to April 2020	-	-	Mild
27.	Gherlone EF et al (2021) [37]	Italy	Cross-sectional	122	M-75.4% F-24.6%	62.5 yrs	July 23, 2020 to September 7, 2020	CAD, DM, Chronic kidney disease, active neoplasia COPD	History of Hospitalization and ICU and Ventilation	Moderate Severe
28.	El Kady DM et al (2021) [38]	Egypt	Online survey	58	M-53.4%; F-46.6%	18-46 yrs	May 15 to June 10, 2020	-	History of Hospitalisation	Mild
29.	Fidan V et al (2021) [39]	Turkey	Cross-sectional	74	M-66.2% F-33.8%	51.4 ± 6.3 yrs	April to October 2020	-	Hospitalized	Mild Moderate

30.	Natto ZS et al (2021) [40]	Saudi Arabia	Cross-sectional study	109	M-67% F-33%	39.3±12.4 yrs	July-October 2020	DM (10.1%); hypertension (7.3%); asthma and arthritis (1.7%)	-	-
31.	Elamrousy WAH et al (2021) [41]	Egypt	Cross-sectional	124	M-74.2%; F-25.8%	50.32 ± 12.47 yrs	2 September 2020, to 10 June 2021	DM (n = 52), hypertension (n = 16), cardiac disease (n = 8), renal disease (n = 4), liver disease (n = 4)	Hospitalized	Severe (58.1%)
32.	Bulut DG et al (2021) [42]	Turkey	Cross-sectional	200	M-75 F-125	20–30 yrs: 89 (62/27), 31–40: 65 (43/22), 41–50: 27 (14/13), 51–60: 15 (4/11), 61–70: 4 (2/2)	September 2020 to March 2021	-	Hospitalized (11.5%)	Moderate Severe
33.	Naser Al et al (2021) [43]	Iraq	Prospective study	338	M-59%; F-41%	Mean age-45 yrs	August 2020 to March 2021	Respiratory diseases, DM, hypertension, heart disease, urogenital diseases, hematological diseases, gastrointestinal diseases	Hospitalized	critical admitted cases-38.6%
34.	Muthyam AK et al (2022) [44]	India	Cross-sectional	100	M-51% F-49%	More than 35 yrs-54%; Less than 35 yrs-46%	-	Immunocompromised state, Multidrug therapy	Hospitalisation	Mild to Moderate
35.	Ganesan A et al (2022) [45]	India	Cross-sectional	500	M-73.4% F-26.6%	53.46 ± 17.50 years	-	-	-	-

36.	El Tantawi M et al (2022) [46]	Multicountry study (Saudi Arabia)	Cross-sectional	434	M-41.5% F-58.5%	18-23 yrs	August 2020 to January 2021	Cancer and COPD	-	Mild
37.	Soares CD et al (2022) [47]	Brazil	Retrospective	14	M-71.5% F-38.5%	58 yrs	-	-	-	-
38.	Tuter G et al (2022) [48]	Turkey	Cross-sectional	204	M-37.3% F-62.7%	53.3 yrs	February 2021 to March 2021	DM hypertension Immunosupression	Hospitalisation ICU	Mild Moderate Severe
39.	Schwab G et al (2022) [49]	Brazil	Cross-sectional	154	M-59.7% F-40.3%	54.60 ± 13.93 years	January 13 to May 28 of 2021	-	Hospitalisation ICU Ventilation	Moderate to Severe (discharged /death)
40.	Chawla J et al (2022) [50]	India	C Cross-sectional	217	M-70% F-30%	50-60 yrs	September and December 2020	DM, hypertension CAD, bronchial Asthma	-	Mild Moderate
41.	Binmadi NO et al (2022) [51]	Saudi Arabia	Cross-sectional	195	M-25% F-75%	33% were 18 to 24 years old and 33% were 25 to 34 years old.	March of 2020 and March of 2022	Immunosupression, hormonal modulation	Hospitalisation ICU Ventilation	Mild Moderate Severe Critical
42.	de Paula Eduardo F et al (2022) [52]	Brazil	Retrospective	519	M-68.2% F-31.8%	51-80 yrs	May 2020 to February 2021	-	ICU	Severe
43.	Villarroel-Dorrego M et al (2022) [53]	Spain	Cross-sectional	55	M-54.5% F-45.5%	51 ± 23.24 y	-	-	-	-
44.	Manifar S et al (2022) [54]	Iran	Cross-sectional	140	M-44.2% F-55.8%	53.78 ± 17.44 yrs	1 September 2020 to 17 October 2020	-	Hospitalisation	Moderate Severe
45.	Bhuyan R et al (2022) [55]	India	Cross-sectional	169 (first wave) 211 (2nd wave)	1st wave- M-35.5%; F-64.5% 2nd wave- M-45.5%; F-55.5%	63 ±17 and 57 ± 18 (1st and 2nd wave)	-	Comorbidities	Hospitalisation ventilator	Mild Moderate Severe
46.	Brandao TB et al (2020) [56]	Brazil	Case series	08	M-05; F-03	53 yrs	-	Hypertension COPD (case 1); DM, obesity,	Hospitalisation	Mild Moderate Severe-Critical

								renal Failure, bariatric surgery, fibromyalgia (case 2); obesity, Parkinson disease, hypertension, COPD (case 3) DM and Hypertension (case 4)		
47.	Dima M et al (2020) [9]	Romania	Case series	03	M:F-2:1	Newborns	May 2020	Diaper erythema	Neonatology Ward	Mild
48.	Tapia ROC et al (2020) [57]	Latin America	Case series	04	F:M--3:1	47.2 ± 6.8 yrs	-	-	Case 2- Hospitalised	Mild (case 1 & 3); hospitalized (case 2); moderate (case 4)
49.	Vaira LA et al (2020) [58]	Italy	Case series	72	M-27; F-45	49.2 yrs	March 31, 2020 and April 6, 2020.	History of head trauma, allergic rhinitis, chronic rhino sinusitis, and psychiatric or neurological disorders.	-	Mild Moderate
50.	Presas CMC et al (2020) [59]	Spain	Case series	03	M:F-2:1	59 yrs	last week of March and the first week of April 2020	DM & hypertension (case 2); Obesity and Hypertension (case 3)	Case 3- Hospitalisation	Case 1- Mild Case 3- Moderate to severe
51.	Sinadinosand Shelswell (2020) [6]	United Kingdom	Case series	03	M:F-2:1	58 yrs		DM and Hypertension (case 2); obesity (case 3)	-	Mild to Moderate
52.	Rodríguez MD et al (2020) [60]	Spain	Case series	03	F:M-2:1	53 yrs	-	-	Case 1 – Home quarantine Case 2 & 3- Hospitalisa	Case 1- Mild Case 2- Moderate Case 3- Moderate

									tion	
53.	Corchuelo and Ulloa (2020) [61]	Colombia	Case report	01	Female	40 yrs	-	-	-	Moderate
54.	Dos Santos et al (2020) [10]	Brazil	Case report	01	Male	67 yrs	March 31, 2020	CAD, autosomal dominant polycystic kidney disease, and kidney transplant, immunosuppression, venous thromboembolism	Hospitalisation in ICU	Severe
55.	Zarch and Hosseinzadeh (2020) [62]	Iran	Case report	01	Female	56 yrs	October 2020	-	-	-
56.	Hjelmeseth J (2020) [63]	Norway	Case report	01	Female	60 yrs	-	-	-	-
57.	Kahraman and Çaşkurlu (2020) [64]	Turkey	Case report	01	Male	51 yrs	18 March 2020	-	-	Moderate
58.	Smith AC et al (2020) [65]	United States	Case report	01	Male	21 yrs	March 19, 2020	-	-	Mild
59.	Maniaci A et al (2020) [66]	Italy	Case report	01	Male	15 yrs	-	-	-	Mild
60.	Melley LE et al (2020) [67]	USA (Pennsylvania	Case report	01	Female	59 yrs	May 2020	-	-	-
61.	Riad A et al (2020) [68]	Egypt	Case report	01	Female	47 yrs	-	Cardiovascular disease DM	-	Moderate

