

# History of Infection Outbreaks and Mental Health Issues: Awareness for Corona-virus Neuropsychiatric Coverage

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## ABSTRACT

The infection outbreaks are not novel but have long historical roots in diverse countries of the world. The infection outbreaks not merely imparted a negative impact on physical health but also adversely affected mental health issues. According to a massive body of researches, the rate of mental health issue among the general population found to be higher. As the ratio of PTSD during the Ebola Virus was 76.4% and depression during SARS-CoV-1 reported as (32.4%). However, the psychiatric morbidity during H1N1 was found to be (8.0%). The causes of neuropsychiatric complication or mental health issues during previous outbreaks were cultural psychological and social issues. In particular, pharmacological treatment found to be the most prevalent reason for developing neuropsychiatric complication or mental health issues. As during all infection outbreaks, multiple drugs and vaccinations have been used to control the spread of viral diseases. The current study provides a detailed description of how the drugs

and vaccination led to neuropsychiatric complication. The PICO method was used to design the research question and through the PRISMA technique, around 15 studies have been included in the current study. The findings of the current study reported substantial neuropsychiatric complication due to the persistent use of drugs and vaccination. The current study finding spread the awareness for coronavirus and related infection coverage.

**Key words:** Infection outbreak, Mental health issues, Neuropsychiatric complication, COVID-19, Medication, Vaccine

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## INTRODUCTION

Infection outbreaks have enormously disrupted human lives and caused a substantial transformation in normal routine life. The infection outbreaks are not novel but have long historical roots in diverse countries of the world (Huremovic D, 2019). Since historical times, the infectious outbreak brings about massive destructions. Apart from disturbed routine, the infection outbreaks have imparted substantial adverse impact on the physical as well as mental health of the people. The physical effects lead to disabilities to high mortality rates and literature is enriched with the evidenced-based studies highlighted the high ratio of mental health issue during the diverse outbreak (Rehman S and Lela U, 2021). According to a massive body of researches, mental health issue among the general population found to be higher.

As the ratio of PTSD during the Ebola Virus was 76.4% and the prevalence of depression during SARS-CoV-1 reported as (32.4%). However, the psychiatric morbidity during H1N1 was (8.0%). Furthermore, the mental health issues among medical staff and survivors were 1.5-75.3% and 13.0 to 94.4% respectively during the previous pandemic (Zürcher SJ, *et al.*, 2020). The magnitude of mental health issues during COVID-19 is also found to be higher like other infection outbreak. According to a recent meta-analysis, the pooled prevalence of insomnia, distress, anxiety and depression during COVID-19 reported as 37.9%, 41.1%, 31.9%, and 31.4% (Wu T, *et al.*, 2021).

The enormity of mental health issues has been devastating during previous pandemics. Therefore the psychologists, physicians, psychiatrist and other medical staff took a toll to mitigate the obnoxious impact of infection outbreak (Rehman S and Lela U, 2020). Several studies indicated that psychological,

mental, and psychical support during the previous pandemic found to be associated with positive mental, psychological and physical health (Chow EJ, *et al.*, 2019). The victim and survivors and their family members reported multiple psychological issues but with the help of the practitioner, they overcome their traumas (Xiong J, *et al.*, 2020). Unfortunately, the magnitude of mental health issues or neuropsychiatric complication during COVID-19 is high and people are taking persistent medication and vaccination to combat the infection.

Unfortunately, the literature reported that persistent exposure to medication and vaccination leads to neuropsychiatric complications (Gunaydin C and Bilge SS, 2018). The evidence-based data is necessary to investigate to validate the connection between medication and neuropsychiatric complication.

Furthermore, there is a dire need to take more precaution and provision physical, psychological and mental health assistance to control the adverse impact of infectious diseases. It can only be done after the identification of nature and levels of management plan during previous infection outbreak. Therefore the current study provides an interesting but alarming picture of infection outbreak and possible management and pharmacological modalities and their side effects for devising a better management plan to combat future and current viral diseases.

