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Is Gene Therapy Really Fruitful for Osteoarthritis?

JAYEETA CHOWDHURY^{*1}, DATTATREYA MUKHERJEE²,^{ID} DEBRAJ MUKHOPADHYAY³ ^{ID}

Strategies have been categorized into two focus areas for the delivery of nucleic acids to weakened, diseased tissues: viral and non-viral gene therapy. In this commentary we address the implementation of osteoarthritis (OA) gene therapy as one of the most prevalent types of arthritis. We mostly concentrate on the gene therapy and cell therapy without a virus. We address briefly the benefits and the drawbacks of viral and non-viral gene therapy and stress upon the nucleic acid transport mechanisms used for transmitting gene to synovial joint articular chondrocytes. While viral gene delivery has become more common because of the efficiency published, considerable efforts have been made to improve the efficiency for transfecting non-viral transmission by promising tools for further use in simple, translational and clinical OA trials. Non-viral gene delivery technology has the ability to change the possible production of OA and osteoarticular disease-modifying therapeutics.

Additional research is required to improve gene expression transfection effectiveness, durability and length of time. Osteoarthritis (OA) is one of the leading reason of disability all around the world and a highest cost contributor to health as well as social care systems.¹ In the aspect of prevalence, OA is the most ordinary chronic and degenerative disease of synovial joints.² The incidences of OA are increasing among the aging population because of the epidemic of obesity.^{3,4} Articular cartilage deterioration and degradation are characterized by OA and result in extreme pain, joint loss and decreased quality of life.⁵ As an alternative way to distribute therapeutic agents, growth factor genes and small regulatory components as microRNA, some methods to gene transmission are proposed.^{6,7} Finally, there have been progresses in the advancement of gene therapy approaches and technology to test them on experimental and translational OA models. Further studies are required, however, to maximize the gene expression transfer efficiency and length.

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World Health Day 2021: Amidst the Backdrop of COVID-19

RASHMI JAISWAL

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The world is currently going through a situation where we can see rising deaths due to COVID-19. If these records continue to hike in the same manner, then the day is not so far when, we will contribute to this and take this list further. With an already strained healthcare system across the globe, all countries are plagued by the emergence of the various waves of the pandemic. With the target to vaccinate the entire global population, the World Health Day 2021 with the theme “Building a Fairer, Healthier World” offers hope for a better, COVID-19 free world.

KEYWORDS: COVID-19, Health, WHO

INTRODUCTION

The World Health Organisation’s (WHO) constitution was implemented worldwide on 7th April, 1950. Since then, the same day is celebrated as “World Health Day” globally.¹ The significance behind marking this day is to spread awareness and make people realise the importance of leading a healthy and stable life. This day mainly emphasizes on drawing attention towards the subject of global health. Today the entire world is concerned about health and lifestyle. Only reason behind this being the recognition of health and diseases escalated throughout the mankind by WHO. During the earlier times when there was no such awareness, people had to suffer dreadfully from chronic diseases without even knowing the cause and cure.²

HISTORY OF PANDEMICS (POST 2000)³

Pandemic is a worldwide spread of a disease. It’s an unfortunate reality, but this has happened quite very often in the past. Addressing the 21st century, some of the major pandemics have occurred that demolished many lives.

SEVERE ACUTE RESPIRATORY

SYNDROME/SARS (2002): First reported in November 2002 in China. It is caused by SARS-CoV. WHO reported 8,096 cases and 774 deaths.

Swine Flu/H1N1 Flu (2009): It was noted for its rapid global spread because of high degree of viral

contagiousness. It was first detected in United States in April, 2009. CDC estimated that 151,700-575,400 people worldwide died from this disease.

Middle East Respiratory Syndrome/ MERS (2012):

It was first observed in June 2012 in Saudi Arabia. It is caused by MERS-CoV which attacks the respiratory system. In total, 27 countries have reported cases, leading to 858 known deaths.

EBOLA (2014):

Ebola outbreak was first reported in March 2014 in West Africa. It was noted for its unprecedented magnitude. The outbreak ended with more than 28,600 cases and 11,325 deaths (as reported by CDC).

ROLE OF WHO DURING COVID-19 PANDEMIC⁴

Dr. Tedros Adhanom, Director General of the World Health Organization once said “A devastating epidemic can start in any country, at any time and kill millions of people because we are not prepared. We are still vulnerable.” (12th February, 2018)

A cluster of pneumonia cases was reported in Wuhan, post which WHO activated the emergency management team on 1st January, 2020. As a response to increasing cases, WHO launched the R&D blueprint on diagnostics, vaccines & therapeutics for the novel coronavirus. The main sight was to improve



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coordination between scientists and global health professionals for global research on corona virus disease. However, many allegations were raised on WHO's credentials for its dereliction of duty for covering up China's failure to handle the crisis.

WHO issued an advisory stating the best way out of this pandemic would be comprehensive approach. WHO suggested all countries to perform maximum possible testing and contact tracing. They suggested to follow social distancing to break the chain of spread.

WORLD HEALTH DAY 2021¹

"Building a Fairer, Healthier World" is a very serious and impactful theme chosen by WHO for this year's World Health Day. Poor and underprivileged people are the first victim of any pandemic as they are unable to avail the proper medical facilities and necessary services at the right time. Which is not fair enough, since we all are equal and should have equal exposure to all medical facilities. On the occasion of world health day, promotional programs, events and activities are launched worldwide to forecast the

awareness related to public health. We need to work all together, to tackle this issue and achieve the motive behind this theme.

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Coronavirus Disease 2019: Prevention and Safety in the Dental Office

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Coronavirus disease 2019 (COVID-19) caused by a single stranded RNA virus originating from Wuhan China has gripped the whole world and evolved rapidly into a public health crisis. SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) is abundantly present in nasopharyngeal and salivary secretions of affected patients and is transmitted by droplets, surface contact, fecal-oral route and by aerosolization during procedures. The dental professionals are particularly at risk because of close contact with the patient and exposure to blood, saliva and droplets. Dental professionals must be fully aware of coronavirus spreading modalities, identification of patients with this infection, so present article introduces the essential knowledge about COVID-19 infection and provide recommended management protocols for dental practitioners based on relevant guidelines, research so that dental professional are better prepared to manage asymptomatic, suspected, and confirmed COVID-19 patients.

KEYWORDS: Coronavirus, Saliva, Disinfection, Triage

INTRODUCTION

What a start for year 2020: coronavirus. Corona virus disease also known as COVID 19 has rapidly evolved into a worldwide health crisis influencing every aspect of life. The corona virus infection started from Wuhan, China and was declared pandemic by world health organization.^{1,2} The novel corona virus was initially named 2019-nCoV and officially called SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2).³ On 11th February 2020, World health organization named the latest strain of coronavirus as COVID 19.⁴ This novel coronavirus is similar to coronavirus species found in bats and pangolins stating zoonotic nature of this disease.^{5,6} Globally, as of 7th February 2021, there have been 105,394,301 confirmed cases of COVID-19, including 2,302,303 deaths and India has reported 10,826,363 confirmed cases of COVID-19 with 154, 996 deaths as reported by WHO situation report and number is increasing each day [Figure 1].⁷ When COVID-19 infection was spreading at an alarming rate, many countries including India imposed lockdown to control the spread of the infection by closing teaching institutions, airports, social gatherings, sports activities, events, bus transport and offices with special guidelines. Besides this, several individuals were self-quarantined and many with travelling history from affected areas were home or institution quarantined to limit the spread of disease.

