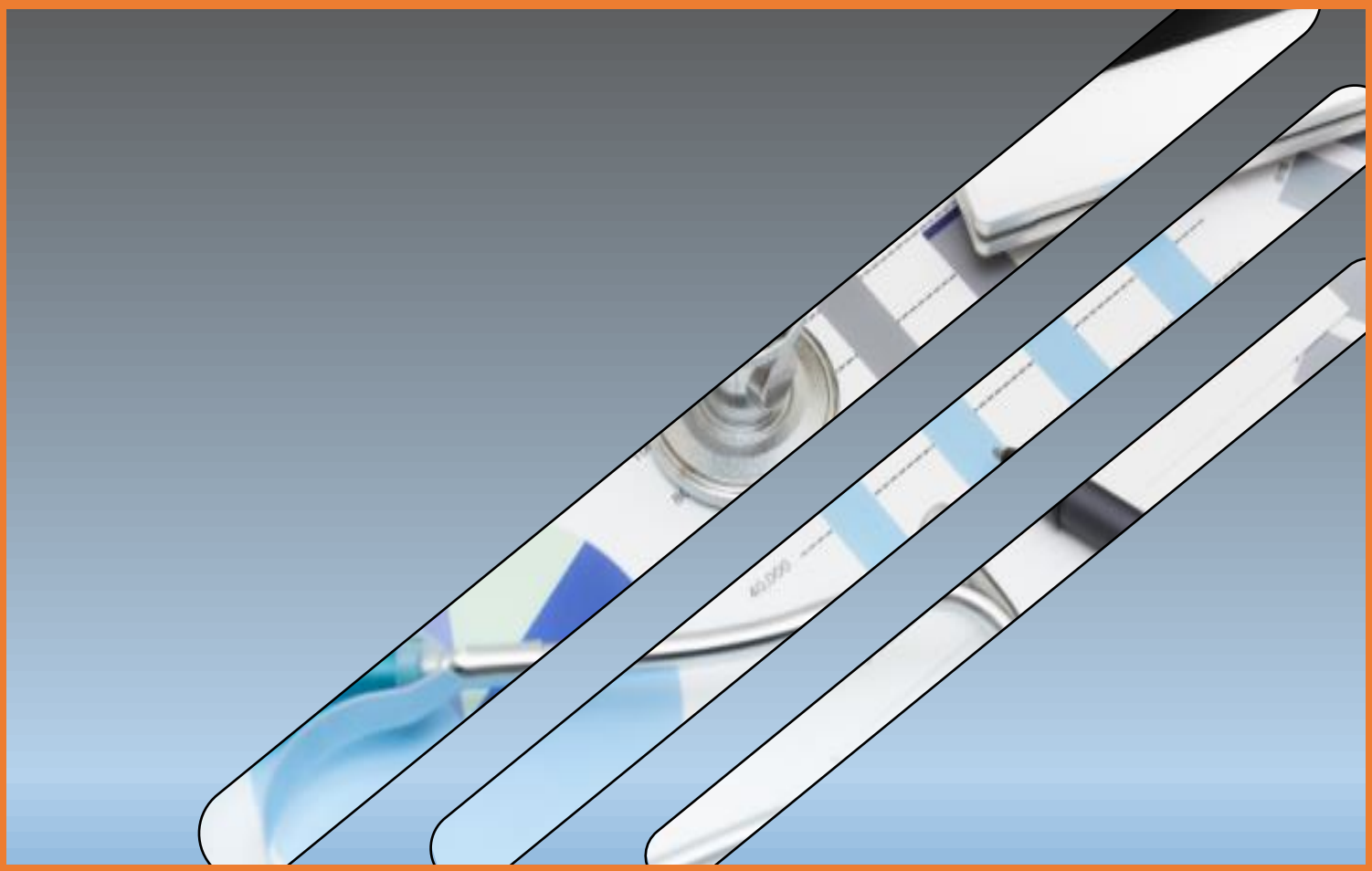

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EDITORIAL COMMENT

Editorial Comment

Dear Authors and Readers

Greetings

As we march towards completing five and a half years of glorious publication in the month of September 2022, this message is to thank you all for your constant support and guidance.

The world today is at a very strange position. Sporadic occurrences as well as outbreaks of various diseases are still plaguing the world. We request you all to stay safe and wish the best of health to all your near and dear ones.

Team IHRJ would also like to thanks its reviewers whose timely inputs have contributed to the success of the journal.

We are looking forward to completing six years of publication and will constantly keep you updated on the developments of the journal.

Regards
Team IHRJ

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REVIEW

QR CODE

A Detailed Study of Covid-19 (Emphasizing its Genomic Variants, Pathogenicity, Phylogenetic Analysis, Epidemiology, and Clinical Measures)

SOMENATH DUTTA *[1], ROHAN GHOSH [1], DEBANJAN GHOSH [1], PRIYASA SANTRA [1], SHILPA DAW [2]

ABSTRACT

Covid-19 (Coronavirus) had spread all over the world. Around 213 countries were affected by the deadly virus and encountered a mob of dead. After analyzing the genome, we can say that the Coronavirus originates in bats and gets transmitted to humans. Although the intermediate source of origin and transmission to humans is unknown, rapid human-to-human transmission has been evinced. SARS-CoV-2 is phylogenetically related to a group of bat viruses known to cause severe acute respiratory syndrome (SARS-CoV). Both viruses (SARS-CoV and SARS-CoV2) belong to the same family of beta coronaviruses. The first case of SARS-CoV2 infection was reported from Wuhan, China. Till now, there have been 577,018,226 confirmed cases of Covid-19 worldwide. More than 6 million people have succumbed to this deadly disease worldwide. Presently, the urgent need to develop a drug and vaccine that could cure this disease is fulfilled. This current review summarizes the origin of SARS-CoV2, its genome structure, pathogenicity and phylogenetic analysis of the virus, and its epidemiology. We have also discussed the existing drugs and approved vaccines that are presently treating humanity. This review aims to compact every possible information regarding Covid-19.

KEYWORDS: SARS-CoV2, Variants, Outbreak, Antiviral Therapies

INTRODUCTION

Viruses are microscopic organisms that can cause infections to almost all kinds of life forms like humans, animals, plants, fungi, and even bacteria. They vary in complexity and consist of genetic material, RNA or DNA, surrounded by a coat of protein, lipid(fat), or glycoprotein. They cannot replicate in the absence of a host. They are the most abundant biological form on the planet.

Several novel diseases have emerged in various geographic areas over the past few decades, including pathogens such as Ebola, Zika, Nipah, and coronaviruses (CoVs).

Coronaviruses are enormous in numbers and common among many animals, even in human bodies. Respiratory and gastrointestinal illnesses are the two most common symptoms of Coronavirus in humans and animals. Various Coronavirus has large peplomers, and it almost looks like a crown under the electron microscope. The name corona denotes “crown” or “halo”.[1,2] A new type of viral infection has been discovered in Wuhan, China, and preliminary genomic sequencing data suggests that this virus is a novel strain of CoV (2019-nCoV), identified as severe acute respiratory syndrome CoV-2 (SARS-CoV-2). Although coronavirus disease 2019 (COVID-19) is thought to have originated in an animal host (zoonotic origin) and then spread from person to person, other routes should not be ruled out. Covid-19 was not considered a deadly virus before 2003. These are almost round in shape, and were causing minor symptoms in immunocompetent people. Runny nose, sore throat, cough, headache, and fever are the main symptoms of Covid-19. The symptoms can last for numerous days. Immunocompromised patients have a chance that the virus could cause a lower respiratory illness like bronchitis and pneumonia.[1-3]

In 2003 the world experienced the first pandemic of the 21st century. Severe Acute Respiratory Syndrome Coronavirus (2003) appeared in Guangdong, China, and it was the cause of 774 deaths and the illness of more than 8000 patients.[1,4,5] After nine years, the strains of Coronavirus immersed in Saudi Arabia, with 2500 cases and 861 deaths with a deadly case-fatality rate of 34.4%, were the terrible result of Middle East Respiratory Syndrome Coronavirus (MERS-CoV).[5]

COVID-19 infection symptoms were first seen in Wuhan's people, and then it gradually began to take on a larger size. In December 2020, many Covid-19 cases were found in the South China seafood markets. Twenty-seven patients of the South China seafood city were found in worse condition. The rest of the cases were in control. On January 9th, 2020, after examining

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Wuhan city, the China government had found shocking reports; on that day, China government published a report about Covid-19. A piece of information on the CDC disclosed Coronavirus (COVID-19) had been found at the main reasonable specialist for 15 to 59 pneumonia cases. On January 10, 2020, the genome of covid-19 became accessible.[6] Then it was kept in the GenBank database (accession number- MN908947). Then Global Researchers took the data and called it influenza (GISAID). In the primary examination of this virus, it was told that the novel Coronavirus (SARS CoV-2) is affected by the SARS-related CoV clade and differs from the inside genome of known bat CoVs.[7] After the COVID-19 discovery, more than 577,018,226 patients were greatly affected, and about 6,401,046 died due to Covid-19 till August 3, 2022, 04:22 GMT. COVID-19 can spread quickly and cause significant illness in older adults and those in poorer health condition.[8,9] The Coronavirus is capable of mutation and recombination, and the genome sequence has already been muted. Some scientists have found that there are two circulating strains in the virus, the deadly strain "L" and the less virulent strain "S".[10,11]

THE ERA OF CORONAVIRUS

Coronavirus is not a new type of virus as it belongs to the subfamily Coronavirinae and with the family Coronaviridae and the order Nidovirales. The members of Coronavirinae subfamily are classified into four types based on their protein sequences and phylogenetic relationship as Alphacoronaviruses, Beta coronaviruses, Gamma coronaviruses, and Delta coronaviruses. Gamma coronavirus and Delta coronavirus are unable to affect humans. However, it can affect birds and might affect mammals[12,13] but Alpha coronaviruses and Beta coronaviruses can cause respiratory illness in human bodies and gastrointestinal disease in animals. Six common coronaviruses (members of Alphacoronaviruses and Betacoronaviruses) can affect humans significantly, as reported in December 2019. HCoV-229E, and HCoV-NL63 belong to the group of Alpha coronaviruses, and the linage A of Beta coronaviruses consists of HCoV-OC43 and HCoV-HKU1 and the deadliest SARS-CoV and MERS-CoV linages to B and C of Betacoronavirus respectively.[12] CoVs are zoonotic pathogens that arise in animal bodies and are later transmitted directly to humans. All Coronaviruses that affect massively in human life originated in bats and are the hosts of many Coronaviruses[3,14]but there is an animal hosts in between bats and humans. Market civets' cats and dromedary camels are the intermediate animal host of SARS-CoV and MERS-CoV, respectively.[14] Primarily in the seafood market in Wuhan city, China, Covid-19 is suspected, so the Chinese authority decided to close the market.[6,12] According to the analysis, the Coviid-19 is similar to SARS, which was named SARS-CoV-2.

ALPHA VARIANT (B.1.1.7)

The variant alpha or B.1.1.7 was first detected in the United Kingdom in September 2020 and emerged with a large number of unusual mutations across the world. As the dominant strain delta came, it started fading the alpha variant case. Compared with the strain that showed up in Wuhan, it has 23 more mutations, according to the American Society for Microbiology. Among these, eight mutations are linked to spike proteins. The N501y mutation in the receptor binding domain enhances its affinity for the human ACE2 receptor, while the P681H mutation can affect the cell's infectivity and replication of the virus. The variant has shown to be nearly 50% more transmissible than other dispersed lineages, according to the Centers for Disease Control and Prevention (CDC). Vaccines producing companies like Pfizer, Moderna vaccines, Johnson & Johnson vaccine have confirmed that the vaccine shots stimulate neutralizing antibodies against the alpha variant.

