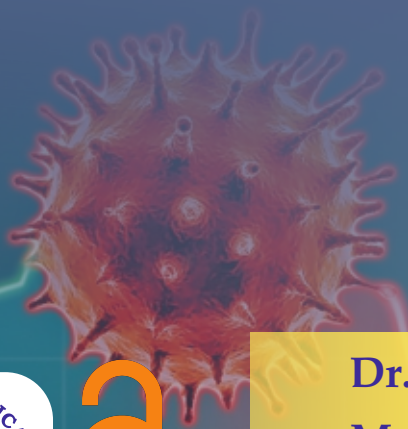
Pandemic Corona Virus vs. Epidemic, and Endemic Virus Diseases: Present, Past, and Future Directions



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INNOVATIVE PUBLICATION

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ISBN : 978-93-91208-61-5

Edition : First, 2022

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Dedication

I dedicated this book to my parents, family members, relatives, wife and son because they gave me strength, focus of heal and courage to share my pharmacy knowledge for successful completion of this book.

I dedicate this book to my all well-wishers who always encourage me an achieving higher goal and motivating me for writing this type of book for medical and paramedical education and research.

Foreword

There are very limited textbooks covering the most advanced aspects of **"Pandemic Corona Virus vs Epidemic, Endemic and Post Pandemic Virus Diseases: Present, Past, and Future Directions."** The need for such a book written in a simple, direct, lucid, and relevant language was appropriately realized. The excellent efforts of Editor-in-Chief, Dr. Suryakanta Swain and co-editors Mr. Bikash Ranjan Jena, and Mr. Debashis Ghose, have resulted in a faithful publication of this textbook covering significant areas related to the pandemic, epidemic, and endemic virus diseases and suggested allopathic, homeopathic, ayurvedic, home remedy, convalescent plasma therapy, etc., for novel coronavirus treatments and prevention guidelines. The current global data for the preclinical and clinical status of drugs-approved vaccines and few vaccines under development for coronavirus infections, and the impact of post-covid-19 on science and technology, current and future directions in academic and industrial research. The subject matter is written with adequate information about the pandemic, epidemic, endemic and post pandemic virus diseases and theoretical background and presented simply for better understanding among the medical, paramedical students, researchers, and scientists across the globe. As a reader, whether you are a student, teacher in India, or abroad, I hope that researchers and academicians would be pleased with this textbook, which should add to your current knowledge, understanding, and insights of theoretical and practical concepts of this selected contents covered. It is a matter of immense pleasure for me to write a foreword for this textbook. I wish the editor-in-chief and co-editors great success in this combined venture. I hope their contribution to medical and paramedical or pharmaceutical sciences literature will contribute endlessly. The chief editor of this textbook, Dr. Suryakanta Swain, is a well-established scientist with extensive academic teaching and research knowledge in pharmaceutical or health sciences. Dr. Suryakanta Swain has been researching pharmaceutical targeting drug delivery systems by applications of quality by design tools for the last 14 years and has patented and published articles of study and review, invited editorials or opinion articles, short communications, thematic issues, national and international books and book chapters in reputed publishers.

Dr. P. K. Mishra,

The Vice-Chancellor
The Assam Kaziranga University, Jorhat, Assam, India

The Readership of the Book

The significant features of this book include:

- Theoretical discussions of the knowledge and information sources about pandemic corona virus vs epidemic, endemic virus and post pandemic diseases among university students of UG, PG, Ph.D. scholars and research scientist.
- This textbook is written as per the current COVID-19 pandemic vs Epidemic, Endemic and Post Pandemic Virus Diseases is a significant challenge to the health of the world population; therefore, these results assessing students' knowledge provide an essential baseline for planning required educational interventions such as types of pandemic corona virus vs epidemic, endemic virus and post pandemic diseases and their treatment and self-quarantine. This textbook also covers the public health-related information and impact of post covid pandemic situation and implementation of protective health measures, including positive hygienic practices such as hand washing to reduce the risk of COVID-19.
- This book also critically discussed the significant areas related to the pandemic corona virus vs epidemic, endemic virus and post pandemic diseases and suggested allopathic, homeopathic, ayurvedic, home remedy, convalescent plasma therapy, etc., for novel coronavirus treatments and prevention guidelines. Apart from that, this textbook eye catch on the current global data for the preclinical and clinical status of drugs-approved vaccines and few vaccines under development for coronavirus infections, and the impact of post-COVID-19 on science and technology, current and future directions in academic and industrial research which will be exceptional as compared to already existing textbooks in a lucid and students friendly for easy understanding and applications. The post-COVID-19 recovery patients or vaccination people's worldwide associated side effects, and adverse drug reactions such as Stevens-Johnson syndrome, Toxic epidermal necrolysis, Mucormycosis, White fungus, Yellow fungus, Zika, Delta, Omicron, IHU and Delmicron Virus are significant blockbusters of this second and third waves of current and post covid situation.
- Concise and advanced information and tabulation.
- Well-explained diagrams.

Editor-in-Chief Brief Biosketch

Dr. Suryakanta Swain

Dr. Suryakanta Swain is currently Professor and Dean Research, Associate/Acting Dean, Founder Principal-cum-Head (Pharmacy), School of Health Sciences at The Assam Kaziranga University, Jorhat, Assam, India. He has 14+ years of rich experience with a blend of teaching, research, and administration. He completed B. Pharm Berhampur University and M. Pharm Biju Patnaik University of Technology (B.P.U.T), Odisha, by qualifying National-level exams such as GATE and NIPER. He completed his Ph. D (Pharmacy) from Berhampur University, Odisha. His Doctoral Research work is on the Design and Evaluation of Mucoadhesive Drug Delivery System of Some Selected Drugs (Rabeprazole Sodium and Venlafaxine HCl) to improve oral Bioavailability. Dr. Swain researches QbD enabled mucoadhesive drug delivery systems, self-emulsifying drug delivery systems, gastro-retentive drug delivery systems, and targeted drug delivery systems. Prof. Swain has published 105 Research/Review/Editorial/ Opinion Articles of Scopus/SCI/Pubmed/SCI-E/JCR/PCI/UGC-care listed International/ National Journals of Publishers such as Springer/Elsevier/Taylor and Francis/Informa Health care/Bentham/Dove Press etc. with highest Journal (Acta Pharmaceutica Sinica B) of Impact factor of 11.413 with more than 1700 Google Scholar citations (H-index=18 and i10-index=34) and 900 Scopus citations (H-index=13), and 27 Research Gate Score (1500 citations). Dr. Swain also Edited 6 National Textbooks as per the New PCI Syllabus of M.Pharm and B.Pharm Courses. He also published 7 International Textbooks and 35 National Book chapters, Received 1 Indian Patent Grant and Published 1 Indian Patent from the Ministry of Commerce, Govt. of India and Patent Innovation already Initiated for Technology Transfer with Pharmaceutical Company and such innovation are also Coverage with Times of India E-News Paper. Prof. Swain has permanent Advisory/Editorial/ Reviewer Board Members in more than 100 National/International Journals and Ph.D. Research Supervisors/UG/PG/Pharm-D Practical External Examiners/Ph.D. Adjudicators/ Examiner and Members of Board of Studies (Co-Chairman)/Academic Council/IQAC/ UDRC/NACC as a Chief School level/NBA coordinator/R & D/External Expert Member of Selection Committee of various Universities such as The Assam Kaziranga University/ Acharya Nagarjuna University/JNTU-Kakinada/JNTU-Hyderabad/Annamalai University/ Biju Patnaik University of Technology/Berhampur University/GITAM University/

Centurion University/Singhania University/AMRI University/SOA University, etc. He is presently guiding 10 Ph.D. Research Scholars and already guided 60+ M. Pharmacy, 40 + B.Pharmacy, and 7 Pharm D 5th year Clinical/Hospital-based projects. Dr. Swain has received several awards, such as Emerging Leader in Health and Medical Sciences Award, Prof. M.L. Khorana Memorial Award, Rajni Bhai V. Patel PharmInnova Competition Award, etc. Dr. Swain has delivered and attended more than 100 AICTE/DST/DBT/PCI/ICMR sponsored at National and International Seminars/Conferences/Workshops/FDPs/SDPs as an Invited Speaker/Resource Person/Guest Lecture/Guest of Honor/Adjudicators etc. He is the life member of several professional bodies such as FIC/APTI/IPA/HAB/IPGA/ISPOR and Members of Reviewer MS Research Australia, Research Management Council, Australia, 2014/Member of Healthcare Advisory Board (HAB), Canada, 2014/ABM International Science and Technology Development INC, Baltimore, USA/Community Member of the Global Community of Information Professionals, Canada 2013/Member of the Pharmacy One Source Community, US 2013/Asian Science Council Editor, Canada/Bentham Science Ambassador/Registered Member of Odisha State Board of Pharmacy Council, 2008/Member of PCI, etc. Dr. Swain is now heading 14 different Programmes and 9 Departments under The Assam Kaziranga University, Jorhat, Assam. He has recently set up six laboratories infrastructure and introduced D and B. Pharmacy new courses and 4 new emerging PG programmes: Master in Optometry, M.Sc. Microbiology, Master in MLT (Medical Microbiology)/MPT (Neurology/Orthopedics), increased 100 intakes of B.Pharm course and designed the new course structures and syllabi for North Eastern Region of India.

Preface

Our prime intention is to cover the contents of the book as comprehensively as possible. Thus, we are delighted to introduce this textbook, **"Pandemic Corona Virus vs Epidemic, Endemic and Post Pandemic Virus Diseases: Present, Past, and Future Directions."** The present book is unique in several aspects. This textbook critically discussed the structure, morphology, family, epidemiology, pathophysiology, life cycle, pathogenesis, and symptoms of the novel coronavirus (COVID-19). Apart from that, epidemic, endemic virus diseases such as Ebola, Nipah, Novel influenza virus H1N1, Lassa fever, zika virus, coxsackie virus, Japanese encephalitis, dengue fever, West Nile virus, chikungunya, etc. viral infections of global outbreak data as compared to coronavirus (COVID-19) are also discussed. Suggested allopathic, homeopathic, ayurvedic, home remedy, convalescent plasma therapy, etc., for novel coronavirus treatments and prevention guidelines. The current global data for the preclinical and clinical status of drugs approved vaccines and few vaccines under development for coronavirus infections, and the impact of post-COVID-19 on science and technology, current and future directions about the coronavirus of which will be exceptional as compared to already existing textbooks in a lucid and researcher friendly for easy understanding and applications in the current COVID situation. In addition to this textbook also covers the health condition and status of post-vaccination that may improve and reduce the long-term effects of the COVID-19 virus. Moreover, briefly enlightened post-covid-19 recovery patients or vaccination people's worldwide associated side effects, and adverse drug reactions such as Stevens-Johnson syndrome, Toxic epidermal necrolysis, Mucormycosis, White fungus, Yellow fungus, Zika, Delta, Omicron, IHU and Delmicron Virus are significant blockbusters of this second and third waves of current and post COVID situation. I am incredibly grateful to all the co-editors in this textbook, who have given up encouragement to write about all the selected contents of this book to create imagination in the mind of medical and paramedical students and Ph.D. scholars. Preparing this textbook took longer than anticipated, and it contains more pages than expected. This present book should be handy to pharma and microbiology students studying medical microbiology, virology, etc. It could help develop their career in the medical and allied health sectors. I think this book might fit any of the above descriptions, depending on the reader's need. I am heartily thankful for my co-editors Mr. Bikash Ranjan Jena, and Mr. Debashis Ghose, for their constant and keen involvement in the compilation, edition, and creation of flow charts and figures during the writing of this textbook. Finally, I would like to thank my loving wife, **Ms. Linarani Swain**, for her love, understanding, and constant support during the time of preparation of this textbook. I would like to thank my loving son **Priyans Swain** for giving me time to make this book.

Acknowledgements

I acknowledge with grateful appreciation the significant contributions of co-editors, Mr. Bikash Ranjan Jena and Mr. Debashis Ghose, in sustaining the vitality of this textbook. I extend my gratitude to all well-wishers, mentors, academic guides and academic colleagues, and industry friends who have shared their thoughts with me. I acknowledge my parents, father-in-law, mother-in-law, brothers, brothers-in-law, sisters-in-law, all relatives, my wife, Mrs. Linarani Swain, and my lovable son Priyans Swain. They supported me a lot during my entire life assignment. It is my proud privilege to express my heart-felt gratitude to the Director, Ms. Rainy Kethan, The Assam Kaziranga University, for her kind consideration of providing this great opportunity to me for writing this textbook. Because of her blessing and encouragement, this book has come to light. I acknowledge my sincere gratitude towards Dr. P.K. Mishra, Honorable Vice-Chancellor, The Assam Kaziranga University, for his extreme support for the successful completion of this textbook. I especially thank the publisher, acquisitions editor, managing editor, copy editor, and production manager of IP Innovative Publication Private Limited, Uttam Nagar, New Delhi contributed so expertly to the planning, preparation, and production of this book.

Dr. Suryakanta Swain

Editor-in-Chief

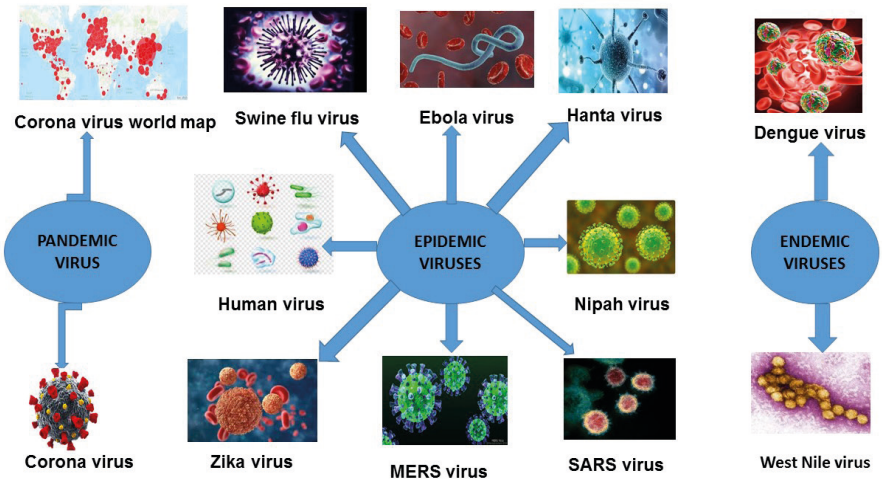
Contents

Abstract

Coronaviruses is regarded as a massive family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East respiratory syndrome, and severe acute respiratory syndrome, which is now another forewarning of the risk of CoVs posed to public health globally as a pandemic. The first case was reported from Wuhan city, China, on 31st December, 2019 and now spreading worldwide, 192,281,116 COVID-19 positive cases are reported till 21st July, 2021. This textbook critically discussed the structure, morphology, family, epidemiology, pathophysiology, life cycle, pathogenesis, and symptoms of the novel coronavirus. Apart from that, epidemic, endemic virus diseases such as Ebola, Nipah, novel influenza virus H1N1, Lassa fever, Zika virus, Coxsackie virus, Japanese encephalitis, Dengue fever, West Nile virus, Chikungunya, etc. viral infections of global outbreak data as compared to coronavirus are also discussed. We concluded with suggested Allopathic, Homeopathic, Ayurvedic, home remedy, convalescent plasma therapy, etc. for novel coronavirus treatments and prevention guidelines. The current global data for the preclinical and clinical status of drugs, vaccines under development for coronavirus infections, the impact of post COVID-19 on science and technology, current and future directions are the primary focus for the readers and researchers. This textbook also covers the current health condition and status of post-vaccination and how that may improve and reduce the long-term effects of the COVID-19 virus. Moreover, briefly enlightened post-COVID-19 recovery patients or vaccination people's worldwide associated side effects, and adverse drug reactions such as Stevens-Johnson syndrome, Toxic epidermal necrolysis, Mucormycosis, White fungus, Yellow fungus, Zika, Delta, Omicron, IHU and delmicron Virus are significant blockbusters of this second and third waves of current and post COVID situation.

Keywrords: COVID-19, Novel influenza H1N1 virus, Hantavirus, Zika virus, Coxsackie virus, Japanese encephalitis.

Graphical Abstract



Chapter 1

Introduction

Human civilization has already been experienced the devastating power of nature through various contagious epidemics and deadly pandemics earlier, like Spanish flu, the life-threatening outbreak in recorded history by killing 50 million people during 1918–20[1]. This pandemic has gone beyond the death toll, and fatalities rates were unpredictable at that time. After 100 years, again, the most significant pandemic era repeated in December 2019; the Wuhan city of China, which is the novel COVID-19 (SARS-CoV-2) biological outbreak. On March 11, as per the official reports of WHO, COVID-19 was declared as a global pandemic because of its severity, rapid spreadability of infections geographically, around the globe[1,2]. Before the emergence of COVID-19, the issue of the threat has already been revealed out during the early twenty-first century, almost 17 years back (In 2003). The prime most severe acute respiratory syndrome (SARS) outbreak in 2003 ruined down over 800 deaths among 8000 cases[3].

Epidemics are out-spread either by the re-emergence of pathogenic organisms or microbes that have been identifiable, existed for a higher-duration on earth upon inanimate objects, or in the creature. Whereas, at this time, immunologically vulnerable populations, or newly-emerging animals, microbes, viruses are reformed due to environmental conditions, social impact[1-4]. The mystery continues, and SARS was ultimately covered through quick patient's isolation, syndromic surveillance, strict enforcement of quarantine of all connections, and in some localised areas prime-most quarantine imposition of the centre of the population[3,4]. SARS was eliminated gradually by a break or draconic measures in all human-to-human transmission routes. Even if the most substantial economic country likes the United States, eight people had laboratory evidence of the potent SARS-CoV infection during SARS. All of those people had travelled history to other parts of the globe, the location where SARS was spreading out[4,5]. By the end of July, 2021, within a matter of two years, while the beginning of coronavirus disease 2019 (COVID-19) outbreak, above 192,281,116 confirmed cases, with

more than 4,134,015 deaths, have been reported worldwide[3,4]. All over the world, even if, in the United States, quarantining measures or isolating millions of people is a great deal or to minimize the effect, but the people who have been potentially uncovered to the coronavirus are being asked to self-isolate for a period of 14 days. During this moment, they can check themselves for symptoms[3-5]. For public welfare, emerging and remerging of infectious agents are signs of global evolution and difficult concept[6,7].