Health care professionals including dental

professionals working as corona warriors are in close contact with infected patients and have highest chance of getting infected.^{8,9} Many health care workers like doctors, nurses have been tested positive for COVID-19, many are quarantined and deaths have also been reported from affected countries including India. Dental professionals have a high risk of getting infected and potentially spreading it to their peers, families, other patients and can become potential carriers of the disease.⁹⁻¹² As viruses can be easily vehiculated by the aerosol generated by most of dental procedures so the aim of the present article is to introduce the essential knowledge about COVID-19 infection in dental settings and provide recommended management protocols for dental practitioners based on relevant guidelines and research so dental professional are better prepared to manage asymptomatic, suspected, confirmed COVID-19 patients.

EPIDEMIOLOGY AND PATHOGENESIS

Genetic and epidemiologic research shows that COVID-19 infection started with a single animal-to-human transmission, followed by sustained human-to-human spread.^{13,14} The common routes of transmission of coronavirus includes direct transmission of respiratory droplets from infected person while speaking, coughing, sneezing to the mouth, nose or eyes or by inhalation into lungs of nearby individuals.^{15,16} SARS-CoV-2 can bind to human



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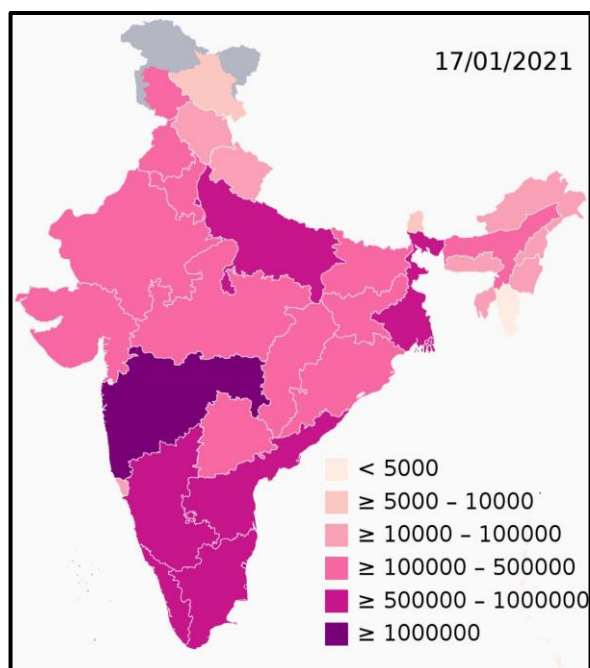


Figure 1. India COVID-19 case density map on 17-01-2021

angiotensin-converting enzyme 2 receptors, which are highly concentrated in salivary glands explaining presence of SARS-CoV-2 in secretory Saliva [Figure 2].¹⁷⁻¹⁹ Coughing or sneezing by an infected person makes SARS-CoV-2 Airborne, leading to recommendation of social distancing to minimize community spread of the disease. In addition, there may be risk of fecal-oral Transmission, as SARS-CoV-2 was found in the stool of patients.²⁰ Symptomatic COVID-19 patients are the main source of transmission but asymptomatic patients and patients in their incubation period are also carriers of SARS-CoV-2.^{13,21} The average incubation period has been found to be 5- 6 days, but it could be as long as 14 days, which is the time duration adopted for medical observation and quarantine.^{22,23} People of all ages are generally susceptible to this disease but

elders with pre-existing chronic diseases like cardiovascular illness, kidney diseases or immunosuppression and close contacts of COVID-19 infected patients including health care workers are at higher risk of COVID-19 infection.^{24,25} Dental care settings invariably carry the risk of infection transmission due to the specificity of its procedures. Pathogenic microorganisms can be transmitted through inhalation of airborne microorganisms, direct exposure of respiratory secretions containing blood, oral fluids and nasal, oral and conjunctival mucosal contact with droplets and aerosols. Indirect transmission can occur by contact with contaminated instruments and clinical environmental surfaces [Figure 3].^{11,26-30}

CLINICAL MANIFESTATIONS

Patients with COVID-19 usually present with clinical symptoms of fever, dry cough, shortness of breath, myalgia and fatigue [Figure 4]. In addition, symptoms like nausea, diarrhoea, vomiting, sore throat, headache, reduced sense of smell, and abnormal taste sensation has also been observed.^{13,31,32} In addition, chest X-ray and computed Tomography demonstrated ground-glass Opacities and bilateral shady patches as most common pattern.³³ Most of the patients have only mild symptoms resembling flu like symptoms and seasonal allergies.³³ Asymptomatic patients can act as potential carriers and source of re-infection. The higher-risk patient population manifests symptoms typical of pneumonia or acute respiratory distress Syndrome.³⁴

DIAGNOSIS AND TREATMENT PLAN

The diagnosis of COVID-19 is based on a combination of epidemiologic information, clinical symptoms, laboratory tests and CT imaging findings.^{9,34} Novel coronavirus nucleic acid can be detected in nasopharyngeal swabs, oropharyngeal swabs, sputum, lower respiratory tract secretions, blood, feces, and