62.	Putra BE et al (2020) [69]	Indonesia	Case report	01	Male	29 yrs	-	Cardiovascular diseases	-	Moderate
63.	Dalipi ZS et al (2021) [70]	Europe	Case report	01	Male	17 yrs	-	-	-	-
64.	Eita AAB et al (2021) [71]	Egypt	Case report	01	Female	31 yrs	-	Irritable Bowel Syndrome Atopy	-	Severe
65.	Cirillo and Colello (2021) [72]	Italy	Case report	01	Female	36 yrs	March 2020	-	-	Mild
66.	Nejabi MB et al (2021) [73]	Afghanistan	Case report	01	Male	62 yrs	-	-	-	Mild
67.	Klein H et al (2021) [74]	Israel	Case report	01	Female (pregnant)	40 yrs	-	-	-	Mild
68.	Ramires MCCH et al (2021) [75]	Brazil	Case report	01	Female	50 yrs	-	Obesity, hypertension, and type2 DM	Hospitalisation Ventilation	Severe
69.	Hocková B et al (2021) [76]	Czech Republic	Case series	03	M:F-3:0	62 yrs		Arterial hypertension, hypercholesterolemia, GERD (case 1); Arterial hypertension, history of MI and septic shock (case 2)	ICU	Severe
70.	Teixeira IS et al (2021) [77]	Brazil	Case series	04	M:F-1:3	57 yrs, 84 yrs, 70 yrs, 64 yrs	-	Hypertension, hypothyroidism, and rectal tumor (case 2); hypertension, hypothyroidism (case 3); bipolar disorder (case 4)	-	-
71.	Emelyanova N et al (2021) [78]	Ukraine	Case report	01	Female	38 yrs	-	-	-	-
72.	Fathi Y et al (2021) [79]	Iran	Case report	01	Female	22 yrs	April 2020	-	Hospitalization (2nd day)	

73.	Shenoy P et al (2022) [80]	India	Case report	01	Female	55 yrs	-	-	-	-
74.	Palaia G et al (2022) [81]	Italy	Case report	01	Female	30 yrs	-	-	-	-
75.	Rafałowicz B et al (2022) [82]	Poland	Case series	06	M-4 F-2	43 yrs, 72 yrs, 53 yrs, 48 yrs, 66 yrs; 71 yrs	January-June 2021	Hypertension and insulin resistance (case 2)	No	

CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; GERD: Gastroesophageal reflux disease; DM: Diabetes mellitus; CLD: Chronic lung disease

Table 2: Oral manifestations of the included studies (n=75)

S. No.	Author & year	Oral manifestation	Site	Type of oral manifestation	Occurrence/duration of oral manifestation	Systemic manifestation
1.	Al-Zaidi and Badr (2020) [12]	Loss of taste (83%)	Tongue	Taste alterations	1 week before systemic symptoms	Fever (63.08%), cough (60.00%), dyspnea (47.69%), sore throat, diarrhea (32.31%), chest pain (30.77%).
2.	Biadsee et al (2020) [13]	Taste alteration (n=67), dry mouth (72), plaque-like changes in the tongue (9), swelling in the oral cavity (10)	Tongue, oral cavity	Taste alteration, tongue manifestation, xerostomia	Along with systemic symptoms	Cough and runny nose (p = 0.018), olfactory dysfunction
3.	Bodnia and Katzenstein (2020) [14]	Total loss of taste (70%)	Tongue	Taste alterations	1-3 weeks (78%), 3-6 weeks (22%)	Fatigue, headache, fever, dry cough and disturbance of the sense of smell
4.	Chen L et al (2020) [15]	Amblygeustia (47.2%), dry mouth (11.1%)	Tongue, oral cavity	Taste alteration, xerostomia	Along with systemic symptoms	Submandibular lymph node enlargement (1); cough (21); fever (20); diarrhea (04); chest tightness (13)
5.	Dell V et al (2020) [16]	Taste disorders (65.5%)	Tongue	Taste alterations	Mean duration: 10 days	Fever (72.1%); cough (47.9%); fatigue (40.3%); dyspnea (21.7%); diarrhea (19.7%)
6.	Kumar L et al (2020) [17]	Taste Dysfunction (28.4%)	Tongue	Taste alterations	Duration: 2-15 days	Malaise (14.2%), sore throat (19.9%), cough (20.6%), fever (48.2%), diarrhea (5.7%), nasal discharge (3.5%) headache (5.7%)
7.	Lechien JR et al (2020) [18]	Gustatory dysfunction (88.8%)	Tongue	Taste alterations	Mean duration: 9.2 ± 6.2 days	Olfactory dysfunction (85.6%)
8.	Paderno A et al (2020) [19]	Gustatory dysfunction (group a-51.9% Group b-78.9%) Partial-36.8% Total-60.1% Unable to assess-3.1%	Tongue	Taste alterations	First symptom in 11.9% (group a) and 10.2% (group b) Mean duration: 9.2 ± 5.4	Olfactory dysfunction, fever, cough, headache, dyspnea, asthenia, diarrhea, nausea, nasal congestion, pharngodynia
9.	Rizzo PB et al (2020) [20]	Loss of taste (n=113)	Tongue	Taste alterations	Mean duration: 9.5 days	Dry cough, fever, headache, sore throat, chest pain, nausea, abdominal pain
10.	Yan CH et al (2020) [21]	Gustatory impairment -71% (p<0.001)	Tongue	Taste alterations	-	Fatigue (81%), fever (70%), anosmia (68%), myalgia or arthralgia (63%), diarrhea (48%), nausea (27%).

11.	Sinjari B et al (2020) [22]	Impaired taste (25%), burning sensation (15%), difficulty in swallowing (20%), dry mouth (30%) (p=0.02)	Oral cavity, tongue	Taste alterations	-	-
12.	Giacomelli A et al (2020) [23]	Dysgeusia (8.5%) Ageusia (1.7%)	Tongue	Taste alterations	Before hospitalization (91%)	Fever (72.8%), cough (37.3%), dyspnea (25.4%), sore throat (1.7%), arthralgia (5.1%), headache (3.4%), asthenia (1.7%), abdominal symptoms (8.5%)
13.	Mascitti H et al (2020) [24]	Oral lichenoid reaction 32.5%; oral enanthema 27.5%; macroglossia 25.0% cheilitis 12.5%; ageusia-20.5%; extensive ulcerations of the tongue2.5%	Lips, tongue, oral cavity and oral mucosa	Red and white lesions, tongue manifestation, taste alteration, vesiculobullous lesion	-	Macular exanthema (80%), face edema (32%), livedo (13%), urticarial rash (8%), purpura (5%), oral lichenoid lesions (33%), and conjunctivitis (18%)
14.	Salehi M et al (2020) [25]	White plaques on the intraoral mucous layer	Mucous membrane	Red and white lesions	-	-
15.	Askin O et al (2020) [26]	Necrosis on maxillary arch (1 case); apthous stomatitis 5.8%; rash and erythema; apthous lesion on side of tongue	Mucous membrane and tongue	Vesiculobullous lesion, tongue manifestation, red and white lesions, periodontal changes	-	Cutaneous findings (36.1%)
16.	Katz J et al (2020) [27]	Recurrent aphthous stomatitis- 0.64%	Oral mucosa	Vesiculobullous lesion	-	-
17.	Fantozzi PJ et al (2021) [28]	Dry mouth-45.9%; swallowing difficulties,-39.2%; dysgeusia-59.5%	Tongue; oral cavity	Taste alteration, xerostomia	First symptom (xerostomia)-19.6%; dysgeusia (87.9%) Duration (xerostomia) -7 days; dysgeusia 6 days	Fever (90.9), cough (46.8), dyspnea (34.3), diarrhea (4.5), sore throat (3.6), fatigue (3.6), myalgia/arthralgia (2.7), vomiting (2.7)
18.	Favia G et al (2021) [29]	Geographic tongue (n=7); fissured tongue (5); ulcerative lesion (65); blisters (19); hyperplasia of papillae (48); angina bullosa (11); candidiasis (28); ulceronecrotic gingivitis (7) Petechiae (14); oral haemorrhage (1) Taste disorders (90%)	Tongue, oral mucosa, lips	Tongue manifestation, vesiculobullous lesion, red and white lesions, periodontal changes, bleeding disorders, taste alteration	Together with general symptoms (26.2%); Duration: one week (41%) After 1 week of general symptoms (32.6%)	Fever, anosmia, cough, sore throat, congestion, runny nose, nausea or vomiting, muscle and body aches, dermatologic manifestation, pneumonia, dyspnea, hypoxia (spo2 < 90%)
19.	Halepas S et al (2021) [30]	Red and/or swollen lips (48.9%); strawberry tongue (10.6%)	Lips, tongue	Lip lesions, tongue manifestation	-	Fever