Coronaviruses are family of enveloped RNA viruses which are zoonotic and being spread out generally amongst human beings, other mammals, birds that causes a respiratory blockage, enteric, hepatic, and neurologic disorders[8,9]. After almost a decade of SARS eradicates, another enormously pathogenic coronavirus, especially in the region of Middle Eastern countries known as the Middle East respiratory syndrome coronavirus (MERS-CoV) has originated[9]. ACE2 acts as a receptor for SARS coronavirus (SARS-CoV) which chiefly attacks the type II category pneumocytes and ciliated bronchial based epithelial cells, whereas the MERS-CoV utilizes the unique dipeptidyl peptidase 4 (shortly DPP4; also regarded as CD26) as a unique receptor and it targets type II pneumocytes as common but having slight modified unciliated bronchial epithelial cells[10]. The deadly SARS-CoV and MERS-CoV were transferred straight to the general people from the market civets and also from Arabian camel or (Dromedary camels) correspondingly. However, both the viruses' contagion is contemplation to have originated in the bats[11–14].

Wide-ranging literature findings signify of these two imperative coronaviruses have a similar structural genomic sequence, but have also been an exceptional discovery in bats, worldwide. In this textbook, we highlighted the origin, evolution, morphology of SARS-CoV and MERS-CoV, their global impact, similarity, and difference against the newest SARS-CoV-2 (COVID-19) [15–17]. Specially, we accentuate the genetic diversity, environmental distribution, interspecies communication, and prospective for the pathogenesis of SARS and MERS-related coronaviruses i.e., SARSr-CoVs and MERSrCoVs correspondingly, observed in bats. These unique concepts can assist in setting up preventive action taken to counteract the threats against future spill over as well as the microbial contaminations to the human race with the novel coronaviruses. The vaccinated individual experiences some mild side effects after getting vaccinated, which are signs that your body is building protection. However, the COVID-19 vaccines are safe, and getting vaccinated will protect you against developing severe COVID-19

disease and dying from COVID-19. Sometimes new variants emerge and disappear, and sometimes the new variants may persist a long time. Multiple variants of the virus that causes COVID-19 have been documented in the United States (US) and globally during this pandemic.

Viruses frequently alternate and become more varied. Scientists' the day by monitoring these sudden changes, counting to the spikes on the virus's surface. By carefully studying these infectious viruses, researchers and scientists can learn how changes to the virus might affect how it spreads and how quickly the community spread has been occurred. These small differences, or variants, have been studied in detail and identified since the beginning of the pandemic era. Some variations allow the virus to spread more efficiently or make it even strong resistant to treatments or vaccines. Those variants need to be monitored more carefully to stop mutation and spreading rates all over the globe. The current pandemic has exaggerated numerous fields of space science, technology organizations, government, private, and government-aided agencies worldwide, leading to compact productivity, reduced gross domestic product (GDP), and economic downturn[18–21].

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Chapter 2

Family, Structure and Morphology of COVID-19 Virus

The COVID-19 virus belongs to the family, coronaviridae, arteriviridae and roniviridae, and subfamilies like's alpha (TGEV, PEDV, FCOV), beta (SARS-COV, MHV, MERS-COV), gamma (IBV) and delta, toronavirinae (Bafinivirus and Toro virus) and its order nidovirals. The structural arrangement of coronavirus particles or virions are spherical in shape, with just about diameters contain 125 nm, as confirmed and display in current studies by cryo-electron tomography and also in cryoelectronic microscopy. A club-shaped spike projection from the surface of the virion is the vital characteristic of coronaviruses. These noted spikes are a denoting the actual quality of virions and provide them the exterior of a solar corona, indicating the species name as coronaviruses. The nucleocapsid is located within the coverage of the stated virion. Coronaviruses have spiralled in the shape of usual nucleocapsids, which is curious amongst positive-sense RNA viruses, but far more frequent for negative-sense RNA viruses (Fig. 1).

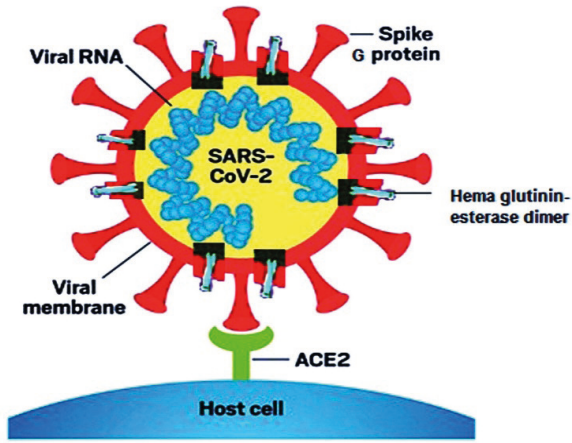

Fig. 1: Structure of coronavirus.

The particles of the coronavirus restrain four chief structural proteins. These are the spike (S), (M), (E), (N) membranes envelope and nucleocapsid proteins. Moreover, total of the proteins are encoded within the 3′ end of the inherent information or viral genome. The S protein (~150 kDa), uses an N-terminal signal progression to gain access to the ER and having the process of N-linked glycosylation. The Virus encoded the S protein, includes the individual spike configuration on the outside of the virus. The trimetric S-glycoprotein conciliates correlation to the specific host receptor. In most, but not all of the category of corona viruses, S is cleaved up utilizing host cell and having furin-alike protease into distinct twice different polypeptides distinguished as S1 and S2[22]. Through the spike molecule, S2 can form the series, whereas S1 can formulate a higher receptor-attaching sphere of the S protein.

In the virion, M protein is noted as the most copious structural protein. For virion appearance, the M protein which is tiny in size (~25–30 kDa) with a three transmembrane denotation. It has a smaller N-terminal end and larger C-terminal glycosylated ectodomain and which elongates 6–8 nm towards viral particle. Most, M proteins have not hold a signal series in spite of being co-translationally inserted in the Endo plasmic reticulum (ER) membrane[23]. The current analysis recommends that the M protein; can remain as a dimer in the virion and might take on two diverse conformations that endorse curvature of the membrane, which adheres to the nucleocapsid. The E-protein (~8–12 kDa) is established in little quantities inside the virion. E-protein from coronaviruses is extremely differing but have a widespread structural design. Most data suggest that the membrane topology of E-protein is unique as it's a transmembrane protein, which is not totally resolved[24]. The E protein has endodomain of N- and C-terminal and possesses ion channel activity. As contrasting to former structural proteins, recombinant viruses lacking of the E protein. The E protein facilitates the congregation and discharge of the virus; however, it also has other utilities. For example, in protein, for SARS-CoV-E, the ion channel activity is not requisite for the replication virus but is necessary for causing pathogenesis.

The N-protein composed of the mere protein enclosed in the nucleocapsid[25]. It is mainly assembling two diverse domains, an N-terminal and C-terminal domain shortly as (NTD) and (CTD), jointly can adhere to the m-RNA *in vitro*, but each area uses diverse technicalities to bind to RNA. The best RNA binding needs assistance from similar domains. N-protein becomes critically phosphorylated, and the concept of phosphorylation has been recommended to make active a structural

alter enhancing the similarity for viral adjacent to RNA of non-viral. The N-protein attaches to the viral genetic material in a conformation having beads-on-a-string form. Two-RNA substrates definite geometry have been recognized for N-protein; the TRSs and the genomic wrapping signal. The genomic covering indication has been established to attach particularly to the digit second or else C-terminal RNA protein domain.

N protein attaches an enter component of the replicase complex, (nsp3) as well as the M-protein[26]. These protein interactions available help jointly the viral genetic based material (genome) to the RTC, and afterward enclose the encapsid genetic documents into viral particles (virion). A well-known fifth number of structural proteins, (Heamagglutinin-esterase) shortly as HE, are located in a division of β-coronaviruses. The protein possesses acetyl-esterase activity and acts as a haemagglutinin, adheres sialic acids on surface glycoprotein's, and these performances are concerned to improve the transport mediated by a membrane transport S-protein. These processes also negotiated cell entry of S-protein and virus multiply through the mucosal layer. Fascinatingly, HE improves the murine hepatitis virus (MHV) neurovirulence; on the other hand, it is chosen next to tissue culture for unknown reasons[27].

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Chapter 3

Epidemiology of COVID-19 Virus

As on 21st July, 2021 global data of the corona virus, a total of 192,281,116 peoples are affected, 4,134,015 peoples have died, and 174,965,113 peoples were recovered. Among the total global infected cases, the total number of active cases is 13,181,988 out of which infected patients, 13,100,195 (99.4%) in mild condition and 81,793 (0.6%) serious or critical conditions and the total number of closed cases so far 179,099,128 out of which 174,965,113 (98%) are recovered or discharged and 4,134,015 (2%) cases are deaths. The five major affected countries with COVID-19 virus cases are USA (35,081,719), India (31,216,337), Brazil (19,419,741), Russia (6,006,536), and France (5,890,062). The major countries mostly affected globally due to coronavirus (COVID-19) infections data information's are depicted in Table 1 as on July 21, 2021, 04:48 GMT[28–31].

Table 1: Corona virus (COVID-19) five major affected countries globally and its percentage of death and percentage of recovery data till 21st July-2021

S No	Name of the Country	No. of patients affected	No. of patients death	No. of patients recovered	Death (%)	Recovered (%)
1	USA	35,081,719	625,363	29,435,171	1.782589388	83.90458575
2	India	31,216,337	418,511	30,390,687	1.340679401	97.35507084
3	Brazil	19,419,741	544,302	18,124,621	2.802828318	93.33091003
4	Russia	6,006,536	149,922	5,382,213	2.495981045	89.60593926
5	France	5,890,062	111,525	5,663,776	1.893443566	96.15817287
All total		97,614,395	1,849,623	88,996,468		

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Chapter 4

Pathophysiology and Lifecycle of COVID-19 Virus

4.1. Attachment and Entry

The proven pathophysiology of COVID-19 enfolds the immediate attachment and aetiology of receptor and its protein analogues. The first add-on of the particles of virus (virion) to the corresponding host cell are initiated by connections stuck involving the S protein and its receptor. The stringent receptor site connecting domains or shortly RBD; inside the S1 section of a COVID-S protein progression relies upon the virus. This result out, with a few pertaining to the RBD at the N-terminal of S1 (MHV). In contrast, other category of SARS-CoV possesses at terminal site of S1 or having C-terminus projection with the RBD. The target s-protein based interaction or else the receptor is found as a principal influential factor for a corona virus to pollute a species containing host active and furthermore bears the virus of tissue tropism. The cellular receptor which bear the peptidases as numerous corona viruses make use of it. It is indistinct that upon what basis the peptidases are significantly employed as an entrance strike yet in the deficiency of the enzymatic pasture of such proteins. Aminopeptidase N (APN) used by many α-corona viruses as a receptor, similarly, (ACE2) used by mostly HCoV-NL63, as well as SARS-CoV accordingly. MHV usually enters throughout the CEACAM1, and newly recognized MERS-CoV which adheres to dipeptidyl-peptidase 4 (shortly as DPP4) to obtain doorway into human being cells.

However, on succeeding the receptor binding, the virus must subsequently gain entrance to the cytosol host cell. This is usually done by of S protein-based acid-dependent proteolytic cleavage like cathepsin (TMPRRS2) or else one more protease, regulated by fusion of the cellular membranes and viral. The S protein cleavage arises at two distinct sites within the S2 portion of the protein, with the earliest cleavage imperative for isolating the RBD and S-protein fusion domains and the second for revealing the fusion peptide (cleavage formed at S2′). Inside the acidified endosomes, usually the incorporation or fusion usually arises, but a few corona viruses, like in case of MHV, a fusion of this arises at

projection of cytomembrane. The segmentation or the Cleavage formed at S2′ appears a grouping peptide to facilitate for inserting towards the layer, which is accompanied by the union of two heptad repeats in S2 generating a not parallel six-helix wrap-up or bundle. The configuration of this wrap up permits for integration of viral and membranes of cell, subsequent infusion, and eventually discharge of the viral genome towards the cell body or the cytoplasm[32-34].

4.2. Replicase Protein Expression

In the corona virus life, the next utmost footstep is the p the reconstruction of the replicase gene is observed from virion genomic RNA, that surround two large ORFS, rep1a, and rep1b, having two co-terminal polyproteins, pp1a and pp1 ab respectively. The virus revived and unifies to consistent both polyproteins as 5′-UUUAAAC-3′ a greasy series, and an RNA pseudo knot to commence the ribosomal margin. The ribosome unrolls the pseudoknot geometry and continues transformation until it run across the rep1a stop codon in the majority of the cases. Uncommonly, the pseudoknot prevents the ribosome from undulating elongation, resulting it to indentation on the oily series, altering the chemical analysis edge by moving back one nucleotide, −1 frameshift, former to the ribosome is capable to congregate the structure of pseudoknot and pull-out translation into rep 1b, formed in the translation of pp1ab. The forecast of in vitro analysis results to be the frame shifting of ribosome to be greater than 25%. It is unidentified accurately to control protein expression.

What is the actual need of viruses to utilize the frame shifting to, at the same time it is made-up to either manage the accurate ratio of rep1b: rep1a proteins so that an appropriate atmosphere can be formed for replication of RNA. The polyproteins assemble the pp1a, and pp1ab encircle the NSPS 1–11 and 1–16, in that order. However, γ-coronaviruses mostly cleaved by the poly-proteins, which are analogous nsp1 having the tendency of 2 or 3 proteases to formulate simple cleave off to replicase based polyproteins. They are the protease of serine category, known as commonly papain-like proteases (shortly PLpro), programmed within nsp3. All the way through the NSP5, which is the chief protease (Mpro) has been programmed, (encoded) so, in steed of the γ-coronaviruses, SARS-CoV and MERS-CoV, on the whole, corona-viruses, encode the two PLpros within nsp3, which only articulate one PLpro. The Mpro is utterly in charge of for the enduring 11 based cleavage units whereas the NSP1/2, NSP2/3, are intended to cleaved off by PLpros as well as NSP3/4 limits. For the smooth production of RNA replication

and transcription of the sub-genomic RNAs, many of the NSPS assemble into the RTC to produce surroundings appropriate for synthesis of RNA. The NSPS also holds other enzymatic domains and applications, counting those significant for replication of RNA, just like the RdRp domain encoded by nsp12. Just like that the RNA helicase domain can be encoded by NSP13 which assimilate activity of RNA 5′-triphosphatase. The NSP14 conceal the exo-ribonuclease (shortly ExoN) implicated in imitation reliability and action associated to N7-methyltransferase; similarly, the NSP16 cover up the 2′-O-methyl-transferase and its accomplishment. In adding up, replication workability, other performances, like clogging up takes place principally towards the NSP16-2′-O-methyltransferase; NSP1; as well as NSP3-deubiquitinase behaving innate immune responses. Apart from that, diverse unidentified additional activities that have been observed for compounds of NendoU and NSP3-ADP-ribose-1”-phosphatase etc. Fascinatingly, ribonucleases NSP15-NendoU and NSP14-ExoN actions are exceptional to the nidovirales order and can be fit thought-out hereditary markers for these categories of viruses[35-38].

4.3. Replication and Transcription

The formation of viral replicase complexes can be followed by viral RNA synthesis that contains cis-acting sequences. Due to active translation and congregation process, the viral RNA synthesis, (genomic or sub-genomic) RNAs are formulated, which give out mRNAs with structural and accessory genes that elucidate replicase polyproteins. The 3′ co-terminal by the complete viral genome is the characteristics of every positive-sense sub-genomic RNA. Hence these can produce a set of, nested based RNAs, distinguishing possessions of the order *nidovirales*. By negative-strand intermediates (approximately 1% possesses poly-uridylate and anti-leader series) the sub-genomic, as well as the genomic RNAs, are produced. Seven stem-loop structures reside within the 5′ UTR and 3′ UTR end bears the genome to facilitate, expand into the 1a gene replicase sequence, and bulged stem-loop, a pseudoknot, and a hypervariable section respectively. Fascinatingly, overlapping arises among the stem-loop and the pseudoknot at the 3′ end so that, cannot formulate at the same time. Consequently, these diverse structures are anticipated to control the interchange stages of RNA synthesis. In contrast, individually, which of the steps are regulated, and their clear-cut action and mechanism are yet mysterious. This was originally thought to occur throughout (synthesis of positive-strand) or else negative-strand RNA addition. A lot of pieces of confirmation currently support this model, due to, anti-leader sequence at the

3′ extension of negative-strand sub-genomic RNAs, hence several concepts like the RdRp avoid all of the TRS-B sequences to construct complete negative-strand genomic RNA and TRS-B sequences directed on the TRS-L consequently. The basic reason behind the questionnaires is highly needed to put on a full standpoint that, how the replication of RNA arises in the family of these viruses, finally, because of homologous and non-homologous recombination. Coronaviruses are as well known for their ability to reunite. The capability of these viruses to reunite is joined to the strand switching capacity of the RdRp. Recombination likely plays a significant role in the evolution of the virus. It is the foundation for targeted RNA union; an overturn heredity device intended to viral recombinants during genome 3′ end positively[39–41].