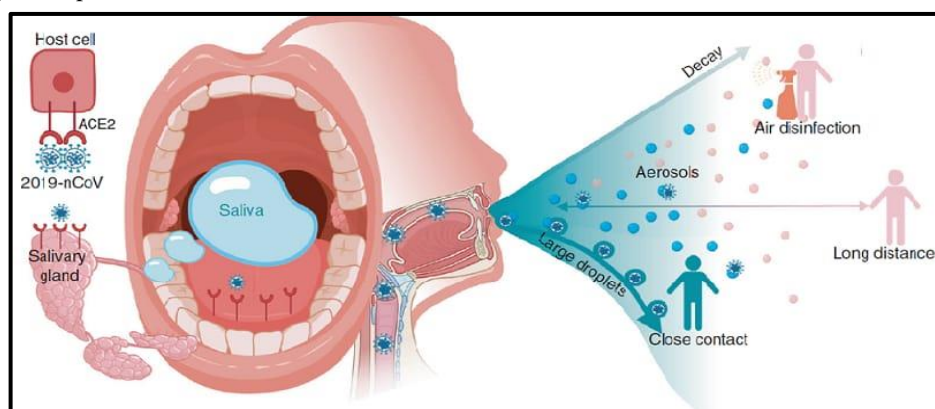


Figure 2. Potential diagnostic value of saliva and transmission of 2019-nCoV

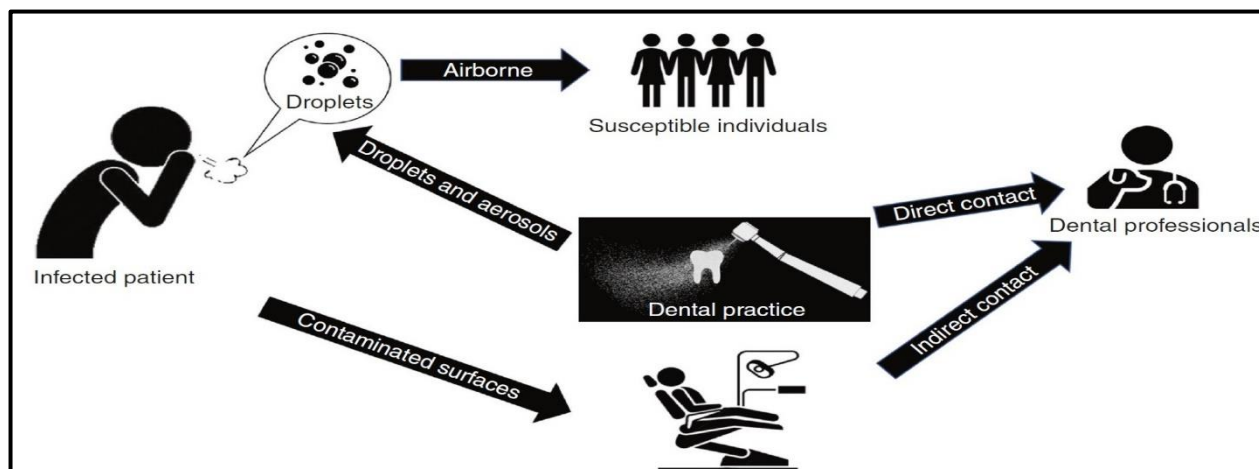


Figure 3. Transmission routes of 2019-nCoV in dental clinics and hospitals

bronchoalveolar lavage using RT-PCR and/or NGS methods. Serological diagnosis of COVID-19 using SARS-CoV-specific secretory immunoglobulin A (SIgA) in saliva has also been demonstrated.³⁵ Researchers had carried out various testing and clinical trials to investigate interventions that were potentially effective against COVID-19 and various medications were recommended for prophylaxis of SARS-CoV-2 infection in selected high-risk individuals.³⁶ The convalescent plasma (CP) use as a potential treatment modality is still questionable due to limited high-quality randomized clinical trial studies.^{37,38} Now corona vaccine is available and it is being given to the people in different countries. COVID-19 management has largely been supportive and is directed at relieving symptoms.⁹ The COVID-19 vaccine was launched on 16th January, 2021 in India.¹⁷ Healthcare and frontline workers are getting the vaccine in first phase and will be followed by persons over 50 years of age and persons under 50 years with comorbid conditions.

PATIENT MANAGEMENT IN DENTAL PRACTICE

As many of the dental procedures involve aerosol generating procedures, the standard protective measures followed in routine clinical work are not sufficient to prevent the spread of COVID-19 infection. Different kinds of patients like Asymptomatic patients, patients in incubation period, unaware of their infection, or choose to conceal their infection can visit for treatment. With increase in cases daily and fear of community spread it is strongly recommended to treat

each dental patient as COVID-19 positive.

TELE SCREENING AND TRIAGE

1. In general, one should avoid walk-in visits.
2. Phone triage of every patient should be carried out at the time of scheduling appointments. When patient arrives at dental clinic a detailed medical history, COVID-19 screening questionnaire to identify any suspected or possible infected COVID-19 patient and assessment of true dental emergency should be done by asking patient about the nature of his dental condition.³⁹

HOW TO IDENTIFY DENTAL EMERGENCY

When a patient calls or visit dental clinic, dentists should use their professional judgment⁸ to decide if a patient need emergency, urgent or non-urgent dental care.^{40,41} Dental emergencies are potentially life threatening and require immediate intervention and include:

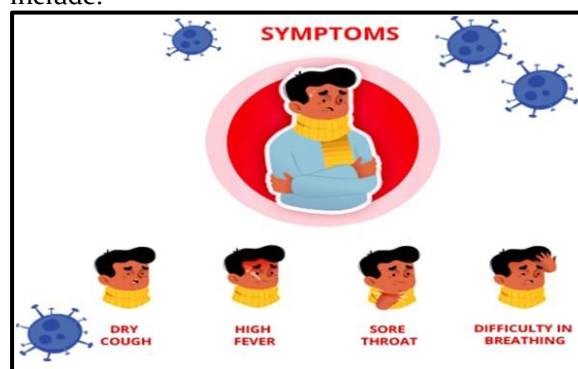


Figure 4. Sign and symptoms of COVID-19

1. Uncontrolled bleeding.
2. Cellulitis or a diffuse soft tissue bacterial infection with intra-oral or extra-oral swelling that potentially compromise the patient's airway.
3. Trauma involving facial bones, potentially compromising the patient's airway.

Urgent dental care involves conditions that require immediate attention to relieve severe pain and/or risk of infection. These should be treated as minimally invasively as possible.

1. Severe dental pain from pulpal inflammation.
2. Pericoronitis or third-molar pain.
3. Surgical post-operative osteitis, dry socket dressing changes.
4. Abscess, or localized bacterial infection resulting in localized pain and swelling
5. Tooth fracture resulting in pain or causing soft tissue trauma.
6. Dental trauma with avulsion/luxation.
7. Dental treatment required prior to critical medical procedures.
8. Final crown/bridge cementation if the temporary restoration is lost, broken or causing gingival irritation.
9. Biopsy of abnormal tissue.

Other urgent dental care:

1. Extensive dental caries or defective restorations causing pain.
2. Suture removal.
3. Denture adjustment on radiation/ oncology patients.
4. Denture adjustments or repairs when function impeded.
5. Replacing temporary filling on endodontic access openings in patients experiencing pain.
6. Snipping or adjustment of an orthodontic wire or appliances piercing or ulcerating the oral mucosa.

ROUTINE OR NON-URGENT DENTAL PROCEDURES INCLUDE BUT ARE NOT LIMITED TO:

1. Initial or periodic oral examinations and recall visits, including routine radiographs.
2. Routine dental cleaning and preventive therapies.
3. Orthodontic procedures other than those to address acute issues (e.g. pain, infection, trauma) or other issues critically necessary to prevent harm to the patient.
4. Extraction of asymptomatic teeth.
5. Restorative dentistry including treatment of

- asymptomatic carious lesions.
6. Aesthetic dental procedures.

Treatment should be deferred for two weeks in suspected or confirmed cases of COVID 19 infection if possible and the patient should be reported to the concerned health authorities to quickly impose quarantine and/or hospitalization depending on the severity of the situation.^{9,41,42,43,44} Positive cases requiring emergency treatment should be referred preferably to emergency department with dental consult. If the dentist cannot delay the treatment or refer the patient then one should follow standard, contact and airborne precautions while treating the patient in negatively pressured rooms or Air Borne Infection Isolation Rooms (AIIRs) if available.^{11,45} Urgent care should be deferred if possible for at least 2 weeks and antibiotics and/or analgesics should be prescribed for dental conditions like tooth pain and/or swelling. In case of asymptomatic patients with contact or travel history treatment should be postponed up to 14 days if possible. If there is no history of contacts and/or symptoms, patients are allowed to visit the dental office with modifications and dental procedures should be performed by following the preventive precautions [Figure 5].

DENTAL OFFICE TRIAGE

1. Patient entering the dental office should be given a surgical mask if he/she is not wearing one.
2. Patients are advised to arrive on time for appointments, not early, to minimize waiting in dental office and to decrease the number of people present.
3. Physical barriers made up of glass or plastic windows should be installed at reception areas to limit close contact with potentially infectious patients.
4. Patient's history should be repeated and body temperature registered through 7a no contact forehead thermometer.¹¹
5. Suspected or confirmed patients of COVID-19 infection should be seated in a separate, well-ventilated waiting area and should follow proper respiratory hygiene.⁴⁵
6. A prominent sign directing the patients to use a hand sanitizer from no touch dispenser should be placed at entrance.
7. Posters and signs about hand hygiene, respiratory hygiene, social distancing and cough etiquette should be displayed at the entrance, waiting areas,