20.	Rekhtman S et al (2021) [31]	Rashes on lips and tongue-5.7% and 2.9%; ulcers on lips and tongue	Lips and tongue	Tongue manifestation, vesiculobullous lesion, lip lesions		Generalized rashes and vesiculobullous lesions present
21.	Maraouf N et al (2021) [32]	Periodontitis-258/568	Periodontium	Periodontal changes	-	-
22.	Nuno-Gonzalez A et al [5] (2021)	Oral mucosal changes (11.7%), transient anterior U-shaped lingual papillitis (11.5 %), tongue swelling (6.6%), aphthous stomatitis (6.9%), burning sensation in the mouth (5.3%), m ucositis (3.9%), glos sitis with patchy depapillation (3.9%), white tongue (1.6%), and enanthema (0.5%), taste disturbances	Tongue, oral mucosa	Tongue manifestation, vesiculobullous lesion, burning sensation	-	-
23.	Subramaniam T et al (2021) [33]	Ulcers on oral mucosa (case 1); burning mouth and mucositis on lower labial mucosa (cases 2,5); papillary atrophy (case 3); reddish-white spots on the palate (case 4); ulcers on lower lip (cases 6,7,8); pallor of lip (case 9)	Oral mucosa, palate, lips, tongue	Tongue manifestation, vesiculobullous lesion, burning sensation, red and white lesions, lip lesions	-	Fever, cough, dyspnea, runny nose, chest tightness, loss of smell
24.	Abubakr N et al (2021) [34]	Dental pain (23%), pain in jaw bones or joint (12.0%), halitosis (10.5%), ulcerations (20.4%), and dry mouth (47.6%)	Teeth, jaw bones, oral cavity	Vesiculobullous lesion, xerostomia, pain in teeth and jaw, tmj disturbances	-	Fever, myalgia, dysphagia, and hyposmia, loss of smell, nasal itching
25.	Song J et al (2021) [35]	Loss of taste (20.6%; median score, 6)	Tongue	Taste alteration	First symptom (0.4%) Recovery time-7 days	Nasal obstruction (8.6%), rhinorrhea (10.3%), nasal itching (4.9%), sneezing (11.0%), loss of smell (11.4%)
26.	Bardellini E et al (2021) [36]	Oral pseudomembranous candidiasis (7.4%), geographic tongue (3.7%), coated tongue (7.4%); taste alteration (11.1%)	Tongue, oral mucosa	Red and white lesions, tongue manifestation	-	Fever, cough, rhinorrhoea, breathing difficulty
27.	Gherlone EF et al (2021) [37]	Salivary gland ectasia-38%; dry mouth-30%; dysgeusia-17%; white plaque-28%; oral ulcers-12%	Salivary glands, tongue, oral mucosa, oral cavity	Salivary gland disorders, xerostomia, red and white lesions, vesiculobullous lesions, taste alteration	-	-
28.	El Kady DM et al (2021) [38]	Dry mouth 39.7%; loss of salt sensation-34.5%, loss of sweet sensation-29.3%, altered food taste-	Tongue, salivary glands, gingiva, oral mucosa	Xerostomia, taste alteration, periodontal changes, salivary gland disorders, vesiculobullous	-	-

		25.9%; tongue redness 8.8%; gingival bleeding 7%; salivary glands infection 22.4%; swellings in the salivary gland or cheek 13.8%; pain or swelling below mandible-10.8%; burning mouth sensation-22.4%; ulcers-17.2%		lesions, burning sensation		
29.	Fidan V et al (2021) [39]	Aphthous-like ulcer (36.5), erythema (25.7), lichen planus (16.2); tongue (31.8), oral mucosa (27.0), gingiva (14.9), palate (5.4)	Tongue/oral mucosa/gingiva/palate-39.7%/34.5%/18.9%/6.9%	Vesiculobullous lesions, red and white lesions, periodontal changes	Oral lesions prior covid-19 diagnosis	-
30.	Natto ZS et al (2021) [40]	Loss of taste-43.4%; erythema/desquamated gingivitis and coated tongue (7.3%); ulcers/blisters (6.4%); pain and soreness (2.8%); dry mouth (0.9%)	Tongue; gingiva; oral mucosa, oral cavity	Vesiculobullous lesions, taste alteration, xerostomia	After systemic symptoms	Cough, fever, sore throat, runny nose, muscle pain, headaches, nausea, and diarrhea
31.	Elamrousy WAH et al (2021) [41]	Oral ulcers (92.8%); dry mouth (84%); loss of taste (55%); hemorrhagic ulcers with crust on lips	Lip/tongue/labial mucosa-42.3%/38.5%/34.6%	Vesiculobullous lesions, lip lesions, taste alteration	-	Asthenia (67.7), breath problems (67.7), cough (67.7), fatigue (19.4), abdominal symptoms (12.9)
32.	Bulut DG et al (2021) [42]	Taste loss (53%), halitosis (21%), oropharyngeal wound and pain (18%), pain in the chewing muscles (16%), pain in the temporomandibular joint (17.5%), gum bleeding (17.5%), dry mouth (38%, after recovery 12.0), aphthous ulcer (14.5%), sensitivity and/or pain in teeth (12%), herpes labialis (8.5%), burning in the tongue (7.5%)	Tongue, gingiva, lips, oral cavity	Taste alteration, TMJ disturbances, xerostomia, burning sensation, vesiculobullous lesion, periodontal changes, teeth pain	-	Presence of symptoms (87.5)
33.	Naser Al et al (2021) [43]	Burning sensation (6%), numbness or tingling of the tongue (2%), white coat of the tongue, gingiva, palate (31.6%, 22.4%, 15.6%), loss of taste (79.5%), aphthous ulcers (24.8%), black discoloration of oral cavity, lips and tongue (4.7%, 6.8%), yellow coating on lips (5.3%)	Tongue, palate, lips, oral mucosa, oral cavity	Burning sensation, tongue manifestation, red and white lesions, vesiculobullous lesion, fungal infection, lip lesions	-	-