4.4. Assembly and Release

The viral structural proteins S, E, subsequent replication, subgenomic RNA synthesis after translation usually entered to ER. These proteins shift along the secretory pathway into the ERGIC. The M protein initiates and responsible for most protein-protein interactions requisite for assembly of coronaviruses but not targeted for virion configuration, since virus-alike particles may not be produced by M protein phrase without help. On the other hand, while M protein is articulated in association with E protein, VLPs are fashioned, signifying the assembly two unified proteins task jointly to create coronavirus envelopes. N protein initiates VLP creation, suggestive of that the union of encapsidated genomes into the ERGIC produces envelopment of the viral genome.

The S protein in adequate is incorporated into virions at this step, which is to transfer to the ERGIC and interrelate with the M protein which is crucial for its enclosure into virions. As compared to both the protein configurations, M protein is moderately plentiful, whereas the E protein is minute quantities in the virion. M protein interactions offer the momentum for the maturation of the envelope. It is unidentified how E protein assists; in stir up the twist of membrane, as E-protein stops the M protein aggregation. In addition to this, The E-protein may also have a detach role in promoting viral release by altering the host secretory pathway. The M protein adheres to the nucleocapsid, and this interaction promotes the production of virion congregation. These interactions have been depicted to the c-terminus of the endodomain of M with CTD 3 of the N-protein. Conversely, it is not clear about the process of nucleocapsid form complexation with virion RNA deals to the ERGIC to act together with M protein and turn out to be included

in the viral envelope. However, the mutation of this signal does not come out to impact the viral count and its mechanism and maximum coronaviruses do not hold the same sequences at this point. By exocytosis, virions are moved towards the cell surface in vesicles. The concept remains unclear that whether the virions utilized the conventional path for way out. Cell-cell fusion can take place in some coronaviruses, as S protein, which does not get combined into the corresponding virions moved to the surface of the cell. Moreover, the interaction has been raised among the nearby infected and uninfected cells, transfer of large freight from the golgi bodies or virus has diverted a divide, single path for its and this results in the formation of bigger nucleated cells, which allow the virus to reach within an infected individual without being detected by virus-intensify antibodies and the complete life cycle of the coronavirus is depicted in Fig. 2[42-44].

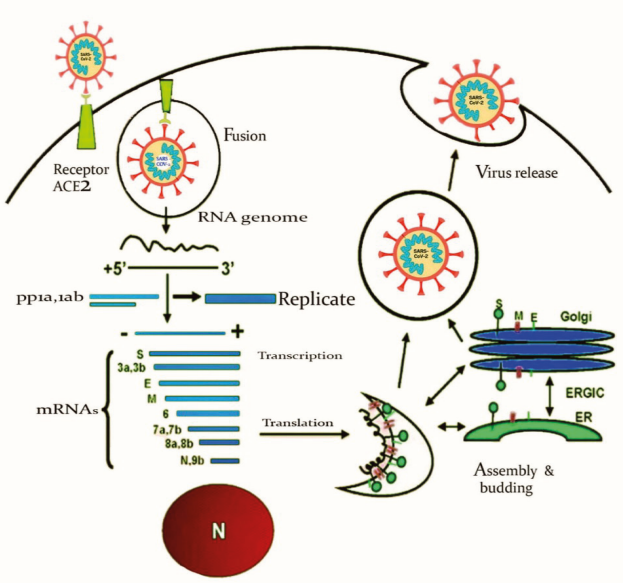

Fig. 2: Schematic representation for life cycle of corona virus (COVID-19).

4.5 Pathogenesis of Coronavirus

4.5.1. Animal Coronaviruses

Coronaviruses produces numerous syndromes in animals, and their competence to create severe diseases like pigs, dogs, chickens, bats, and cats led to momentous research on these kind viruses during the 20th century. For instance, the most

reliable and certain PEDV and TGEV are the category of viruses of Animal corona viruses which causes cruel gastroenteritis nuisance in youthful piglets, leading to key mortality, and morbidity economic losses to a greater extent. For the first period, PEDV recently emerged in North America, resulting in major fatalities of young piglets. PHEV mostly results in the enteric infection but the same moment can infect and transmit the CNS resulting in vomiting, encephalitis, and wasting in pigs. In domestic cats, usually, FCoV is a new virus which normally causes asymptomatic illness results to a persistent illness, and alteration transforms the virus into FIPV, a new enormously virulent strain of FCoV. FIPV (macrophage-tropic) formed due to the redevelopment stage of a lethal syndrome called as feline infectious peritonitis (FIP) that has a shape of wet and dried up forms, equal to the human disease, sarcoidosis.

FIPV causes chemokine expression and lymphocyte depletion, ensuing in lethal disease. In animals like, rats, cattle, Bovine and Rat (CoVs), and also in IBV which create mild to moderate severe RTI respectively. Bovine CoV creates consequential losses in the cattle and has spread to contaminate a diversity of ruminants, including elk, deer, and camels. The virus causes diarrhoea, all leading to loss of weight, dehydration, lower production of milk, as well as the depression. Renal disease can also be formed by a few strains of IBV, which is a γ-coronavirus that affects the urogenital tract of chickens. IBV considerably diminishes production off egg and weight gain, resulting in substantial losses in the chicken manufacturing industries each year.

Currently, a novel coronavirus named SW1 was recognized in a deceased Beluga whale. Huge numbers of virions were documented in the liver of the dead whale with breakdown of acute liver followed by respiratory failures. Liver tissue sequence can recognize the virus as a coronavirus, rather identifying in electron microscopic images. Based on the phylogenetic study, it was consequently determined to be a new coronavirus (γ-CoV) which may have a causative agent of disease in whales. Over the past some decades, additionally, there has been a powerful interest in recognizing the novel bat CoVs, as these are likely to be the definitive source for SARS-CoV and MERS-CoV. In association with these hundreds of novel bats, coronaviruses have been found out ultimately. Another new collection of nidoviruses, namely mesoniviridae, were newly recognized as the initial nidoviruses to totally contaminate insect hosts that are closely related to the roniviruses but are extremely contradictory as they shape, and appearance is~20 kb, deteriorating within the big and tiny nidoviruses. The largely intentional

animal coronavirus is murine hepatitis virus (MHV), which creates a selection of outcomes in mice, counting respiratory, enteric, hepatic, and neurologic disorders. These infections frequently serve as beneficial models of disease. For instance, in susceptible A/J and C3H/HeJ mice, MHV-1 cause respiratory problems, A59 and MHV-3 persuade brutal hepatitis, while JHMV leads to encephalitis. Amusingly, A59 and attenuated versions of JHMV leads to chronic demyelinating infirmity, that analogous to multiple sclerosis (MS).

This result to building the MHV contagion one of the excellent models for this debilitating human syndrome. Early studies suggested that demyelination was relay on the rapid replication of the viral genome in oligo-dendrocytes in the province of the brain and spinal cord of CNS. Moreover, further new information shows that the disease is immune-mediated as the immune-deficient (Absence of T and B cells) mice do not build up demyelination, but addition up subsequent virus-oriented T-cells restores the demyelination development. Ultimately the chosen MHV can be premeditated under BSL2 laboratory circumstances, just as the SARS-CoV or MERS-CoV, offers a more appropriate animal model. In tissue culture cells, these factors build MHV, a wonderful model for analysing the rudiments of replication (viral genome) pathogenesis, and immune tendency to defence against the coronaviruses[45,46].

4.5.2. Human Corona Viruses

Former to the outbreak, of the SARS-CoV viruses were only reflections to produce mild, respiratory self-limiting complications in human beings. Two of the most promising, infective and devastating human coronaviruses are α-coronaviruses (HCoV-229E and HCoV-NL63). In contrast, the other two of this generations are β-coronaviruses (HCoV-OC43 and HCoV-HKU1), HCoV-229E as well as HCoV-OC43, which were secluded almost 50 years ago whereas HCoV-NL63 and HCoV-HKU1 were merely newly recognized next to the SARS-CoV epidemic. The species of HCoV-229E keep apart, around the globe have, only negligible string divergence, while that of HCoV-OC43, which possesses the identical site, but out-of-the-way in diverse years, can illustrate imperative hereditary changeability and resolution. These viruses are pervasive in the human, (almost 15–30%) result to RTI infections every passing year with brutal illness in new born babies and elder people, and individuals with preliminary respiratory complications. HCoV-NL63 is also associated with acute laryngo-tracheitis (croup). It has been found that human corona virus (HCoVs) has the tendency to generate the Multiple sclerosis (MS).

SARS-CoV, are belongs to second categories of corona virus, that was recognized as the prime causative factor of the SARS and its devastating outbreak resulted during 2002–2003 on Guangdong region of China.

In particular, the countries of Southeast Asia and Toronto, Canada for quite a lot of months, moreover, the outbreak resulted in the damage of approximately 40 billion in financial progress, as the virus almost close down numerous activities in the concerned country. In Hong Kong city, the outbreak was first started in a hotel and eventually being broadened to approximately 24 countries. During the endemic, intimately associated viruses were split out from several unusual animals includes raccoon dogs with palm civets (Himalayan zones) Conversely, it's broadly accepted that SARS-CoV emerged in bats since a massive number of bats (species of chinese horseshoe) enfold genetic sequences of SARS-CoVs and hold forensic authentication for a prior contagion with an associated CoV. In reality, two new-fangled bat, such as SARS-related CoVs were freshly documented that is further similar to SARS-CoV, then any previous virus recognized to date. They also used the ACE2 inhibitor, which is established to utilize a similar receptor as that of the human virus. These can reveal additional confirmation that SARS-CoV emerged especially from bats. Although in a few human beings within wet animal markets, had forensic evidence of SARS-CoV infirmity leads to the previous contagion outbreak, as these individuals had no conspicuous symptoms or seems to be (Asymptomatic) Thus, it is liable that an intimately connected virus disseminated in the wet creatures or markets with full of animas for a long year, earlier than a series of components accelerated its widespread into the generously proportioned population. The transmission of SARS-CoV was to some extent judegeful, as it simply spread through straight get in touch with contaminated persons after the instigation of sickness. Hence, the outbreak was covered within healthcare and household remedies, apart from few cases of more spreading performance were one entity was able to contaminate numerous contacts due to improved growth of elevated viral spike multiplicity or else capability to aerosolize the pandemic virus.

As a consequence of the moderately incompetent spreadability of SARS-CoV has seen and further could controlled from first to last, with the use of quarantine measures. Only a little figure of SARS cases observed after the epidemic was under controlled during the June 2003 as the SARS-CoV, infects the cells of epithelial tissue inside the lungs initially. The virus subsequently is competent of unproductive infection as it is inward bound macrophages and contain uniform

dendritic cells. Instead of this, the infectivity of such cell types might be significant in suggesting cytokines (Pro-inflammatory), which might add to the disease. In detail, lots of chemokines including the cytokines are twisted by such cell types and are prominent in the serum of SARS-CoV contaminated carriers or individuals. The accurate process of lung injury and the reason for brutal ailment in human leftovers undecided. Viral titters come out to diminish when rigorous complications emerge in both in animal models as well as in human beings. Moreover, the specified animals contaminated with SARS-CoV (such as rodents) strains demonstrate parallel clinically description and outcome to the human ailment, counting a reliant on age, and harshness of illness. Pro-inflammatory cytokines and compact T-cell responses can be revealed by such animals, which also exhibit increased levels of the pathological immune response of infection. During the start of the twenty-first century in 2003, the SARS-CoV epidemic was stable and could be controlled. After that, the virus has not been completely eradicated; in the region of Middle East during 2012, a second novel human CoV has emerged.

In Kingdom of Saudi Arabia (Western Asian) and other countries in the Middle East regions, the epidemic contagion virus, named MERS-CoV, was originated, which was found to be the main co-factor in a couple of extremely infectious respiratory tract disorders or (RTI). The outbreak was quite being serious as the mortality rate is high (of ~50%) in the early stages. Even if the infrequent cases sustained all through the rest of the year-end, the outbreak was not accelerated in early 2013, but in April 2014, a point of around 200 plus cases and almost 40 death cases have reported. Later the dangerous thought evolved that virus had mutated and genetically multiplied RNA, and it was even stronger for person-to-person communication or spreadability. However, the enlarged number of cases reported and resulted from the improved finding of seasonal growth rate in birthing camels. As per the research of the European Centre for Disease, during August 27, in 2014, a total figure of 855 cases with 333 deceased and an overall fatality rate (40%) are prevented and controlled in the MERS-CoV virus. MERS-CoV is a β-coronavirus belongs to group 2c; identical in structure as that of bat coronaviruses, HKU4 and HKU5. Serological or forensic investigations have identified Somali camel might be the usual host for MERS-CoV and its antibodies found as in Somali camels of the Middle East. For, MERS-CoV active replication, the cell lines from the camels are the appropriate agents to be indulgent in Saudi Arabia, more persuasive confirmation for recent studies predicting the identical MERS-CoVs in both dromedary camels and in case of human cases. One of these surveys in close

proximities in the human case, had straight contact with a contaminated camel, and the virus isolated from this patient was ready for mutant strain. At present, it leftovers to be resolute that the quantity of MERS-CoV cases can be recognized to a transitional host as contrasting to human-to-human communication.

It was revealed that the human-to-camel spreadability rate is the first factor in this outbreak. The predominating receptor for MERS-CoV is Dipeptidyl peptidase 4 (DPP4). The virus is solitary capable of using the receptor from certain important groups of mammals and creatures, like specifically in bats, humans, camels, rabbits, and horses to ascertain infectivity. To evaluate the potential vaccines or antiviral therapy, unluckily for researchers, the virus is incompetent of contaminating mouse cells because of differences in the structure of DPP4, building it hard. In recent times, a modest animal model for MERS-CoV was originated to initiate the human DPP4 genome into the lungs of a mouse using an Adenoviral vector. This perfect arrangement makes it achievable to test remedial association and invention of novel drug molecules, monoclonal antibodies and powerful vaccines for MERS-CoV in any kind of animal sensitive to adenoviral gene transfer[47,48].

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Chapter 5

Signs and Symptoms

The main sign and symptoms are observed after 2–14 days of exposure or incubation period of COVID-19 virus in the human body such as:

1. High fever	7. Chills and rigors
2. Dry cough	8. Diarrhoea
3. Breathing difficulties (or Shortness of breath) like asthma, pneumonia	9. Body aches
4. Sneezing	10. Headache
5. Runny nose and sore throat	11. Gastrointestinal problems
6. Chest tightness	

In chronic cases, due to impairment in kidney, liver and respiratory functioning leads to kidney, liver and respiratory failure and finally leads to patient death. Apart from that literature also reported recently that corona infected person may be never developing any above symptoms (Asymptomatic) and in some patients not yet symptomatic (Pre-symptomatic). Other new sign and symptoms of corona affected patients reported at least two of these underneath symptoms:

1. Fever	5. Headache
2. Chills	6. Sore throat
3. Repeated vibration with chills	7. New loss of taste or smell[49].
4. Muscle pain	

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Chapter 6

Suggested Treatments, Prevention and Management Guidelines

6.1. Allopathic Treatments

6.1.1. Favipiravir

As per current literature, 20th Jun, 2020, 19:26 IST, Favipiravir ('FabiFlu®') of Glenmark Pharmaceutical Ltd., Mumbai product shows clinical improvements of up to 88% is the first drug got Indian regulatory approval with quick reduction in viral load within 4 days between the age generations from 20 to >90 years, including in patients with co-morbid circumstances like diabetes and cardiac disorder suffering from mild to moderate COVID-19 infections. Mechanism of action of this drug is most selectively and potently inhibiting the RNA dependent-RNA polymerase of RNA infectious viruses (Fight antiviral drug approved to fight against corona virus for mild to moderate infected patients)[50].

6.1.2. Remdesivir

Gilead Sciences' Veklury (remdesivir), another most capable drug candidate for the management of COVID-19 patients after failure of clinical trials of hydroxycholorquine globally. The renowned Indian drug regulating authority, DCGI granted the marketing authorization such company in the form of injection or lyophilised powder for injection dosages form of 5 mg/mL and 100 mg respectively for the treatment of critically affected COVID-19 patients for "restricted emergency use and other Indian generic Pharma manufacturers, such as Cipla, Jubilant Lifesciences Hetero Labs, and Mylan as well as a Pakistani firm, Ferozsons Laboratories also got such approval for marketing across the globe[51].

6.2. Homeopathic Treatments

Arsenic album-30c: Indication: Two drops of sesame oil should be added in each nostril each morning for the prevention of corona virus (healing based on the

teaching of Hippocrates and Galen), and it was reported by Dasgupta A. Feb 7, 2020, on Indian Authorities propose use of homeopathy to prevent coronavirus[52].

6.3. Ayurvedic Treatments

Home remedies to fight the symptoms of the coronavirus attacks are as follows:

1. Lemon tea: Kills the sore throat problems and removes the harmful infection from the air passageway or blockage.
2. Ginger tea: Eases your anxiety and headaches, caused by respiratory tract infections.
3. Lemon honey tea: Soothes your airway passage and soften your rough coughs, dry sneeze.
4. Mint tea: Helpful in stopping the runny nose and helps in easy breathing or inhalation.
5. Certain ayurvedic agents or ligands such as nimbin, curcumin, withaferin-A, piperine, mangiferin, andrographolide, quercetin, luteolin, zingiberene, b-caryophyllene, eugenol, gallic acid etc. showed pharmacological actions like antiviral, antimicrobial, anti-inflammatory, antioxidant, antidiabetic, anticancer and immunomodulatory activities etc. might be useful treatment therapy during this pandemic situation in order to control the corona viral infections and also boost the immunity of peoples who are already infected with secondary infections[52].

6.4. Home Treatments

1. Dissolve 1–2 tablespoons of honey in 1 cup of herbal tea (herbs like madhuyasthi, basil, peppermint, vasa)
2. Prepare fruit and green vegetable salads using detoxifying foods such as beetroot, radishes, cabbage, and broccoli. Boil and mix them gently, if you wish a cooked meal.
3. Yoga is one more approach to detoxify your body mechanisms. It is an excellent form of cleansing your body and mind [53].