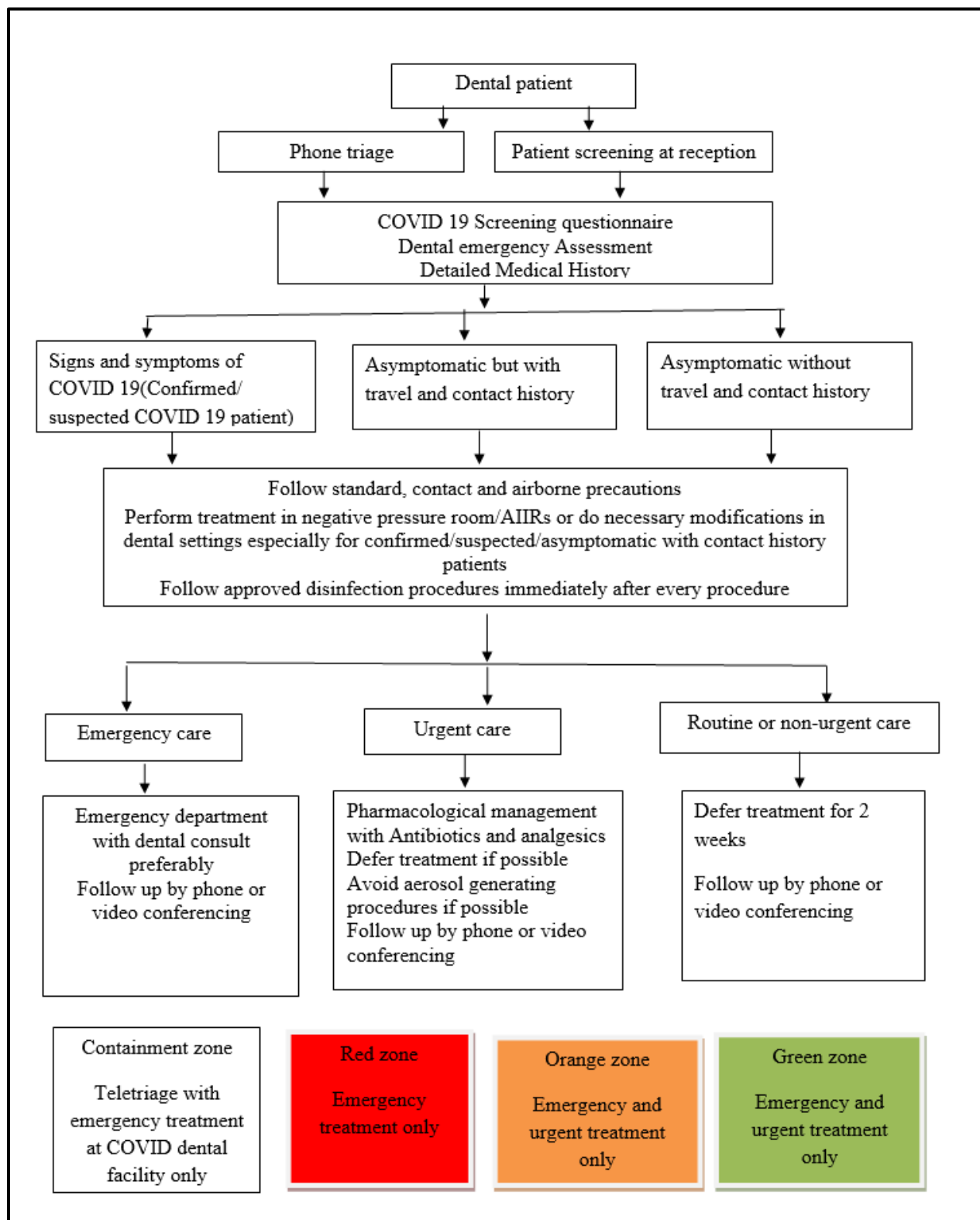


Figure 5. An overview of patient screening and management in dental office

elevators, and cafeteria.^{47,48}

8. Remove all potentially contaminated objects (i.e., tables, magazines, toys) which could facilitate cross infection.

9. Number of patients should be limited in waiting area and distance of one meter should be kept between the chairs.⁴⁹ Accompanying persons should be advised to wait outside the dental office.

10. Clothing, cellular telephones, and bags are encouraged to be left in the waiting room. Public areas, including door handles, chairs and bathrooms should be cleaned and disinfected frequently.

DENTAL TREATMENT GUIDELINES

Dental treatment may pose significant risks for dental practitioners and patients. Every dental patient appearing healthy should be considered contagious as the person can be possessing virus despite the absence of clinical manifestations. During dental procedures involving production of aerosols there is a risk of inhalation of small particles and droplets potentially carrying microorganisms by the dental workers so, it is important to safeguard our patients' health via establishing contagion risk reduction protocol and a safer work environment.

1. Pre-procedural one minute mouth rinse with 0.2% to 1% povidone-iodine, 0.05% to 0.1% cetylpyridinium chloride, or 1% hydrogen peroxide before dental procedure is one of the most efficient ways to reduce the proportion of microorganisms in oral cavity.^{11,50}

2. The dental practitioner should perform careful hand washing using alcohol based formulations or water and soap for at least 20 seconds.^[51] The department for infections control of the Stomatology Hospital in West China (Sichuan University) proposed a "two-before and three-after" protocol for hands hygiene.¹¹

3. Dental practitioners should follow all the standard, contact, and airborne precautions including the appropriate use of personal protective equipment including long-sleeved water resistant gown, face masks, glasses or face shield, overshoes, head cap. Face masks like National Institute for Occupational Safety and Health-certified N95, European Standard Filtering Face Piece 2 (EU FFP2), or equivalent, when running aerosol generation procedures and EU FFP3 respirators complying with European Standard 149 (EN 149) or equivalent should be used during emergency for suspected or confirmed COVID-19 patients. There should be a dedicated area for donning and doffing of PPE.^[51,52,53]

4. Disposable (single-use) devices such as mouth mirror, syringes, and blood pressure cuff should be used to prevent cross contamination.

5. Dental instruments required in a dental procedure should be prepared in advance to make the procedure fast and limit contamination.

6. Working surfaces, the dental chair, and devices can be protected from direct contamination by using disposable coverings.

7. Extra oral imaging techniques like panoramic radiography or cone-beam computed tomographic imaging should be preferred than intraoral to avoid gag or cough.⁹ If intraoral imaging is unavoidable, sensors should be double covered to prevent perforation and cross contamination.

8. Rubber dam should be used to minimize splatter generation and extra high volume suction should be used to prevent spreading of aerosol and spatter. Use of a complete four-handed operatory is also desirable.^{54,55}

9. Ultrasonic instruments, high-speed handpieces, and 3-way syringes should be used minimal to reduce the risk of generating contaminated aerosols. Anti-retraction dental hand piece with specially designed anti-retractive valves or other anti-reflux designs are strongly recommended.⁵⁵

10. Digital dental impressions should be preferred over traditional ones and traditional impressions should be immediately disinfected with the use alcohol based disinfectants sealed in an envelope and sent to the laboratory. Since cast models are usually contaminated with many microbial species and are difficult to sanitize, prefer models made of synthetic materials.⁵⁶

11. Dentists should minimize utilizing rotary instruments for preparing a cavity and atraumatic restorative procedures can be done in selective cases. Pulp devitalization can be performed for a carious tooth with symptomatic irreversible pulpitis, followed by filling material.

12. Treatment of fracture, luxation, or avulsion of tooth should be decided by the age, trauma severity, apex formation and duration of tooth avulsion. If suturing is needed absorbable suture is preferred.

13. Cases with severe oral and maxillofacial compound injuries should be admitted to the hospital immediately and treated accordingly.

14. After the procedure, all the disposable protections should be removed. The reusable tools and materials should be cleansed, sterilized, and carefully preserved.

15. As coronavirus may live up to 9 days on an inert

surface with preference for humid condition clinical staff should disinfect inert surfaces using chemicals effective against COVID-19 and keep a dry atmosphere to mitigate the 2019-nCoV spread.^{27,57} Recent WHO guidelines deemed water and detergent followed by disinfectants (.1% sodium hypochlorite or 5% bleach 1:50 dilution) effective against COVID-19.⁵⁸

16. Ventilation systems providing air movement from a clean (DHCP workstation or area) to contaminated (clinical area) direction should be installed and properly maintained. Use of indoor portable air cleaning system equipped with HEPA filter and UV light is advisable.

17. The medical and domestic waste produced after treatment of suspected or confirmed COVID-19 cases is considered to be infectious medical waste and should be disposed off in a double-layer yellow waste bags with a “gooseneck” knot in compliance with the requirements of medical waste disposal.