BETA VARIANT (B.1.351)

The strain was first detected in South Africa, spread faster than earlier variants, and derived from the second wave of pandemics. The variant was also designated as Variant of Concern (VOC). It carried eight distinct mutations, out of which notable mutations included N501Y, K417N, and E484K, which aides bind more tightly to the human receptors. K417N changes the shape of viral proteins, and E484K helps the variant escape from the immune system. The variant has shown to be nearly 50% more transmissible than other variants, and vaccines have less efficacy than other previous strains. The 501Y.V2 variant showed complete escape from neutralizing antibodies in 48% of patients treated with convalescent serum obtained from patients who had previously had Covid-19. Pfizer had 75% efficacy against the variant.

GAMMA VARIANT (P.1)

The gamma variant samples were first collected from Brazil in November 2020 and were designated as a variant of concern on January 11, 2021. The variant was also labeled as "previously circulating VOC" in March 2022. The gamma is closely related to the beta variant

and nearly has the same spike protein mutations. Unlike beta, it carries eight additional sequence changes in its spike: L18F, T20N, P26S, D138Y, R190S, D614G, H655Y, and T1027I. The gamma infection has a higher viral load and is more transmissible than other variants. The variant is relatively resistant to neutralization by convalescent plasma and vaccine (Moderna or Pfizer vaccination). According to the CDC, it showed less susceptibility to monoclonal antibody treatments, including bamlanivimab and etesevimab.

DELTA VARIANT (B.1.617.2)

The variant was first reported in India and classified as a variant of concern according to the WHO in May 2021. Rapidly it became the dominant variant in the US but was replaced by omicron in December 2021. The Delta variant has a faster growth rate than the alpha variant. The variant is identified by T19R, del157/158, L452R, T478K, D614G, P681R, D950N mutations L452R and D614G mutation aids if firm attachment to human receptors. In contrast, P681R mutation is caused by changing an amino acid beside the furin cleavage site enabling the virus to infect human cells. The variant emerged as the most transmissible variant, nearly 60% more contagious than the alpha. Vaccines like Pfizer showed 88% efficacy against the delta variant.

OMICRON (B.1.1.529)

First detected in South Africa and was assigned as a variant of concern (VOC) on November 24, 2021. The variant is highly mutated and showed more than 30 mutations in spike proteins, of which ten mutations are present in the receptor-binding domain (RBD). It also showed similarities between the beta and lambda variants. The omicron variant has two sub-variants denoted as BA.1 and BA.2, sharing 32 mutations but having 28 mutations differing between them. BA.1 is nearly four times more transmissible than the delta variant. Unlike BA.2, BA.1 has a deletion in the S protein.[15]

PHYLOGENETICS ANALYSIS OF SARS COV2

During the early stages of an outbreak, identifying a developing pathogen's sources was crucial since was enabling focused containment measures. Until December 2019, four betacoronavirus strains—HKU1, MERS-CoV, OC43, and SARS-CoV—were linked to severe human illnesses. In Wuhan, central China, researchers first characterized the fifth strain, a new beta coronavirus called SARS-CoV-2, which causes pneumonia in humans. Bats serve as both a natural host and a place where coronaviruses grow. It has been suggested that the bat reservoir is where most of the human coronaviruses come from to achieve this.

This novel beta coronavirus called SARS-CoV-2 causes human pneumonia. The fifth strain was initially reported in Wuhan, Central China. Bats, serving as a natural host, promote the outspread of coronaviruses. To do this, it has been proposed that the bat reservoir is the source of the bulk of human coronaviruses. Several researchers have recently recognized the genetic similarity between SARS-CoV-2 and the betacoronavirus of the subgenus Sarbecovirus. The novel virus' genomic sequence shares 96.2 % of its sequence with the bat. As illustrated in Fig.1, the SARS-related Coronavirus was discovered in Wuhan, China; however, it differs from the SARS-CoV (about 79%) or MERS-CoV (about 50%) genomes. Here the phylogenetic tree has been constructed by emphasizing the genomic variations within the different emerging mutant strains, where we find the beta variant to be the closes neighbor of initial SARS CoV2 strains.[16,17]

SARS-CoV-2

SARS-CoV-2 Coronaviruses belong to members of the Coronavirinae subfamily of the Coronaviridae family, which includes four genera: Alphacoronavirus, Beta coronavirus, Gamma coronavirus, and Delta coronavirus. SARS-CoV's genome (27–32 kb) is a single-stranded positive-sense RNA (+ssRNA) more significant than any other RNA virus. The nucleocapsid protein (N) produces the virus's capsid outside the genome. The viral genome is packed by an envelope that is associated with three structural proteins: membrane protein (M), spike protein (S), and envelope protein (E). The genome size of SARS-CoV-2, which was recently sequenced as a member of the coronavirus family, is around 29.9 kb. The genome of SARS-CoV-2 include four structural proteins (S, E, M, and N) and sixteen non-structural proteins (nsp1-16).[8]

Spike Protein: Coronavirus's S protein or spike protein is located on the virion surface in a looming out form. This is a class I viral transmembrane protein with multifunctional ability and higher transmembrane abundancy. The size of this protein varies from 1,160 amino acids to 1,400 amino acid residues. Apart from playing a significant role in the infection by virion entry, it also acts as a critical factor for host range determination and tissue tropism. This is a trimer protein, and its ectodomains (in all CoVs) have similar

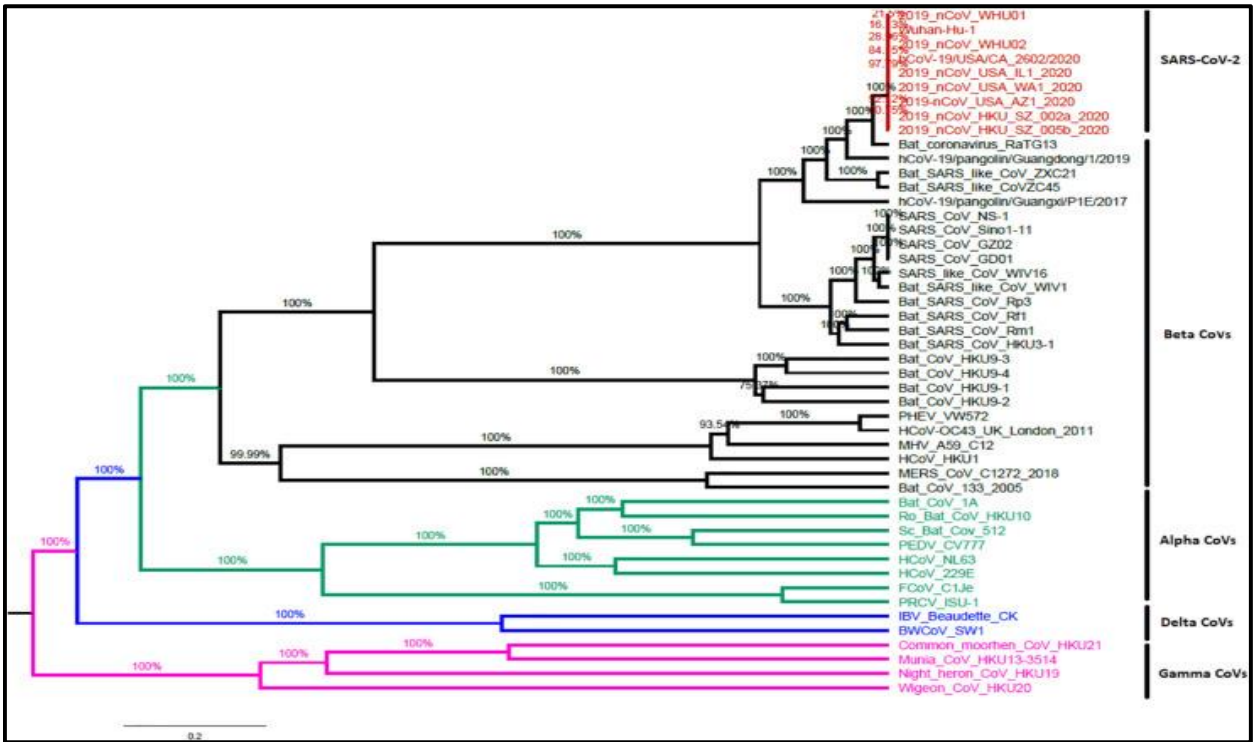

Figure 1. Whole genome-based phylogenetic tree of CoVs constructed with the maximum-likelihood method (Junejo et al. 2020)

domain organization. This organization involves two subunits, S1 and S2, among which the first is concerned with receptor binding while the other one is concerned with fusion. The C-terminal domain of the S1 subunit consists of the Receptor Binding motif (RBM).

Membrane Protein: M protein is concerned with defining the shape of the viral envelope as it exists in the maximum number among the viral protein. Binding to the nucleocapsid serves as the central organizer of the coronavirus assembly. Coronavirus's M protein contains varying amino acid contents, yet an overall structural similarity within the different genera is maintained. It comprises three transmembrane domains, flanked by a long carboxy-terminus inside the virion and a short amino acid terminus outside of it. The viral scaffold is generally maintained by M-M interaction.

Envelope Protein: E proteins of Coronavirus are the smallest and most mysterious of the significant structural proteins. This is an integral membrane polypeptide acting as a virion and possesses multifunctional capability in pathogenesis, assembly, and virion release. The alteration of virulence of Coronavirus is dependent on the action of this protein. It has three domains: an effective C-terminal, a large

Nucleocapsid Protein: The N protein of Coronavirus serves the versatile function. It includes a role in complex formation with the viral genome, and also it facilitates M protein interaction at the time of virion assembly, followed by enhancement of the transcription efficiency of the virus. It has three highly distinct and conserved domains: a CTD, an NTD, and an RNA-binding domain or a linker region (LKR). The NTD binds with the 3" end of the viral genome, probably via electrostatic interactions, and is highly diverged in length and sequence.[18]

GENOMIC STRUCTURE & REPLICATION

The world is aware of the trending novel zoonotic Coronavirus (SARS-COV-2), popularly called Covid-19, whose infection started in Wuhan in December 2019.[19] The Coronavirus family contains many contagious viruses- IBV-Beaudette, BCoVENT, hCoV-229E, MHV-A59, TGEV-Purdue 115, PEDV-CV777, etc. The range of their lengths is 27,317 to 31,357 nucleotides making the Coronavirus genome the largest one among all the RNA viruses. The members of this family have been known to contaminate humans and other vertebrates, causing respiratory and GIT-related issues. The organization of this genome is somewhat similar to older Nidovirus.[20] Before the pandemic spread, there were only two

viruses that were common in causing human infections, hCoV-229E, and hCoV-OC43. After the contamination started, the discovery of more strains was observed- SARS-CoV, hCoV-NL63, hCoV-HKU1 and MERS-CoV. Out of these, SARS-Cov and MERS-Cov are highly virulent and have the highest mortality rate. Interestingly, both of them have been derived from bats. At the 5' terminal end, the two-thirds portion of the genome codes for replication and transcription, while the leftover one-third codes for structural and accessory proteins of the virus. The research on these one-third proteins is compulsory to determine the drug treatments and develop vaccines against the virus.[21] SARS-CoV and MERS-CoV both are highly pathogenic and derived from the bat. But some phylogenetic research has revealed that though Coronavirus can enter the cell through human receptors, it doesn't transmit directly. Rather, it needs an animal host that stays close to humans to spread it. So, for SARS-CoV, it is raccoon dogs; for MERS-CoV, it is domestic riding camels. SARS CoV-2, the reason for the pandemic is 96% identical to bat SARS-like coronavirus gnomically. The virus is spherical in shape, with single-stranded positive-sense RNA 26 to 32 kb in size. The structural features show that it is crownlike, possessing clover leaf-shaped projections (made up of glycosylated proteins) from the viral envelope known as spike proteins. Except for spike proteins, they have 3 other proteins present: the membrane, envelope, and nucleocapsid ones (Figure-2).[22]

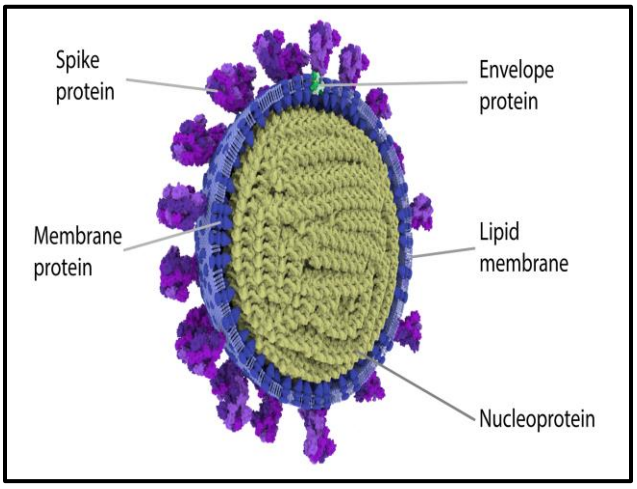

Figure 2. Structure of Coronavirus (David et al. 2020)

Almost 66% of the genome consists of two open reading frames overlapping code for 16 non-structural proteins, which involve RNA-dependent RNA polymerase, proteases, primase, helicase, etc. Jointly forming a viral replication system.