## METHODS

### Development of research question

The authentic and logical research question enhance the worth of the study findings. Hence PICO technique was used to generate an authentic research question. PICO is an acronym P (Population), I (Issue), C (Comparison/ not applicable), and O (Outcome). The above mentioned four steps facilitated in developing

the logical research question. The P or population refers to (world-wide victim, survivors or general population), issues (Infection outbreak), and outcome (management modalities.). PICO is valid and authentic strategy to research and review articles considering the relevance of research question. All the component of PICO generated a reliable and valid research question.

What is the history of infection outbreak and how it will help in coverage of COVID-19)?

**Search strategies**

The search strategies was to use the relevant key terms along with the Boolean words i.e. “OR” and “AND”. Infectious outbreak and mental health issues, psychiatry of pandemic, historical pandemic and neuropsychiatric complications, mental health response to infectious diseases, viral diseases and psychiatry and COVID-19 phrases have been used to find the relevant article. The following electronic databases have been used in the current study (Figure 1).

- PubMed
- Scopus
- Goggle Scholar
- NCBI
- Ovid
- CENTRAL
- JSTORE
- Science Direct

**Inclusion and exclusion criteria**

The inclusion and exclusion criteria have been listed below.

- Merely the medical, psychiatric and psychological articles have been included in the current study.
- The published articles from 2018-2021 have been included in the review process.

**PRISMA Chart**

The PRISMA flow chart has been used for the screening of the articles (Moher D, et al., 2010).

**Quality assessment**

The Health Evidence Quality Assessment Tool was used to assess the quality of the articles (Practice tools, 2018). Primarily the articles with high number 8-9 or moderate number (6-7) have been included in the current study.

**Data extraction**

After the documentation of the chosen article into study characteristic table, the underlying management and assessment themes have been extracted.

In sum, the current study would provide an overview of the assessment and management of the previous and current infection outbreak. The implications will be discussed in reference to develop policies to manage the pre and post pandemic effect for future outbreak.

**RESULTS**

Influenza, Infectious mononucleosis, HIV/AIDS, Rubella, Spanish flu, Swine flu H1N1, Avian influenza H7H9, Middle East respiratory syndrome coronavirus (MERS-CoV), SARS-COV-1 and COVID-19 originated at China, South Africa and the United States. The high prevalence and mortality rates have been found globally. The management plan for all infectious outbreak has been found as isolation and quarantine (Table 1).

The Oseltamivir, LopavinaVir/ritonavir, Ribavirin, Glycyrrhizin, Chloroquine, Interferons, Monoclonal antibody therapy, zanamivir, antiviral therapies, Antipyretics and anti-inflammatory medications prophylactic vaccines, Ganciclovir, valganciclovir, Antiviral medication, neuraminidase inhibitors (NAIs), cap-dependent endonuclease inhibitor, adamantanes ZMapp, Interferon and ribavirin have been reported as the most widely used medicine. DNA, Live attenuated vaccine, viral vector vaccine and Adenovirus Type 5 Vaccine were the frequently used vaccines (Table 2).