6.5. Convalescent Plasma Therapy

The convalescent plasma therapy is another potential approach for treatment corona virus as per current literature approach. The main approach of such therapy

is to use the antibodies of the already recovered patients' blood and inserted in to the active cases, especially for immunisation of health workers, families of patients and other tremendous-risk connections with the COVID-19 viruses for prevention only but not for fully cures. A study was conducted by John Hopkins, immunologists and he found that some risks associated with such therapy such as more infections or re-infections and may affects the immune system of the patients by suppressing the body's natural immune response during and after transferred blood to the patients[54].

6.6. Prevention and Management Guidelines

1. Always you should avoid direct contact of the hand to mouth parts; by touching your nose eyes, and mouth with unwashed hands.
2. As a prophylactic measure everyone should avoid intimate contact with people who are feeling unusual or sick and having some symptoms.
3. It will be better to stay behind at home when you are sick and weak.
4. Directed to cover always your sneeze or dry cough with the help of tissue paper, then throw the tissue in the trash and should avoid spitting in public.
5. Instructed to clean and disinfectant regularly, to the touched in animate objects and surfaces using a standard household cleaning spray or wipe.
6. It is advisable or better to use handkerchief, when any one is coughing or sneezing in environment. The patient has to wear out a protective covering or face mask for preventive measures.
7. Every time before cooking carefully cook the meat items and eggs for the killing of germs and microbes.
8. The sick animals and animals that have died of specific diseases should not be eaten.
9. Always avoid the intimate contact with stray animals, as well as the sick animals, spoiled meat, waste and available fluids in the market.
10. As per precautionary measure it has been advised always, washing of your hands routinely with soap and water for at least 20–30 seconds particularly after moving to the bathroom, prior to taking food items, if it is visibly unclean and after blowing your nose, coughing or sneezing (Its effective to use an alcohol-based hand sanitizer with at least 60% alcohol if soap and water are not readily available).

11. Similarly, numerous other potential techniques that have established helpful in the management and confinement, of COVID-19 are explained below:
12. Regulates-applicability of boundary controls to protect the motion of individuals to and from infected zones.
13. Early recognition of suspected cases as well as to instruct the society on the severe risk factors, symptoms, recommend trouble-free entrance to test, standard possible trials in any medical track contact with infected individuals.
14. Mark out the possible contacts-a labour-intensive method of production which tracks easily infected persons through its actions from the movement of infectivity to distinguish all the persons.
15. Immediate quarantine and to isolate an individual suspected of illness from social contact with other peoples for a particular episode of time that enfolds the disease incubation instance.
16. Safety measure of using fitting apparatus, equipment's to shield the Medical workers like nurses, pharmacist, and doctors, lab-technicians who are dealing with patients and who cannot avoid contact with infected individuals.
17. Avoid Social distancing for community spread and safety measures has to be incorporated (cancel events, closing institutions, work from home, etc.)
18. Effective Instruction, educating, promoting the society-to encourage activities like frequent hand washing and avoiding gathering and groups, etc.
19. In the course of social distancing related policies, economic measures-to offer reinforcement to peoples and businesses and to boost acquiescence
20. All of these processes and potential measures are prepared and intend to limit the population exposed to contamination. At the same time to diminish and eradicate the transmission rate between the individuals of the population. This reinforcement marks in a pulling down of the pandemic arc of confirmed cases over time. As an effect, the falling peak in the number of cases wants the utmost therapeutic care and quarantine steps for early recovery. This unifies the capability of the therapeutically system to offer brilliance care to those infected and lessen the death rate. This, on the other hand, signifies a strong impact that strengthened

the pressure on the Medical system. This imparts more is the possible deceased or death rate, as investments are not competent to gather the stipulations as well so, medical workers exceed their demand to provide the utmost care. Pulling down the curve also extends the point in-time scale magnitude of outbreak; so that any feasible vaccine can at several future point be applied to speedily boost immunity within the population[55,56].

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Chapter 7

Epidemic Viruses

The endless new contagious disease is again entering into the health of human life, devoid of warning spontaneously. The comeback of infective illnesses started in the 21st century and decade before in the early 1990s. The threat goes on and spread-out year after year to human civilization. Among the infectious diseases, the significant conditions as Epidemic, and contagious are mainly Ebola (in 1976–2018), HIV (in 1983), Nipha (in 1998), SARS (2003), MERS (2012–2013), different types of human viruses including Novel influenza virus H1N1 (in 2009), Yellow fever (Urban Yellow Fever (YF) during 2016 in Africa, Lassa Fever in West Africa by rats (in 1969–2018) as well as the most recent outbreak case (in china) of Hantavirus which already originated during 1950–53 at various regions of America. The description, cause, and characteristics of some specific transmittable diseases as below[57–59].

7.1. Ebola

According to the precedent origin and record, the prevalence of Ebola virus disease seen in the Western African Ebola virus epidemic during 2013–2016 with incubation period 2–21 days. This has ruined the first loss of endurance and seconds most of the socioeconomic predicament, absolute survival in the countries and regions, predominantly in several areas like Guinea, Liberia, and Sierra Leone. The mode of transmission of this virus first from wild animals to humans and then transmitted progressively to the large populations through community transmission. Around 50% is counted as the average fatality rate during such epidemics, and 25–90% is the case fatality rate outbreaks as per the earlier reports. Community engagement is a crucial aspect of productively scheming outbreaks. Feeble surveillance systems and pitiable public health infrastructure contributed to the complexity surrounding the containment of this deadliest outbreak. It hastily extends to prior Guinea's bordering countries, Liberia and Sierra Leone, with rapid contagion. By July 2014, the explosion expands to the capitals of all three countries. This was the first time EVD extended from more isolated, rural areas and into densely populated urban centers, providing an unprecedented opportunity for transmission[60–62].

7.2. Nipah

It is a zoonotic RNA virus that belongs to genus Henipavirus, and family paramyxoviridae. This virus is more contagious and observed in Malaysia's country, which originated around 20 years back, i.e., in 1998. Its outbreak falls in the southeast region of Asia results in 265 cases of acute encephalitis with 105 deaths. The mode of transmission to humans from animals and it infects a wide range of animals. It causes brutal illness and even life death in people, making it a community healthiness concern. Moreover, it can be spread out straight among the people or all through infected foods. Bats are the causative agents and probable natural depot of Henipaviruses. In infected people, it causes a series of disorders, from subclinical contagion to the acute respiratory infirmity and fatal encephalitis[63–66].

7.3. SARS

The severe acute respiratory syndrome is typically known as SARS (transmitted from civet cats to humans), which was undiscovered earlier than 2003. In Asian countries, it has diminished the life of beyond 8,000 people, wipe out around 800 deaths concerning many lives resulting in terror and fear the world diagonally and inflicting massive economic smash up. In November 2002, the severe acute respiratory syndrome coronavirus (SARS-CoV) seen in China, and then in July 2003, 8000, positive cases reported in the other 26 countries. The resemblance between SARS-CoV and new SARS-CoV-2 (new COVID-19) is conspicuous, not only in the specified name. The complete genome or virus homology to the origin, mode of transmissions of SARS-CoV-2, has almost 86% resemblance with SARS-CoV1. In contrast, the COVID-19 will be dissimilar from SARS concerning the infectious period, transmissibility, clinical sternness, and degree of population increase [67,68].

7.4. MERS

In Saudi Arabia, 2012, a new virus MERS-CoV of coronavirus family emerged, causing an epidemic responsible for the viral respiratory syndrome known as MERS with 1000 cases, around 400 deaths. The common symptoms of this virus infected person are cough followed by fever, shortness of breath, GI tract disorders, diarrhoea, and pneumonia and some cases also asymptomatic, even if the patient becomes positive for contamination as it having characteristics of the zoonotic virus. Gradually this virus also spreads globally, and one-third of infected patients died due to this virus, mainly South Asia and African countries[69-72].

7.5. HCoV-229E

HCoV-229E human virus under the family coronaviridae and belongs to the genus, Alphacoronavirus, and order, Nidovirales. This virus has single-strand RNA and enters into the host cell by binding the APN receptor, and this virus mostly infected to humans and bats. This human coronavirus (HCoV-229E) cause and effect towards lower respiratory tract infections as well as inflammation of the outer ear along with common cold. There is no confirmation of this category of illness-causing enteric infection in human beings[73].

7.6. HCoV-NL63

It is new species of coronavirus belongs to family coronaviridae, under the above categorization of setracovirus, and it comes under the phylum: incertaesedis with the order: nidovirales. In the Netherlands, 2004, 7 years old child suffering from bronchiolitis and other respiratory disorders has first identified the presence of such an HCoV-NL63 corona human virus. Such virus characteristics have an inner envelope, positive-sense, single-strand RNA, and bind to the ACE2 receptor of the host cell. Afterward, the virus strain is known to infect mostly children with an impaired immune system and upper or lower respiratory tract disorders. Upper respiratory like rales, irregular chest problems, and X-ray, gaseous exchange, sever fever associated with cough, mucus fluid-filled inside the nasal cavity, or lower respiratory disorders like bronchiolitis and croup, which was observed predominantly in younger kids. HCoV-NL63 is the causative factor or mediator for the etiologic of all respiratory syndromes with a rate of around 10%[74].

7.7. HCoV-HKU1

It is a human coronavirus related to the advanced classification of Embecovirus and connected to the family: Coronaviridae. This virus first detected from a 71-year-old man who suffered from fever and cough, and the primary source of this virus originated from infected mice. The upper respiratory disease, common cold, bronchiolitis, and pneumonia are the significant symptoms seen in the case of HCoV-HKU1 infected illness present in humans. Two cases first reported in Hong Kong in January 2005[75,76].

7.8. HCoV-OC43

It is a type of beta-coronavirus 1 under the family coronaviridae, and this virus mainly infected to humans and cattle. The mechanism of transmission of this virus

through replication having single-strand RNA and more infectious due to active enveloped, with positive-sense. The pathogenesis towards its host cell by fastening to the N-acetyl-9-O-acetylneuraminic acid receptor located in the cell surface[77].

7.9. Canine Coronavirus

Canine coronavirus is a classic coronavirus which comes under family: *coronaviridae* and to the order of *nidovirales*. It has a surface morphology contain an envelope, with positive-sense, the single-stranded RNA component of Alpha coronavirus 1. It forms an extremely infectious intestinal disorder globally in the case of dogs. The mode of transmission of this contagious virus strains into the host cell through the attachment of the APN receptor. This virus generally produces diarrhoea or inflammation of the GI tract in the case of contaminated dogs primarily recognized in the year 1971. The capable strains of this enteric canine coronavirus have been identified with several properties, counting pantropic strains of the enteric virus. The accretion of point mutations inside the genome and genetic additions causing the advancement of canine coronavirus results in a usual appearance of viruses among distorted genomic and morphological characteristics, together with their tropism and virulence[78].

7.10. Feline Coronavirus

It is a type of alpha coronavirus and more contagious. It belongs to the family coronaviridae having 29,190 nucleotides polyadenylated RNA genome, capped, enveloped, and positive-strand RNA. This virus transmitted from cats to other vectors, so it called feline coronavirus. Different categories of such viruses are canine coronavirus (CCV), gastroenteritis virus (TGEV), raccoon dog's coronavirus (RDCoV), and Chinese ferret badger coronavirus (CFBCoV). The infirmity with FCoV can result in a different series of cryptograms as clinically in noticeable infections leads to an extremely lethal illness called feline infectious peritonitis (FIP). Therapeutic research in the case of FIP is unclear and not cooperative in building an inequality identification. The feline enteric coronavirus (FECV) and feline infectious peritonitis virus (FIPV) are the two biological groups of feline coronaviruses observed due to in vivo mutation take place inside the already infected cat GI tract[79].

7.11. Miniopterus Bat Coronavirus 1

It is a positive-sense RNA virus or alpha-corona virus having single-stranded, enveloped, and large RNA genome showing replication and observed in the corona-

shape framework and cell characteristics (Fig. 3). The severe acute respiratory syndrome is seen in bats but not found in human life. Different types of diverse coronaviruses with suitable examples are mention in Table 2[80,81].

Table 2: Different types of human corona viruses with specific examples

Types of human corona virus	Examples of types of human corona virus
Alpha coronavirus 1	HCoV-229E, HCoV-NL63, Canine coronavirus, Canine coronavirus type I, Canine coronavirus strain Elmo/02
Beta coronavirus	HCoV-OC43, HCoV-HKU1
Canine coronavirus type II	Canine coronavirus strain NTU336/F/2008
Feline coronavirus	Feline coronavirus Type-I, Feline coronavirus C1Je, Feline coronavirus type II, Feline infectious peritonitis virus WSU 79-1146
Porcine respiratory coronavirus	Porcine respiratory coronavirus ISU-1
Transmissible gastroenteritis virus	Transmissible gastroenteritis virus Transmissible gastroenteritis virus virulent Purdue
Human coronavirus 229E	Human coronavirus NL63, Human coronavirus NL63 Amsterdam 1
Porcine respiratory coronavirus	Porcine respiratory coronavirus ISU-1
Miniopterus bat coronavirus 1	Miniopterus bat coronavirus 1A, Miniopterus bat coronavirus 1A AFCD62, Miniopterus bat coronavirus 1B, Miniopterus bat coronavirus 1B AFCD307, Miniopterus bat coronavirus HKU8, Miniopterus bat coronavirus HKU8 AFCD77/08/05 Mm
Porcine epidemic diarrhoea virus	Porcine epidemic diarrhoea virus CV777
Rhinolophus bat coronavirus HKU2	Rhinolophus bat coronavirus HKU2/HK/46/2006
Scotophilus bat coronavirus 512	Scotophilus bat coronavirus 512/2005

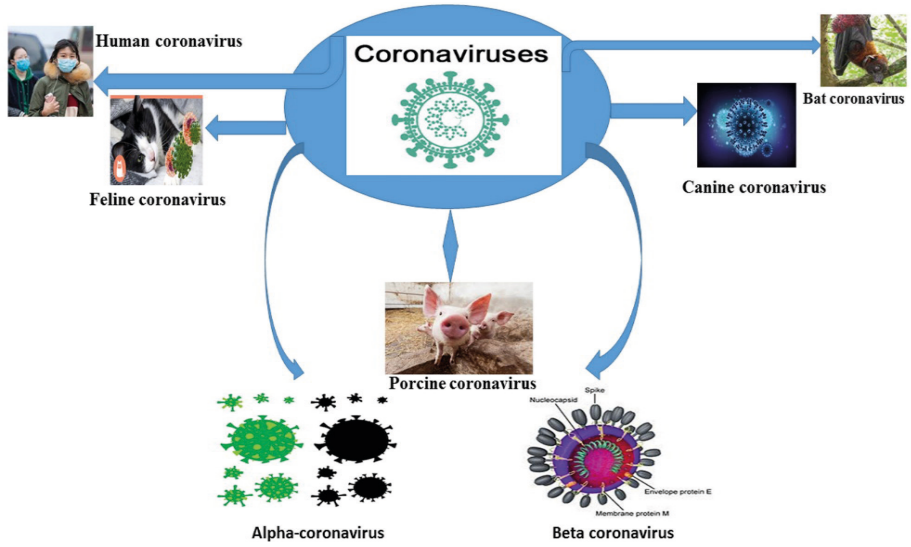

Fig. 3: Schematic representation of various types of corona viruses.

7.12. Hantavirus or Ortho-hantavirus

This virus is seen in rodents or rats and transmitted to humans through their urine, saliva, or faeces. It causes significant complications such as Hantavirus pulmonary or cardiopulmonary syndrome and haemorrhagic fever with renal syndrome. It is a single-stranded, enveloped, negative-sense RNA virus belongs to the family hantaviridae. Over the last, some decades, perceptive and recognition of Hantavirus infection have dramatically expanded worldwide. The terror of Hantavirus outbreaks has been coming to the attention of the world during the Korean conflict, i.e., the American-Korean war during 1950–53. A total of 265 cases, 105 deaths in the southeast region of Asia (Malaysia), the total number of soldiers infected 3000 during the Korean War. In other countries like the U.S, a total of 728 cases, Canada 109 cases, in Germany during 2017, a total of 1713 infections cases is reported. According to the Global Times reports, recently, a man from Yunnan tested positive for Hantavirus. In March 2020; He has passed away due to severe infection. Approximately 32, other people have been suspected and identified for the virus. The earlier diseases outbreak data of radar chart (Fig. 4) compared to the current pandemic virus (COVID-19) global data as of 8th July, 2020 is shown in Table 3 and 4[82–85].

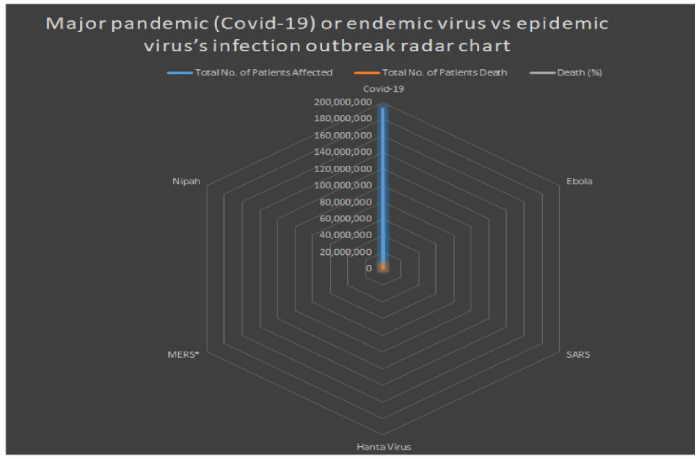

Fig. 4: Major pandemic (COVID-19) vs endemic virus and epidemic virus's infection outbreak radar chart.