These irregular proteins are the main therapeutic targets to find a cure for the disease. The remaining one-third of the genome contains the proteins not involved in replication but cause suppression of the immune system and enhance pathogenesis.[23] A unique feature own by this virus is that it can also outspread by people showing no symptoms at all. Reports have disclosed that this virus can spread among cats but meager chances among dogs. Whether this can spread from domestic animals to humans is still untold.

EPIDEMIOLOGY

In the past two decades, China has experienced three major respiratory virus outbreaks that have escalated into epidemics: the H5N1 avian flu in 1997, SARS-CoV in 2003, and the ongoing SARS-CoV-2 (since 2019). The first infections of SARS-CoV-2 have direct links to the Hunan seafood market; later sources of infection were diseased people. Presently, human-to-human transmission is the primary mode of disease transmission worldwide. The intermediate host thought to have caused the outbreak is believed to be snakes or pangolins, although this has yet to be validated. Travel and importation were crucial in bringing SARS-CoV-2 to Korea, Japan, the Middle East, Europe, and especially India. SARS-CoV-2, which is of international concern, was labeled as a public health crisis by the World Health Organization (WHO) on January 30, 2020, and a controlled pandemic on March 11, 2020. According to the Chinese Centre for Disease Control and Prevention (CCDC), person to person transmission via respiratory droplets and contact are the most common routes of infection for humans. There has been no reliable evidence of vertical (intrauterine) transmission described in the literature thus far.[24]

As of June 10, there have been 532,201,219 cases and 6,305,358 deaths globally and 43,205,106 cases and 524,747 deaths in India.[25]

PATHOPHYSIOLOGY OF SARS COV-2

SARS-CoV-2 has a diameter of 60 nm to 140 nm with discrete spikes ranging in size from 9 nm to 12 nm, giving the virus the appearance of a solar corona. Coronaviruses can adapt to and infect new hosts via genetic recombination and variation. Although bats are assumed to be a natural reservoir for SARS-CoV-2, it

has been proposed that humans acquired the infection via an intermediary host, such as the pangolin.

The current state of knowledge on the human immune response elicited by severe acute respiratory syndrome coronavirus (SARS-CoV-2) is described. SARS-CoV-2 infects cells by binding to the angiotensin converting enzyme 2 receptor (ACE2) via the viral structural spike (S) protein. The host cell's serine protease type 2 transmembrane serine protease (TMPRSS2) increases viral uptake by cleaving ACE2 and activating the SARS-CoV-2 S protein. In the early stages, viral copy levels in the lower respiratory tract can be high.

Infected cells and alveolar macrophages, as well as recruited T lymphocytes, monocytes, and neutrophils emit inflammatory signalling molecules. Late-stage pulmonary edema can cause hyaline membrane development in the alveolar gaps, which is consistent with early-phase acute respiratory distress syndrome.[26]

REPORTED DRUGS AND VACCINES

Till now there are few antiviral treatments or vaccines of Coronavirus. Scientists are mainly focusing on the symptoms of the respiratory system as per the protocol issued by the health authority in each country, following WHO protocol.[8,9]

The Coronavirus leads to such epidemic in our world for the third times. As we have already fought with the two epidemics, formerly we can use the experience to create treatment plans against this. At this time scientists are using different types of drugs and medication to the positive patients and get a promising result. Also, vaccines are being developed to restrict the viral propagation from one host to another by elevating the immune system.

COVID-19 Treatment Guidelines external symbols are provided by the National Institutes of Health (NIH) to assist healthcare providers in working with their patients and determining the appropriate treatment options. COVID-19 can be treated at home or in an outpatient environment in a variety of ways. They are as follows.

Nirmatrelvir with ritonavir (Paxlovid) is an experimental antiviral therapy for adults and children aged 12 and up. It is eaten orally at home. It should be started as soon as possible, and no later than five days after the onset of your symptoms.

Remdesivir (Veklury) is an antiviral drug that can be used by both adults and children. Treatment involves intravenous (IV) fluids at a medical facility for three days. It should start as soon as possible and within seven days of the onset of your symptoms.

Bebtelovimab external icon is an experimental monoclonal antibody therapy for adults and children aged 12 and above. A single IV injection of bebtelovimab is administered by a healthcare practitioner. It should begin as soon as feasible and no later than seven days after your symptoms begin.

Molnupiravir (Lagevrio) is an antiviral medication for individuals aged 18 and up. It is taken orally at home (orally). It should begin as soon as feasible and no later than seven days after your symptoms begin.[27]

REPORTED VACCINES

Grouping into categories of vaccine construction, the reported vaccines are enlisted below.

RNA vaccines and DNA vaccines: Pfizer–BioNTech is a mRNA vaccine developed by the American corporation Pfizer and the German company BioNTech, COVID-19 is marketed under the trade name Comirnaty. Fosun Pharma distributes Comirnaty in Taiwan, Macau, and Hong Kong.

Moderna is created by the collaboration of Coalition for Epidemic Preparedness Innovations, the National Institute of Allergy and Infectious Diseases, the United States Biomedical Advanced Research and Development Authority, and the American corporation Moderna. It is also known as Spikevax. Men under the age of 30 in Finland are not eligible for the Moderna vaccine as a preventative measure to reduce a very low risk of myocarditis.

ZyCoV-D is a COVID-19 vaccine based on a DNA plasmid produced by the Indian pharmaceutical business Cadila Healthcare with funding from the Biotechnology Industry Research Assistance Council.

Adenovirus vector vaccines: Oxford-AstraZeneca COVID-19 vaccine, marketed as Vaxzevria and Covishield, is a viral vector vaccine developed by the British University of Oxford, the British-Swedish firm AstraZeneca, and the Coalition for Epidemic Preparedness Innovations. Because of a few isolated reports of a rare blood clot disease, Finland, Denmark,

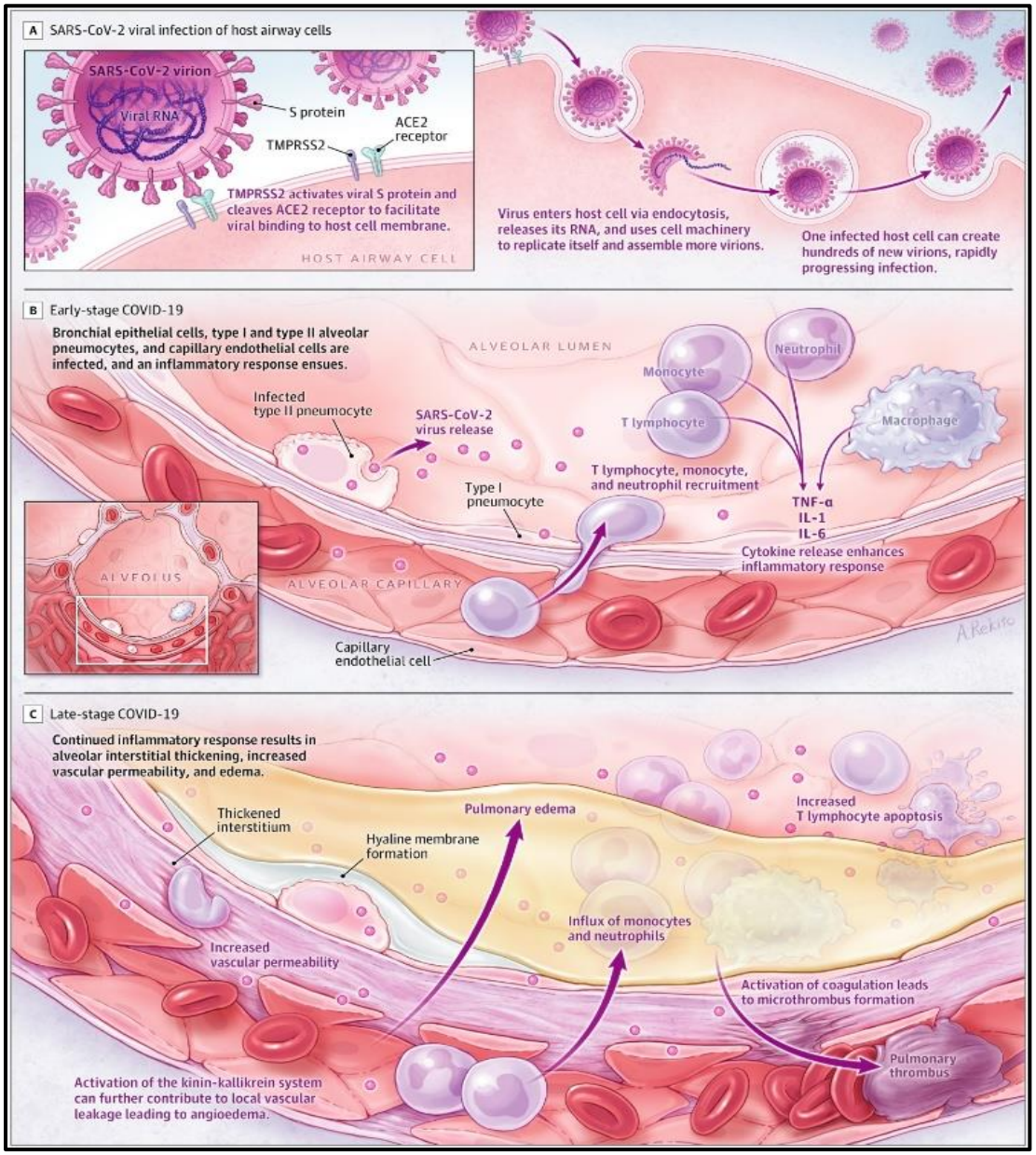

Figure 3. Mechanism of interaction of the SARS CoV-2 virus with human ACE-2 receptor (Wiersinga et al. 2020).

and Norway have stopped using the Oxford-AstraZeneca vaccine. Following the demise of a susceptible recipient, Slovakia discontinued its use. In August 2021, Japan began offering the vaccination to those 40 years of age or older to slow the spread of the Delta form. Over 1.3 billion people have received the AstraZeneca vaccination, making it the most well-liked and broadly accepted vaccine on a global scale. In comparison to other vaccines, the AstraZeneca vaccine is given in the most nations.

Janssen COVID-19 is collaboratively designed by The Beth Israel Deaconess Medical Center and Janssen Pharmaceutica. This is a viral vector vaccine in nature and it is also referred to as COVID-19 Vaccine Johnson & Johnson and COVID-19 Vaccine Janssen. Due to a potential connection between the Janssen vaccination and a rare blood clot disorder, Denmark, Finland, and Norway stopped using the vaccine in favour of other options. Finland started using the Janssen adenovirus vector vaccine in October 2021. Due to the extremely low risk of thrombosis in younger age groups, it is only made accessible to people who are 65 and older.