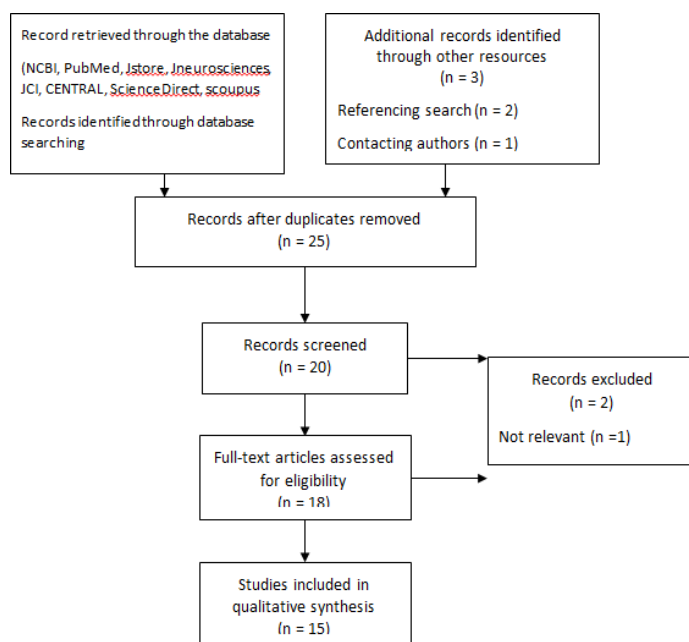


Figure 1: PRISMA flow chart for the selection of articles to be reviewed

Table 1: The following table shows the infection, epidemiology and medication

Authors (Year)	Infection	Originated	Epidemiology	Symptoms	Management	Medications or vaccination
WLE/NBI	WLE/NBI	WLE/NBI	WLE/NBI	WLE/NBI	WLE/NBI	WLE/NBI
(Khalafalla, <i>et al.</i> , 2017)	Ebola virus	South Africa	20% to 80% Mortality	Fever, vomiting, diarrhea, fatigue, headache, loss of appetite, bleeding	isolation	ZMapp, Interferon and ribavirin Adenovirus Type 5 Vaccine
(Chen LH and Wilson ME, 2020)	Yellow Fever	Africa	60,000 deaths	Fever, Headache, nausea, Dizziness, loss of appetite	Sterile insect technology, Insecticide-treated materials, dose-sparing strategies	Arvicidal agents Vector control
(Chow EJ, <i>et al.</i> , 2019)	Influenza	United States	291,000-646,000 respiratory deaths	pneumonia, and respiratory failure	Self-limiting	Antiviral medication, neuraminidase inhibitors (NAIs) (e.g., oral oseltamivir, inhaled zanamivir, and intravenous peramivir); cap-dependent endonuclease inhibitor (baloxavirmarboxil); and adamantanes (e.g., amantadine and rimantadine)
(Mohseni M, <i>et al.</i> , 2021)	Infectious mononucleosis	US	95% of the population worldwide	Cervical lymph node enlargement, sore throat, fever and fatigue, tonsillar pharyngitis	Touching or mating restriction	Antipyretics and anti-inflammatory medications prophylactic vaccines, Ganciclovir and valganciclovir
(Simon V, <i>et al.</i> , 2006)	HIV/AIDS	South Africa	25 million mortality	Skin rash, headache, fatigue, herpes zoster,	Touching or mating restriction	Single compound tablets, Fixed-dose combination tablets DNA vaccine
(Grant GB, <i>et al.</i> , 2017)	Rubella	6 countries	(78%) of 194 countries	Mild fever and rash illness during pregnancy	Vaccination	rubella-containing vaccine (RCV), measles-containing vaccine
(Martini M, <i>et al.</i> , 2017)	Spanish Flu	Spain	50 million mortality cases worldwide	Coughing, fever and headaches	Quarantine or isolation	no vaccines or antivirals
(Dandagi GL and Byahatti SM, 2011)	Swine Flu H1N1	China	30,000 confirmed cases, 1235 Mortality	Sore throat, chills, fever, muscle pains, severe headache, coughing, general discomfort and coughing	Inhibition of smoking, close contact with live pigs, use of gloves and social distancing	Oseltamivirders, Zanamivir Adults Vaxiflu-S33 vaccine, Nasovac vaccine
(Tanner WD, <i>et al.</i> , 2015)	Avain Influenza H7H9	China	20,000	Acute respiratory tract infection	Social distancing	Antiviral drug, Oseltamivir, zanamivir
(Tanner WD, <i>et al.</i> , 2015)	Middle East respiratory syndrome coronavirus (MERS-CoV)	Jordan	43%	High fever, cough and acute lower respiratory symptoms	Social distancing	Ribavirin, Lopinavir/ritonavir
(Tong TR, 2006)	SARS-CoV-1	10% of the 8000 mortality	China	Acute respiratory distress and respiratory failure	Isolation	Ribavirin Glycyrrhizin, Chloroquine, Interferons, Monoclonal antibody therapy
(Rehman S and Lela U, 2021)	COVID-19	2,74,488 Mortality	China	Respiratory issue, sore throat, fever, cold	Isolation and Quarantine	Oseltamivir, Lopinavir/ritonavir Live Attenuated Vaccine Viral vector vaccine