7.13. Influenza H1N1 Virus

The influenza A (H1N1) is a swine flu-origin (S-OIV) virus having segments of genetic material seen in humans. The recent H1N1 virus appears to be a fusion of three famous sequences i.e., human influenza RNA and avian, associated with porcine. In the previous two decades, the genomic analysis demonstrated a similar appearance and connectivity to standard reasserting swine influenza A. The inimitable virus subsequently has been isolated in countries of Asia, North America as well as in Europe. During the 1918 pandemic, a sum of 40–50 million deaths rates seen international transmission of a human influenza A (H1N1) virus. In India solely, an approximate quantity of 4.9 million surplus deaths has found out, signifying 2% of the community, which later continued to globally. In 1957, H1N1 inexplicably vanished due to equally contests and resistance to such virus among the peoples and with the occurrence of new H2N2 virus strain and became pandemic. At that moment, around two hundred and thirty persons had serological proof of infectivity leads to one death. Later, on, in January 1976, Fort Dix, New Jersey, around 76 new cases are reported in army soldiers with increased respiratory illness and spread to other countries such as North-Eastern China, Hong Kong, Soviet Union and became epidemic in November 1977. Especially in young adults, it creates a moderately mild sickness, and genetic evidence revealed the similarity of spreadability of virus-related fatality or death rates in 1950 and 1977.

The recurrence was the assumption because of the accidental release of the H1N1 virus from the laboratory with the fading inhabitant's immunity of an infected person [86].

7.14. Zika Virus

Zika virus (ZIKAV) illness is a re-emerging syndrome of mosquitoes. This is produced as of single-stranded RNA arbovirus. Currently, the ZIKAV disease has become a worldwide physical condition difficulty or health issue chiefly subsequent to two foremost outbreaks occurred at the Federal States (Yap Island) of Micronesia as well as the French Polynesia in 2007 and 2013, correspondingly. Also, a major epidemic outbreak in Brazil arises during 2015, the fresh unrecognized merciless complications of ZIKAV infection, like Guillain-Barre syndrome and microcephaly. These syndromes were documented during then, at least 86 diverse countries have reported continual broadcast of ZIKAV infectivity and epidemiological relevance. At present, merely a small number of literature and information have profiled the chemokine and cytokine comeback to the virus amongst diverse populations of patients with ZIKAV illness based on its host and pathogen-specific factors. Moreover, supplementary studies addressing the dynamics of chemokine and cytokine productions amongst diverse communities of patients with ZIKAV illness are needed[87].

7.15. Human Enteroviruses (Coxsackie Virus-A6, A10, A16 and A71)

The first coxsackievirus A10 strain case in South America with the identification of HFMD (Hand-foot-and-mouth disease) is noted. The viral strain corresponds to the lineage concerned in vital European outbreaks and almost certainly entered Uruguay after 2017 with the origin of the Greek era. This investigation calls out for the support of the regional surveillance of HFMD. HFMD is noted as an acute viral ailment associated with high occurrence in human beings younger than five years old, categorized by a vesicular exanthema, principally located in hands, feet, and oral mucosa, connected with the infectivity by diverse Human Enteroviruses i.e. groups of coxsackie-virus (CV) A6, A10, A16 as well as Enterovirus A71. However, during the middle of the early April and June 2019, at some point in outbreak of this disorder in which at least 179 children from Paysandu Province-Uruguay were infected. The CVA10 belongs to the family picornaviridae *and genus* enterovirus *that* comes out within Human Enterovirus Species A. Later this contagion of the

virus became a rising cause of the severe health issues and physical stipulations throughout the last one decade involving neurological complications [88].

7.16. Lassa Fever

In the 1950s, the Lassa fever is first described but the root cause of Lassa disease was not recognized up to the end of 1969. The vital family of arenaviridae is the origin of this single-stranded RNA virus. Around 80% of people who turn out to be contagious with the Lassa virus developed no systematic symptoms. Approximately, 1 in 5 infectivity's ending up in severe sickness, wherever the virus affects persistent organs like the liver, spleen and kidneys. Lassa fever is a zoonotic infection, meaning that humans turn out to be contaminated from contact with contaminated animals. The rodent (Multimammate rat with genus Mastomys) is the animal host of this virus. "Mastomys rats stained with Lassa virus doesn't turn out to be ill, whereas they can lead to the virus in their urine and faces. The primary symptom of such an infection is acute viral haemorrhagic fever with 2-21 days' incubation period and mostly seen in West Africa. It is transferred to human to human or laboratory communication by touching the food items or household remedies stained with rodent feces or urine. Primarily in the medical care center, a health sector for sufficient illness prophylactic and control measures has to be carried out for this disease. Gradually based on the severity, the infection identified to be endemic in several regions of countries of Liberia, Guinea, Sierra, Nigeria, and West Africa, etc. with a fatality rate of 1% in a general and hospitalized case fatality rate of 15% but almost positively exists and isolated in several countries of as well. An early sympathetic concern with rehydration and supportive symptomatic management improves the survival rate of the population[89].

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Chapter 8

Endemics Virus

The term endemic is derived from Greek en meaning in and demics meaning people. It is applicable to explain an infection that is occurred at an approximately steady level within a civilization or nation. Every Nation may encompass an infection that is distinctive and definite reported endemic viral infections are summarized as below:

8.1. Dengue Virus (DENV)

Dengue or Flavivirus is belongs to family Flaviviridae and it is a contagion mosquito-(*Aedes*) borne disease mainly affected in Asia zone of Southeast. It is transmitted to human and identified by serotypes of 1–4 cryptogram of DENV. As per the literature report so far dengue infections 50–100 million peoples are infected globally, and 50, 0000 individuals are required treatments every year. The haemorrhagic shock, hyperthermia, and organ failure are the major complications of dengue affected patients with an incubation period of 5–8 days. The preventive measures for this virus to inject vaccine of live attenuated tetravalent Dengvaxia® to the healthy individuals (9–45 years) and maintain volume of body fluid regularly[90].

8.2. West Nile Virus (WNV)

West Nile virus is a zoonotic flavivirus infection are mainly seen in arthropod such as birds and horses. The birds give out to be the reservoir for this category and mode of transmission arises through the mosquitoes. WNV is mostly found out in countries of West Asia, including the zones or regions of Middle East, and North America, Africa and Europe. The Mammals are well thought-out the dead-end causing hosts which don't donate to the endemic multiply of the pathogen. The standard incubation period for this flavivirus lasts for 2–14 days. The humans those found after a prolonged rate of infection, results out about 20% will experience a mild, distracted illness appearance of elevated temperature or fever, myalgia, stress and headache. Occasionally observed with rashes, and lymphadenopathy; <1% will raise out rigorous neurological disorders[91].

8.3. Japanese Encephalitis (JEV)

Japanese encephalitis is an arthropod-borne Flavivirus virus having 6–16 days' incubation period. It is mostly seen in western pacific south-east Asia and other 24 countries across the globe and became endemic according to the transmission of the virus. The mainstream of confirmed cases is unfocused or asymptomatic; however, clinical symptoms have only been observed in the case of individuals less than 1%, who develop fever, stress, headache, and distorted mental condition, followed by convulsions. In comatose patients, mortality rises from 30 to 40–50% after the occurrence of encephalitis. Due to proper intensive medical care and in time vaccination, 30–50% of infected peoples recovered from Japanese encephalitis due to improved neuropsychological consequence[92].

8.4. Chikungunya (CHIKV)

Chikungunya virus (CHIKV) is also called Alphavirus about the *Togaviridae* groups of family, mostly being observed and transmitted by mosquitoes of the Aedes family in Asian regions. Most of the contaminated patients become symptomatic after an incubation phase of 2–4 days (normal range of 1–12 days). The CHIKV categorized by the commencement of sharp febrile infirmity and appearance of maculopapular rashes. The main symptoms are severe joint pain followed by arthralgia for up to 2 years. The first case of chikungunya is reported in the year 1999 in South Indonesia through the serological test, and again outbreaks in the year 2001 to 2003, and 2008. Gradually the cases are reduced in the rate of 10.1/1000 and seen through the cohort's serological study[93].

8.5. Measles (MV)

Measles is a contagious virus (Person to person) with an incubation period of 12–16 days. It belongs to family *Paramyxoviridae*, and it is high risks to the newborn baby with a lack of passive antibodies and also adults age 20–30 years. The primary complications of measles are a fever with sickness, conjunctivitis, maculopapular, cough, coryza, erythematous (3–5 days), and Koplik's spots. The severity of measles infected patients (40%) are more contaminated and prone to relative immunosuppression with pneumonia [94].

8.6. Rabies (RABV)

Rabies is a type of Bat Lyssaviruses and transmitted from animal strains to humans through saliva and ultimately causes lethal illness to the brains or central nervous

system. The mortality rates of rabies virus almost 50 or 100 per year. The animal dogs mainly spread out this virus and transmitted rabies virus from dogs to other wildlife animals through the whole vital tissue. The most contagion rates about 95% worldwide are the Asian and African continent death counts among the cumulative reported transmission[95].

8.7. Avian Influenza (AI)

Avian influenza is the subtypes of H5N1 and H7N9 belongs to family *Orthomyxoviridae,* and it is a contagious virus under the category respiratory disorder. The first Avian H5N1 influenza reported case was seen in Hong Kong in 1997 and later spreads to the southeast of Asia than Indonesia in December 2003 through poultry and declared as endemic. In July 2005, monthly 5 to 3 cases have been reported in humans from chicken even through control measures to secure further communication, and the rate of spreading of influenza in human's further decreases gradually in the year 2008[96].

8.8. Hepatitis-A Virus (HAV)

Hepatitis A virus strain is a food-borne infection mostly seen in 90% of the human race, the leading kids below ten years of age in Indonesia. Later, endemic zones of the population show less acute infections of Hepatitis A due to increased community-based resistance. Further contaminations spread to older generations from airdrops lower-age kids, which turns out to be a lucid enhancement in hygiene. This turn-down observed in seroprevalence between kids, and young people noticed in Indonesia and other continents. Alternations of the epidemiologic prototype have quantifiable and community fitness implications, but somehow the unified worldwide the causative infectivity and the early vaccination may economical for the management of Hepatitis A virus illness. Utilizing travel medicine guidelines for individuals travelling to Indonesia, HAV immunization usually suggested for safety measures[97].

8.9. Seasonal Influenza and Influenza-like Illnesses

Influenza viruses (A, B, and C) belong to the family Orthomyxoviridae and mainly causes respiratory syndromes in human. The Influenza A targets and infects around 5–15% of the human civilization every year. Most of the time, this virus spread infection, and maximum active cases seen in tropical Indonesia regions. Storms *et al.,* 2011 conducted a study and found that 76% positive PCR test with

the occurrence of influenza virus or influenza-like illness observe in patients with critical respiratory problems in the month of December-May every year, but 36% had other brutal disorders during the weeks with maximum influenza-based activity. MoH-RI suggested antiviral oseltamivir medicine or vaccines in early stages or practical implementation of drug programs across Indonesia, to reduce the influenza cases up to 15% during the endemic[98].

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Chapter 9

Global Current Preclinical and Clinical Status of COVID-19 Vaccine

A lot of new drugs, including monoclonal antibodies, immunoglobulins, and vaccines are now in pipelines and already designed to treat the novel COVID-19, which, at this moment called pandemic globally. Numerous Pharmaceutical giant companies like Pfizer, Novartis, GSK, Bayer, Abbot, Sanofi as well as World top most Biopharmaceutical and vaccine manufacturing companies, like Gilead Sciences, Zhejiang Hisun, Airway Therapeutics, CMG Biotech, Regeneron and Government and Private research organizations etc. are working 24/7 to bring out novel molecules. These vaccines will fight against this contagious syndrome of COVID-19 with fewer periods. The complete data of the preclinical and clinical status of ongoing trials of drugs, drug therapy, and its potential options are demonstrated in Table 4 and the list of recent novel coronavirus (COVID-19) vaccines and manufacturing companies in various stages of development, across the world till 20th December, 2020 are depicted in Table 5 [99–141].

Table 3: Global data of pandemic (COVID-19) virus vs epidemic viruses till 21st July, 2021

Name of virus and year of origin	Virus origin country	Subtypes of virus	Major animals source	Five major affected countries	Name of detection and diagnostic tests	No. of patients affected globally	No. of patients death globally	Fatality rate (%)
COVID-19 2019-2020 (As on 21st July-2021)	China	229E (alpha coronavirus) NL63 (alpha coronavirus) OC43 (beta coronavirus) HKU1 (beta coronavirus) MERS-CoV, SARS-CoV SARS-CoV-2	Ant-eating pangolin and Bat	USA, India, Brazil, Russia, and France	Real-time reverse-transcription polymerase chain reaction (rRT-PCR) assays, rRT-PCR assay, Nasopharyngeal and oropharyngeal swabs test, ELISA, or enzyme-linked immunosorbent assay, is a screening test used to detect the presence and concentration of specific antibodies that bind to a viral protein.	192,281,116	4,134,015	2.1499984

Ebola 1976 2014-2016 (Outbreak)	DRC (Democratic Republic of Congo)	Zaire, Sudan, Bundibugyo, Tai Forest (formerly known as Côte d'Ivoire), and Reston	Wild animal or fruit bat. Besides bats, other wild animals sometimes infected with EBOV include several monkey species, chimpanzees, gorillas, baboons, and duikers	Democratic Republic of Congo, Sudan, Gabon, Cote d'Ivoire, South Africa, Uganda. Congo, Guinea, Sierra Leone and Liberia; one of America, United States of America and one of Europe, Spain. Guinea, Liberia and Sierra Leone. It also affected Italy, Mali, Nigeria, Senegal, Spain, the United Kingdom and the United States.	Reverse transcription polymerase chain reaction (RT-PCR) for detection of Ebola virus RNA and antigens in blood samples	33687	14693	43.61
Nipah 1998-1999	Malaysia and Singapore	RNA virus in the genus Henipavirus	Sick Pigs or Fruit Bats	Malaysia and Singapore, Bangladesh and India	NAAT, eg, PCR and sequencing), IgG/ IgM/antigen ELISA, Immunofluorescence assay, histopathology, and virus isolation and neutralisation.	265	105	39.62

SARS (Severe Acute Respiratory Syndrome) 2002-2003	China, Canada, Hong Kong Special Administrative Region of China, Chinese Taipei, Singapore, and Hanoi in Viet Nam.	SARS-CoV-2	Bats, Civet cats	Southern China, Toronto in Canada, Hong Kong Special Administrative Region of China, Chinese Taipei, Singapore, and Hanoi in Viet Nam.	Real-time reverse transcriptase–polymerase chain reaction (rRT-PCR) of nasopharyngeal swabs typically has been used to confirm the clinical diagnosis.	8000	800	10
MERS* (Middle East respiratory syndrome) 2012-2015	South Arabia	MERS-CoV	Dromedary camels and Bats	South Arabia, Middle East, Africa and South Asia, Egypt, Oman, Qatar, Algeria, Austria, Bahrain, China, France, Germany, Greece, Islamic Republic of Iran, Italy, Jordan, Kuwait, Lebanon, Malaysia, the Netherlands, Philippines, Republic of Korea, Kingdom of Saudi Arabia, Thailand, Tunisia, Turkey, United Arab Emirates, United Kingdom, United States, and Yemen.	Gold standard in-house RT-rtPCR assays as well as virus culture in Vero and LLC-MK2 cells. A colorectal adenocarcinoma (Caco-2) epithelial cell line has since been recommended for isolation of infections MERS-CoV. PCR-based techniques are the preferred method for MERS-CoV detection.	1000	400	40

Hantavirus 1950-1953 2017, 2020	China		Rodents (rodent-borne), Rat, deer mice	China, US, Canada, Germany	Serologic Assays Tests based on specific viral antigens from SNV have since been developed and are now widely used for the routine diagnosis of HPS. CDC uses an enzyme-linked immunosorbent assay (ELISA) to detect IgM antibodies to SNV and to diagnose acute infections with other hantaviruses.	5582	1	0.018

Table 4: Present preclinical and clinical status of proposed drug substances used for preventive measures for treatment of corona virus (COVID-19) worldwide till 21st July, 2021

Name of drugs and available brands	Therapeutic category	Recommended dose	Stages of pre-clinical and clinical trial status against novel COVID-19	Manufacturing companies details	References
Remdesivir (GS-5734)	Adenosine triphosphate analog. Broad-spectrum antiviral I	A five-day and ten-day dosing regimen of an intravenous formulation.	Remdesivir has demonstrated significant activity and prominent results in a case involving American patient in preclinical trials, and Chinese in vitro tests in Phase III Clinical trial involving a total of 761, patients in a randomized, placebo-controlled, double-blind study at multiple hospitals in Wuhan, China. Analysis was carried out by the Centres for Disease Control and Prevention COVID-19 response team.	Gilead Sciences Inc. Foster City, California, United States.	[99-101]
Favilavir (or T-705 or Avigan)	Experimental antiviral drug. Pyrazinecarbox amide derivative viral RNA polymerase inhibitor.	600 mg tid with 1600 mg first loading dosage for not more than 14 days.	The drug has reportedly revealed effectiveness in managing the syndrome with minimal side effects. Initially the trials involved a total number of 340 patients, and it has a "high degree of protection," as the drug has already been developed and approved for usage in treating flu. According to China science and technology ministry, later according to Japanese Ministry, the clinical trial involving 70 patients. The clinical trial is being conducted in Shenzhen, Guangdong province. Estimated study completion: June 2020.	Zhejiang Hisun Pharmaceutical, China	[102, 103]