CONCLUSION

With rampant spread of COVID-19 infection worldwide and cases increasing, dental care professionals now will be treating this subset of patient population on daily basis. Several dental practices have either modified their services according to recommended guidelines, or closed down practices for an uncertain period causing serious financial challenges impacting economical condition of the sector. Dental professionals must be fully aware of 2019-nCoV spreading modalities, identification of COVID-19 patients, most importantly self-protection, protection of people and adoption of strict preventive measures. Corona vaccines are available and being administered phase wise but covering the whole population especially in India is a challenge. Dentistry has an important role to play during this pandemic so further assessment of the implications of COVID-19 outbreak in dental practice is urgently needed and in coming time entire profession might show a significant change.

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Anaphylactic Reactions to COVID-19 Vaccine

SACHLEEN KAUR

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The SARS-CoV-2 coronavirus responsible for the COVID-19 pandemic has led to a major health crisis and high mortality rates. Progression to a severe and potentially fatal form of COVID-19 is associated not only with massive viral replication, but also with an inappropriate inflammatory response against the SARS-CoV-2 virus. Therefore, drug strategies may target not only the viral infection itself, but also inappropriate immunoinflammatory responses. Numerous wide-ranging medications have been attempted to improve the prognosis and outcome of COVID-19, especially among hospitalized patients due to an acute respiratory distress syndrome. Vaccination against COVID-19 is an essential global intervention to control the current pandemic situation. Vaccines often cause adverse events; however, the vast majority of adverse events following immunization are due to the protective immune response induced by the vaccine, and not due to an allergic reaction. It is important to know that how can SARS-CoV-2 vaccines be administered with minimal risk of allergic reactions. In fact, currently available mRNA vaccines may usually be administered readily even to patients with allergies. The following review describes the risk of severe anaphylaxis and provides practical tips for safe vaccination.

KEYWORDS: Anaphylaxis, COVID-19, Vaccination, Allergy

INTRODUCTION

Vaccines against SARS-CoV-2 infection have recently become available and have been used in various countries around the world since end of 2020. Although overall good tolerability has been reported, several anaphylactic reactions have been described following vaccination. Vaccination against COVID-19 is an essential global intervention to control the current pandemic. Vaccines often result in adverse events which are majorly a consequence of the vaccine stimulating a protective immune response, and not allergic reactions. Anaphylaxis as an adverse event following immunization is uncommon, occurring at a rate of less than 1 per million doses for most vaccines.¹ Ideally, patients with a history of severe allergy should not be vaccinated, but given the high prevalence of allergic diseases, this may result in several people being necessarily deprived of vaccination, making herd immunity more difficult to achieve. The current recommendation of the European regulatory authority states that patients with known allergy to the ingredients contained in the vaccine should not be vaccinated. It has furthermore been noted that a very small number of severe allergic reactions have occurred since vaccination was started. Vaccinations should generally be administered under medical supervision which allows for emergency treatment. People who develop a severe allergic reaction after

the first vaccination should not be administered the second dose of the vaccine.

Allergic reactions to vaccines are very rare and are usually induced by sensitization of the vaccinated person to ingredients of the vaccine. Besides the specific viral mRNA vaccines contain a number of additives which may theoretically precipitate an allergic reaction. Allergic or allergy-like reactions can possibly be precipitated by polyethylene glycol (PEG) also known as macrogol which is present as an additive in new vaccines for stabilization of nanoparticles and may also be present in many other oral or intravenous preparations.² PEG is known to give rise to harmless, delayed-onset contact allergic reactions as well as isolated cases of immediate-type reactions including anaphylaxis.^{3,4} Another possible mechanism currently being discussed is complement-mediated mast cell activation by PEG specific IgG and/or IgM antibodies also known as complement-activation-related-pseudoallergy.⁵

Many healthy individuals are known to have specific antibodies against PEG. Allergic reactions may be due to immunologically mediated hypersensitivity reactions of varying severity to foreign substances, only some of which are life-threatening. Anaphylaxis is the maximum variant of an immediate-type



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allergic reaction which manifests in various organ systems and may be potentially life threatening. This must be distinguished from non-IgE-mediated immediate reactions. Polysorbate 80 is also one of the ingredient of some of the current non-mRNA-based COVID vaccines and this molecule has also been reported to cause anaphylaxis-like reactions in animal studies⁶ but there are only a few cases of adverse events in human subjects.^{7,8}

RECOMMENDATIONS FOR PRACTICE

Possible adverse reactions after vaccination include anaphylaxis, which occurs very rarely, as well as marked local reactions, worsening of symptoms of an existing allergic disease, which may very rarely evolve into a life-threatening condition only after several days. The current focus is on the possibility of acute anaphylaxis. A previous severe allergic reaction to any component of the SARS-CoV-2 vaccine is an absolute contraindication to vaccination. Other risk constellations from an allergological point of view include patients with a history of anaphylaxis to an indeterminate triggering agent, to previous vaccinations or medication with pre-existent mastocytosis. However, anaphylaxis after insect bites or foodstuffs does not constitute a contraindication to COVID-19 vaccination with mRNA vaccines, according to current state of knowledge. As a precautionary measure, patients with a history of anaphylactic reaction to foodstuffs were excluded from certain vaccinations, since residual components of food allergens may trigger allergic reactions during vaccinations in isolated cases. Patients with food allergy are not expected to be at higher risk of allergy to COVID-19 vaccination. Detailed medical history should be evaluated for potential risk to the patient. If the constellation is unclear, allergy testing should be undertaken in a timely manner before vaccination to determine the triggering substance.

Patients may be vaccinated if they are found to have anaphylaxis to defined drugs or additives not included in the vaccine. This procedure requires appropriate information and education of both immunization teams as well as individuals willing to be vaccinated. It is likely that absolute contraindications to SARS-CoV-2 vaccination are rare in patients with underlying allergies. However, the frequency of severe allergic reactions to mRNA-based vaccines, their underlying mechanism and individuals at particular risk must be observed very

carefully over time. Notification regarding the implementation of SARS-CoV-2 vaccination should provide guidance regarding the need for allergological evaluation in case a history of certain risk factors is present. This facilitates an initial discussion including medical history at the vaccination center. Anti-allergic premedication should be considered in addition to the specified provision of emergency medical care in the event that allergological tests yield equivocal results. This may be considered for instance in patients with a history of perioperative or contrast-induced anaphylaxis or of anaphylaxis of indeterminate origin. Antihistamines and an oral glucocorticoid should be administered prophylactically. Premedication may also be considered in subjects who are evidently very afraid of possible vaccine reactions following rational explanation in an attempt to prevent nocebo reactions. The injection may be given after obtaining a brief history and exclusion of contraindications which should be checked from the labelling document of the vaccine provided by the manufacturer. A 30-minute post-injection follow-up is recommended in people with a history of anaphylaxis due to possible side effects. The vaccination team must be informed about the possibility of anaphylaxis and trained in its acute treatment. Necessary medication and supplies must be available on site, including epinephrine auto-injectors.

CONCLUSION

The worldwide incidence of allergies has increased over the past several decades. Drug-induced anaphylactic reactions are a rare but real problem in clinical medicine. A blanket exclusion of all patients with allergy from SARS-CoV-2 vaccination is irrational and should be avoided. Adequate allergological testing should be performed in the presence of an appropriate history in order to determine the true risk of anaphylaxis after SARS-CoV-2 vaccination. This is best done before a vaccination appointment. All individuals administering vaccination should be explicitly trained in the identification and management of anaphylactic reactions and must have access to necessary equipment, including epinephrine auto-injectors. Pharmacological premedication with histamine H₁ and H₂ antagonists plus glucocorticoids prior to vaccination may be considered in equivocal cases and in patients with hypochondriac anxiety. It is important to report any

severe allergic reaction related to vaccination. We have analyzed the risk of anaphylaxis due to COVID-19 vaccination from an allergological perspective and also highlighted the basic principles for prevention and therapy of anaphylactic reactions and proposed measures for practical management of vaccination against SARS-CoV-2. There is a further need to evaluate the risk of anaphylaxis for the recently approved COVID-19 mRNA vaccines by analyzing the data available in the current literature.