Sputnik V COVID-19 vaccine belongs to the viral vector vaccine type, which is manufactured by the Russian

Gamaleya Research Institute of Epidemiology and Microbiology. Sputnik Light is a reformed type of the prior, which consists of the first dose of the Sputnik V vaccine, and is based on the Ad26 vector.

Convidecia is a viral vector vaccine created by the Beijing Institute of Biotechnology of the Academy of Military Medical Sciences and the CanSino Biologics firm in China.

Inactivated virus vaccines: Sinopharm BIBP vaccine belongs to inactivated virus vaccine manufactured by the China National Pharmaceutical Group (Sinopharm) and its Beijing Institute of Biological Products.

CoronaVac vaccine is an inactivated viral vaccine for COVID 19 manufactured by Sinovac Biotech in China.

Covaxin was developed by the Indian company Bharat Biotech in cooperation with the Indian Council of Medical Research–National Institute of Virology. It is an inactivated virus vaccine. As with the inactivated polio vaccine, Covaxin makes use of an older, less sophisticated method of manufacturing.

Valneva vaccine comprises inactivated (killed) particles of the original strain of SARS-CoV-2 (the virus that causes COVID-19).

Sinopharm WIBP vaccine is developed by the collaboration of the China National Pharmaceutical Group (Sinopharm) and its Wuhan Institute of Biological Products.

Subunit vaccines: NVX-CoV2373 is a subunit COVID-19 vaccine candidate developed by Novavax and the Coalition for Epidemic Preparedness Innovations (CEPI) that is now being tested in India under the brand name Covovax.

Although the manufacturers refer to NVX-CoV2373 as a "recombinant nanoparticle vaccine," it has been called both a protein subunit vaccine and a vaccine against virus-like particles.

Abdala is a subunit vaccine was created by the Cuban Center for Genetic Engineering and Biotechnology.

EpiVacCorona is manufactured by the Russian State Research Center of Virology and Biotechnology VECTOR. To make the vaccine, a big carrier protein is linked to three chemically produced peptides (short fragments of a viral spike protein). An MBP and a viral nucleocapsid protein have been fused together to produce this protein.

Zifivax, also known as ZF2001 or ZF-UZ-VAC-2001, is an adjuvanted protein subunit COVID-19 vaccine that was developed by Anhui Zhifei Longcom in partnership with the Institute of Microbiology at the Chinese Academy of Sciences. ZF2001 was given the marketing name Zifivax. At this time, there are 29,000 people taking part in clinical trials for the vaccine candidate in countries like China, Ecuador, Malaysia, Pakistan, and Uzbekistan.

Soberana 02 or Soberana 2, also known by its technical designation FINLAY-FR-2, is a COVID-19 vaccine manufactured by the Finlay Organization, a Cuban institute for epidemiological research. It was created in conjunction with Iran's Pasteur Institute of Iran and is known as PastoCovac.[27]

CONCLUSION

The COVID-19 pandemic created a significant risk to the global public health systems. The consecutive two to three years of the pandemic by the rising numbers of infections and deaths have caused the international community to undergo a severe phase by the tireless struggle of the researchers and medical practitioner, along with other first-line workers has retrieved the health scenario of the world. Our review paper has inculcated information regarding genomic variants, pathogenicity, phylogenetic analysis, epidemiology, and clinical measures. We have cultivated the best to provide a void less details of every possible head. The different proteins involved in this disease and the drugs or vaccines reported for the control have been in prime focus along with its genomic variations. This study is done to sum up the complete documentation of the COVID 19 diseases from its onset till today.

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AUTHOR AFFILIATIONS: (*Corresponding Author)

1. Pondicherry Central University, Puducherry, 605014, India. [https://orcid.org/0000-0002-9580-6386, (Somenath Dutta), https://orcid.org/0000-0001-9128-2389, (Rohan Ghosh), https://orcid.org/0000-0001-7220-9928, (Debanjam Ghosh), https://orcid.org/0000-0002-4286-1437, (Priyasa Santra)]
2. Sharabeshwara College of Nursing, Karnataka, 583102, India (https://orcid.org/0000-0002-5946-8797).

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Contact Corresponding Author at: sduttabiotech[at]gmail[dot]com

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REVIEW

QR CODE

Unfair Jeopardy of Third and Fourth Hand Smoking

NIDHI THAKUR[*1], LALITA KUMARI[2], KRISHNA CHAUHAN[2]

ABSTRACT

Smoking-related illnesses and fatalities continue to be a significant public health issue because it is still the world's biggest cause. The harmful effects of active smoking and second hand smoke on health are now well documented. Third-hand smoke (THS) and fourth-hand smoke exposure, on the other hand, are relatively new terms that have only recently been defined in the context of environmental and public health. Third-hand smoke is composed of pollutants that accumulate indoors when tobacco is smoked. Third-hand smoke is constituted of chemicals that adhere to surfaces. THS contains tobacco smoke components that can linger on interior surfaces and in dust for months before being gaseously released back into the atmosphere. Humans who have been exposed to third parties are more likely to develop cancer, have DNA damage, and heal wounds more slowly. Pregnant women are at an increased risk of stillbirth, premature birth, and sudden infant death syndrome (crib death). Smoking is a learned behaviour. Like third hand smoke fourth hand smoke also pose a potential health threat to children and young adults. When people see their role models, on-screen celebrities, friends, and co-workers smoking, the behaviour becomes normalised and acceptable. It is too early to predict the combined health effects of third and fourth hand smoke. Probably the most important intervention would be to raise public awareness of the problem, which adds yet another reason to remain active in the anti-smoking campaign.

KEYWORDS: Smoking, Tobacco, Exposure, Health, Environment

INTRODUCTION

Tobacco smoking is the six out of eight leading cause of death in the world. Tobacco smoking comprises of two types which includes active and passive smoking. Active or current smoking is defined as regular cigarette smoking for duration more than 6 months at the time of examination whereas passive smoking is defined as breathing in other people's tobacco smoke.[1] It is the exposure to smoking more than once per week and for longer than 1 year. Passive smoking includes second hand smoke, third hand smoke, and fourth-hand smoke. Under passive smoking second hand smoking is the common and dangerous as it comes from burning or heating tobacco through a cigarette, electric cigarette, hookah, pipe or cigar also from the air a smoker exhales while smoking. However 3rd and 4th hand smoke also prevail in our surrounding environment and do have the ill effects on one's health so here we will talk about the effects of third and fourth hand smoke.

THIRD HAND SMOKE

In the environmental and public health fields, third hand smoking is a relatively new phenomenon. This concept was first proposed by Winickoff et al. in Pediatrics in 2009, but it was popularised by the New York Times when they published an article on the subject titled: A New Cigarette Hazard: 'Third Hand Smoke'

Third hand smoke is made up of the pollutants that settle indoors when tobacco is smoked. The chemicals in third hand smoke include nicotine as well as cancer – causing substances such as formaldehyde and naphthalene.[2] Third hand smoke build up on the surfaces over time and in dust after tobacco has been smoked, they are re emitted into gas phase or react with other compounds in the environment to form secondary pollutants. Third hand smoke exposure consist of unintentional intake of tobacco smoke that occur in the absence of concurrent smoking mainly through inhalation but also via ingestion and dermal routes.

Third hand smoke possess a potential health hazard to non-smokers especially in children than adults owing to hand-to-mouth and dermal exposure from contact with contaminated surfaces like floors, toys, pacifiers toys and they also tend to spend more time indoors.[3]

Exposure to third hand smoke occur by mainly three routes. First, by oral route when pollutants enter mouth through fingers and objects. second by breathing in the particles and chemicals in the air and third through dermal route when it absorbs third hand smoke when skin comes in contact with the surfaces. Third hand exposure in humans display increased risk of cancer, damage DNA, delayed wound healing,

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altered inflammatory response, impaired collagen deposition, headache, earache, triggers asthma attacks, worsens respiratory illness and decrease immunity.[4] In pregnant women there is increased risk for still birth, premature birth and sudden infant death syndrome (crib death). The only way to safeguard non-smokers, especially young children, from the dangers of third-hand smoke is to prohibit smoking in all indoor areas, including automobiles.[5]

FOURTH HAND SMOKE

Smoking is a learned behaviour. Observing role models, on-screen actors, acquaintances, and co-workers smoke normalises the behaviour, making smoking "the cool thing." This has a significant impact on the populace who respect and revere them, inculcating smoking as a symbol of glamour and increasing the attractiveness quotient to be perceived in the same way as on-screen personae— "rich, gorgeous, charismatic, and powerful"—even if it is causing havoc. Children and teens are particularly vulnerable.[6]

A total of 1,85,000 children and teenagers were "recruited to cigarette smoking by their exposure to on-screen smoking," according to a study by the Ontario Tobacco Research Unit, published by the Centre for Tobacco Control Research and Education, University of California, San Francisco, US, during the 10-year research period alone. Whatever harmful messages you may have heard about smoking, they are reversed when you witness a friend, colleague, or role model smoking. You will want to imitate them.

Visual mapping of smoking in outdoor bars and cafes across Wellington city was done as part of a study published by BioMed Central Public Health, New Zealand, which came to the conclusion that high rates of smoking normalised the behaviour and made it socially acceptable, encouraging younger people to start smoking and decreasing the likelihood of smokers quitting or even attempting to quit.

Fourth hand smoke has a number of benefits when it comes to peers, including friends and co-workers. For one, it helps manage tension, with phrases like "I NEED A SMOKE" implying that the other person may have found a method to escape the stress you both may be experiencing at the time. Therefore, a non-smoker who is around smokers feels left out, leading them to start smoking in order to experience a sense of belonging. Watching your friends and co-workers smoke might function as a trigger, making fourth hand smoke considerably worse for individuals who have given up smoking.

Therefore, "we need a few of people who denounce smoking for a person who even unwittingly praises it."

CONCLUSION

The use of tobacco can be decreased by outright banning tobacco advertisements, promotions, and sponsorships. Both direct and indirect kinds are covered. Television, radio, billboards, and social media platforms are examples of direct formats. Brand sharing, price reductions, and free distribution are indirect types. The most effective strategy to lower health care expenses and tobacco usage is through cigarette taxes, especially among teenagers, young people, and low-income individuals.

The World Health Organization (WHO) introduced "the MPOWER" in 2007 as a useful and affordable worldwide measure for tobacco use prevention which includes the following:

- Deter people from smoking
- Provide support for quitting smoking Inform people about the hazards of tobacco
- Enforce restrictions on tobacco sponsorship, promotion, and advertising.
- Increase tobacco taxes.[7]

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AUTHOR AFFILIATIONS: (*Corresponding Author)
1. BDS Final Year Student (https://orcid.org/0000-0002-6251-6921).
2. Intern, [(https://orcid.org/0000-0001-7407-8351, Lalita Kumari), (https://orcid.org/0000-0001-8917-3060, Krishna Chauhan)
Himachal Dental College, Sundernagar, Himachal Pradesh India

Source of support: Nil, **Conflict of interest:** None declared

Contact Corresponding Author at: nidhi.thkr1999[at]gmail[dot]com

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ORIGINAL RESEARCH

QR CODE

Knowledge, Attitude and Practice of Smoking Cessation Advice among Dental Students in Delhi-NCR

SUMEDHA KUSHWAHA[1], WAIROKPAM BHOOMIKA DEVI[2]

ABSTRACT

INTRODUCTION: The problem of tobacco abuse is not recent and has been documented well in history in various cultures all over the world. Dental colleges house vast number of potential tobacco cessation counsellors as budding health professionals who are in direct contact with patients

AIM: The main objective of present study was to assess the knowledge, attitude and practice of smoking cessation advice among dental students in Delhi-NCR.