Sildenafil (Revatio, Viagra)	Phosphodiesterase (PDE) inhibitors.	Sildenafil citrate tablets 0.1g/day for 14 days.	Clinical trial involving Phase 3, 10 participants. Observe the efficacy and safety of G1, drug in patients with COVID-19 under clinical actual diagnosis and treatment conditions. Rate of disease remission. & Time of entering the critical stage analysis Time outline 14 days.	Tongji Hospital, Hubei, China	[104, 105]
Lopinavir and Retonavir (Kaletra, Aluvia)	Anti-HIV, Antiretroviral Protease inhibitors, Combination protease Inhibitor and host.	Adults 500 mg once, twice a day, 2 weeks.	A total of 199 patients with laboratory-confirmed SARS-CoV-2 infection underwent randomization. Clinical trials COVID-19, clinical studies SARS, in vitro and clinical studies SARS-CoV, in vivo studies MERS-CoV2.	Abbott Laboratories, Abbott Park Business Centre, Lake Bluff, Illinois, United States.	[106]
Baloxavir marboxil (Xofluza)	Antiviral (End nuclease inhibitor)	80 mg on day 1, afterwards 80 mg on day 4; and on day 7 as required. (Over ally, Not more than 3 times administration).	Employed for management of influenza vaccine of phase II & III Clinical trials. Anticipated for various influenza infections like A (H1N1), influenza A (H3N2), or influenza B infections, and novel corona virus pneumonia (COVID-19).	Genentech, (member of the Roche Group), US.	[107-109]
AT-100	A recombinant human surfactant protein D (rhSP-D)		AT-100 has revealed better efficacy in preclinical studies in reducing swelling and illness in the lungs, while also generating an immune response in opposition to various respiratory syndromes.	Airway Therapeutics LLC, US.	[110, 111]

Corticosteroids	Steroid hormones (glucocorticoids) with effective Drug component: Methylprednisolone	Methylprednisolone 40 mg q 12h for 5 days.	Clinical trial COVID-191, and studies related to SARS, MERS, has carried out. Phase III clinical trial performed for H1N15. Recently Efficacy and Safety of Corticosteroids in COVID-19: A Prospective Randomized Controlled Trails has started with approx. 400 participants on February 14, 2020 and estimated completion date on May 30 2020, for Novel Coronavirus Pneumonia.	Symbiotech Pharma Lab Pvt. Ltd., Indore, India	[112-114]
mRNA-1273		25 microgram (mcg), 100 mcg, 250 mcg dose. Levels of mRNA-1273 given on a two-dose vaccination schedule 28 days.	The first US clinical trial of a COVID-19 vaccine which is mRNA-1273, has in progress at Kaiser Permanente Washington Health Research Institute (KPWHRI) in Seattle. The open-label Phase I trial has carried out with dosage levels of 25μg, 100μg, 250μg dose levels of drug employed on a two-dose vaccination scheduled with enroll of 45 healthy adult volunteers of ages 18 to 55 over approximately 6 weeks, the company has already started formulations of mRNA-1273 material for the Phase II study.	Modern and Vaccine Research Centre, Cambridge, Massachusetts, US.	[115, 116]
Danoprevir + ritonavir	(HCV) protease inhibitor and Nucleoside Inhibitor	Danoprevir 100 mg single dose before and after administration of ritonavir 100 mg twice daily for 10 days.	National Health Commission of the People's Republic of China issued the implementation of the oral hepatitis C protease inhibitor Ganovo (Danoprevir, ASC-08), in combination with ritonavir, to extravagance the COVID-19 patients. A total of 11 number of patients are enrolled in clinical trial and undergone better treatment under Diagnosis and Treatment Program for Novel Corona virus Infection.	Ascletis Pharma Inc., Jianghan Road Binjiang Di Hangzhou, China	[117-119]

Sirolimus (Rapamycin, Rapamune®)	Immunosuppressant and mTor inhibitor IL2	solution in a concentration of one mg/ml, Influenza: 1 mg 1xday. Severe H1N1 pneumonia: 2mg 1xday.	In vitro studies MERS-CoV: Huh7 cells; Sirolimus mostly retained inhibitory activity adjacent to MERS-CoV; whether it was added pre- or post-infection during stages of clinical trials.	Pfizer Ltd., New Work, USA	[120, 121]
Novaferon, Nova	Anti-cancer; Recombinant protein produced by DNA-shuffling of IFN-α	20g/ time, atomized inhalation (in one trial, in combination with Arbidol tid. Arbidol Tablets 200mg/ time, p.o.tid).	Clinical trials initiated for COVID-19 Randomised controlled trial. N=90 with COVID-19 randomised to Novaferon.	Genova Biotech, Beijing, China	[122, 133]
Chloroquine or Hydroxychloroquine; (Resochin)	Antimalarial agent, heme polymerase inhibitor; Malaria prophylaxis and treatment	Hydroxychloroquine 0.1 oral 2/ day, Hydroxychloroquine 0.2 oral 2/ day (Now WHO banned to take such medications for covid patients)	Double blind n=300 with COVOID-19, randomised 1:1:1 to hydrochloroquine (0.1/0.2 oral /day) Estimated study completion: August 31, 2020/December 31, 2020.	Bayer, Germany	[124]
Abidol (Umifenovir)	Non-nucleoside broad spectrum agent, Antiviral activity	Arbidol Tablets 200mg/ time, P.O.TID. Ordinary treatment plus a regimen of arbidol (100mg) (oral, tid, 200mg each time, taking for 7-14 days).	Intended for in vitro study of SARS-CoV: -(GMK-AH-1 cells) - Arbidol and arbidol mesylate were revealed to contain a straight antiviral outcome in early viral replication in the cultured cells. (Russian).	JSC Pharmstandard Tomskchempharm, Russia	[125, 126]

Lopinavir/Ritonavir vs Chloroquine	Anti-HIV, antiretroviral protease combination with heme inhibitors Polymerase inhibitor (antimalarial).	lopinavir 200 mg/ Ritonavir 50 mg twice daily with 0.1 oral 2/ day of hydroxychloroquine	Multicentre, open labelled, randomized clinical trial N=150 with mild COVID-19 Randomised to Lopinavir/Ritonavir, Hydroxychloroquine, or Conventional treatment. Mild and sever symptoms randomized to n=59 (Mild) and n=14 (severe) with combination therapy of Chloroquine + lopinavir/ritonavir.	1. Abbott Laboratories, United States. 2. BAYER, Germany	[127-130]
Darunavir (with cobicistat) Prezcobix	(HIV-1) Protease inhibitor	Darunavir 800 mg/ Cobicistat 150 mg QD.	Conventional treatment for Phase 3, randomized, open label clinical trial initiated with number of (N=30) patients with COVID-19.	Cipla labs, Mumbai, India	[131]
IFN-β1b (Betaseron®/ Betaferon®, Extavia®)	Antiretroviral	62.5 (a quarter of the dose) every other day, increasing gradually over 19 days to arrive at the suggested dose of 250 micrograms (μg) should be administered every other day	The analysis has been carried out by using SARS-CoV (invitro), and MERS-CoV(invivo) treatment trails have been implemented.	Schering AG, germany, Marketed by Bayer Pharma., Germany, New version of IFN-β1b marketed by Novartis, Basel, Switzerland	[132]
Ribavirin + Ritonavir + Lopinavir	Nucleoside Inhibitor + Protease inhibitor	Lopinavir 400 mg/ ritonavir 100 mg orally twice daily should be administred, plus (2) ribavirin 2.4 gm or 101-240 mg orally as a recommended dosage	Clinical trial has completed for SARS. Clinical trial: (1) lopinavir 400 mg/ritonavir 100 mg orally 2 times has been given, with (2) as a loading dose Ribavirin 2.4 g orally followed by 1.2 g orally every 12 hours. Duration of treatment up to 10 days. Case study: ribavirin 600mg 2x day and lopinavir + ritonavir 1000mg 1x day.	CMG Biotech, New Delhi, INDIA, and Abbott Laboratories, Abbott Park United States.	[133, 134]

Ribavirin + Corticosteroids	Nucleoside Inhibitor+ Steroid hormones (Glucocorticoids) with effective Drug component: Methylprednisolone	Methylprednisolone 40 mg q 12h for 5 days with ribavirin 2.4 gm or 101-240 mg orally	Potential observational revision of 2002 SARS-CoV infected patients who received standard regimen with ribavirin (14 days) and corticosteroids (21 days); clinical outcomes were implemented for 3 weeks.	CMG Biotech, New Delhi, INDIA with	[135-137]
INO-4800	DNA vaccine against novel Covoid 19.	Two doses of the vaccine 28 days apart	The companies already started pre-clinical testing for clinical product manufacturing during January 10, 2020. The company has also prepared 3,000 doses for human clinical trials using 30 healthy volunteers, which is expected to begin in April 2020 in the US, followed by China, and South Korea. A phase I clinical trial is planned to be conducted in parallel in China, by Beijing Ad vaccine. Results from the clinical trials are predictable to be accessible in September 2020.	Inovio Pharmaceuticals, Wateridge Circle San Diego, CA and Beijing Advaccine Biotechnology, Beijing.	[138]
REGN3048-305 and Kevzara (sarilumab)	Monoclonal antibodies [R REGN3048 and REGN3051, and Kevzara (fully monoclonal antibody, interleukin-6 (IL-6) receptor antagonist]	Minimum one or two doses (low dose, high doses) of the vaccine for 1-2 Months based upon disease conditions of patients	The mutual combination of neutralizing monoclonal antibodies like REGN3048 and REGN3051 is being premeditated against Novel Covoid-19 in a first-in-human clinical trial sponsored by the National Institute of Allergy and Infectious Diseases (NIAID). The safety and tolerability of the drug will be analyzed in 48 patients. Especially for Phase II & III clinical trial in patients with severe COVID-19 infection Regeneron has partnered with Sanofi to evaluated Kevzara has initiated successfully for up to 400 patients in U.S.	1. Regeneron Pharmaceuticals, Inc. Eastview, near Tarrytown, New York. 2. Regeneration Pharma Partnership with Sanofi, Paris, France.	[139-141]

Table 5: List of novel coronavirus (COVID-19) vaccines and manufacturing companies in various stages of development, and early approval for emergency uses across the world till 21st July, 2021

Name of novel coronavirus vaccines	Name of Manufacturing company under development with other international collaborations	Developing country	Applications and purposes	Manufacturing company official web link	Current preclinical and clinical trial status
Fusogenix DNA vaccine 1. Covigenix - VAX-001 Spike protein 2. Covigenix - VAX-002 Multiple epitopes	Entos Pharmaceuticals In partnership with ImmunoPrecise , Johnson & Johnson Innovation J Labs, MERCK, OOISIN Biotechnologies	Canada	Fusogenix drug delivery platform is a proteo-lipid vehicle that introduces genetic payload directly into the cells. It developing an optimised payload containing multiple protein epitopes derived from SARS-COV-2 proteins, which will stimulate an immune response in the body to prevent COVID-19 infection.	https://www.entospharma.com/about	The company completed preclinical testing for safety and efficiency. Covigenix-VAX-001 entered Phase- I clinical trials.
ChAdOx1 nCoV-19 AZD2816 Vaccine	University of Oxford	United Kingdom	This vaccine is on under clinical trial planned to be conducted the study by taking approximately 510 volunteers aged between 18 years and 55 years. The studies are initiated against the B.1.351 variant of concern 2,250 participants across UK, South Africa, Brazil and Poland. AZD2816 will be administered to individuals who have previously been fully vaccinated with two doses of the original Oxford-AstraZeneca vaccine or an mRNA vaccine, at least three months after their last injection. The study aims to assess the immune response to the Beta variant of concern with the new vaccine.	http://www.ox.ac.uk/news-and-events/coronavirus-research	Competed phase III human trials and applied for approval. Phase II/III trial initiated since 27th June 2021.

Gimsilumab	Roivant Sciences	United States	The drug targets granulocyte-macrophage colony stimulating factor (GM-CSF), which is a pro-inflammatory cytokine found in high levels in the serum of COVID-19 patients and targeting GM-CSF is expected to reduce lung damage and reduce mortality rate in COVID-19 patients.	https://roivant.com/#contact	Currently in Phase III development stage
T-COVIDTM	Altimmune and University of Alabama at Birmingham (UAB) collaborations	United States	Single-dose intranasal therapeutic for the treatment of early COVID-19. Currently immunogenicity studies followed by development of phase one clinical trial material under progress against COVID-19 virus.	https://altimmune.com/pipeline/	Preclinical animal studies completed and phase III clinical trial during the third quarter of 2020. Completed Phase I and II clinical trials
NasoVAX™			A recombinant intranasal vaccine that is being developed for both seasonal and pandemic use. NasoVAX can activate the humoral, mucosal and cellular immune arms in unison for a more comprehensive immune response.		Preclinical animal studies completed. Completed Phase I clinical trials.

TJM2	I-Mab Biopharma	China	It is a neutralising antibody, as a treatment for cytokine storm in patients suffering from a severe case of coronavirus infection and the drug targets the human granulocyte-macrophage colony-stimulating factor (GM-CSF), which is responsible for acute and chronic inflammation. TJM2 in reducing or preventing cytokine release syndrome (CRS) and neurotoxicity associated with CAR-T therapy through collaborations.	http://www.i-mabbiopharma.com/en/Pipeline.aspx	I-Mab seeks approval for COVID-19 trial in South Korea during March 31st, 2020. Completed Phase I clinical trials.
Coronavirus vaccine	Medicago and Laval University's Infectious Disease Research Centre collaborations and also partial research funded by Canadian Institutes for Health Research (CIHR).	Canada	To develop antibodies against SARS-CoV-2 bu successfully producing virus-like particles (VLPs) of the coronavirus just 20 days after obtaining the SARS-CoV-2 gene (virus causing the COVID-19 disease).	https://www.medicago.com/en/	Preclinical study completed Phase I/II/III trial completed and applied for registration.

AT-100 (rhSP-D)	Airway Therapeutics, Inc	Basel, Switzerland as well as its affiliate in Toronto, Canada	This vaccine showed efficacy in preclinical studies in reducing inflammation and infection in the lungs, while also generating an immune response against various respiratory diseases. A novel recombinant human protein rhSP-D – an engineered version of an endogenous protein – that reduces inflammation and infection while modulating the immune response to break the cycle of injury and inflammation.	https://www.airwaytherapeutics.com/pipeline/	Pre-clinical studies completed and clinical trials Phase I under developmental stage.
TZLS-501	Tiziana Life Sciences	United Kingdom	It binds to human anti-interleukin-6 receptor (IL-6R) receptor and preventing lung damage and elevated levels of IL-6 and also depleting the amount of IL-6 circulating in the body thereby reducing chronic lung inflammation.	https://www.tizianalifesciences.com/our-drugs/anti-il-6r/	Pre-Clinical trials completed on May 2021 and filed IND.

OYA1	OyaGen	United States	It shows strong antiviral efficacy against coronavirus in laboratory essays and it is more effective than chlorpromazine HCl in inhibiting SARS-CoV-2 from replicating in cell culture.	http://www.oyageninc.com/wordpress/drugs	COVID-19: OyaGen assesses candidate; Airway files for testing. Pre-IND discussions with the FDA have confirmed studies, human Phase I clinical trials initiated.
BPI-002	BeyondSpring	United States	This vaccine able to activate CD4+ helper T cells and CD8+ cytotoxic T cells and generating an immune response in the body and may helpful for corona virus infections.	https://www.beyondspringpharma.com/pipelineoverview/index.aspx	BPI-002 can potentially function as an adjuvant to provide improved long-term humoral (B-cell dependent) protection against future viral infections (COVID-19). Investigational new drug-enabling studies and efforts related to manufacturing and safety testing have been initiated.

INO-4800/ CELLECTRA® (Device)	Inovio Pharmaceuticals and Beijing Advaccine Biotechnology and grant supported by Coalition for Epidemic Preparedness Innovations (CEPI).	United States	Preclinical trials are ongoing and the design for human clinical trials have been completed and plans for large-scale manufacturing have also been developed. The studies will evaluate the safety, tolerability and immunogenicity of INO-4800, a Prophylactic Vaccine Against SARS-CoV-2	https://clinicaltrials.gov/ct2/show/NCT04336410	Phase I clinical trials completed by May 27 2021.
NP-120 (Ifenprodil) NP-121 (Radiprodil)	Algernon Pharmaceuticals	Canada	It is an N-methyl-d-aspartate (NDMA) receptor glutamate receptor antagonist sold under the brand name Cerocal and efficacy in improving survivability in mice infected with H5N1. It possess a similar phenylethanolamine pharmacophore as NP-120 (Ifenprodil), in its initial IPF in vivo animal study. In the study, both compounds, at the same dose, reduced fibrosis to a similar extent.	https://algernonpharmaceuticals.com/ipf-np-120/	NP-120 (Ifenprodil) is already approved with an established safety history,in Preclinical animal models. Completed Phase I clinical trials and now moves to Phase II.
APN01	University of British Columbia and APEIRON Biologics	Canada	The research revealed that the ACE2 protein was the main receptor for the SARS virus and the clinical trial will test the drug's efficacy in reducing the viral load in patients.	https://news.ubc.ca/2020/03/06/ubc-researchers-get-funding-to-help-in-global-response-to-covid-19/	APN01-1-01 completed Phase II clinical trials

mRNA-1273 vaccine	Moderna, Inc., (Nasdaq: MRNA) a clinical stage biotechnology company and Vaccine Research Center and collaboration the Vaccine Research Center, a unit of the National Institute of Allergy and Infectious Diseases (NIAID).	Canda	The vaccine targets the Spike (S) protein of the coronavirus and a total of 45 males and females aged between 18 and 45 have been enrolled for the trial. The participants will be divided into three cohorts who will be administered 25 microgram (mcg), 100mcg or 250mcg dose 28 days apart.	https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-first-participant-dosed-nih-led-phase-1-study	Moderna got early FDA approval for emergency uses
Avian Coronavirus Infectious Bronchitis Virus (IBV) vaccine	MIGAL Research Institute	Israel	The vaccine has demonstrated efficacy in pre-clinical trials conducted by the Volcani Institute.	https://www.migal.org.il/en	Phase I completed and under Phase II initial development
TNX-1800	Tonix Pharmaceuticals and collaborated with Southern Research, a non-profit research organisation.	United States	The vaccine is a modified horsepox virus developed using Tonix's proprietary horsepox vaccine platform and to express a protein derived from the virus that causes the coronavirus infection.	https://www.tonixpharma.com/pipeline/tnx-1800-coronavirus-vaccine	Now under Phase II/III trials study.
Brilacidin	Innovation Pharmaceuticals and agreements with university in the US and 12 biocontainment labs in the US for evaluation of Brilacidin as a treatment for COVID-19.	United States	It shows antibacterial, anti-inflammatory and immunomodulatory properties in several clinical trials and earlier reported for inflammatory bowel disease and oral mucositis in cancer patients.	http://www.ipharminc.com/brilacidin-1	Phase III human trials for other clinical indications ongoing.