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Interactions Between Anti-Epileptic Drugs and Contraceptives: A Review

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Around half of the pregnancies in women with epilepsy are unplanned and the choice of contraceptive method in epileptic women is important, since it requires considering their possible pharmacological interactions with certain types of anti-epileptic drugs. Drugs from this class which induce hepatic enzyme activity may alter the metabolism of most hormonal methods of contraception, and this may affect their contraceptive efficacy. Hormonal contraception is regarded as highly effective, but its interaction with anti-epileptics may accelerate the metabolism of the latter with the consequent risk of failure, reduction of plasma concentration predisposing to seizures, risk of unwanted pregnancies, abortions, teratogenicity, maternal or fetal complications and difficulty in the management of epilepsy during pregnancy. In case of prescribing both medications, the combined use with a barrier method should be considered. Family planning counselling at the first visit has been shown to influence the choice of the contraceptive method. In conclusion, the different therapeutic options should be analyzed together with the epileptic patients in order to achieve and optimize the best goal for each one. This article reviews these issues and offers practical recommendations for the management of contraception in epileptic patients.

KEYWORDS: Epilepsy, Contraception, Anti-Seizure Drugs, Pregnancy

INTRODUCTION

Epilepsy is a chronic neurological disease, characterized by recurrent seizures resulting from abnormal neuronal discharge in the central nervous system. Around 65 million subjects are affected by it globally.¹ Changes in seizure patterns have been reported in women during puberty, the menstrual cycle, pregnancy and menopause, related to hormone steroid levels.² Estrogens are generally considered proconvulsants via the glutamate receptor excitatory pathway, while progesterone and its metabolites are anticonvulsants via the inhibitory effect via the neuronal membrane receptor, enhancing GABA-A mediated chloride conductance.²⁻⁴ The seizure fluctuations that occur during the menstrual cycle are responsible for one third of cases and are defined as catamenial epilepsy.²⁻⁴ The drug-drug interaction between anticonvulsant drugs and contraceptives was first suggested in the early 1970s.⁵ Therefore, contraception management in these women is critical because of the potential maternal fetal risk due to failure in the choice of method.^{1,6,7} There may also be difficulty managing seizure activity, caused by poor adherence to the drug treatment or physiological changes in the pharmacokinetics of the anticonvulsant medication during pregnancy.⁸ There are currently different methods of birth control available: non-hormonal contraception such as: copper intrauterine devices, barrier methods, surgical

and hormonal, transdermal patches subdermal implants, vaginal rings, and finally levonorgestrel-releasing intrauterine devices. Another form of contraceptive use is emergency hormonal contraception. The failure rate is approximately 1% in healthy women, but 3-6% in women with epilepsy. This occurs despite the fact that fertility in this group of patients is reduced by one third, either due to social reasons or organic reasons.⁹ The estrogen component found in most formulations of oral combined contraceptives is ethinylestradiol.

More than 30% of the ethinylestradiol undergoes metabolism in the intestinal wall, mainly by sulfotransferase - dependent conjugation. Subsequently its biotransformation continues in the liver catalyzed by cytochrome P450 enzyme complex enzymes, uridine diphosphate glucuronyltransferase 1A1 and sulfotransferase-dependent conjugation, and finally, it is hydroxylated to inactive metabolites predominantly by cytochrome P450 3A4. These hydroxylated and methylated metabolites are present free and conjugated to glucuronides and sulfate.⁹ Glucuronidation is inhibited by valproate and induced by phenobarbital, phenytoin, carbamazepine, oxcarbazepine and high dose topiramate, accelerating the metabolism of ethinylestradiol.¹⁰ Ethinylestradiol can also induce the enzymes uridine diphosphate



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glucuronyl transferase, affecting drugs that are primarily metabolized by this pathway, such as lamotrigine.⁹ Similar to ethinylestradiol, the metabolism of the progestogen component also involves cytochrome P450 by hydroxylation, reduction, deacetylation and finally sulfation and glucuronidation.⁹ Its metabolism may be accelerated if combined with carbamazepine, oxcarbazepine, lamotrigine, phenytoin and phenobarbital.¹⁰ The first-generation of anticonvulsant drugs includes phenobarbital, phenytoin, valproate, diazepam, clonazepam, carbamazepine, ethosuximide and primidone.¹¹ The second-generation drugs include felbamate, gabapentin, clobazam, lamotrigine, levetiracetam, pregabalin, tiagabine, topiramate, vigabatrin and zonisamide.¹²

Finally, with the aim of obtaining minimal or no adverse effects with anticonvulsant properties, the door was opened to the third generation: brivaracetam, eslicarbazepine acetate, lacosamide, rufinamide, stiripentol, perampanel.¹³ Based on their mechanism of hepatic metabolism, anticonvulsant drugs may be classified as P450 enzyme-inducing and non-enzyme-inducing antiepileptic drugs. P450 system enzyme inducers include phenobarbital, phenytoin, carbamazepine, oxcarbazepine, eslicarbazepine, felbamate, primidone, rufinamide, lacosamide, and topiramate (at dose greater than 200 mg/day). These drugs induce the cytochrome P450 enzymes from the liver, being able to accelerate the metabolism of combined or progestogen-only oral contraceptives and progestogen implants (subdermal) reducing their effectiveness.^{2,9}

Oxcarbazepine has a low enzyme induction potential, but unfortunately exerts a similar effect to carbamazepine on hormonal contraceptives.^{9,14} Therefore, if oral contraception is indicated, use in combination with a barrier method such as condom or vaginal diaphragm is suggested.^{15,16} These anticonvulsant drugs do not alter the efficacy of depot medroxyprogesterone acetate injection, copper intrauterine device or levonorgestrel release, therefore these may be another option.¹⁶ In turn, these drugs used as monotherapy increase sex hormone-binding globulin levels, both in males and females, resulting in decreased levels of testosterone and bioavailable estradiol, increasing its metabolism with subsequent reduction in its plasma concentration.¹⁵ With some drugs, the extent of enzyme induction may be dose-dependent, difficult to quantify and subject to large variation between individuals, as occurs with

topiramate. No enzyme inducers of the P450 system are namely levetiracetam, gabapentin, topiramate (at doses below 200 mg per day), zonisamide, clobazam, tiagabine, brivaracetam and vigabatrin. This group does not affect contraceptive efficacy, so epileptic women can choose any method of contraception or emergency contraception.¹⁶ The drug lamotrigine has minimal effects on the efficacy of combined contraceptives, however, the use of this type of contraception increases clearance, reducing the plasma concentration of lamotrigine by 45 to 60% and predisposing to epilepsy seizures. If this is the option chosen by the epileptic woman, the dose of lamotrigine should be increased and to reduce its toxicity. Along with levetiracetam, it is recommended during pregnancy because of its low risk of teratogenicity. Enzyme inhibitor anticonvulsant drugs valproate is used as a first option in many women with generalized epilepsy and in unclassified epilepsy, achieving control with low doses. It is highly teratogenic in a dose-dependent manner, and genetic factors and individual susceptibility may be involved. It has been described to act as an antagonist of folic acid.¹⁷ A significantly lower intelligence quotient was detected in children of women treated with valproate, as well as a lower verbal, nonverbal and spatial response and the need for an 8-fold higher education intervention. Intrauterine exposure to this drug is associated with an increased risk of autism spectrum disorders, hyperactivity, dyspraxia and attention deficit disorder.⁸ Stiripentol inhibits cytochrome P450 3A4. There are no publications on the interaction of this drug with contraceptives, so its action on this pathway is assumed to be mild.¹⁴