**Table 2: The drugs and vaccines have been used to treat viral infections and the below mentioned suggested the massive body of neuropsychiatric complication or mental health issues due to the persistent use of medication.**

Infection disease	Drug/Vaccine	Neuropsychiatric complication and mental health issues
Ebola Virus	ZMapp, interferon and ribavirin Adenovirus Type 5 Vector Vaccine	Interferon causes depression, suicidal behavior, manic syndrome, anxiety disorders, psychotic disorders and delirium associated with an array of unspecific psychiatric symptoms: fatigue, irritability, psycho-motor retardation, decreased libido, insomnia, concentration difficulties and attention deficit problem (Coman HG, <i>et al.</i> , 2013). Ribavirin develops depression, anxiety and poor life quality (Rehman S and Lela U, 2021). No psychiatric complication was found to be associated with zMapp. Adenovirus Type 5 Vector vaccines develop depression, hallucination and disorganized thinking patterns.
Yellow fever	Arvicidal agents vector control	Antiviral agents lead to psychiatric and behavioral abnormalities.
Influenza	Antiviral medication, neuraminidase inhibitors (NAIs) (e.g., oral oseltamivir, inhaled zanamivir, and intravenous peramivir); cap-dependent endonuclease inhibitor (baloxavirmarboxil); and adamantanes (e.g., amantadine and rimantadine	Antiviral agents lead to psychiatric and behavioral abnormalities (Cespedes MS and Aberg JA, 2016). Nueuraaminidase e.g. zannmivir and peramivir leads to hallucinations Oseltamivir causes nausea, behavioural issue, delirium, convulsion, panic attacks, loss of consciousness and depressive mood (Han N, <i>et al.</i> , 2020) Baloxavirmarboxil and adamantine cause disturbed consciousness, coma, delirium, hallucinations, delusions, and confusion (PMDA, 2018).
Infectious mononucleosis	Antipyretics and anti-inflammatory medications	Anti-inflammatory and antipyretics leads to Parkinson’s, Schizophrenia and Alzheimer (Gunaydin C and Bilge SS, 2018)
HIV/AIDS Swine Flu H1N1	Efavirenz Single compound tablets, Fixed-dose combination tablets DNA vaccine Oseltamivolders, Zanamivir Adults Vaxiflu-S33 vaccine, Nasovac vaccine	Efavirenz causes dizziness, insomnia, headache, abnormal dreams and impaired concentration dizziness, insomnia, headache, abnormal dreams and impaired concentration (Rawal G, <i>et al.</i> , 2016). DNA vaccine Oseltamivir causes nausea, behavioural issue, delirium, convulsion, panic attacks, loss of consciousness and depressive mood (Rehman S and Lela U, 2021). zannmivir and peramivir leads to hallucinations.
Middle East respiratory syndrome coronavirus (MERS-CoV) SARS-CoV-1	Ribavirin, Lopinavir/ritonavir Ribavirin Chloroquine, Interferons, Monoclonal antibody therapy	Ribavirin develops depression, anxiety and poor life quality Lopinavir/ritonavir leads to delusion, dizziness, anxiety, and nightmare (Rehman S and Lela U, 2021). Ribavirin causes depression, anxiety and poor life quality Chlorine causes psychosis (Rehman S and Lela U, 2021). Chloroquine and interferon develops psychosis, insomnia, visual and auditory hallucination (Gaida R, <i>et al.</i> , 2016). Monoclonal antibody develops schizophrenia and psychosis (Maxwell NM, <i>et al.</i> , 2015).
COVID-19	Oseltamivir Lopinavir/ritonavir(LPV/r) Favipiravir Ribavirin COVAX19, bac-TRL-spike, Covaxin (BBV152), Zy-CoV-D, SCB2019, GX-19 and DNA plasmid Viral vector vaccine Live Attenuated Vaccine	Oseltamivir caused nausea, behavioural issue, delirium, convulsion, panic attacks, loss of consciousness and depressive mood Lopinavir/ritonavir leads to delusion, dizziness, anxiety, and nightmare (Rehman S and Lela U, 2021). Not only medication but diverse vaccines have also been used for COVID-19 management. The names of the vaccines are mRNA1273, COVAX19, bac-TRL-spike, Covaxin (BBV152), ZyCoV-D, SCB2019, GX-19 and DNA. Hence, the Lentiviral Minigiene and pathogen-specific aAPC vaccine is expected to be available in 2024. The previous pandemic vaccination found to be detrimental for the metal health of the people. Hence the current and upcoming vaccine must be checked before its application (Rehman S and Lela U, 2021) Viral vector vaccine led to Alzheimer and Parkinson’s disease. Live Attenuated Vaccine leads to mental health issues.