Recombinant subunit vaccine	Clover Biopharmaceuticals using its patented Trimer-Tag© technology and also collaborating with GSK to develop a vaccine using the latter's pandemic adjuvant system.	China	Recombinant subunit vaccine based on the trimeric S protein (S-Trimer) of the COVID-19 coronavirus, which is responsible for binding with the host cell and causing a viral infection.	http://www.cloverbiopharma.com/index.php?m=content&c=index&a=lists&catid=42	Phase-II completed Phase III clinical trials ongoing.
Vaxart's coronavirus vaccine	Vaxart's company	United States	It is an oral recombinant vaccine in tablet formulation using its proprietary oral vaccine platform, VAAST and its genome of 2019-nCOV to be tested in pre-clinical models for mucosal and systemic immune responses.	https://investors.vaxart.com/news-releases/news-release-details/vaxart-announces-positive-pre-clinical-data-its-oral-covid-19	Completed Phase-II clinical trial study.
CytoDyn-leronlimab (PRO 140)	CytoDyn company	United States	This drug is a CCR5 antagonist potential coronavirus drug. This drug is already approved by USFDA for phase two clinical trials for treatment of HIV	https://www.cytodyn.com/pipeline/covid-19	Currently enrolling patients in three clinical trials.
Linear DNA Vaccine	Applied DNA Sciences and Takis Biotech	United States	Polymerase Chain Reaction (PCR)-based DNA manufacturing technology will be used to develop the vaccine for corona virus for effective without being inserted into the patient's genome.	https://adnas.com/	Applied for preclinical tests.

BXT-25	BIOXYTRAN	United States	It is used to treat for Acute Respiratory Distress Syndrome (ARDS) in late-stage patients infected with the coronavirus. The other application for diffusion of oxygen to the blood is comprised in patients suffering from ARDS leading to fluid build-up in the lungs for quick recovery of patients from corona virus	https://www.bioxytraninc.com/about#pipeline	To start clinical trials
Covaxin & BBV154 intranasal vaccine	Bharat Biotech is developed in collaboration with the Indian Council of Medical Research (ICMR)-National Institute of Virology (NIV).	India	Inactivated vaccine is developed and manufactured in Bharat Biotech's BSL-3 (Bio-Safety Level 3) high containment facility. Intranasal vaccine stimulates a broad immune response – neutralizing IgG, mucosal IgA, and T cell responses.	https://www.bharatbiotech.com/	Drug regulator recently granted permission to initiate phase III human clinical trials for COVID-19 vaccine with 25,800 participants, >2400 volunteers were above 60 years of age and >4500 with comorbid conditions. Covaxin. Demonstrated 77.8% vaccine efficacy against symptomatic COVID-19 disease, through evaluation of 130 confirmed cases, with 24 observed in the vaccine

					group versus 106 in the placebo group. The efficacy against severe symptomatic COVID-19 disease is shown to be 93.4%. The efficacy data demonstrates 63.6% protection against asymptomatic COVID-19. Efficacy data demonstrates 65.2% protection against the SARS-CoV-2, B.1.617.2 Delta variant Completed preclinical testing on Mice, Hamsters and Rhesus Macaques.
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Chapter 10

Impact of Post COVID-19 on Science and Technology

The global outbreak of COVID-19 response demands the strengthened applications of science and technology. The current pandemic has exaggerated numerous fields of space, science, technology-organizations, government, private, government-aided agencies worldwide, leading to compact productivity, reduced gross domestic product, (GDP), and economic downturn[142]. On the other hand, it has also opened an abundant novel funding research outline in a figure of governmental agencies and various research firms all over the globe. The chosen examples, like polymerase chain reaction (PCR)-based testing kits approved by Japan for faster testing and improving regime with the rising command for simpler and rapid analysis. Moreover, the influence of the COVID-19 pandemic leading to declined efficiency, hits all-time lowest level on several programs, affecting the human race in both developed and emerging economies. The impact and interactions extend over almost all the sectors ranging from manufacturing to trade, real estate, tourism, transport, education, healthcare, and so on. Revolutionary changes have also been observed in topmost world space researches like National Aeronautics and Space Administration (NASA), intergovernmental organizations like European Space Agency (ESA), and Japan Aerospace Exploration Agency (JAXA), closure of commercial aerospace like Rocket Lab and Bigelow Aerospace etc. By the meantime, the internet traffic and telecommunications sectors reflect its huge strain or a sharp rise in usage; as teleconferencing, video communications has served as a substitute or replacement for cancelled events as well as daily big business meetings and social contacts. These also act as a source of avoiding social problems and overcrowding. However, the extent of the economic impact will rely on how the virulent disease outbreak unfolds and the repression strategy of any Nation [143]. The fruits of scientific research, counting capable vaccines, those have to be developed, targeted and shared universally. Several such initiatives, strategies are in place; but must be scaled up efficiently as per demands. Although

the result from the crisis is both amplifying familiar risks and creating new things, but the innovatory changes at this scale create pioneer openings, new challenges, and roots to build back the nation even better[144].

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Chapter 11

COVID-19 (SARS-COV-2) Variants and its Origin

Viruses constantly transform mutation. The emerging of new virus variants is now observed in some leading countries like the US, South Africa, Brazil, etc. In association with expert networks, WHO, national authorities, institutions, and researchers, have been closely monitoring and judging the evolution of SARS-CoV-2 since January 2020. In recent times, thousands of assorted variants of COVID-19 are socializing across the ecosphere due to mutagenic alternation or changes in genetic sequence. Viruses mutate all time, and most changes are inconsequential and life-threatening, but others can make the disease more infectious and complicated. These potentially concerning changes are called "variants of concern" and are reserved under the closest monitoring by health officials, doctors, and the WHO and Centre for Disease and Control (CDC) official warnings globally. The notable variant of COVID-19 is to spread more easily and quickly than other variants, which may lead to complex cases of COVID-19 and increased count of fatality rate progressively. An increase in cases will put more strain on healthcare resources, lead to more hospitalizations and potentially more deaths. Therefore far, studies recommend that the recent authorized USFDA approved vaccines like Covishield (Oxford-AstraZeneca, US), DCGI approved Covaxin (Bharat Biotech, India), Sputnik V (Russia) work on the circulating variants up to some extent. A clear implication of the emerged variants and SARS-CoV-2 (B.1.1.7 as Alpha, B.1.351 as Beta, B.1.617.2 as Delta, and P.1 as Gamma). They recently generated (B.1.525 as Eta, B.1.526 as Iota, and B.1.617.1 as Kappa) novel expanding sources of viruses are enlisted in Table 6 and depicted in Fig. 5[145–160].

Table 6: List of different types of SARS-CoV-2 variants, origin and detected country/city name in India and Abroad

Types of SARS-CoV-2 variants	Origin country/ region	Detected country/ spreading city	Year of origin	References
B.1.1.7 (Alpha)	United Kingdom	United States	Earliest identified samples Sep 2020. Date of designation 18 December 2020	[151, 152]
B.1.351 (Beta)	South Africa	United States	December 2020 (SA) End of Date of designation Dec 2020, and closely monitored in January 2021 (US)	[152–154]
P.1 (Gamma)	Brazil	UK and 10 more countries	Nov 2020 early detection date of designation Jan 2021	[152–154]
B.1.617.2 (Delta)	UK, India,	Chandigarh, Kerala India, Europe, North America, and Africa	December 2020 documented samples, Date of designation 4 Apr 2021.	[152–155]
Lineage B.1.525 (Eta)	UK	Dermark, France, Spain, Switzerland, Germany, USA, UK, and many more	Multiple countries, Dec-2020, designation date, VOI on 17 mar 2021	[155, 156]
B.1.526 (Iota)	UK	USA, UK (Britain)	United States of America, Nov-2020, Date of VOI on 24-Mar-2021	[156, 157]
(B.1.617.1 (Kappa)	India	India	India, Oct-2020, Date of designation 4-Apr-2021	[156, 158]

Types of SARS-CoV-2 variants	Origin country/ region	Detected country/ spreading city	Year of origin	References
C.37 **(Lambda)**	Peru	Argentina, Brazil, Colombia, Ecuador, and Mexico, and has since spread to the UK	15 June 2021, but was first identified in Peru in August 2020	[155, 159]
B.1.1.529 **(Omicron)**	Botswana, South Africa	United Kingdom, Israel, Denmark, Europe	26 November 2021	[182]
B.1.640.2 **(IHU)**	France	Mediterranee Infection institute in Marseille, southeastern France	December 2021	[183]
Double variant of Covid-1 **(Delmicron)**	US	US and Europe	December 2021	[184]

**VOI: Variant of Interest*

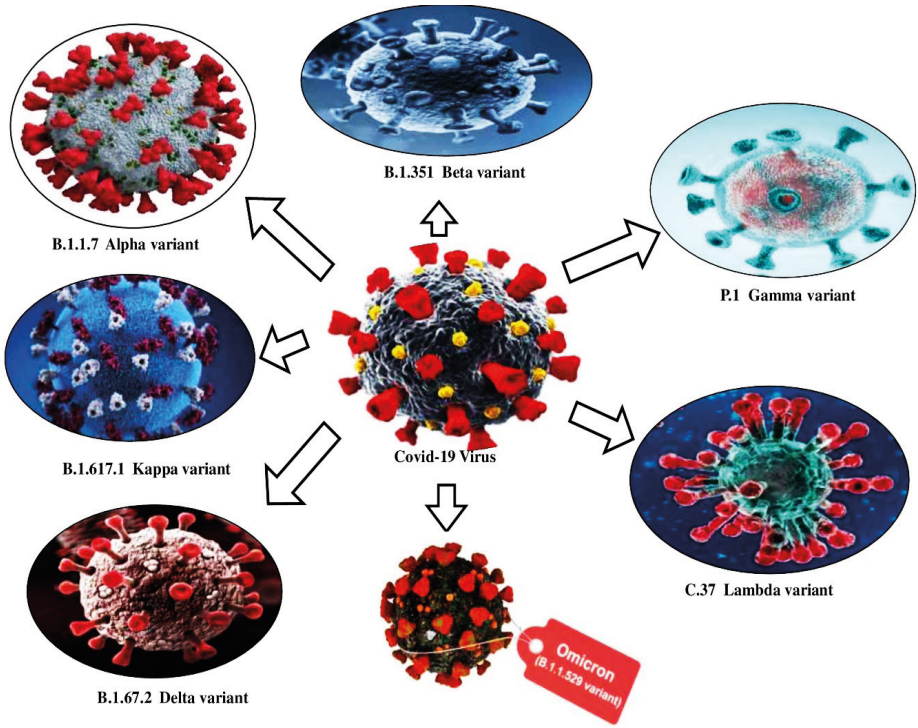

Fig. 5: Different emerging variants of SARS COVID-19 virus.

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Chapter 12

Post-Vaccination Associated Side Effects, Adverse Drug Reactions (ADRS), and Reported Case Studies

12.1. Mild-to-Moderate Side Effects (MTMS)

The individuals or vaccinated person should not move outside within the window period of 7–14 days. They should follow some preventive measures, stay at home, and compulsory wearing of masks even though if they are vaccinated to spread infections. After vaccinations, the common ADRs may observe slight fever, muscle aches, and body pain or back pain. These are signs that the body's immune system responds to the vaccine, specifically the antigen (a substance that triggers an immune response), gearing up to fight the virus. These side effects usually go away on their own after a few days after vaccination. Common and mild or moderate side effects are sound: they show us that the vaccine is working. Experiencing no side effects doesn't mean the vaccine is ineffective. It means everybody responds differently[145,146].

12.2. Stevens Johnson Syndrome (SJS)

The most severe cutaneous adverse reaction is known as "SCAR," popularly as Stevens-Johnson syndrome. This adverse reaction is almost equivalent to that of Toxic Epidermal Necrolysis (SJS/TEN) is the) which was often observed as a lethal consequence. Toxic Epidermal Necrolysis (TEN) is usually detected as a rare severe Cutaneous Adverse Reaction. It displays an acute onset characterized by erythematous or violaceous patches, atypical targetoid lesions, bullae, erosions, and skin detachment. It differs from Stevens-Johnson syndrome (SJS) only in the percentage of skin involvement, which is 10 and is greater than 30% of the body surface. The typical SCAR has been detected after administration of some drug-induced treatments and post-vaccination[145].

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Chapter 13

Reported Case Studies

13.1. Toxic Epidermal Necrolysis

The first case of toxic epidermal necrolysis (TEN) was observed in a case report of a patient of a 78-year-old female with COVID-19 treated with hydroxychloroquine. As per the results revealed along with COVID-19, she has also suffered from cardiometabolic syndrome[146]. Another critical case report was observed in a 60-year-old male who presented with fever, oral ulceration, and skin rash three days after the first dose of COVID-19 vaccination. He visited a local physician and was prescribed paracetamol and levocetirizine despite not control the symptoms. Gradually the rashes became generalized in distribution. Afterward, the patient was undergoing treatment and completer the diagnosis of SJS; the patient was started on oral cyclosporine 300 mg, and the patient improved ultimately after seven days[147]. Doctors of AIIMS first detected Bhubaneswar, Odisha, which incidentally was the first case post-COVID-19 vaccination. The post-COVID-19 patients reported case studies and significant signs, symptoms, fatality rate, and identification test in Table 7 and Fig. 6. The pre-and post COVID-19 vaccination health conditions (Fig. 7).

Table 7: The major signs, symptoms, mortality rate and identification test of the few post COVID-19 reported case

Name of the reported case diseases in a COVID-19 infected and recovery patients	County and name of city first reported	Total no. of patents infected till date (13.07.2021)	Major signs and symptoms	Mortality Rate/No. of death reported	Identification test	References
Toxic epidermal necrolysis (TEN)	England in 1922 and 1956 (identified) first reported	1–2 per million per year	Widespread skin pain, Blisters and large areas of peeling skin (skin reaction to the dose), HIV, Cancer.	20–50%	Dermatological test/ Skin test, Skin biopsy	[145, 170]
Mucormycosis (Black fungus)	Argentina, Chikkamagaluru, Karnataka, India	40,854 cases in so far (India)	Black lesions on nasal bridge, Nasal or sinus congestion, one sided swelling of face, Fever etc.	80%	HRCT scan, microscopic examination of sample, patient history, physical exam	[160, 161, 171]
White fungus	Uttar Pradesh, India	197 cases in India	Whiteness of tongue, mouth lungs, the brain, and the food pipes can be infected. Loss of taste. Pain while eating or swallowing.	54%	Microscopic examination the sample	[162, 163, 172]
Yellow fungus	Ghaziabad, New Delhi, India	10,000 cases total all-over globe.	Loss of weight, weariness, loss of appetite and lethargy	1.61 %	Endoscopy *test*	[169, 172]

Zika virus	Uganda & United Republic of Tanzania.	13 as per US Territories, 14 in kerala state of India.	Fever, conjunctivitis, Joint and muscle pain, babies born with abnormally small head	50 reported deaths	Blood test	[166, 168]
Delta virus	Kerla, India & Great Britain	51 cases reported in India and Highest case in the State of Maharashtra in India. 63 cases reported globally.	Cough, loss of smell, headache, sore throat, runny nose, and fever	>20 death cases reported	PCR test	[173, 174]
Omicron	South Africa. Most dominant variant in United states.	United Kingdom, Denmark, Germany, India. In India - total of 1,892 cases till January 04, 2022.	Body ache, generalised weakness, fatigue, headache and fever	India has reported 1892 omicron cases found across 23 states, total cases in globe 324,268,862 as on Dec 25, 2021	RT-PCR test	[185-187]
Delmicron	US and Europe	US and Europe	Scratchy throat, sneezing, mild temperature and extreme body ache	Not specific more cases	RT-PCR test	[188]
IHU	France	Mediterranee Infection institute in Marseille, southeastern France	Respiratory symptoms	It has 46 mutations, 12 cases reported in France	RT-PCR test	[183]

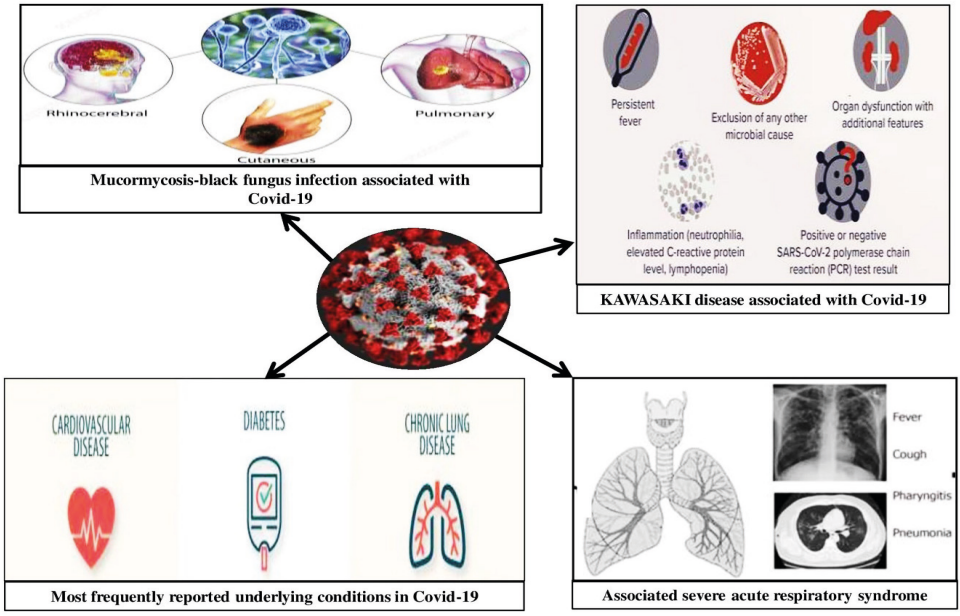

Fig. 6: Major symptoms, infections, and diseases associated with COVID-19 virus pre-and vaccinated persons.