34.	Muthyam AK et al (2022) [44]	Dry mouth (44%) followed by swallowing difficulty, mouth ulcerations, chewing problems, gum bleeding, and burning sensation, altered taste (72%); fissured tongue, halitosis, and loss of taste-2%	Gums, tongue, oral mucosa, oral cavity	Xerostomia, vesiculobullous lesions, taste alteration, periodontal changes, tongue manifestation, burning sensation	Altered taste lasted more than 1 week-53%	Weakness (8%), cough and cold (4%), and body pain (2%)
35.	Ganesan A et al (2022) [45]	Gustatory disturbance-51.2; dry mouth=28%; erythema, ulcers and depapillation of tongue-15.5% A statistically significant correlation between oral manifestations and disease severity ($p \leq 0.001$).	Tongue, oral mucosa	Xerostomia, tongue manifestation, taste alteration	-	-
36.	El Tantawi M et al (2022) [46]	Dry mouth (11.1% vs 7.5%, $p = 0.009$) and change in taste (11.5% vs 2.7%, $p < 0.001$) were greater in covid-19 person; leukoplakia-4.6%; ulcers & hairy tongue-2.3%;gingival inflammation-13.1%	Oral cavity, tongue, gingiva	Vesiculobullous lesions, xerostomia	-	-
37.	Soares CD et al (2022) [47]	Lesions in the palate/tongue/lips or palate- 57.1%, 29%/ 14.3%.	Tongue, lips, palate	Vesiculobullous lesions	-	Anosmia, fever, and headache.
38.	Tuter G et al (2022) [48]	Dry mouth (44.2%); oral lesions (22.4%); oral mucosa (15.2%); tongue (10.8%).	Tongue, Oral mucosa	Vesiculobullous lesions, xerostomia	-	-
39.	Schwab G et al (2022) [49]	Ageusia – 11.0%; opportunistic oral infections such as pseudomembranous candidiasis and herpes simplex-4.5%	Tongue, oral mucosa	Vesiculobullous lesions, taste alteration, red and white lesions	-	Cough – 72.7%; dyspnoea – 63.0%; fever – 53.9%; anosmia – 14.3%
40.	Chawla J et al (2022) [50]	Dry mouth (38%) ($p=0.03$); Dysgeusia (32%) ($p=0.04$); Vesiculobullous lesion-13%; Oral ulcers-3.7%	Oral cavity, tongue	Vesiculobullous lesions, xerostomia, taste alteration	-	Cough/sore throat/shortness of breath/running nose-30%/20%/7%/11%
41.	Binmadi NO et al (2022) [51]	Distortion of taste-60%; dry mouth-42%, oral ulcerations-11%, gingivitis/petechiae/ candidiasis-6%; necrotizing periodontal disease/vesiculobullous lesions/erythema migrans/geographic tongue-4%	Gingiva, tongue, oral mucosa, oral cavity	Vesiculobullous lesions, xerostomia, taste alteration, periodontal changes, red and white lesions, bleeding disorders, tongue manifestation	Concurrently-47%, after the general symptoms-43%, and before the general symptoms-9%	Fever (95%), headache (65%,), fatigue (65%), cough (63%), myalgia/arthralgia (53%), loss of smell (53%), sore throat (50%), shortness of breath or dyspnea (40%), nausea or vomiting (21%), and diarrhea (15%).

42.	de Paula Eduardo F et al (2022) [52]	Saliva alterations-24.4%; dryness-9.9%; tongue coating-3%; sialorhea-3.3%; petechiae-10.5%; oral bleeding-7.5%	Oral mucosa, tongue	Xerostomia, salivary gland disorders, bleeding disorders, tongue manifestation	-	-
43.	Villarroel-Dorrego M et al (2022) [53]	Hemorrhagic ulcerative lesions-7.3%; erythematous and pseudomembranous forms of candidiasis-12.7%; angular cheilitis-1.5%; total loss of taste-60%; burning mouth-36.4%; dry mouth-27.3%	Tongue, oral mucosa	Xerostomia, bleeding disorders, red and white lesions, vesiculobullous lesions, taste alteration, burning sensation	-	-
44.	Manifar S et al (2022) [54]	Dry mouth-68.6% ($p < 0.001$) Dysgeusia-51.4% ($p < 0.001$) Hypogeusia-49.3%; halitosis-31.4%; metallic taste-29.3%	Tongue, oral cavity	Xerostomia, taste alteration	-	Gastrointestinal symptoms, smell defects, asthma, skin rashes, cough, malaise, myalgia, anorexia, respiratory distress, olfactory dysfunction
45.	Bhuyan R et al (2022) [55]	Burning sensation-2.4%; dry mouth-2.4%; loss of taste-31% ($p<0.001$); mouth ulcer-2.4%. Bleeding gum-2.4%.	Oral cavity, gums, tongue	Xerostomia, taste alteration, burning sensation, vesiculobullous lesion, periodontal changes	-	-
46.	Brandao TB et al (2020) [56]	Multiple aphthous-like ulcers covered with mucopurulent membrane in the Upper and lower lip mucosa and tongue (cases 1,2,4,5); ulcers on tongue and hard palate (case 3); ulcers on tongue and aguesia (cases 6,7, 8)	Lips, tongue, palate	Vesiculobullous ulcers, taste alteration, tongue manifestation	06-10 days	Chest tightness, fever, cough (cases 1,5,7,8); cough, Fever, dyspnea (cases 2,6); Abdominal distension, fever, mild dyspnea (cases 3 and 4)
47.	Dima M et al (2020) [9]	Oral candidiasis	Oral mucosa	Red and white lesions	-	Epistaxis and diaper erythema (all 3 cases); palpebral edema (newborn 2)
48.	Tapia ROC et al (2020) [57]	Bulla on the hard palate (x6mm) (case 1); diffuse purple macule (x12mm) and papule-plaque (x8mm) on the left and right palatal mucosa (case 2); tongue enlarge-ment (case 3); Burning mouth sensation and reddish macules on hard palate (case 4)	Palate, oral mucosa, tongue	Vesiculobullous lesion, red and white lesions, burning sensation, tongue manifestation		Fever, myalgia, dysphagia, and hyposmia
49.	Vaira LA et al (2020) [58]	Hypogeusia (33 cases) Complete ageusia (1 case)	Tongue	Taste alteration		Fever, cough, nasal obstruction, sore throat, hyposmia, anosmia, pneumonia

50.	Presas CMC et al (2020) [59]	Dysgeusia (case 1); multiple ulcers On palate (case 2); pain on tongue, blisters in lip mucosa and Desquamative gingivitis (case 3)	Tongue, lips,	Taste alteration, periodontal changes, vesiculobullous lesions	Along with systemic symptoms	Asthenia; hyposmia, and enlargement of lymph nodes in the neck (cases 1 and 3) Fever and diarrhea (case 2)
51.	Sinadinosand Shelswell (2020) [6]	Pain in palate (case 1); pain and ulcerations in palate (case 2), pain in tongue, blisters of the labial mucosa; desquamative gingivitis (case 3)	Palate, tongue, gums, lips	Tongue manifestation, periodontal changes, vesiculobullous lesions	-	Sore throat (case 1) Pneumonia (case 3)
52.	Rodríguez MD et al (2020) [60]	Dysgeusia, aphthous-like lesions, burning sensation, and tongue depapillation (case 1); burning mouth sensation and unilateral commissural fissures (case 2); dry mouth, lesions on the tongue, palate, and commissure (case 3)	Tongue, palate, oral mucosa	Taste alteration, xerostomia, vesiculobullous lesions, tongue manifestation, burning sensation	Before presentation (case 1); after discharge (case 2); with systemic symptoms (case 3)	Fever, malaise, and anosmia, diarrhea, and pneumonia (cases 1 and 3)
53.	Corchuelo and Ulloa (2020) [61]	Reddish plaques on the lower lip, dark brown pigmentation and aphthous ulcers in the gums, whitish area in tongue	Lower lips, gums, oral mucosa	Red and white lesions, vesiculubullous lesions, tongue manifestation	Mean duration: 8-10 days	-
54.	Dos Santos et al (2020) [10]	Hypogeusia, white plaque, multiple pinpoint yellowish ulcers in the tongue, nodule in lower lip (1cm)	Tongue, lower lip, oral mucosa	Taste alteration, vesiculobullous lesions, tongue manifestation	Mean duration: 14 days	Respiratory symptoms and progressive dyspnea on exertion, Fever and diarrhea.
55.	Zarch and Hosseinzadeh (2020) [62]	Vesicles on lower lip mucosa	Lip mucosa	Vesiculobullous lesions	2 days before systemic symptoms	High fever, Fatigue, and lack of appetite
56.	Hjelmeseth J (2020) [63]	Total ageusia	Tongue	Taste alteration	-	-
57.	Kahraman and Çaşkurlu (2020) [64]	Erythematous surface (hard palate), few petechiae in the midline and numerous pustular enanthema near the soft palate border	Palate	Bleeding disorders, vesiculobullous lesions	Mean duration: 10 days	Sore throat Fever, fatigue, severe dry cough, inability to taste or smell,
58.	Smith AC et al (2020) [65]	Loss of taste	Tongue	Taste alteration	Before general symptoms	Frontal headache, loss of smell, headache, loose stools
59.	Maniaci A et al (2020) [66]	Transient loss of taste	Tongue	Taste alteration	Mean duration: 12 days	Fever, sore throat, runny nose, presence of erythematous skin le-sions on the lower limbs, asthenia
60.	Melley LE et al (2020) [67]	Loss of taste	Tongue	Taste alteration	1 week before systemic presentation	Shortness of breath, Fatigue, and loss of appetite