## DISCUSSION

The current study highlighted the most prevalent previous infection outbreak during human history. Nature, symptoms, management and pharmaceuticals interventions have been discussed in details. The retrieved information would be helpful in the management of current disease COVID-19 and upcoming viral diseases. The differences and similarities help in devising better management plan to mitigate the obnoxious viral infections.

### Prevalence and symptoms

The prevalence of infection outbreaks have been high and caused substantial mortality throughout the world. The high mortality rate was reported despite taking crucial safety measures. The current study suggested the huge prevalence and mortality rate during Ebola virus (20%-80%), yellow fever (60,000), influenza (291,000-646,000), Infectious mononucleosis (90%), HIV/AIDS (25 million), Rubella (78%), Spanish Flu (50 million). A substantial number of people died during diverse pandemics; hence it can be assumed that the family members of the survivors undergo many psychological and emotional disturbances.

### Management

All infection outbreaks were transmittable diseases and as a management modality, social distancing was imposed as a safety measure. Apart from social distancing, various types of drugs and vaccination have been used.

### Drugs and vaccine

Multiple vaccine and drugs have been manufactured during.

#### Ribavirin

The ribavirin medication has been used for Ebola Virus, Middle East respiratory syndrome coronavirus (MERS-CoV), SARS-CoV-1 infection and COVID-19. The recent studies suggested that ribavirin is associated with neuropsychiatric complications such as anxiety, depression and poor quality of life (Coman HG, *et al.*, 2013).

#### Interferon drug

Ebola virus and SARS-CoV-1 have also been treated with the use of interferon drug. According to the literature, it is reported to be associated with anxiety disorder, manic syndrome, depression, delirium, psychomotor retardation, insomnia, and attention deficit hyperactivity disorder [2].

#### Oseltamivir

Another drug Oseltamivir has been used to treat various infections i.e. Swine Flu H1N1 and influenza. According to a massive body of researches, the Oseltamivir was also leading to many neuropsychiatric complications and the most prominent were convulsion, nausea, panic attacks, depressive mood, loss of consciousness and delirium [2]. Convenience-Medication outside hospital settings. The therapy could be terminated easily at any stage. It offers suitability for personal administration. It is non-invasive, keeping away from the inconveniences of the parental therapy.

#### Lopinavir/ritonavir

Lopinavir/ritonavir used to treat Middle East respiratory syndrome coronavirus (MERS-CoV) and COVID-19. It leads to delusion, dizziness, anxiety, and nightmare [2].

#### Zanamivir adults

Zanamivir has been used to treat Influenza and found to be associated with hallucinations (Cespedes MS and Aberg JA, 2016). Transdermal patch is cost effective, due to easy techniques and safe materials which increase productivity.