Literature suggests increase in risk of seizures during contraception. A birth control registry was conducted in 1144 epileptic women, aged 18 to 47 years to find out the impact of contraceptive methods on seizures in different antiepileptic drug category users. For each category of anticonvulsant drugs, they reported an approximately 4.5-fold increased risk of seizures while taking hormonal contraception versus non-hormonal.³ Within specific types of hormonal contraception, a 68% higher incidence of seizures was reported with hormonal patches when compared to users of combined oral contraceptives, probably due to higher ethinylestradiol levels, because gastrointestinal absorption and the first step of hepatic metabolism are avoided.³ And those who used the progestogen-only contraceptive pill had a 62% increase in seizures. This could be due to the low progestin content; whose contraceptive action is more

on cervical mucus than on hormone suppression. Within monotherapy, lamotrigine and valproate presented increased attacks when combined with hormonal contraception.¹³ The precise mechanism by which hormonal based contraceptives may increase the risk of epileptic seizures remains unknown, as there is little evidence regarding the neuroactive properties of the synthetic steroids of contraceptives.

Three potential pathways have been proposed: by classic genomic action estrogens in the central nervous system binds to specific receptors, dimerize and modify neuronal gene expression. Due to nongenomic effects through membrane receptor activation, regardless of the pathway, they can generate changes in neuronal structure, plasticity, direct excitatory effects on the neuronal membrane and postsynaptic regulation of different neurotransmitters. Finally, indirect effects due to alteration of the metabolism of anticonvulsant drugs via induction of the hepatic cytochrome P450 enzyme system, leading to drug-drug interactions and thus reducing therapeutic efficacy when administered together.¹⁴ A retrospective, observational cohort study with case-control analysis was described, conducted from the United Kingdom Health Improvement Network database with 2,201 epileptic women aged 20 to 44 years. This study showed no association between combined oral contraceptives or the progestogen-only hormonal pill and the risk of epilepsy. However, the limitation of this study was low utilization of contraceptives.¹⁸ Another study on epileptic women reported that 63% had received family planning information, however, 54% reported a previous pregnancy. About half of these women were not using contraception and among those who were users, 11% were at risk of potential interaction between oral contraceptives and enzyme-inducing anti-epileptic drugs. 80% received folic acid during pregnancy, although most started supplementation in the second trimester of pregnancy.¹⁹

Another study reports that 65% of the women had had at least one unwanted pregnancy, 30.3% of them did not use a contraceptive method considered highly effective, correlated to lower income, younger age and less access to health insurance.²⁰ 14.5% used hormonal contraception in combination with enzyme-inducing anti-epileptic drugs that could compromise contraceptive efficacy and 50% did not take folic acid before or during pregnancy. Among users with reversible contraceptive methods, 40.6% discontinued it. When compared with the various anti-epileptic

drugs, combination with enzyme inducers most commonly caused the discontinuation of contraceptive methods. Only 25.4% of epileptic women had consulted with their neurologist regarding the choice of contraceptive method. The most common reasons for discontinuation were concern about reliability (13.9%), menstrual problems (13.5%) and increased seizures (8.6%).²¹ A study by Espinera et al. showed how counselling with the epileptologist may influence the choice of contraceptive method.²² Patients who did not desire to get pregnant, when advised about the intrauterine device as a first choice of birth control, were more willing to change to this contraceptive method and were more successful if this topic was addressed at the first neurological consultation. Another survey of neurologists from Brazil reported that 76% conducted family planning counseling, 81% recommended the use of copper intrauterine device, 60% simultaneously prescribed anticonvulsant drugs and hormonal contraception. Although 93% were aware that it could contraindicate the use of some contraceptives, they were unaware of the specific mechanism of interaction between both drugs.²³

During pregnancy, most epileptic women experience improvement of epilepsy, especially those treated with monotherapy and even remain seizure-free, as demonstrated by the European and International Registry of Antiepileptic Drugs and Pregnancy.²⁴ Only 2.6% of pregnant women needed to increase the dose or add a second anticonvulsant drug. In addition, there is a 4.9% risk of malformations in children of women receiving anticonvulsants during pregnancy versus 2.2% in the general healthy population. The use of an anticonvulsant drug in monotherapy doubles the risk, while combination therapy triples it. Prior folic acid supplementation is associated with neurodevelopmental benefits, where children born to pharmacologically treated epileptic mothers, without prior exposure to folic acid, are at increased risk of autistic traits, and this is inversely associated with maternal plasma folate concentration and folic acid dose. Therefore, when planning to get pregnant, it is recommended to start taking folic acid, at least until the first trimester of pregnancy.

CONCLUSION

Epilepsy in women is influenced by physiological variations in the secretion of sex hormones during the menstrual cycle in reproductive life. Therefore, it is important to know aspects of treatment that are

specific at this stage, such as the combination of anticonvulsant drugs and contraceptives, menstrual cycle-related seizures and their adverse effects. It is important to discuss with epileptic patients regarding the adverse effects, preference, efficacy, risks and benefits of the different methods of contraception, as well as the possible interactions with some anticonvulsant drugs in order to optimize the best method. With advancement in the pharmaceutical industry, we have a greater selection of anticonvulsant drugs, with better efficacy and tolerance and fewer drug interactions. The concept of monotherapy or rational combination therapy is important in women who are sexually active and who do not want to conceive, so they should be oriented on the most effective form of contraception.

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Depression Among Delivery Agents and its Determinants due to the COVID-19 Pandemic

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INTRODUCTION: The outbreak of the COVID-19 Pandemic has led to depression and anxiety in many people.

AIM: To assess depression and its determinants among delivery agents in the Union Territory of Jammu and Kashmir and Punjab State, India.

MATERIALS AND METHOD: The present study was online, cross sectional in nature and was conducted among 1248 delivery agents. The level of depression was assessed using a modified version of the Centre for Epidemiological studies- Depression scale (CES-D). Data analysis was done using descriptive statistics and student's independent t-test followed by the modified Bonferroni post-hoc test applied using SPSS version 21.0.

RESULTS: The overall prevalence of depression was found to be 53.7%; Most of the agents belonged to the lower class (59.3%) and Lower Middle Class (36.1%) group. The highest percentage of depression was observed as a result of mortgage (91.3%, non-significant), followed by the fear of losing their job (88.8%) due to the COVID-19 pandemic ($p=0.03$), and fear of getting COVID-19 (85.9%, non-significant difference). Delivery agents having their own transport seemed to have the lowest depression (26.7%, $p=0.04$).

CONCLUSION: Based on the results of the present study, governmental and industrial policies towards the benefit of the delivery agents is advised and during these testing times, assurance of job security and paid leaves in case of contracting COVID-19 should be beneficial.

KEYWORDS: COVID-19, Depression, Questionnaire

INTRODUCTION

The recent COVID pandemic has strained the economy and led to various job losses.¹ As people were forced to stay in the protection of homes during the lockdown, few essential services were still functional, namely healthcare, police, delivery of essential goods, etc. With a phased "unlock" protocol in India, people preferred to stay indoors and chose to order online for home delivery of goods. These deliveries were undertaken by delivery agents employed by various agencies.