61.	Riad A et al (2020) [68]	Painful white patches on the dorsal surface of the tongue and palate, mild tongue pain	Tongue, palate, oral mucosa	Tongue manifestation, red and white lesions	2 weeks before diagnosis	Sore throat, generalised myalgia, and Fatigue with intermittent fever
62.	Putra BE et al (2020) [69]	Stomatitis aphthous	Oral mucosa	Vesiculobullous lesions	Day 7	Fever, back pain, myalgia, sore throat, dry cough, rhinorrhea, anosmia
63.	Dalipi ZS et al (2021) [70]	Loss of taste Bullous and erosive erythematous lesions of lips and oral mucosa	Tongue, lips	Taste alteration, vesiculobullous lesions, lip lesions	Loss of taste-2 weeks before diagnosis	Fever, cough, headache, muscle pain, loss of smell, dark red, purpuric, irregular maculopapular lesions on abdomen
64.	Eita AAB et al (2021) [71]	Dysgeusia and greasy tongue coat	Tongue	Taste alteration, tongue manifestation	Before systemic symptoms	Sore throat, fever (38° C), nasal congestion, conjunctivitis, nausea, Abdominal pain, diarrhea, fatigue, severe joint pain.
65.	Cirillo and Colello (2021) [72]	Loss of taste	Tongue	Taste alteration	1 week before presentation	Loss of smell, headache, fatigue, and muscle pain
66.	Nejabi MB et al (2021) [73]	Fissured tongue, white scars and painful erosive ulcer on the Dorsal surface of the tongue	Tongue	Tongue manifestation	After 1 week of general symptoms	Fever, cough, taste alterations, olfactory dysfunction, and chest tightness
67.	Klein H et al (2021) [74]	Loss of taste	Tongue	Taste alteration	From 4th to 6 weeks	Fever, dry cough, chest pain, sore throat, diarrhea, nausea, headache, and back pain.
68.	Ramires MCCH et al (2021) [75]	Crusted ulcers on lip vermilion (both upper and lower lips	Lips	Vesiculobullous lesions	2 weeks after the onset of fever	Flu-like syndrome; evere and progressive dyspnea (spo2 = 88 %)
69.	Hocková B et al (2021) [76]	Oral lesions at the dorsal surface of the tongue (case 1); multiple lesions located on the tongue dorsum and labial mucosa (case 2); lesions on upper and lower lip (case 3)	Tongue and lips	Vesiculobullous lesions	After the diagnosis (all 3 cases)	Headache, fever, dry cough, and dyspnoea
70.	Teixeira IS et al (2021) [77]	Painful vesiculobullous lip lesions	Lips	Vesiculobullous lesions	After 4 days (case 1); after 10 days (case 2); after 11 days (case 3); after 19 days (case 4)	Headache, myalgia, and dyspnea
71.	EmelyanovaN et al (2021) [78]	Unusual tongue appearance and burning sensation, intermittent bleeding of gums, severe dryness in the oral cavity and persistent distortion of taste	Tongue, gums, oral mucosa	Burning sensation, periodontal changes, taste alteration, tongue manifestation, xerostomia	Third day (dysgeusia) and fifth day (xerostomia) after systemic symptoms	Rhinorrhea, coughing and increased body temperature to 38.5°
72.	Fathi Y et al (2021) [79]	Oral pain, ulcerative lesions on oral mucosa, hemorrhagic crusts on lips	Oral mucosa and lips	Vesiculobullous lesions, lip lesions,	3rd day (oral pain)	Fever, abdominal pain, nausea and occasional vomiting
73.	Shenoy P et al (2022) [80]	Ulcer with irregular borders on the dorsum of the tongue surrounded by a scrapable whitish plaque	Tongue	Tongue manifestation, red and white lesions	Systemic symptoms-3 weeks prior	Fever, cough, chest tightness

74.	Palaia G et al (2022) [81]	Extensive erosions involving lips, ulcers on the hard palate, blisters and ulcers on the dorsal surface of the tongue cheek mucosa	Palate, lips, oral mucosa	Vesiculobullous lesions	7 days prior to general symptoms (duration of oral lesions-14 days)	Bilateral cutaneous lesions were also evident on the hands. Low-grade fever
75.	Rafałowicz B et al (2022) [82]	Unilateral aphthous-like lesions on the left side of the hard palate (case 1 & 5); hemorrhagic changes on the palate and cheilitis (case 2); smooth tongue with intensely red-purple mucosa (case 3); angioma type lesion on the right side of the palate (case 4); mycosis of the tongue, extensive lesions on the palate, spontaneous bleeding, cheilitis (case 6)	Hard palate, tongue; lips	Vesiculobullous lesions, red and white lesions, fungal infection, tongue manifestation, bleeding disorders	-	Fever, malaise, taste disorders, anosmia, and pneumonia (case 1); dyspnea, persistent diarrhea, and vomiting (case 2); loss of smell and taste and fever for 9 days (case 4 & 5)

Supplementary table 1: Treatment of oral lesions for COVID-19 patient

Author & year	Treatment given for oral lesions	Resolution time	General treatment for COVID-19	Outcome of COVID-19
Sinadinos and Shelswell (2020) [6]	Valaciclovir and topical antiseptics (chlorhexidine and hyaluronic acid)-cases 1 and 3; topical antiseptic mouthwash (case 2)	10 days (cases 1 and 3), 7 days (case 2)	-	All 3 recovered
Dima M et al (2020) [9]	Nystatin for the oral candidiasis.	15 days 21 days (newborn 3)	Vitamin D, topical cream for erythema (cases 1 and 2); Ampicillin (100 mg/kgc/d), Gentamicin (4 mg/kgc/d), aminophylline (3 _ 0.3mL/d), and Fluconazole iv (6 mg/kgc) (newborn 3)	All 3 cases recovered
Dos santos et al (2020) [10]	Oral nystatin (100,000 IU/mL, 8/8h, for 30 days), chlorhexidine digluconate (0.12%) 1% hydrogen peroxide	44 days	Fluconazole 200mg/100mL, Meropeném-1000mg, 8/8hs, Sulfamethoxazole+Trimetropin-400mg +80mg, 1.5 ampule, 8/8hs for 10 days Enoxaparin sodium - 60mg/day.	Recovered
Favia G et al (2021) [29]	Hyaluronic acid gel and chlorhexidine 2% mouthwash, miconazole nitrate twice a day in patients with cytological diagnosis of candidiasis, tranexamic acid for local hemorrhages	14-21 days	-	Good recovery

Naser Al et al (2021) [43]	Chlorhexidine 0.2% mouthwash (35%), Nystatin (15%), Mycoheal (8%), Anginovag spray (22%) Fluconazole (13%), Kenalog spray (6%), Amphotericin B (1%)	7.7 days	-	98% responded to treatment
Soares CD et al (2022) [47]	Most patients with chronic ulcers were treated with topical corticosteroids and the lesions resolved after 1 to 2 weeks.	2 weeks	-	All recovered
Brandao TB et al (2020) [56]	Daily photobiomodulation therapy (PBMT)-10 days; 0.12% chlorhexidine mouthwash	11-14 days	Intravenous acyclovir-250 mg/m 2-3 times a day for 10 days.	Recovered (06 cases); critical condition (cases 2 & 4)
Tapia ROC et al (2020) [57]	Topical Mometasone furoate 0.1% in solution after oral hygiene and clorhexidine 0.12% mouthwash	14 days	Acetaminophen 500mg every 6 h for 4 days and Fexofenadine 180 mg every 24 h per 10 days (case 1,2); Dexanethasone 8mg (case 2)	Recovered
Presas CMC et al (2020) [59]	Topical Antiseptics, chlorhexidine and hyaluronic acid mouthwash (Cases 1 & 2); prednisolone 30 mg per day (case 3)	10 days	Valaciclovir 500 mg every 8 hr for 10 days (case 1); antibiotics, corticosteroids, and lopinavir 200 mg, ritonavir 50 mg, hydroxychloroquine 200 mg) (case 3)	Recovered
Rodrígue z MD et al (2022) [60]	triamcinolone acetonide 0.05% (case 1); ointment containing neomycin, nystatin, and triamcinolone acetonide and chlorhexidine mouthwash (case 2); Nystatin solution rinses (case 3)	10 days (cases 1 and 2); 15 days (case 3);	-	All 3 recovered
Corchuel o and Ulloa (2020) [61]	Nystatin oral suspension-3 ml (300,000 I.U) every 6 h; Chlorhexidine gluconate (0.12%)	14 days	-	Recovered
Kahrama n and Çaşkurlu (2020) [64]	Antibiotherapy	14 days	Clarithromycin 500 mg b.i.d. immediately after the diagnosis	Recovered
Smith AC et al (2020) [65]	-	21days	Fluticasone, Loratadine, and nasal spray	Recovered
Melley LE et al (2020) [67]	-	15days	Hydroxychloroquine 400 mg, azithromycin 500 mg	Recovered
Riad A et al (2021) [68]	Topical antifungal, nystatin (Micostatin) and antibacterial mouthwash, chlorhexidine 0.2%, twice daily (case 1); topical antifungal *miconazole* (Daktarin Gel) (cases 2 and 3); systemic antifungal *fluconazole* (Flucoral) (case 3)	10 days (case 1); 4 days (case 2); 7 days (case 3)	*Azithromycin* (Zithromax, *levofloxacin* (Uniloxam), *r ivaroxaban* (Xarelto), and *lactoferrin* (Pravotin) (case 1)	All 3 recovered