#### Chloroquine

Chloroquine and Interferon was manufactured to treat SARS-CoV-1 and it has been observed through literature that both medicines origins psychosis, insomnia, visual and auditory hallucination (Rawal G, *et al.*, 2016).

#### Monoclonal antibody therapy

Monoclonal antibody often used to treat SARS-CoV-1 and develops schizophrenia and psychosis (Gaida R, *et al.*, 2016).

#### Interferons

Interferon was manufactured to treat SARS-CoV-1 and it has been observed through literature that both medicines origins psychosis, insomnia, visual and auditory hallucination (Rawal G, *et al.*, 2016).

#### Efavirenz-HIV/AIDS

Single compound tablets, fixed-dose combination tablets has been effectively used for the treatment of HIV/AIDS. Efavirenz causes dizziness, insomnia, headache, abnormal dreams and impaired concentration dizziness, insomnia, headache, abnormal dreams and impaired concentration (Rawal G, *et al.*, 2016).

#### Antiviral medication

Antiviral agents used to treat Influenza and Yellow fever and leads to psychiatric and behavioural abnormalities. Apart from antiviral agent neuraminidase inhibitors (NAIs) (e.g., oral oseltamivir, inhaled zanamivir, and intravenous peramivir); Nueuraaminidase e.g. zanamivir and peramivir also used to treat influenza and led to hallucinations. cap-dependent endonuclease inhibitor (baloxavirmarboxil); and adamantanes (e.g., amantadine and rimantadine. Baloxavirmarboxil and adamantine used to treat influenza and cause disturbed consciousness, coma, delirium, hallucinations, delusions, and confusion (PMDA, 2018).

#### Vaccination

The names of the vaccines are mRNA1273, COVAX19, bac-TRL-spike, Covaxin (BBV152), ZyCoV-D, SCB2019, GX-19 and DNA. Hence, the Lentiviral Minigiene and pathogen-specific aAPC vaccine are expected to be available in 2024 [2].

Adenovirus Type 5 Vector/Adenovirus type 5 vector vaccines have been manufactured to control the spread of the Ebola Virus and SARS-COV-2. The recent literature depicted that the adenovirus type 5 vector vaccines leads to hallucination, depression and disorganized thinking pattern [2].

#### Viral vector vaccine

Viral vector vaccine is effective for COVID-19 management but found to be associated with Alzheimer and Parkinson disease (Essali N, *et al.*, 2019).

mRNA. mRNA high tracked FDA approved vaccine to control the spread of COVID-19. The mRNA-1273 and BNT162b1 are the two forms of mRNA vaccine and effective within 25 to 10 µg dose (Choudhury S, *et al.*, 2016).

#### DNA vaccine

A DNA vaccine is the main innovative drug to stimulate adaptive immune functioning within seven days against HIV, Nipah virus, Lassa virus and Filovirus (Essali N, *et al.*, 2019).

#### Live attenuated vaccine (LAV)

LAV inserted through the nasal spray and deletes the NS1 gene. Live attenuated gene is effective to spread the COVID-19 infection. According to literature the persistent use of live attenuated vaccine causes neuropsychiatric complication. The DNA and Live attenuated vaccina-

tion are not associated with any neuropsychiatric complication. However, the previous pandemic vaccination found to be detrimental to the mental health of the people. Hence the current and upcoming vaccine must be checked before its application (Moderna Inc, 2020).

## CONCLUSION

Infection outbreak has been widespread throughout the human history and brings about substantial issues. Hence with the help of a medical, psychological and psychiatric practitioner, the obnoxious consequences have been controlled. Despite huge improvement in management modalities, since more attention from medical, psychological, pharmacological practitioners are required. As the medications and vaccination are still creating neuropsychiatric complication, therefore more advancement in this area is needed. Furthermore, we should be papered to handle more viral disaster with the best medication, equipment and pre-and post-pandemic management.

## THE FUNDING AND DISCLOSURE

No funding is available.

## CONFLICT OF INTEREST

The authors declared no interest.

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