An important fact to understand is the unpredictability of this disease as it leads to loss and control one's freedom.² Such conditions lead to certain mental and social disorders that could disrupt one's activities; and this, coupled with the constant fear of getting sick aggravates/worsens the situation. It has been observed that during pandemics various communities experience stress and anxiety to some extent, and disorders of psychological nature are widespread.³ Literature also suggests that people kept in isolation and/or quarantine experience increased levels of anxiety, anger, confusion, and/or stress.⁴

The relationship between environment and the onset of depression and depressive symptoms are more prevalent among workers; especially among those with

job stress, low-skill work and a lower job status.⁵ The reasons for the same can be attributed to high expectations from the job, a lesser or lower social support in the workplace, imbalances in effort put and reward(s) gained, job dissatisfaction and fear of losing one's job.⁶

One of the most exposed groups to the COVID-19 virus have been the delivery agents as they deliver packages/food etc from door to door. Not only they have to deliver goods on time, they are constantly on calls, are on the move constantly and are at various risks. Hence, the present study was undertaken with the aim to assess depression and its determinants among delivery agents in the Union Territory of Jammu and Kashmir and Punjab State, India.

MATERIALS AND METHOD

An online, cross sectional study was conducted by distributing a questionnaire via google forms among various app-based delivery agents (couriers, food delivery, etc) based in the Union Territory of Jammu and Kashmir and Punjab State, India from 25th June, 2020 to 1st December, 2020. Ethical approval was obtained from the study sites prior to data collection, and consent was assumed as completing the survey



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questions. Data was obtained via simple random sampling as well as snowball sampling as the link was distributed to known delivery agents and they were asked to forward the same to their colleagues. Participation in the study was purely voluntary and the delivery agents were free to leave filling the questionnaire at any time. They were assured of the confidentiality of their data and no personal details were collected.

Data was obtained through the modified version of the Centre for Epidemiological studies- Depression scale (CES-D)⁷, was close ended (pre-validated and pre-tested) and had a Cronbach's Alpha (α) of 0.76. The questionnaire was translated and back-translated in Hindi and Punjabi by a language expert. The questionnaire was distributed in both languages (with separate links to both), had 26 questions divided into five sections.

Statistics: Descriptive statistics were applied; data was presented using tables and graphs. The student's independent t-test followed by the modified Bonferroni post-hoc test was used to find the association between the variables using SPSS version 21.0.

RESULTS

At the end of the study period, a total of 1248 completed responses were obtained and their characteristics are shown in table 1. Most of the delivery agents (56.2%) belonged to the age group of 21–30 years followed by 18–21 years (26.1). Most of the agents belonged to the lower class (59.3%) and lower middle class (36.1%).

Age (In Years)	n,%
18-21	326(26.1)
21-30	701(56.2)
30-40	211(16.9)
>40	10(0.8)
Socio economic class	
Upper Class 2 (0.4)	0(0)
Upper Middle 16 (2.8)	1(0.2)
Middle 187 (32.8)	55(4.4)
Lower Middle 273 (47.9)	451(36.1)
Lower Class 92 (16.1)	741(59.3)

Table 1. Distribution of study subjects according to age and socio-economic status

The overall percentage of depression among delivery agents was found to be 53.7%, with the highest

percentage of depression was observed as a result of mortgage (91.3%, non-significant difference), followed by the fear of losing their job (88.8%) due to the COVID-19 pandemic and it was found to be significant ($p=0.03$), and the fear of getting COVID-19 as a result of their job (85.9%, non-significant difference). Delivery agents having their own transport seemed to have the lowest depression (26.7%, $p=0.04$) and as seen in table 2.

The sources of loan availed and it's relation with depression in the 563 (45.1%) of delivery agents is depicted in table 3. Those availing loans from a private lender (63%), multiple sources (62.6%) and close relative(s) (50.2%) showed to have the maximum depression, while the least was depression was observed among those availing loan from a nationalized bank (48.7%). All the observations were found to be statistically significant ($p=0.02$).

DISCUSSION

Through the findings of the present study, it was revealed that in these COVID-19 times, 53.7% delivery agents in the Union Territory of Jammu and Kashmir and Punjab State, India were facing a significant amount of depression especially those having loan (60.2%) or mortgage (91.3%). A high percentage of depression was also seen among the delivery agents due the fear of getting COVID-19 or job loss due to it.

The overall percentage of depression was found to be 53.7% this is on the higher side as compared to farmers (33.9%)⁶ and lower in comparison to cab drivers (60.5%)⁸ and auto-rickshaw drivers (90%).⁹ It is to note that the present study was done during the COVID-19 pandemic and hence, the reported percentages of depression could have increased. As per Bueno-Notivol J. et al., a pooled 25% of depression in community based studies was seven times higher as compared to 3.44% in 2017 and this does show light on the effect of COVID-19 on the mental health of people.¹⁰

Only 26.7% of delivery agents having their own transport reported depression and the association was found to be significant. As per results of a systematic review by Amit N et al.¹¹, evidence was presented to support the unfortunate fact that being in debt is related to depression, anxiety, stress, or suicide ideation among Asian participants. In the same context, farmers who are caught in high debt traps are prone to mental health problems and suicides.^{6,12}

Variable	Depression		n,%	p- value
	Present	Absent		
Overall Depression	666 (53.7)	582 (46.3)	1248(100%)	0.01*
Own Transport				
Present	223 (26.7)	613 (73.3)	836 (66.6)	0.04*
Absent	100(24.3)	312 (75.7)	412(33.1)	
Loan				
Present	339(60.2)	224(39.8)	563(45.1)	0.04*
Absent	201(29.3)	484(70.7)	685(54.9)	
Mortgage				
Present	188(91.3)	18(8.7)	206(16.5)	NS
Absent	300(24.0)	948(76)	1042(83.5)	
Fear of getting COVID-19				
Present	699(85.9)	114(14.1)	813(65.1)	NS
Absent	123(28.3)	312(71.7)	435(34.9)	
Fear of Loss of Job (due to COVID-19)				
Present	891(88.8)	112 (11.2)	1003 (80.4)	0.03*
Absent	183(74.7)	62 (25.3)	245(19.6)	

Table 2. Illustrating the association between depression and its determinants (Independent samples t-test : P-value <0.05 is significant)

Fear of contracting COVID-19 and fear of loss of jobs was reported by 85.9% and 88.8% of the delivery agents respectively. Threat to job security was predictive of depression and cognitive function in the entire sample such that those with higher levels of perceived job security had lower depression and better cognitive function. This was supported by the findings of Mahmud MS et al.¹³ whose empirical results stated that due to the outbreak of COVID-19, and its fear, people are becoming depressed and anxious about their future career which has been attributed in creating a long-term, negative effect on human psychology.

Source of Loan	Depression		n,%	p- value
	Present	Absent		
Nationalized Bank	92(48.7)	97(51.3)	189(33.6)	0.02*
Private Lender	63(63)	37(37)	100(17.8)	
Multiple Sources	45(62.6)	28(38.4)	73(12.9)	
Close Relative(s)	101(50.2)	100(49.8)	201(35.7)	

Table 3. Association between source of loan and depression

This study is prone to certain limitations, the first being the limited number of literature on the effects of

COVID-19 on depression among people. A comprehensive literature search did not reveal any study pertaining to depression among delivery agents. Therefore, comparisons were made with other populations sharing almost the same experience (cab drivers, truck drivers, farmers, etc). Second, due to the self-reported nature of the questionnaire, it is possible that the delivery agents might have either “under” or “over” reported their feelings regarding depression. However, due to the nature of the study and keeping various factors in account (data taken from delivery agents pan-India, assurance of data confidentiality, voluntary participation), the results can be generalized for all delivery riders.

CONCLUSION

The results of the present study showed that depression among delivery agents is on the higher side and in light of the current pandemic situation, the government and employers should keep certain checks in place, assure the delivery agents regarding their job, thus alleviating future “job-related anxiety”. The riders should be provided with financial assistance and “paid” leaves in case they contract COVID-19 while performing their duty with due diligence.

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