Putra BE et al (2020) [69]	Oral hygiene regimen and mouthwash	21 days	Azithromycin 500 mg, hydroxychloroquine-400 mg (10 days), oseltamivir-75 mg (10 days), vitamin C-1000 mg (14 days), vitamin D-5000 IU (14 days) On day six, the lesions lessened	Recovered
Dalipi ZS et al (2021) [70]	Antibiotic therapy with penicillin and anticoagulant therapy with Fraxiparine solution for injection 0.4 mL, antiseptic mouthwash (0.2% chlorhexidine solution mouthwash twice per day for 14 days	21 days	Systemic corticosteroids, vitamins (C, B complex), and locally applied tablets (panthenol-calcium with pantothenic acid)	Recovered
Eita AAB (2021) [71]	0.12% chlorhexidine mouth rinse and nystatin oral drops 100.000 I.U/ml 2-3 times daily). Daily vitamin C (1000 mg) and zinc (50 mg)	28 days	*Azithromycin 500 mg/day, paracetamol 500 mg 2 tablets ×3 times daily, zinc (50 mg), and vitamin C (1000 mg) supplements*	Recovered
Nejabi MB et al (2021) [73]	Intravenous Acyclovir 5 mg/kg for 7 days; PMBT-10 days; Chlorhexidine 0.12%, H2O2-1%)	14 days	Azithromycin 500 mg daily for one week and ceftriaxone 1g twice a day for 3 days. antifungal agents (fluconazole 200 mg tablets for 1 week)	Recovered
Ramires MCCH et al (2021) [75]	Photodynamic therapy for 2 days, methylene blue at 0.01 % was applied over all lesions. After 5 min (time pre-irradiation), the laser device Therapy EC® was used at 660 nm. A total of 30 points were distributed throughout the affected areas: 20 points on the upper and 10 on the lower lip.	Healed after 4 days of therapy	-	Recovered
Teixeira IS et al (2021) [77]	For PBMT, a laser device Laser DUO® was used at 660 nm, on contact mode, point by point, with 100 mW, 33 J/cm2, 0.5 J, and 5 s per point. Then, aPDT technique was performed, with methylene blue at 0.01 % applied over all lesions and after 3 min, the same laser parameters were used.	Marked improvement after 72 hrs	*Azithromycin and ceftriaxone. dexamethasone*	Recovered
Fathi Y et al (2021) [79]	Removal of dental plaque and chlorhexidine mouthwash (twice a day). Valacyclovir for 5 days	Resolved after 4 days	Metronidazole, ceftriaxone, meropenem, ribavirin and hydroxychloroquine were administered and supplemental oxygen was given	-
Shenoy P et al (2022) [80]	Tab Fluconazole, Clotrimazole mouth paint, Chlorhexidine 0.12% mouth rinse.		Anticoagulants, corticosteroids and multivitamins. Medications include Inj.Enoxararin, Inj. Pantop, Tab.Shelcal HD, Neb.Budecort, Inj.Predmet 40 mg, Cap.Meganeuron	Succumbed to disease.

Rafałowicz B et al (2022) [82]	Semiconductor laser therapy with the Smart bio stimulation function-five treatments at 3-day intervals (case 1); aliva-stimulating tablets SST (Sinclair Pharmaceuticals), Kserostemin (artificial saliva) (Aflofarm), and mouthwash with chlorhexidine three times a day for a period of 14 days (case 3); antifungal Nystatin (Teva) antibiotic was administered at a dose of 100,000 IU/mL four times a day along with vitamin A + E + F (Gorvita) ointment on the lips (case 6)	192 days (case 1); 2 weeks (case 3); 60 days (case 5)	-	-

Global Journals Guidelines Handbook 2023

www.GlobalJournals.org

Memberships

Fellows/Associates of Medical Research Council

FMRC/AMRC Memberships

Introduction

FMRC/AMRC is the most prestigious membership of Global Journals accredited by Open Association of Research Society, U.S.A (OARS). The credentials of Fellow and Associate designations signify that the researcher has gained the knowledge of the fundamental and high-level concepts, and is a subject matter expert, proficient in an expertise course covering the professional code of conduct, and follows recognized standards of practice. The credentials are designated only to the researchers, scientists, and professionals that have been selected by a rigorous process by our Editorial Board and Management Board.

Associates of FMRC/AMRC are scientists and researchers from around the world are working on projects/researches that have huge potentials. Members support Global Journals' mission to advance technology for humanity and the profession.

FMRC

Fellow of Medical Research Council

FELLOW OF MEDICAL RESEARCH COUNCIL is the most prestigious membership of Global Journals. It is an award and membership granted to individuals that the Open Association of Research Society judges to have made a 'substantial contribution to the improvement of computer science, technology, and electronics engineering.

The primary objective is to recognize the leaders in research and scientific fields of the current era with a global perspective and to create a channel between them and other researchers for better exposure and knowledge sharing. Members are most eminent scientists, engineers, and technologists from all across the world. Fellows are elected for life through a peer review process on the basis of excellence in the respective domain. There is no limit on the number of new nominations made in any year. Each year, the Open Association of Research Society elect up to 12 new Fellow Members.

To the institution

Get letter of appreciation

Global Journals sends a letter of appreciation of author to the Dean or CEO of the University or Company of which author is a part, signed by editor in chief or chief author.

Exclusive Network

Get access to a closed network

A FMRC member gets access to a closed network of Tier 1 researchers and scientists with direct communication channel through our website. Fellows can reach out to other members or researchers directly. They should also be open to reaching out by other.

Career | Credibility | Exclusive | Reputation

Certificate

Certificate, LoR and Laser-Momento

Fellows receive a printed copy of a certificate signed by our Chief Author that may be used for academic purposes and a personal recommendation letter to the dean of member's university.

Career | Credibility | Exclusive | Reputation

Designation

Get honored title of membership

Fellows can use the honored title of membership. The “FMRC” is an honored title which is accorded to a person’s name viz. Dr. John E. Hall, Ph.D., FMRC or William Walldroff, M.S., FMRC.

Career | Credibility | Exclusive | Reputation

Recognition on the Platform

Better visibility and citation

All the Fellow members of FMRC get a badge of "Leading Member of Global Journals" on the Research Community that distinguishes them from others. Additionally, the profile is also partially maintained by our team for better visibility and citation. All fellows get a dedicated page on the website with their biography.

Career | Credibility | Reputation

Future Work

Get discounts on the future publications

Fellows receive discounts on the future publications with Global Journals up to 60%. Through our recommendation programs, members also receive discounts on publications made with OARS affiliated organizations.

Career | Financial

GJ Internal Account

Unlimited forward of Emails

Fellows get secure and fast GJ work emails with unlimited storage of emails that they may use them as their primary email. For example,
john [AT] globaljournals [DOT] org.