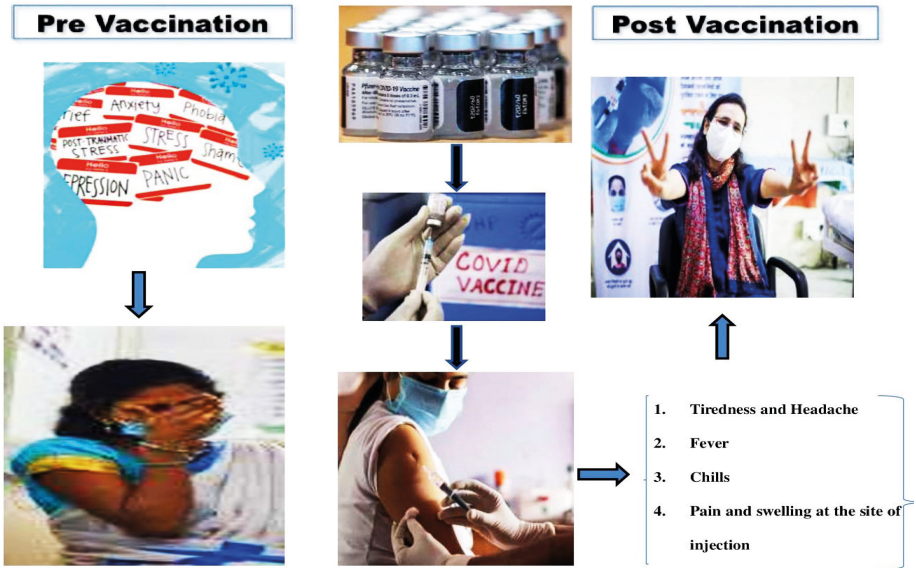

Fig. 7: Pre and post COVID-19 vaccination health conditions.

13.2. Black Fungus or Mucormycosis

Mucormycosis (also known as zygomycosis) is a stern activity as a rare fungal infection produced by a group of molds called mucormycosis, which is observed as post-Covid complications. These molds live all through the atmosphere. In general, Mucormycosis will happen to people with prior health difficulties or take medicines that lower the energetic body's capacity to contest microorganisms. The major targeting organs include the sinuses, respiratory tract (lungs) after inhalation of infected fungal spores from the environment. Other reasons include categories of skin injury[148–152]. However, the central and state government has clarified that the fatality rate in the Country is less than the nation's average. The unadorned increase in Black Fungus causes is a significant concern for Odisha amid the shortage of Amphotericin B Doses. In the second wave of Covid, the Odisha State of India has reported 112 deaths in April, 711 fatalities in May, a record of 77 during June-July 2021[153].

13.3. White Fungus

White fungus is becoming an infection materializing typically amongst COVID-19 positive patients, immune-compromised people with hysterical diabetes. It may be experiential in the case of people with severe cases of intake of steroids. In recent evidence, Bihar's Patna, the state in India, reported 4 cases of White Fungus. In contrast to Black Fungus, the White Fungus is a type of fungal infection, being notified in COVID-19 patients, emphasizing the body defense mechanism or low immunity power. Therefore far, only a minority of cases have been reported as it's not a new infection as it remained and existed previously[154–160].

13.4. Yellow Fungus

Yellow fungus (mucor septics) is a fungal infection that spreads through infectious surroundings or air, leading to ultimately distinct facial disfiguration that sees the aftermath of the COVID-19 outbreak. This fungus primarily attacks the body's vital internal organs and physiology compared to black and white fungus. The injury instigated by the yellow fungus is even more severe. Hence, people must start to observe the symptoms if they arise from day one and consult with a physician. Transmission of the yellow fungus has been occurred when an individual inhales the hollow container or moulds, initiates the environment, contaminated food materials, or old storage of food. Yellow fungus isn't contagious; hence, it cannot

usually transmit from one individual to other. Most of the signs of yellow fungus include loss of weight, weariness, appetite, etc. Other symptoms could be the creation and leakage of pus and sunken eyes[161–165].

13.5. Zika Virus

The unexpected outbreak of coronavirus (SARS-CoV-2) has outshone another emerging viral threat: the Zika flavivirus. Zika virus is a typical mosquito-borne infection name as vector Aedes aegypti mosquito. It was later recognized in humans in 1952 in Uganda and the United Republic of Tanzania. The virus infection was the first case documented in Uganda in 1947 in monkeys. The major outbreaks of Zika virus illness have been chronicled in prime countries like Africa, the Americas, Asia, and the Pacific. The significant symptoms include fever, mild to moderate conjunctivitis, the occurrence of rashes, pain in joints, neurological disorders, headache, etc. The period for infection lasted for 2–7 days. One of the substantial uncertainties is that pregnant women can permit the Zika virus to the fetus. There is a durable implication of an association between Zika virus contagion and foetal microcephaly[166,167].

13.6. Delta Virus

In December 2020, India was the first Country to identify the Delta virus, a dominant variant strain of SARS-CoV-2 (B.1.617.2) is known as the Delta virus. It is initially found in India and then spread to Great Britain. The common symptoms of such infected virus strains are cough, loss of smell, headache, sore throat, runny nose, and fever, and now it is a more dangerous seeker and fatal than the earlier strain of the covid virus. Primarily this strain attacks more of the non-vaccinated people than vaccinated one. The Vaccine manufacturer, Johnson & Johnson Company, reported that their vaccine has more potential and effectiveness against such variants of Delta strain than the original strain of the virus[168–174].

13.7. Omicron

As scientists around the world already predicted that the virus is expected to evolve as new strains, in November 2021 the most contagious variant namely Omicron has been reported in South Africa[175]. At its appearance only, researchers alarmed people about the large number of mutations in Omicron, which has never been seen in a microorganism before. Repeated multiple mutations in spike proteins has made this variant extremely transmissible in any age group of people[176]. WHO

has therefore declared this variant as a Variant of Concern (VoC). It is primarily not very easy to detect Omicron infection by observing symptoms. Where most of the cases are found asymptomatic, genome sequencing is the most reliable way to confirm Omicron infection till now. As on 9th January, 2022, a total of 3,623 Omicron cases has been reported in India[177]. Overcoming infection from Omicron will not be easier as this variant can evade neutralising antibody immunity induced by vaccination by booster dose of Covaxin (Bharath Biotech, Hyderabad, India) and Covishield (Astrazeneca, Oxford joint association) and previous SARS-CoV-2 infection to a large extent. Omicron infections are rapidly expanding worldwide in the face of high levels of Delta infections. Generally, the ability of one variant to induce immunity which can cross-neutralize another variant varies by variant. Although the immunity induced by Beta infection does not cross-neutralize Delta well. The concern which is being studied by researchers now is whether Omicron-induced neutralizing immunity also improves neutralizing immunity against the Delta variant or not. However, Government of different countries are planning for a Booster dose of vaccine for overcoming this rapid spread in all over the places after considering ineffectiveness of current vaccines against Omicron. Getting a booster vaccine may protect people from becoming ill in the hospital by 88 percent, which is only slightly less than previous variants[178].

13.8. Delmicron (Delta Plus Omicron)

At present circumstances, peoples are more scared about the new emerging variant of Delmicron which is a causative virus having dual infection to a healthy individual. Viruses are emerged due to mutation, and variations of different species are even became challenging day by day[179]. An infection of Delmicron arises when an individual is co-infected simultaneously with variants of Delta among with that of Omicron. It can mostly arises in the method of a reinfection. The major symtoms of Delmicron is similar to SARS-CoV-2 infection like cold-and flu like signs have principally remained with appreance of scratchy throat, sneezing, slight fever and thrilling body ache[180]. After delmicron, the Israel informed a double symptom based infection called as flurona (involved both covid with flu). Same moment, while whole Universe is suspecting the “Delmicron” and facing troubles with Delta and with Omicron, due to grouping of both variant, Israel becomes the highlighting country who has reported recently its initial case of ‘flurona[181]. The scientist all over the globe are now concerned about the vaccination programmes and to eradicate the further mutations of Delmicron and other forthcoming variants

with addition of double booster doses of strong vaccines like Covishield, Covaxin (India), Sputnik V (Russia) etc[182–186].

13.9. B.1.640.2 (IHU)

A new strain B.1.640.2 named as IHU was found in south-eastern France with many similarities like Omicron, although WHO has classified it as a variant under monitoring (VUM). With new emerging strains which are powerful in transmissions, it is not necessary that they will be lethal like Delta variant. IHU is currently limited in few geographical areas only and can be well prevented with existing vaccines[187–188].

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Chapter 14

Current and Future Directions

In the present scenario, the whole world faces the deadliest pandemic epoch of the COVID-19 virus and brought devastating pain of sanction worldwide. Hence, immediate anticipatory steps and the prophylactic measure have to be carried out by the Government, which will work out strictly, in due course by the people of every state, country, and continent around the globe. Moreover, now all the countries are taking the preventative measure and crucial steps to fight for human existence, against the threats. These can result to be prompt patient isolation, lock-down of all the activities in the nation to prevent the spreading counts of virus and fatality rate. As per WHO, close contact with people should be avoided for the patients who already infected with COVID-19 and along with significant problems of acute respiratory infections (ARI) for at least ten days; otherwise, there is more transmission of through air droplets, inanimate surfaces, or unclean hands. Hence, Social distancing, rigorous measure has to be maintained stringently among the people as well as the entire community for reducing the rapid contaminations rate. Especially the surface disinfectants like 0.1% sodium hypochlorite or around 60-71% alcohol (Ethyl alcohol) will apply to all public places, which helps to reduce virus infectivity on the surfaces or inanimate objects drastically. Eventually, the fastest implementation of countermeasures has to be followed by the health workers such as doctors, pharmacists, staff nurses, and lab technicians, etc. to treat, track, and isolate the patient. Recent reports imply the fastest developing COVID-19 vaccines by renowned pharmaceutical and biotech firms that readily enter into human clinical trials across the globe. Among all of those, seven vaccines are highly influential as they are prepared within the stipulated timelines. The prime most vaccines include Inactivated vaccine, CoronaVac, AZD1222, mRNA-1273, etc. developing by the institutions are Henan Provincial Centre for Disease Control and Prevention, Sinovac Research and Development Co., Ltd., The University of Oxford, the Jenner Institute and Kaiser Permanente Washington Health Research Institute are first entering human Clinical Trial Phase III and now available across the globe. Ad5-nCoV developed by Tongji Hospital; Wuhan, China enters

into phase III trial announcements within several months expected to finish off. Similarly, the mRNA-1273 by US-based Biotech firm Moderna, and INO-4800 by Inovio Pharmaceuticals, which completed recently Phase III trials and move to an emergency use of Moderna's COVID-19 vaccine as per the approval of FDA. Similarly, BNT162 developed by the German-based company BioNTech and US Pharma giant Pfizer, is one of the four impending vaccines relied upon the messenger RNA, an ideology that will launch the immunization with a couple of months to a year ahead. Among these, contest records about six Indian companies are also stepping forward to bring about the novel vaccine for COVID-19 virus pandemic global attack, either individually or in association with international companies or research organizations, according to current updates from the press trust of India. Out of that, four of these prospective vaccines are currently listed on the global candidate's list of WHO. These involve continuous hard work, brainstorming activities being made by the researchers and scientists of Zydus Cadila Pharmaceutical, Ahmadabad, Biological E Ltd., Hyderabad, and Serum Institute of India, Pune. Moreover, the researcher and scientist should always be aware and get ready with antidotes for further contagion pandemics shortly. Global changes can be made for eradication of infectious viruses by complete social health care system, promote new crisis management protocols, combine efforts of medical, pharmaceutical, biotechnological research, and developments, strengthen and reform intergovernmental or international organizations like OECD, WHO, CDC, etc can work reciprocally to reduce the financial inability or economic hardships of the country, against the precarious pandemic or epidemic outbreak soon.

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Chapter 15

Conclusion

The only available options are excellent public health tools for effective management of emerged viruses in the deficiency of vaccines. By proper individual isolations, quarantine for one to two weeks, and social distancing among the people should be the highest priority for a healthy nation. As it is noticed that, the spread of the emerging zoonotic virus (COVID-19) is becoming more complex week after week, wave after wave, so to minimize the infections only by developing effective vaccines globally. Till now, there are so many drugs and vaccines are developed which are currently under consideration for emergency uses based on rationale and confirmation concerning the efficacy of for proper management of COVID-19 as well as proof of safety from long-time usage in clinical practices. Scientific data from high-quality, harmonized, clinical trials approaching from diverse locations world-wide are immediately essential to execute the current research. The first endeavour of this textbook is to intensify the preparation of frontline immunity based novel molecules, vaccines, and designing of prearranged stratagem, smarter analysis tools for detecting the disease bit earlier, as well as conquering steps to triumph over the contagion of pandemic, epidemic and endemic causing deadliest viruses. The coronavirus outbreak has resulted in a global pandemic situation that was difficult to manage. Additionally, the high mortality rates of COVID-19 have caused a large-scale psychiatric agony, which in the long term may lead to an increase in stress, anxiety, depression, worsening the mental health condition in the population globally. Therefore, an overall health analysis focusing on mental health management is needed to solve the health catastrophe associated with the virus and other associated infections. A comprehensive and multidisciplinary approach is required, where health conditions are specifically addressed and include psychological aspects and other related symptoms and side effects related to the disease. Therefore, an effective vaccination should be considered to prevent drug reactions and implement other treatments to improve immunity. The healthcare personnel should spread awareness about the importance of vaccination and deal with infections. The COVID-19 vaccine, if accepted widely, has a significant

potential to end this pandemic. In conclusion, new methods are necessary for the disease's prolonged course to enable a fully functional health recovery post-COVID-19 vaccination and will be the biggest challenge.

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List of Abbreviations

ACE 2: Angiotensin-converting enzyme 2

ADRs: Adverse drug reactions

APN: Aminopeptidase N

CDC: Centre for Disease and Control

CTD: C-terminal domain

CV: Coxsackie virus

DCGI: Drug Controller General of India

DPP4: Dipeptidyl peptidase 4

ER: Endoplasmic reticulum

ERGIC: Endoplasmic reticulum Golgi intermediate compartment

ESA: European space agency

EVD: Ebola virus disease

ExoN: Exoribonuclease

FCoV: Feline enteric coronavirus

FIP: Feline infectious peritonitis

FIPV: Feline infectious peritonitis virus

H1N1: Human influenza A virus

HE: Hemagglutinin-esterase

HFMD: Hand-foot-and-mouth disease

IBV: Infectious bronchitis virus

JAXA: Japan aerospace exploration agency

MERS-CoV: Middle East respiratory syndrome coronavirus

MHV: Murine hepatitis virus

MS: Multiple sclerosis

MTMS: Mild-to-moderate side effects

NASA: National aeronautics and space administration

NendoU: NSP15-endoribonuclease

Niv: Nipah virus

NSPs: Non-structural proteins

NTD: N-terminal domain

OECD: Organization for economic co-operation and development

PEDV: Porcine Epidemic Diarrhoea Virus

PHEV: Porcine hemagglutinating encephalomyelitis virus

RBD: Receptor binding domains

RdRp: RNA-dependent RNA polymerase

RNA: Ribonucleic acid

RTC: Replicase-transcriptase complex

RTI**:** Respiratory Tract Infections

SARS: Severe acute respiratory syndrome

SCAR: Serious cutaneous adverse reaction

S-OIV: Swine-origin influenza A virus

TEN: Toxic epidermal necrolysis

TGEV: Transmissible Gastroenteritis Virus

UN DESA: United Nations department of economic and social affairs

USFDA: United States Food and Drug Administration

VOI: Variants of Interest

WHO: World Health Organization

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Pandemic Corona Virus vs. Epidemic, and Endemic Virus Diseases: Present, Past, and Future Directions

About The Book

The overview of the book includes the Pandemic Corona Virus vs Epidemic, Endemic and Post Pandemic Virus Diseases. For novel coronavirus treatments and prevention guidelines, it suggests allopathic, homeopathic, ayurvedic, home remedy, convalescent plasma therapy, etc. The current global data for the preclinical and clinical status of drugs-approved vaccines and few vaccines under development for coronavirus infections, and the impact of post-COVID-19 on science and technology, current and future directions in academic and industrial research. The primary arena is to explain the health condition and status of post-vaccination that may improve and reduce the long-term effects of the COVID-19 virus. Moreover, briefly enlightened post-COVID-19 recovery patients or vaccination people's worldwide associated side effects, and adverse drug reactions such as Stevens-Johnson syndrome, Toxic epidermal necrolysis, Mucormycosis, White fungus, Yellow fungus, Zika, Delta, Omicron, IHU, and Delmicron viruses are significant blockbusters of this second and third waves of current and post covid situation. The subject matter is written with adequate information about the pandemic, epidemic, endemic, and post-pandemic virus diseases and theoretical background and presented simply for better understanding among the medical, paramedical students, researchers, and scientists across the globe. This book is also handy for budding scientists and pharmaceutical professionals.

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ISBN 978-93-91208-61-5