MATERIALS AND METHOD: A cross sectional study was conducted among 2953 undergraduate clinical students of third year, fourth year and Internship were enrolled in the study from 18 dental colleges in Delhi- National Capital Region (NCR) using a pre-tested, self-administered questionnaire was employed as an instrument. The questionnaire's content, face and criterion validity were checked and reliability was tested using Cronbach's Alpha and Inter Class Co-relation. Statistical analysis used included quantitative statistics, student t test and ANOVA

RESULTS: Students demonstrated considerable knowledge regarding smoking related policies in the institution, technique and products used for smoking cessation and impact of smoking on oral health, general health and treatments to be performed. However, only half of them had a positive attitude towards tobacco cessation counselling to patients and practice this in the hospital setting.

CONCLUSION: Based on the results of the study, there is a need to further motivate students on smoking cessation advice.

KEYWORDS: Undergraduate Dental Students, Smoking Cessation, NRT, Tobacco

INTRODUCTION

Nearly half of all cancers in Indian men and a quarter of all cancers in Indian women, are attributed to high prevalence of tobacco use.[1] The problem of tobacco abuse is not recent and has been documented well in history in various cultures all over the world.[2] It is a negative social trend and an important public health problem. Aligning with the international strategies, India was amongst the first few countries to ratify the WHO Framework Convention on Tobacco Control (FCTC) in 2004.[3] Besides this, at national level, comprehensive tobacco control legislation –Cigarette and other Tobacco Products Act (COTPA) was enacted in 2003. The National Tobacco Control Program in India (2007-2008) works at National, State and District levels.[4] Recently, it has been advised by the Dental Council of India to open a tobacco cessation centre in every dental college.[5] It is an appreciable move as colleges house vast number of potential tobacco cessation counsellors as budding health professionals who are in direct contact with patients. Specifically, dental professionals encounter patients of various ages and may notice signs of tobacco use at a very early stage and are therefore in an exceptional position to offer preventive care.[6] They can serve as role models for the patients and the society and encourage governments to put in place tobacco control measures.[7]

MATERIALS AND METHOD

Cross-Sectional study was conducted to assess knowledge, attitude and practice of smoking cessation advice among undergraduate clinical dental students in Delhi- National Capital Region (NCR). A total of 18 dental colleges are present in Delhi-NCR according to the Dental Council of India5. Four of these are Government and rest are Private. Ethical clearance was sought, a request letter was sent to Head of Institution and written consent was obtained to conduct the study. Undergraduate clinical students of third year, fourth year and Internship; belonging to regular and supplementary batches; willing to participate in the study by providing a written consent were included in the study. However, students who were absent on the day of the study or did not give informed consent or were a part of the dental institution which did not grant

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permission to conduct the study or whose questionnaires were incompletely filled at the time of analysis were excluded from the study. A pre-tested, self-administered questionnaire was employed as an instrument. All questions were close ended. The content, face and criterion validity were checked. Reliability of the questionnaire was tested using Cronbach's Alpha and Inter Class Co-relation. A method of Convenience sampling was employed. 4500 students constituted the total population. 3225 questionnaires were distributed and filled, out which 272 questionnaires were excluded as they were incomplete, giving us a final sample size of 2953 students. Current Smokers were defined as those respondents who reported smoking at least 100 cigarettes in their lifetime and who, at the time of survey, smoked either every day or some days. Ever Smokers were defined as those respondents who reported smoking at least 100 cigarettes in their lifetime and who, at the time of the survey, did not smoke. Never Smokers were those respondents who reported never having smoked 100 cigarettes.[8]

RESULTS

Out of the total 2953 students, 30.4% were males 69.6% were females. 32.9% of the total were from third year, 31.5% from fourth year and 35.6% from internship. 92.7% sample of the total was from Private and rest from Government colleges. 79.9% constituted never smokers and rest smokers- out of whom 4.7% were ever smokers and 15.4% were current smokers. Out of all 899 males in the study- 8.7% were ever smokers, 29% were current smokers and 62.3% were never smokers. Whereas, among 2054 females- ever smokers constituted only 3.0%, current smokers 9.4% and never smokers 87.6%. The difference of smoking between the two genders was found to be highly significant (p=0.001).

When compared year wise, it was found that from 973 third year students 3.8%, 10.1% and 86.1% were ever, current and never smokers respectively. Out of the 928 fourth year students 5.4%, 17.2%, 77.4% were ever, current and never smokers respectively Among the 1052 interns 4.9%, 18.7% and 76.4% were ever, current and never smokers respectively. The difference was found to be statistically significant (p=0.002). Out of 139 ever smokers and 455 current smokers only 38% and 57% tried to quit respectively. The difference between the groups was found to be statistically significant (p=0.02).

Table 1 depicts percentage wise depiction for questions regarding knowledge about a written smoking policy in the college, presence of a tobacco cessation centre in the college, presence of smoking cessation pamphlets and posters in the waiting area, knowledge of 5A's and 4R's tobacco cessation technique, use of NRT in tobacco cessation, anti-depressants being used in tobacco cessation, relevance of taking history of smoking prior to implant placement, whether you advise a smoker to abstain from smoking pre and post oral surgery and whether a smoker when tested for bleeding on probing, shows less bleeding.

Table 2 depicts attitude of the respondent towards the subject of smoking cessation advice on a five-point

Questions regarding Knowledge	Yes n(%)	No n(%)	Don't Know n(%)
Does your college have a written smoking policy?	764 (25.9%)	1192 (40.4%)	997 (33.7%)
Does your college have a tobacco cessation centre?	1644 (55.7%)	823 (27.9%)	486 (16.4%)
Does your institute provide smoking cessation pamphlets and posters in waiting area to educate patients about hazards of smoking?	1382 (46.8%)	970 (32.8%)	601 (20.4%)
Are you aware about the 5A's and 4R's of tobacco cessation technique?	1128 (38.2%)	1003 (34%)	822 (27.8%)
Is NRT used in tobacco cessation?	1401 (47.4%)	387 (13.1%)	1165 (39.5%)
Can Anti-Depressants be used in tobacco cessation?	1519 (51.5%)	668 (22.6%)	766 (25.9%)
If you are considering a patient for implant placement, would it be relevant to ask whether they have history of smoking?	2318 (78.6%)	324 (10.9%)	311 (10.5%)
If you have a patient for oral surgery, would you advise them to abstain from smoking pre and post surgery?	2374 (80.5%)	137 (4.6%)	442 (14.9%)
A smokers when tested for bleeding on probing, shows less bleeding?	1726 (58.5%)	709 (24%)	518 (17.5%)

Table 1. Percentage wise distribution of questions related to Knowledge

Likert Scale. Strong agreement, agreement, disagreement, strong disagreement was sought for whether a dental student should regularly advice patients to quit tobacco, if dental students should be given any specific and formal training on tobacco cessation techniques, whether equal priority should be given to tobacco cessation counselling and dental treatment if dental student's motivation is effective in cessation, whether they perceive tobacco cessation as an important part of the curriculum, whether tobacco use was a personal decision by patients, if there are too many barriers that prevent a student from helping patients to quit smoking and whether a dental student who himself smokes is ineffective in giving tobacco cessation advice.

Table 3 show descriptive data of the practice of the respondent towards the subject of smoking cessation advice on a four point Likert Scale. Questions included, if students asked about their patient's smoking status, whether they offer smoking cessation counselling to their patients, if students motivate their patients to quit smoking, whether they advise patients to quit tobacco through cold turkey method, whether they inform patients about the benefits of quitting, if they assist patients to give up smoking, if they arrange follow-up visits to discuss cessation with tobacco using patients, if they discussed Nicotine Replacement Therapy with their patients, whether students kept a record of the patient smoking status, whether students recommend the use of approved pharmacotherapy except in special circumstances.

Table 4 depicts statistically significant association between gender and knowledge, attitude and practice for various questions. Knowledge of institute having a

tobacco cessation centre (p=0.016), waiting area in the institute providing pamphlets and posters to educate about the hazards of smoking (p=0.025), awareness of 4A and 5R technique for tobacco cessation (p=0.03) and NRT being used in tobacco cessation (p=0.036). Attitude of dental students for regularly and effectively advising their patients to quit tobacco (p=0.03), dental students be given specific and formal training on tobacco cessation techniques (p=0.008) and effectiveness of students to motivate patients for tobacco cessation (p=0.027). The practice of tobacco cessation among dental students like arranging for follow up visits to discuss tobacco cessation (p=0.05),

Questions Regarding Attitude	Strongly Agree	Agree	Disagree	Strongly Disagree	Don't Know
Dental students should regularly and effectively advice their patients to quit tobacco use.	2313 (78.3%)	463 (15.7%)	126 (4.3%)	35 (1.2%)	16 (0.5%)
Dental students should be given specific and formal training on tobacco cessation techniques.	1835 (62.3%)	923 (31.2%)	148 (5.0%)	28 (0.9%)	19 (0.6%)
Tobacco cessation counselling should be given equal priority as the dental treatment.	1685 (57.1%)	1148 (38.9%)	60 (2.0%)	4 (0.1%)	56 (1.9%)
If dental students motivate patients, they are effective in cessation counselling.	1432 (48.5%)	1292 (43.7%)	115 (3.9%)	15 (0.5%)	99 (3.4%)
Tobacco cessation should be an important part of the dental curriculum.	1468 (49.8%)	1354 (45.8%)	88 (3%)	18 (0.6%)	25 (0.8%)
Tobacco use by patients is a personal decision.	1034 (35.1%)	1464 (49.5%)	306 (10.4%)	48 (1.6%)	101 (3.4%)
Non –smokers should be informed about the harmful effects of second and third hand smoking.	1423 (48.2%)	1299 (44%)	124 (4.2%)	24 (0.8%)	83 (2.8%)
There are too many barriers that prevent me from helping patients to quit smoking.	759 (25.7%)	1143 (38.7%)	769 (26.0%)	117 (4%)	165 (5.6%)
A dental student who himself smokes is ineffective in giving tobacco cessation advice.	891 (30.3%)	1037 (35.1%)	661 (22.4%)	152 (5.1%)	212 (7.1%)

Table 2. Percentage wise distribution of questions related to Attitude

discussing NRT with patients (p=0.018) and use of approved pharmacotherapy (p=0.04).

Table 5 shows a significant association between year of study and various questions regarding knowledge, attitude and practice of students regarding tobacco cessation advice. Knowledge of whether the college had a written smoking policy (p=0.03), the presence of a tobacco cessation centre in the college campus(p=0.006), awareness of 4A and 5R technique for tobacco cessation (p=0.01), NRT being used in tobacco cessation(p=0.02), anti depressants used for tobacco cessation (p=0.01), consideration of smoking status with respect to implant placement (p=0.03) and presence of less bleeding on probing in smokers(p=0.04) were found to be significant. Attitudes of the students, the opinions of dental students regularly and effectively advising patients to quit tobacco (p=0.02), the effectiveness of dental students in motivating patients to quit are effective (p=0.01) and informing non smokers about the harmful effects of second hand smoking (p=0.008) Practice of smoking cessation among the dental students, only discussion of NRT with patients (p=0.01) was found to be significant.

Table 6 depicts tobacco use association with the knowledge, attitude and practice of the students towards smoking cessation advice. Questions regarding knowledge of the presence of a tobacco cessation centre (p=0.01), NRT being used in tobacco cessation (p=0.009), advising smokers to abstain from smoking pre and post oral surgery (p=0.05) and testing of smokers for presence of bleeding on probing (p=0.05) were found to be statistically significant. When tobacco use was related with the attitude of the students regarding tobacco cessation counselling- the opinions of dental students regularly and effectively advising patients to quit tobacco (p=0.01), dental students to be given specific and formal training on tobacco cessation techniques (p=0.04), tobacco cessation to be an important part of the dental curriculum (p=0.016) and ineffectiveness of a smoker to give tobacco cessation advice (p=0.031) were found to be statistically significant.