Career | Credibility | Reputation

Premium Tools

Access to all the premium tools

To take future researches to the zenith, fellows receive access to all the premium tools that Global Journals have to offer along with the partnership with some of the best marketing leading tools out there.

Financial

Conferences & Events

Organize seminar/conference

Fellows are authorized to organize symposium/seminar/conference on behalf of Global Journal Incorporation (USA). They can also participate in the same organized by another institution as representative of Global Journal. In both the cases, it is mandatory for him to discuss with us and obtain our consent. Additionally, they get free research conferences (and others) alerts.

Career | Credibility | Financial

Early Invitations

Early invitations to all the symposiums, seminars, conferences

All fellows receive the early invitations to all the symposiums, seminars, conferences and webinars hosted by Global Journals in their subject.

Exclusive

Publishing Articles & Books

Earn 60% of sales proceeds

Fellows can publish articles (limited) without any fees. Also, they can earn up to 70% of sales proceeds from the sale of reference/review books/literature/publishing of research paper. The FMRC member can decide its price and we can help in making the right decision.

Exclusive | Financial

Reviewers

Get a remuneration of 15% of author fees

Fellow members are eligible to join as a paid peer reviewer at Global Journals Incorporation (USA) and can get a remuneration of 15% of author fees, taken from the author of a respective paper.

Financial

Access to Editorial Board

Become a member of the Editorial Board

Fellows and Associates may join as a member of the Editorial Board of Global Journals Incorporation (USA) after successful completion of three years as Fellow and as Peer Reviewer.

Career | Credibility | Exclusive | Reputation

And Much More

Get access to scientific museums and observatories across the globe

All members get access to 5 selected scientific museums and observatories across the globe. All researches published with Global Journals will be kept under deep archival facilities across regions for future protections and disaster recovery. They get 10 GB free secure cloud access for storing research files.

ASSOCIATE OF MEDICAL RESEARCH COUNCIL

ASSOCIATE OF MEDICAL RESEARCH COUNCIL is the membership of Global Journals awarded to individuals that the Open Association of Research Society judges to have made a 'substantial contribution to the improvement of computer science, technology, and electronics engineering.

The primary objective is to recognize the leaders in research and scientific fields of the current era with a global perspective and to create a channel between them and other researchers for better exposure and knowledge sharing. Members are most eminent scientists, engineers, and technologists from all across the world. Associate membership can later be promoted to Fellow Membership. Associates are elected for life through a peer review process on the basis of excellence in the respective domain. There is no limit on the number of new nominations made in any year. Each year, the Open Association of Research Society elect up to 12 new Associate Members.

To the institution

Get letter of appreciation

Global Journals sends a letter of appreciation of author to the Dean or CEO of the University or Company of which author is a part, signed by editor in chief or chief author.

Exclusive Network

Get access to a closed network

A AMRC member gets access to a closed network of Tier 2 researchers and scientists with direct communication channel through our website. Associates can reach out to other members or researchers directly. They should also be open to reaching out by other.

Career | Credibility | Exclusive | Reputation

Certificate

Certificate, LoR and Laser-Momento

Associates receive a printed copy of a certificate signed by our Chief Author that may be used for academic purposes and a personal recommendation letter to the dean of member's university.

Career | Credibility | Exclusive | Reputation

Designation

Get honored title of membership

Associates can use the honored title of membership. The “AMRC” is an honored title which is accorded to a person’s name viz. Dr. John E. Hall, Ph.D., AMRC or William Walldroff, M.S., AMRC.

Career | Credibility | Exclusive | Reputation

Recognition on the Platform

Better visibility and citation

All the Associate members of AMRC get a badge of "Leading Member of Global Journals" on the Research Community that distinguishes them from others. Additionally, the profile is also partially maintained by our team for better visibility and citation.

Career | Credibility | Reputation

Future Work

Get discounts on the future publications

Associates receive discounts on future publications with Global Journals up to 30%. Through our recommendation programs, members also receive discounts on publications made with OARS affiliated organizations.

Career | Financial

GJ Account

Unlimited forward of Emails

Associates get secure and fast GJ work emails with 5GB forward of emails that they may use them as their primary email. For example,
john [AT] globaljournals [DOT] org.

Career | Credibility | Reputation

Premium Tools

Access to all the premium tools

To take future researches to the zenith, fellows receive access to almost all the premium tools that Global Journals have to offer along with the partnership with some of the best marketing leading tools out there.

Financial

Conferences & Events

Organize seminar/conference

Associates are authorized to organize symposium/seminar/conference on behalf of Global Journal Incorporation (USA). They can also participate in the same organized by another institution as representative of Global Journal. In both the cases, it is mandatory for him to discuss with us and obtain our consent. Additionally, they get free research conferences (and others) alerts.

Career | Credibility | Financial

Early Invitations

Early invitations to all the symposiums, seminars, conferences

All associates receive the early invitations to all the symposiums, seminars, conferences and webinars hosted by Global Journals in their subject.

Exclusive

Publishing Articles & Books

Earn 60% of sales proceeds

Associates can publish articles (limited) without any fees. Also, they can earn up to 30-40% of sales proceeds from the sale of reference/review books/literature/publishing of research paper

Exclusive | Financial

Reviewers

Get a remuneration of 15% of author fees

Associate members are eligible to join as a paid peer reviewer at Global Journals Incorporation (USA) and can get a remuneration of 15% of author fees, taken from the author of a respective paper.

Financial

And Much More

Get access to scientific museums and observatories across the globe

All members get access to 2 selected scientific museums and observatories across the globe. All researches published with Global Journals will be kept under deep archival facilities across regions for future protections and disaster recovery. They get 5 GB free secure cloud access for storing research files.

Associate	Fellow	Research Group	Basic
$4800 **lifetime designation**	$6800 **lifetime designation**	$12500.00 **organizational**	APC **per article**
Certificate, LoR and Momento **2** discounted publishing/year **Gradation** of Research **10** research contacts/day **1 GB** Cloud Storage **GJ** Community Access	**Certificate,** LoR and Momento **Unlimited** discounted publishing/year **Gradation** of Research **Unlimited** research contacts/day **5 GB** Cloud Storage **Online Presense** Assistance **GJ** Community Access	**Certificates,** LoRs and Momentos **Unlimited** free publishing/year **Gradation** of Research **Unlimited** research contacts/day **Unlimited** Cloud Storage **Online Presense** Assistance **GJ** Community Access	**GJ** Community Access

Preferred Author Guidelines

We accept the manuscript submissions in any standard (generic) format.

We typeset manuscripts using advanced typesetting tools like Adobe In Design, CorelDraw, TeXnicCenter, and TeXStudio. We usually recommend authors submit their research using any standard format they are comfortable with, and let Global Journals do the rest.

Alternatively, you can download our basic template from https://globaljournals.org/Template

Authors should submit their complete paper/article, including text illustrations, graphics, conclusions, artwork, and tables. Authors who are not able to submit manuscript using the form above can email the manuscript department at submit@globaljournals.org or get in touch with chiefeditor@globaljournals.org if they wish to send the abstract before submission.

Before and during Submission

Authors must ensure the information provided during the submission of a paper is authentic. Please go through the following checklist before submitting:

1. Authors must go through the complete author guideline and understand and *agree to Global Journals' ethics and code of conduct,* along with author responsibilities.
2. Authors must accept the privacy policy, terms, and conditions of Global Journals.
3. Ensure corresponding author's email address and postal address are accurate and reachable.
4. Manuscript to be submitted must include keywords, an abstract, a paper title, co-author(s') names and details (email address, name, phone number, and institution), figures and illustrations in vector format including appropriate captions, tables, including titles and footnotes, a conclusion, results, acknowledgments and references.
5. Authors should submit paper in a ZIP archive if any supplementary files are required along with the paper.
6. Proper permissions must be acquired for the use of any copyrighted material.
7. Manuscript submitted *must not have been submitted or published elsewhere* and all authors must be aware of the submission.

Declaration of Conflicts of Interest

It is required for authors to declare all financial, institutional, and personal relationships with other individuals and organizations that could influence (bias) their research.

Policy on Plagiarism

Plagiarism is not acceptable in Global Journals submissions at all.