DISCUSSION

The study conducted by Antal M et al.[6] was in accordance to high percentage of females in the study. The study done by Murugaboopathy et al.[9] was in agreement with our results of significant difference

Practice of tobacco cessation	Never	Sometimes	Often	Always
Do you ask about your patient's smoking status?	412 (13.9%)	631 (21.4%)	427 (14.5%)	1483 (50.2%)
Do you offer smoking cessation counselling to your patients?	384 (13%)	914 (30.9%)	819 (27.7%)	836 (28.4%)
Do you motivate patient to quit smoking?	301 (10.3%)	614 (20.6%)	691 (23.4%)	1347 (45.7%)
Do you advice patients to quit "cold turkey" (in one go)?	812 (27.5%)	746 (25.3%)	557 (18.9%)	838 (28.3%)
Do you explain patient about the impact of smoking tobacco on general and oral health?	185 (6.2%)	626 (20.9%)	739 (24.6%)	1403 (48.3%)
Do you inform patients about the benefits of quitting?	198 (6.6%)	567 (18.9%)	760 (25.3%)	1428 (49.2%)
Do you assist patients to give up smoking?	799 (27%)	880 (29.8%)	691 (23.4%)	583 (19.8%)
Do you arrange follow-up visits to discuss cessation with tobacco using patients?	975 (33.1%),	853 (28.9%)	392 (13.2%)	733 (24.8%)
Do you discuss nicotine replacement therapy with your patients?	912 (30.9%),	991 (33.6%)	475 (16%)	575 (19.5%).
Do you keep record of patient smoking status?	931 (31.5%)	819 (27.7%)	488 (16.5%)	715 (24.3%)
Do you recommend the use of approved pharmacotherapy except in special circumstances?	1008 (34.1%)	1209 (40.9%)	375 (12.7%)	361 (12.3%)

Table 3. Percentage wise distribution of questions related to Practice

Questions related to Knowledge	Options	Male	Female	Total	P Value
Does your college have a tobacco cessation centre?	Yes	527	1117	1644	0.016*
	No	253	570	823	
	Don't Know	119	367	486	
Does your institute provide smoking cessation pamphlets and posters in waiting area to educate patients about hazards of smoking?	Yes	450	932	1382	0.025*
	No	289	681	970	
	Don't Know	160	441	601	
Are you aware about the 5A's and 4R's of tobacco cessation technique?	Yes	346	782	1128	0.03*
	No	281	722	1003	
	Don't Know	272	550	822	
Is NRT used in tobacco cessation?	Yes	434	967	1401	0.036*
	No	136	252	388	
	Don't Know	329	835	1164	
Questions related to Attitude					
Dental students should regularly and effectively advice their patients to quit tobacco use.	Strongly Agree	720	1593	2313	0.03*
	Agree	129	334	463	
	Disagree	38	88	126	
	Strongly Disagree	4	31	35	
	Don't Know	8	8	16	
Dental students should be given specific and formal training on tobacco cessation techniques.	Strongly Agree	563	1272	1835	0.008*
	Agree	278	645	923	
	Disagree	51	97	148	
	Strongly Disagree	0	28	28	
	Don't Know	7	12	19	
Do you arrange follow-up visits to discuss cessation with tobacco using patients?	Never	258	717	975	0.05*
	Sometimes	262	591	853	
	Often	143	249	392	
	Always	236	497	733	
Do you discuss nicotine replacement therapy with your patients?	Never	256	656	912	0.018*
	Sometimes	288	703	991	
	Often	168	307	475	
	Always	187	388	575	
Do you recommend the use of approved pharmacotherapy except in special circumstances?	Never	276	732	1008	0.04*
	Sometimes	388	821	1209	
	Often	127	248	375	
	Always	108	253	361	
Questions related to Practice					
Do you arrange follow-up visits to discuss cessation with tobacco using patients?	Never	258	717	975	0.05*
	Sometimes	262	591	853	
	Often	143	249	392	
	Always	236	497	733	
Do you discuss nicotine replacement therapy with your patients?	Never	256	656	912	0.018*
	Sometimes	288	703	991	
	Often	168	307	475	
	Always	187	388	575	
Do you recommend the use of approved pharmacotherapy except in special circumstances?	Never	276	732	1008	0.04*
	Sometimes	388	821	1209	
	Often	127	248	375	
	Always	108	253	361	

Table 4. Association between Gender and Knowledge, Attitude and Practice towards smoking cessation advice. *p value less than 0.05 was considered to be significant

between smoking status of males and females. Reason can be an increased number of females; who are non smokers. GHPSS Data reveals that smoking prevalence among Indian dental third year students was low (9.6%) with 2.4% female smoking population, depicting similar results as our study.[10] However,

Questions regarding Knowledge		Year of study			P value
		3rd Year	4th Year	Internship	
Does your college have a written smoking policy?	Yes	306	205	253	0.031*
	No	346	392	454	
	Don't Know	321	331	345	
Does your college have a tobacco cessation centre?	Yes	503	524	617	0.006*
	No	280	273	270	
	Don't Know	190	131	165	
Are you aware about the 5A's and 4R's of tobacco cessation technique?	Yes	362	316	450	0.01*
	No	366	376	261	
	Don't Know	245	236	341	
Is NRT used in tobacco cessation?	Yes	382	438	581	0.02*
	No	137	140	110	
	Don't Know	454	348	361	
Can Anti-Depressants be used in tobacco cessation?	Yes	472	450	597	0.01*
	No	227	224	217	
	Don't Know	274	254	238	
If you are considering a patient for implant placement, would it be relevant to ask whether they have history of smoking?	Yes	777	729	812	0.03*
	No	79	102	143	
	Don't Know	117	97	97	
A smoker when tested for bleeding on probing, shows less bleeding?	Yes	504	522	700	0.04*
	No	260	231	218	
	Don't Know	209	175	134	
Questions regarding Attitude					
Dental students should regularly and effectively advice their patients to quit tobacco use.	Strongly Agree	764	706	843	0.02*
	Agree	168	138	157	
	Disagree	36	49	41	
	Strongly Disagree	1	25	9	
	Don't Know	4	10	2	
If dental students motivate patients, they are effective in cessation counselling.	Strongly Agree	465	463	504	0.010*
	Agree	439	381	472	
	Disagree	22	42	51	
	Strongly Disagree	9	3	3	
	Don't Know	37	39	22	
Non –smokers should be informed about the harmful effects of second and third hand smoking.	Strongly Agree	467	487	469	0.008*
	Agree	427	380	492	
	Disagree	37	34	53	
	Strongly Disagree	5	7	12	
	Don't Know	37	20	26	
Questions regarding Practice					
Do you discuss nicotine replacement therapy with your patients?	Never	331	316	265	0.01*
	Sometimes	316	293	382	
	Often	138	152	185	
	Always	188	167	220	

Table 5. Association between Year of study and Knowledge, Attitude and Practice towards smoking cessation advice. *p value less than 0.05 was considered to be significant

studies done by Bell GR et al.[11], GHPSS- data of Albania (30.1%) with 27.1% female smokers and Republic of Serbia, Belgrades (42.5%) with 47.2% females were found out be in contrast to our results.[12] Several studies also reported similar results, where it was found that 70% of smokers had the intent to quit, 34% made an

Questions regarding Knowledge	Options	Tobacco Use		
		Don't Use	Use	
Does your college have a tobacco cessation centre?	Yes	1350	294	0.01*
	No	634	189	
	Don't Know	374	112	
	Total	2358	595	
Is NRT used in tobacco cessation?	Yes	1145	256	0.009*
	No	291	96	
	Don't Know	922	243	
If you have a patient for oral surgery, would you advise them to abstain from smoking pre and post surgery?	Yes	1881	493	0.05*
	No	107	30	
	Don't Know	370	72	
A smokers when tested for bleeding on probing, shows less bleeding?	Yes	1404	322	0.05*
	No	549	160	
	Don't Know	405	113	
Questions regarding Attitude				
Dental students should regularly and effectively advice their patients to quit tobacco use.	Strongly Agree	1868	445	0.01*
	Agree	375	88	
	Disagree	89	37	
	Strongly Disagree	22	13	
	Don't Know	4	12	
Dental students should be given specific and formal training on tobacco cessation techniques.	Strongly Agree	1491	344	0.04*
	Agree	730	193	
	Disagree	107	41	
	Strongly Disagree	18	10	
	Don't Know	12	7	
Tobacco cessation should be an important part of the dental curriculum.	Strongly Agree	1192	276	0.016*
	Agree	1074	280	
	Disagree	65	23	
	Strongly Disagree	10	8	
	Don't Know	17	8	
	Total	2358	595	
A dental student who himself smokes is ineffective in giving tobacco cessation advice.	Strongly Agree	692	199	0.031*
	Agree	858	179	
	Disagree	519	142	
	Strongly Disagree	122	30	
	Don't Know	167	45	

Table 6. Association between Tobacco Use and Knowledge, Attitude and Practice towards smoking cessation advice. *p value less than 0.05 was considered to be significant

attempt to quit but only 2.5% were successful.[13-17] The studies done by Rajasundaram P et al (98.2%)[18], was in contrast with our results depicting a high percentage of students being aware of the smoking policy. The study done by Tangade P. et al in which more than 90% of the respondents agreed and 82% were ready to do further course regarding cessation also[19] was in accordance and in disagreement with Murugaboopathy V et al. (45%).[9] When gender was compared with practice of tobacco cessation advice, Vannobbergen et al, found significant difference between the genders and showed females are more effective in providing cessation advice.[20] Our study results reveal that not even half of the study population (35.5%) of students prescribe NRT to patients which is in accordance with Singla A et al, where only 12.5% dentists prescribed NRT[21] and in contrast with the results of study of Tangade P et al.[19], which showed 70% of students prescribe NRT5 According to our study there was no significant difference found between the year of study and tobacco cessation advice given by students. Similar results were found by Tangade P et al.[19], (63%) and Tomar SL,(60%)[22] where students routinely ask about patients tobacco use.

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AUTHOR AFFILIATIONS: (*Corresponding Author)
1. Ph.D Student, Population Health Sciences, Temerty Faculty of Medicine, Institute of Medical Sciences, University of Toronto (https://orcid.org/0000-0001-9145-7257)
2. Department of Paediatric and Preventive Dentistry, Dental College, RIMS, Lamphelpat, Imphal, Manipur, India

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Contact Corresponding Author at: sumedha.kushwaha90@gmail.com

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ORIGINAL RESEARCH

QR CODE

Demographic and Clinical Profile of Oral Submucous Fibrosis: A Retrospective Study

MOIN IFTIKHAR SHAPOO[1], MOHAMMAD YUNIS SALEEM BHAT*[2], DHEERAJ SHARMA[3], ATOOFA ZARGAR[4]

ABSTRACT

BACKGROUND: Oral Submucous Fibrosis (OSMF) is a potentially malignant disorder which is irreversible in nature and has high morbidity and high malignant transformation rate and hence demands focus on prevention of the disease at population and individual level.

AIMS: Assessment of risk factors and the role of habit variables such as duration and frequency in the severity of OSMF and to ascertain the association of gender predilection for different habits and severity of OSMF.

MATERIALS AND METHOD: This descriptive retrospective study of 1801 OSMF patients was carried out at the Dental hospital in the rural population of Gwalior region. The clinicodemographic data including details of habits was collected for a period of 5 years, from January 2016 to December 2021. Collected data was analysed using Systat version 12 software.