Plagiarized content will not be considered for publication. We reserve the right to inform authors' institutions about plagiarism detected either before or after publication. If plagiarism is identified, we will follow COPE guidelines:

Authors are solely responsible for all the plagiarism that is found. The author must not fabricate, falsify or plagiarize existing research data. The following, if copied, will be considered plagiarism:

- Words (language)
- Ideas
- Findings
- Writings
- Diagrams
- Graphs
- Illustrations
- Lectures

- Printed material
- Graphic representations
- Computer programs
- Electronic material
- Any other original work

Authorship Policies

Global Journals follows the definition of authorship set up by the Open Association of Research Society, USA. According to its guidelines, authorship criteria must be based on:

1. Substantial contributions to the conception and acquisition of data, analysis, and interpretation of findings.
2. Drafting the paper and revising it critically regarding important academic content.
3. Final approval of the version of the paper to be published.

Changes in Authorship

The corresponding author should mention the name and complete details of all co-authors during submission and in manuscript. We support addition, rearrangement, manipulation, and deletions in authors list till the early view publication of the journal. We expect that corresponding author will notify all co-authors of submission. We follow COPE guidelines for changes in authorship.

Copyright

During submission of the manuscript, the author is confirming an exclusive license agreement with Global Journals which gives Global Journals the authority to reproduce, reuse, and republish authors' research. We also believe in flexible copyright terms where copyright may remain with authors/employers/institutions as well. Contact your editor after acceptance to choose your copyright policy. You may follow this form for copyright transfers.

Appealing Decisions

Unless specified in the notification, the Editorial Board's decision on publication of the paper is final and cannot be appealed before making the major change in the manuscript.

Acknowledgments

Contributors to the research other than authors credited should be mentioned in Acknowledgments. The source of funding for the research can be included. Suppliers of resources may be mentioned along with their addresses.

Declaration of funding sources

Global Journals is in partnership with various universities, laboratories, and other institutions worldwide in the research domain. Authors are requested to disclose their source of funding during every stage of their research, such as making analysis, performing laboratory operations, computing data, and using institutional resources, from writing an article to its submission. This will also help authors to get reimbursements by requesting an open access publication letter from Global Journals and submitting to the respective funding source.

Preparing your Manuscript

Authors can submit papers and articles in an acceptable file format: MS Word (doc, docx), LaTeX (.tex, .zip or .rar including all of your files), Adobe PDF (.pdf), rich text format (.rtf), simple text document (.txt), Open Document Text (.odt), and Apple Pages (.pages). Our professional layout editors will format the entire paper according to our official guidelines. This is one of the highlights of publishing with Global Journals—authors should not be concerned about the formatting of their paper. Global Journals accepts articles and manuscripts in every major language, be it Spanish, Chinese, Japanese, Portuguese, Russian, French, German, Dutch, Italian, Greek, or any other national language, but the title, subtitle, and abstract should be in English. This will facilitate indexing and the pre-peer review process.

The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.

Manuscript Style Instruction (Optional)

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11'", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

Structure and Format of Manuscript

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

a) A title which should be relevant to the theme of the paper.
b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
c) Up to 10 keywords that precisely identify the paper's subject, purpose, and focus.
d) An introduction, giving fundamental background objectives.
e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition, sources of information must be given, and numerical methods must be specified by reference.
f) Results which should be presented concisely by well-designed tables and figures.
g) Suitable statistical data should also be given.
h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
j) There should be brief acknowledgments.
k) There ought to be references in the conventional format. Global Journals recommends APA format.

Authors should carefully consider the preparation of papers to ensure that they communicate effectively. Papers are much more likely to be accepted if they are carefully designed and laid out, contain few or no errors, are summarizing, and follow instructions. They will also be published with much fewer delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and suggestions to improve brevity.

Format Structure

It is necessary that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

All manuscripts submitted to Global Journals should include:

Title

The title page must carry an informative title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) where the work was carried out.

Author details

The full postal address of any related author(s) must be specified.

Abstract

The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Keywords

A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy: planning of a list of possible keywords and phrases to try.

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning searching. Think about the most important concepts related to research work. Ask, “What words would a source have to include to be truly valuable in a research paper?” Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

Numerical Methods

Numerical methods used should be transparent and, where appropriate, supported by references.

Abbreviations

Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

Formulas and equations

Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

Tables, Figures, and Figure Legends

Tables: Tables should be cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g., Table 4, a self-explanatory caption, and be on a separate sheet. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.

Figures

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

Preparation of Eletronic Figures for Publication

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/ photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). Please give the data for figures in black and white or submit a Color Work Agreement form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution at final image size ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs): >350 dpi; figures containing both halftone and line images: >650 dpi.

Color charges: Authors are advised to pay the full cost for the reproduction of their color artwork. Hence, please note that if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a Color Work Agreement form before your paper can be published. Also, you can email your editor to remove the color fee after acceptance of the paper.

Tips for writing a good quality Medical Research Paper

1. Choosing the topic: In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

2. Think like evaluators: If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

3. Ask your guides: If you are having any difficulty with your research, then do not hesitate to share your difficulty with your guide (if you have one). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work, then ask your supervisor to help you with an alternative. He or she might also provide you with a list of essential readings.

4. Use of computer is recommended: As you are doing research in the field of medical research then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

5. Use the internet for help: An excellent start for your paper is using Google. It is a wondrous search engine, where you can have your doubts resolved. You may also read some answers for the frequent question of how to write your research paper or find a model research paper. You can download books from the internet. If you have all the required books, place importance on reading, selecting, and analyzing the specified information. Then sketch out your research paper. Use big pictures: You may use encyclopedias like Wikipedia to get pictures with the best resolution. At Global Journals, you should strictly follow here.

6. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

7. Revise what you wrote: When you write anything, always read it, summarize it, and then finalize it.

8. Make every effort: Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

9. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several unnecessary diagrams will degrade the quality of your paper by creating a hodgepodge. So always try to include diagrams which were made by you to improve the readability of your paper. Use of direct quotes: When you do research relevant to literature, history, or current affairs, then use of quotes becomes essential, but if the study is relevant to science, use of quotes is not preferable.

10. Use proper verb tense: Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

11. Pick a good study spot: Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

12. Know what you know: Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. Arrangement of information: Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

15. Never start at the last minute: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

16. Multitasking in research is not good: Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

17. Never copy others' work: Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

18. Go to seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.

20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. Adding unnecessary information: Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. Report concluded results: Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. Upon conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

The introduction: This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear: Adhere to recommended page limits.

Mistakes to avoid:

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

Reason for writing the article—theory, overall issue, purpose.

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

Introduction:

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.

The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

Approach:

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

Procedures (methods and materials):

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

Materials may be reported in part of a section or else they may be recognized along with your measures.

Methods:

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

Approach:

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

What to keep away from:

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

What to stay away from:

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

Figures and tables:

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

Discussion:

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."

Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

The Administration Rules

Administration Rules to Be Strictly Followed before Submitting Your Research Paper to Global Journals Inc.

Please read the following rules and regulations carefully before submitting your research paper to Global Journals Inc. to avoid rejection.

Segment draft and final research paper: You have to strictly follow the template of a research paper, failing which your paper may get rejected. You are expected to write each part of the paper wholly on your own. The peer reviewers need to identify your own perspective of the concepts in your own terms. Please do not extract straight from any other source, and do not rephrase someone else's analysis. Do not allow anyone else to proofread your manuscript.

Written material: You may discuss this with your guides and key sources. Do not copy anyone else's paper, even if this is only imitation, otherwise it will be rejected on the grounds of plagiarism, which is illegal. Various methods to avoid plagiarism are strictly applied by us to every paper, and, if found guilty, you may be blacklisted, which could affect your career adversely. To guard yourself and others from possible illegal use, please do not permit anyone to use or even read your paper and file.

Criterion for Grading a Research Paper (Compilation) by Global Journals

Please note that following table is only a Grading of "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals.

Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

INDEX

save our planet

Global Journal of Medical Research

Visit us on the Web at www.GlobalJournals.org | www.MedicalResearchJournal.org
or email us at helpdesk@globaljournals.org

ISSN 9755896