RESULTS: The average age of the patient in the study was 32.8 years, with 16.5:1 M:F ratio. Significantly higher proportions of females (69.6%) were illiterate and belonged to low socioeconomic status. There was a statistically significant increase for areca nut chewing (OR=0.135(0.054-0.342), P < 0.0001), gutkha chewing (OR=22.32(10.421-47.817), P < 0.0001), tobacco chewing (OR= 0.111(0.04-0.308), p<0.0001), smoking habits (OR=30.791(7.472-126.89), P < 0.0001) and alcohol (OR=12.692(3.077-52.347, p < 0.0001) in males when compared with females. The maximum patients were seen in stage II (37%) and stage III (34%), followed by stage I (18.73%) and stage IV (10.3%) and the severity of OSMF was more in subjects who had the habits for longer duration.

CONCLUSION: There was a definite gender predilection for various habits and their variables (frequency, duration), educational and socioeconomic status, clinical features and disease severity. Significant correlation was also found between habit variables (duration, frequency) and severity of the disease.

KEYWORDS: Areca Nut, Clinical Grading, Gender, Gutkha, Oral Submucous Fibrosis, Oral Cancer

INTRODUCTION

Schwartz in 1952 first described Oral Submucous Fibrosis (OSMF) as "Atropicaidiopathica mucosae oris" while Jens J. Pindborg in 1966 described it as "an insidious, chronic disease that affects any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by, or associated with, the formation of vesicles, it is always associated with a juxtaepithelial inflammatory reaction followed by fibroelastic change of the lamina propria and epithelial atrophy that leads to stiffness of the oral mucosa and causes trismus and an inability to eat".[1] Along with the features mentioned above, OSMF, a potentially malignant disorder (PMD) is also characterized by clinical features such as progressive reduction of mouth opening, reduced tongue movement, blanching and leathery texture of the oral mucosa, depapillation of the tongue, and shrunken uvula.[2,3]

Areca nut-chewing, in any formulation, has been considered the main etiological agent even though multifactorial etiopathogenesis has been reported.[1] The disease has shown predominance towards Asian population and more exclusively in Indian population which could be attributed to the areca nut chewing habit in these regions. Prevalence of OSMF in Indian rural population has been reported ranging up to 0.4%.[4] Illiteracy, lack of awareness of ill effects of various habits, lower socioeconomic status and peer-pressure plays an important role in development of OSMF in rural population. The premalignant lesions caused by gutkha, areca nut, tobacco and related products can be reversed by quitting the habits at an earlier stage and by early diagnosis and proper treatment. Thus, it proves the importance of identifying the high-risk group and educating them about ill-effect of areca nut, tobacco, along with early diagnosis, treatment and prevention of debilitating diseases caused by these habits. These observations

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justified our surge for the present study to assess the risk factors and clinical presentations of OSMF in the rural population. The role of critical components of a habit such as duration, frequency, and chewing time in the clinical grading of OSMF and its gender specificity is lacking in the present scenario of evidence-based dentistry.[5,6] Thus, this study was also carried out to correlate these habit factors to the clinical grading of OSMF, in addition to its demographic and clinical profile in this rural population of western Maharashtra.

MATERIALS AND METHOD

An Observational Descriptive retrospective study of 1801 patients with a clinically diagnosed OSMF was carried out in the Department of Oral and Maxillofacial Surgery, after approval from institutional ethical committee. The data was collected for a period of 5 years from January 2016 to December 2021, from the detailed case records of these patients. Patients with a clinical diagnosis of OSMF, in the age group of 15 to 90 years were selected. Patients with known history of systemic disorders causing limitation of mouth opening like anemia and scleroderma and patients with a history of previous treatment for OSMF were excluded from the study. Data was collected in the context of details of demographics, involved habits, sites of lesion, signs and symptoms, clinical grading etc. The OSMF patients were divided in five categories based on age groups and duration of the habit and into four groups according to their frequencies of habits (per day). The different types of habits such as chewing of Gutkha, Areca nut, Pan masala, Betel quid, Smokeless tobacco, Smoking and Alcohol were recorded in detail in terms of duration and frequency. The patients were divided into single & multiple habits. The clinical grading into four stages according to their clinical presentation of the disease was done using Khanna and Andrade (1995) classification.[7] The data was collected and recorded in tabulated format in excel sheet. All statistical analyses were performed using Systat version 12 software. Descriptive measures like mean values and standard deviations for continuous variables and percentage for categorical variables were calculated. The OSMF cases were classified by gender for comparison purposes. Estimation of odds ratio (OR)along with 95% confidence intervals was made for comparing risk of OSMF by gender. Tests of significance like unpaired t-test for comparing means and Chi-square test of association were performed for comparing percentages of two independent samples(male vs. females). A value of $P < 0.05$ was considered statistically significant.

RESULTS

Demographics

In the present study males were predominant, out of 1801 patients, 1699 (94.30%) were male. The male to female ratio was 16.5:1. The youngest patient was 15years of age whereas the oldest patient was 88 years old. Majority (68.3%) of the OSMF cases belonged to 20-39 years of age group. The average age of the patient in the study was 32.8 years. The mean age for males (n = 1699) was 32.2 ± 11.3 (range 15–84) years and for females (n = 102) it was 42.9 ± 15.4 (range 15–88) years. Thus, occurrence of OSMF in younger age group(<30 years) was significantly higher in males as compared to females(P = 0.0001).69.6% of females with OSMF had a low socioeconomic status which was a significant observation when compared to males (14.9%).Similarly, proportion of illiterate females was also significantly higher (69.6%) when compared with illiterate men (12.8%) (Table 1).

Study Variable	Male (n=1688)		Female (n=102)		Total (n=1790)		Test of significance
	No.	%	No.	%	No.	%	
Age group (years)							
10-19	97	5.7	2	2	99	5.5	
20-29	725	43	16	15.7	741	41.4	
30-39	459	27	26	25.5	481	26.9	*p<0.0001
40-49	263	15.4	23	22.5	283	15.8	
>50	155	8.9	35	34.3	186	10.4	
Education							
Illiterate	216	12.8	71	69.6	287	16	
Non Graduate	805	47.7	31	30.4	836	46.7	*p<0.0001
Graduate	539	31.9	0	0	539	30.1	
PG	128	7.6	0	0	128	7.2	
Socio Economic Status							
Lower	251	14.9	71	69.6	322	18	*p<0.0001
Lower Middle	769	45.6	23	22.5	792	44.2	
Middle	574	34	8	7.8	582	32.5	
Upper Middle	93	5.5	0	0	93	5.2	
Upper	1	0.1	0	0	1	0.1	

Table 1. Demographics of OSMF patients

Habits

Out of 1801 patients, 61.56% (n = 1111) patients had multiple (more than one) habits,37.71% (n = 676) patients had exclusive habits (only one habit), while

Risk Factors	Male (N=631)	Female (N=44)	OR(95% CI)	P value
	n (%)	n (%)		
Areca nut				
Yes	422 (66.9)	6 (13.6)	12.788(5.321-30.732)	<0.0001
No	212 (33.1)	38 (86.4)		
Guthka				
Yes	57 (8.6)	22 (50)	0.094 (0.049-0.180)	<0.0001
No	577 (91.4)	22 (50)		
Tobacco (Non smoked)				
Yes	156 (24.2)	16 (36.4)	0.560(0.295-1.063)	0.076
No	480 (75.8)	28 (63.6)		
Smoking				
Yes	2 (0.3)	--	-	-
No	629 (99.7)	--		

Table 2. Sex wise Risk Distribution with Single Risk Factor of OSMF

0.7% (n = 14) patients did not give history of any habit (table 2, 3).

Exclusive habits

Table 2 shows the risk distribution of OSMF cases having exclusive habits (n =675). Females have shown statistically significant predilection for exclusive gutkha chewing habit [OR = 0.094 (0.049-0.180), P =0.0001] when compared with males, followed by tobacco chewing habit [OR=0.560(0.295-1.063),P=0.076] which however was not statistically significant. Significant predilection for exclusive areca nut [OR =12.788(5.321-30.732)P =<0.0001]was found more in males as compared to females.

Multiple habits

Table 3 shows the risk distribution of OSMF patients with multiple habits (n =1111). There was a statistically significant predilection for areca nut chewing (OR=0.135(0.054-0.342), P < 0.0001), gutkha chewing (OR=22.32(10.421-47.817), P < 0.0001), tobacco chewing (OR= 0.111(0.04-0.308), P<0.0001), smoking habits (OR=30.791(7.472-126.89), P < 0.0001) and alcohol (OR=12.692(3.077-52.347), p < 0.0001) in males when compared with females.

Table 4 shows the gender-wise distribution of signs/symptoms in OSMF cases at first presentation. Vesicles /ulcerations [OR= 0.605(0.383-0.956),P= 0.031] and shrunken uvula [OR =0.616(0.408-0.929),P 0.021] were found to be significantly more prevalent in females when compared with males (Table 4).

Clinical grading

Out of 1801 patients, 339 cases(18.7%) were of stage I, 667(37%) patients were having stage II OSMF,610(34%)

Risk Factors	Male (N=1045)	Female (N=57)	OR(95% CI)	P value
	n (%)	n (%)		
Areca nut				
Yes	611 (58.5)	52 (91.2)	0.135(0.054-0.342)	<0.0001
No	434 (41.5)	5 (8.8)		
Guthka				
Yes	828 (78.5)	8 (14)	22.32(10.421-47.817)	<0.0001
No	225 (21.5)	49 (86)		
Tobacco (Non smoked)				
Yes	624 (59.4)	53 (93)	0.111(0.04-0.308)	<0.0001
No	424 (40.6)	4 (7)		
Smoking				
Yes	552 (52.8)	2 (3.5)	30.791(7.472-126.89)	<0.0001
No	493 (47.2)	55 (96.5)		
Alcohol				
Yes	330 (31.6)	2 (3.5)	12.692(3.077-52.347)	<0.0001
No	715 (68.4)	55 (96.5)		

Table 3. Sex wise Risk Distribution with Single Risk Factor of OSMF

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No	715 (68.4)	55 (96.5)		

Table 4. Symptoms and Sex wise Risk Distribution

cases had stage III while 185(10.3%) patients had stage IV OSMF (Table 5).

Prevalence of OSMF was also recorded based on age groups. It was more(41.4%) in group II (age 20-29 years) patients while it was least (5.53%) in group I (upto 19 years) patients. The stage I OSMF was more prevalent in group I patients and stage II OSMF was more prevalent in group V (above 50 years) patients. The highest prevalence of stage IV (14.4%) OSMF was in group IV(40-49 years) patients whereas the stage III (36.4%) OSMF had highest prevalence in group II (20-29 years) patients. By applying Chi square test significant association was found between age group and clinical staging of OSMF($P < 0.001$) (Table 5).

Table 6 depicts the gender-wise distribution of clinical grading of OSMF, where32.35% females were affected with stage III and stage II OSMF, each, while 37.26% males had stage II and 34.06% had stage III OSMF. Stage I OSMF was present in 18.84% males and 16.67% females whereas stage IV OSMF was seen in 18.63% females and 9.83% males.

In the present study 26 cases (25 male, 1 female) were of squamous cell carcinomas(IVB)which accounts for 1.5% malignancy potential in our study. One hundred and fifty-nine(141 male, 18 female) patients(8.8%)were having other precancerous lesion associated with OSMF (IVA).By applying Chi square test significant association was found between gender and clinical staging of OSMF($P < 0.001$) (Table 6).

Duration and frequency of the habits

Table 7 shows prevalence of OSMF based on duration

Stage	Age Groups					Total
	Upto 19 Group I	20-29 Group II	30-39 Group III	40-49 Group IV	50 & above Group V	
I	28(28.3)	149 (20.1)	85(17.7)	49(16.3)	27(14.5)	338(18.7)
II	35(35.4)	255 (34.4)	185(38.5)	112(38.9)	77(41.4)	664(37.0)
III	30(30.3)	270(36.4)	164(33.5)	86(30.4)	61(32.8)	611(34.0)
IVA	5 (5)	65 (8.6)	40 (8.3)	30 (10.6)	20 (10.7)	160 (8.8%)
IVB	1 (1)	3 (0.4)	12 (2)	11 (3.8)	1 (0.5)	27 (1.5%)
Total	99(100.0)	742(100.0)	486(100.0)	288(100.0)	186(100.0)	1801(100.0)
Chi Square=37.573, df=16, P=0.0017						

Table 5. Association between age groups and clinical grading of OSMF

Stage	Male		Female		Total
	No. (%)		No (%)		
I	318 (94.9)	18.8%	17 (5.1)	16.6%	335 (100%)
II	629 (95)	37.3%	33 (5)	32.4%	662 (100%)
III	575 (94.5)	34.1%	33 (5.5)	32.4%	608 (100%)
IVA	141 (88.6)	8.3%	18 (11.4)	17.7%	159 (100%)
IVB	25 (96.2)	1.5%	1 (3.8)	0.9%	26 (100%)
Total	1688	100%	102	100%	1790

Table 6. Association between genders and clinical grading of OSMF

of the habits. Duration of habit was divided in 5 groups. A higher prevalence was recorded in Group A (up to 5 years)[721 (40.2%)] followed by Group B (6-10 years)[420 (23.3%)], Group C (11-15 years)[261 (14.3%)], Group E (more than 20 years) [203 (11.2%)]and Group D (16-20 years)[197 (11%)]. This prevalence was statically significant (P < 0.0001) (Table 7).

Frequency of habit was divided in four groups. Prevalence of OSMF was more in Group 2 (6-10 times/day) [616 (34.2%)] and group 3(11-15 times/day) [549 (30.3%)]in comparison to group 1 (up to 5 times/day)[368 (20.6%)] and Group 4 (more than 16 times/day) [268 (14.9%)]. The prevalence was statistically significant (P < 0.0001) (Table 8).

DISCUSSION

Prevalence of OSMF has been estimated to range from 0.1 to 30% based on geographical location, sample size, and sampling methodology.[8] The prevalence of OSMF in India, having a broad age range of 11 to 60 years, has been estimated to range from 0.2–2.3% in males and 1.2–4.6% in females.[3,8]

The present study showed a higher prevalence of OSMF in males (16.5:1), which is similar to the studies reporting a varying but higher male prevalence with male: female ratio ranging from 2.4:1 to 40:1.[5,9-14]Biradar et al in their study reported all were male patients.[15]However, few studies have reported female preponderance.[16-18]The higher involvement of males in all studies, reflects their easy access to the abusive habits when compared with females.

In the present study, the youngest patient was 15 years of age whereas the oldest patient was 88 years old. The average age of the patient in the study was 32.8 +11.8 years, which is in the similar range with previous studies.[5,19, 20]Majority of the OSMF cases (68.3%) belonged to 20-39 years of age group. This is in

Stage	Duration of the habits					Total
	Upto 5 years	6-10 years	11-15 years	16-20 years	> 20 years	
I	147 (20.5%)	81 (18.7%)	44 (17.2%)	39 (19.9%)	27 (13.4%)	338(18.7)
II	255 (35.5%)	150 (36%)	103 (39.8%)	64 (32.7%)	91 (44.6%)	663(37.0)
III	252 (34.8%)	150 (36%)	81 (31.7%)	67 (34.2%)	61 (30.2%)	610(34.0)
IVA	65 (9%)	33 (7.9%)	23 (7.8%)	24 (11.7%)	18 (8.9%)	163 (8.8%)
IVB	2 (0.2%)	6 (1.4%)	10 (3.5%)	3 (1.5%)	6 (2.9%)	27 (1.5%)
Total	721 (40.2%)	420 (23.3%)	261 (14.3%)	197 (11%)	203 (11.2%)	1801(100.0)
Value of χ^2 =31.971, d.f.=16, significant, p=0.0101						

Table 7. Association between duration of habit and clinical grading of OSMF

Stage	Duration of the habits					Total
	Upto 5 years	6-10 years	11-15 years	16-20 years	> 20 years	
I	147 (20.5%)	81 (18.7%)	44 (17.2%)	39 (19.9%)	27 (13.4%)	338(18.7)
II	255 (35.5%)	150 (36%)	103 (39.8%)	64 (32.7%)	91 (44.6%)	663(37.0)
III	252 (34.8%)	150 (36%)	81 (31.7%)	67 (34.2%)	61 (30.2%)	610(34.0)
IVA	65 (9%)	33 (7.9%)	23 (7.8%)	24 (11.7%)	18 (8.9%)	163 (8.8%)
IVB	2 (0.2%)	6 (1.4%)	10 (3.5%)	3 (1.5%)	6 (2.9%)	27 (1.5%)
Total	721 (40.2%)	420 (23.3%)	261 (14.3%)	197 (11%)	203 (11.2%)	1801(100.0)
Value of χ^2 =31.971, d.f.=16, significant, p=0.0101						

Table 8. Association between habit frequencies and clinical grading of OSMF

consistent with the earlier studies by Sirsat and Khanolkar,[21] Sinor et al,[16] Ahmad et al.[2] and Shah et al.[20] During the recent years, with the arrival of attractive and convenient packaging in the forms of sachet, beguiling advertisements linking it to the social status and most importantly easy availability has led to an increase in consumption of gutkha and pan masala among the younger population, which is also noted in the present study.[2]

Most of the OSMF patients (62.2%) in the present study belonged to lower middle and lower socioeconomic class. Shiau and Kwan[22]and Ramanathan et al[23]alsomade a similar observations with most cases from Indian populationbeing from low socioeconomic group of the society. McGurk and Crag[24] studied Asian community settled in United Kingdom and they found that most of the OSMF patients were from a low or middle-income group. The reason might be attributed to poor nutritional quality of food with low vitamins, iron and use of more spices and chillies to make the food tasty, coupled with lack of health consciousness.[2]

Apart from areca-nut chewing being considered as the main causative agent, other contributory risk factors for etiopathogenesis of OSMF includes chewing of smokeless tobacco, high intake of chillies, toxic levels of copper in foodstuffs, vitamin deficiencies, malnutrition resulting in low levels of serum proteins, anaemia and genetic predisposition.[8] Areca-nut consumption is estimated to be by 10-20% of World's population in different forms.[8] Areca-nut chewing in its various forms is widely prevalent in the India, giving rise to an increased prevalence of OSMF, from an estimated 2,50,000 cases in 1980 to an estimated 5 million people in 2002.[5] Moreover, recent data suggests that prevalence of OSMF in India has increased from 0.03% to 6.42%.[23] A marked increase in incidence has been observed after the widespread marketing of commercial products known as Gutkha (mixture of tobacco and areca-nut), sold in single-use packets.[8]

In present study, areca nut chewing and the use of tobacco for teeth cleaning were proportionately higher in females which are attributable primarily to the local cultural practices and easy availability of areca nut and tobacco. Inversely, gutkha chewing and tobacco smoking was more prevalent in males. Seedat and Van Wyk[17]from South Africa and Hazare et al [5]from India had similar observations in their studies. In various epidemiological studies on OSMF, the investigators found a strong association between gutkha, areca nut chewing and OSMF and pointed that these habits led to OSMF.[2,5,10,12,14,16] In the present study, 13 patients (0.7%) reported no history of any habits.

Burning sensation of oral mucosa (81.34%) and inability to open the mouth wide due to fibrotic bands, were the chief complaints in the present study, which can be considered as the diagnostic signs of the disease.[5,11,28]

In present study, majority of patients were seen in stage II (37%) and stage III (34%) OSMF, followed by stage I (18.73%) and stage IV (10.3%) OSMF. These findings are in consistent with the study by Srivastvaet al.[14]Kumar et al.[12] found stage II was more prevalent followed by stage IV, III and stage I in their study where as in the study conducted by Hazare et al[5], majority of OSMF (48.3%) cases were in grade III followed by grade II. The less prevalence of stage I in the present study as well as in various other hospital-based studies may be due to

the fact that in the early cases significant changes, especially limited mouth opening, are not seen, and unless there are any significant symptoms or dysfunction of affected part/organ, patients usually donot approach the doctor. A population screening study revealed majority of patients in asymptomatic stage, stage I OSMF was more prevalent.

In the present study, posterior one-third of oral cavity involving both buccal mucosa, retromolar area and soft palate were predominantly affected, which is similar to the observations from two studies from Maharashtra state. Contrary to these findings, a study from Kerala state, reported labial mucosa to be significantly affected, which represents a regional variation with respect to various chewing habits practised in different parts of India.[5]

Although the prevalence based on duration and frequency of habit was variable in the present study, a generalized observation made was that 59.8% of the patient had habit duration for more than 5 years and 79.4% of the patient had frequency of more than 5 times in a day. As most of the patient were in stage II and stage III OSMF, it led us to conclude that the severity was more in subjects who were chewing for longer duration and frequencies. These findings were in accordance with the previous studies.[11,12]

Malignant transformation of OSMF

Patients with OSMF have been reportedwith higher risk of developing oral squamous cellcarcinoma (OSCC), compared to other PMDs.[8]In the present study 26 cases (25 male, 1 female) were of squamous cell carcinomas (IVB) which accounts for 1.5% malignancy potential.In 1970, a 17-year follow upstudy reported malignant transformation in 7.6% of OSMF cases.[29]Studies with smaller follow up periods also have reported malignant transformation rates ranging from 1.9 to 9%, depending on diagnostic criteria and duration of follow up.[8]A recent study from India has reported malignant transformation in 25.77% of OSMF cases indicating the alarming malignant potential of OSMF.[23]

We can conclude from the present study that habit variables in the form of duration, frequency, have increased significance in correlation to severity of clinical grading of OSMF. It was also found that there is a marked difference in the habits, their frequency and duration, signs and symptoms and disease severity in females when compared with males seeking dental care for OSMF at tertiary level, in the Western Indian rural population.

Limitations of the present study includes that since it was a retrospective study, control group was not there and there were a smaller number of females in the study. Also amount/quantity of gutkha/areca nut, its duration in the mouth, style of chewing gutkha-swallowing/spitting and association of prevalence and severity of OSMF with different types of habits were not included. Hence, a well-designed, large, multicentric, prospective study including matched control groups is recommended.

In conclusion, primary prevention for a potentially malignant disorder such as OSMF needs to be improvedat national, state, and individual levels and should involve education of the public regarding the ill effects of areca nut and tobacco along with harsher laws and punishments to restrict the sale of gutkha and similar products. More focus should be on early diagnosis since many patients come so late to diagnosis that interventions are of limited efficacy and despite the efforts taken cure is almost impossible. Further, having multiple habits such as chewing tobacco or areca-nut products, imbibing unhealthy amounts of alcohol, abusing other drugs and often having dietary deficiencies increases the risk of co-morbidities such as metabolic syndromes, respiratory, gastrointestinal/liver and cardiovascular diseases.[8,31]Depending on their dominant symptoms, patients may seek consultation/treatment by either a primary care physicians (PCP) or an oral physicians/dentists. Thus an interdisciplinary approach that may help in early diagnosis of OSMF/potentially malignant disorders and OSCC, with integrated management of both oral and systemic symptoms, improving long term prognosis, reducing suffering and improving quality of life is crucial. Hence all health care professions must work together as a team with the primary goal of prevention.

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AUTHOR AFFILIATIONS: (*Corresponding Author)
1. Senior Registrar, Trauma Centre Government Medical College & Hospital Doda Jammu & Kashmir
2. Professor, Department of Dentistry, Govt Medical College & Hospital, Doda, Jammu & Kashmir (Corresponding Author)
3. Senior Registrar, Department of Dentistry, Govt Medical College & Hospital Doda, Jammu & Kashmir
4. Senior Registrar, Department of Dentistry, Govt Medical College & Hospital Doda, Jammu & Kashmir

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Contact Corresponding Author at: dryunissaleem1969[at]gmail[dot]com