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ARTICLE

Climate Induced Virus Generated Communicable Diseases: Management Issues and Failures

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ABSTRACT

In the present review article human diseases caused by various groups of pathogens have been explained with its etiology, epidemiology and treatment. In addition, effect of climatic changes on parasites and pathogens has been demarcated with rising incidences of diseases. In response to environmental changes, mainly external and internal microenvironment of body and drug regimens taken by patients; virus is regularly changing its form and new mutant variants are coming out. These are circulating in many Indian states and cross border countries and causing high infectivity and mortality in human patients. These variants with new mutations are challenging existing drugs and other prophylactic measures and massively disrupting functions of a tissue, organ, or entire organism. Diseases caused by viruses are showing new trends in virulence, with high infectivity, morbidity and mortality. Due to climatic effect and drug resistance and new mutations in pathogens disease burden has been exacerbated enormously at global level. In all cases of helminthes, protozoan's, fungi, bacteria, virus pathogens and parasites available drug structure seem to be failed or their usefulness has been much reduced due to evolution of new mutant variants with multiple drug resistance. There are serious failures at the level of operation, management and control of disease. The utmost failure is due to lack of appropriate vaccine, drug regimens, clinical care and awareness among people. These are major reasons that is why diseases become uncontrolled and unmanageable.

1. Introduction

A disease is an abnormal state in which human body faces disruption of functions of a tissue, organ, or entire organism due to invasion by some pathogen or parasite. Though, disease can be symptomatically identified but in a few cases its occurrence does not display any symptoms and patient remains asymptomatic. Disease may be caused by accident due to any causative agent passes on the man through some vector, through air, water or by contact. A disease passes through three phases i.e. initiation, progression and phase of recovery. There are numerous diseases, which display characteristic cause, specific set of symptoms, etiology and epidemiology. Among them major reasons are invasion by viruses, bacteria, fungi, smoking, genetic defects and life style. Life style diseases are caused due to eating habits, smoking, drinking, fast food, hot items, abnormal day periodicity and un-natural

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behavior of living (Table 1). There are two major categories of diseases: communicable and non-communicable. Communicable diseases are spread by vectors mainly insects, through drinking water, food, soil, and vegetables. But there are diseases which spread from person to person, zoonotic which transmit directly from animal to person or by any other mode. Transmission of communicable disease also takes place due to inhalation of aerosols present in the air, dust particles, contact with contaminated surfaces, blood transfusion, organs transplantation and unsafe sexual contact. Common cold, flu, influenza, rabies, SARS, and AIDS, are examples of communicable diseases.

After 2001 there has seen a sudden emergence of viral and bacterial diseases in tropical and subtropical countries. There is a surge of microbial and parasitic diseases in these climatic regions of the world. Most of the Southeast Asian countries and Australia [1] are in grip of mosquito-borne flaviviruses [2] arboviruses and alphaviruses enzootics [3]. Four viruses Ebola, Avian flu, MERS and

Table 1. General, personal, physiological, infectious and public related health disorders.

General health	**Physiological problems**	**Public Disorders**		**Infectious diseases**
Allergies	Heart disease	Bowel or bladder problems	AIDS/HIV	Encephalitis
Cold and flu	Asthma.	Chronic Fatigue Syndrome	Autoimmune disorders	Malaria
Vomiting and diarrhea	Obesity/ Eating disorders	Injury	Diabetes (genetic)	Diarrhea
Fatigue,	Diabetes	Mental health and depression	Eating disorders	Jaundice
Meningitis,	Stress and Headaches	Overweight and obesity	Digestive Disorders	Leptospirosis
Mononucelosis	Depression and anxiety	Pain	Food allergies and intolerances	Brucellossis
Sinusitis	Gastrointestinal problems	Pressure sores or ulcers	Heart health	Hookworm infection
Sore throat	Insomnia	Heart Disease	Goiter	Influenza
Urinary tract infection	Alzheimer's disease.	Learning Disabilities	Overweight and obesity	Tuberculosis and Leprosy
Vaginal infection	Accelerated aging.	Limb Loss	Osteoporosis	Urinary tract infection
West Nile Virus	Premature death.	*Methicillin-resistant Staphylococcus aureus* (MRSA) Infections	Atherosclerosis	Respiratory Virus
Fever,	Over weight	Musculoskeletal Disorders	Arthritis	Filariasis
Hay fever,	Alcoholism	Hypothyroidism	Hyperthyroidism	Acute Respiratory Syndrome
Headache,	Sprains and strains	High cholesterol and high triglycerides	Cardiovascular	Gastroenteritis problems
Heart burn	Muscle spasm, Migraine, Burns	Heartburn and gastro esophageal reflux disease,	Nephritis, breathing disorders, High blood pressure	AIDS

**Diseases in bold letters will be considered in first category for investigation.*

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SARS have been reported highly lethal in 2016 (UNEP report, WHO and World Bank). Most of the disease causing viruses have acquired mutations and showing new trends in virulence, high infectivity, morbidity and mortality. Similarly diseases caused by protozoan parasites are hovering with much enhanced parasitemia with extreme adaptability, and resistance to all existing drug spectrums.

Most of the virus generated diseases are suddenly emerging due to climatic effects, drug regimens and immune defense of host body. Most of the new mutant strains of viruses i.e. Rhinovirus, , Respiratory Syncytial Virus, Herpes Simplex Virus, Adeno virus, cytomegalovirus, influenza virus Type A, Type B, parainfluenza virus, SARS corona virus, poliovirus, HTLV-1, gastroenteritis virus, adenovirus, rotavirus, Norovirus, Astrovirus, corona virus, pancreatitis coxackie virus, Hepatitis virus A, B, C, D, E, dengue, West Nile Virus, Rabies acquired resistance against modern pharmaceutics and are circulating in between various hosts. Most of the virus generated diseases are on rise because of attainment of new genetic variations and resistance to therapeutic drugs and vaccines [4]. Recently, W.H. O. has alarmed many countries about new waves of infection caused by Ebola virus, Hantavirus associated with HCPS, Hendra virus, highly pathogenic virus H5N1, Lassa fever virus, lymphocyte choriomeningitis virus, monkey pox virus, Nipah virus, Rabies and Rubella, Rota virus B, Chikungunia virus and Yellow fever virus. Since 2000 many virus diseases have been re-emerged after prolonging time. Every year incidence rate of sexually transmitted diseases, Herpes simplex virus type 2, human papillomavirus, SARS and H1N1 is increasing. All these viruses changed its intensity of infection, morbidity and mortality rate; even spite of clinical and therapeutic care, mortality rate is not lower down.

2. Viral Diseases

2.1 Japanese Encephalitis

Japanese encephalitis is a major public health problem in the Southeast Asian countries that is responsible for high morbidity and mortality in pediatric groups. Disease occurs almost every year [6]. It is a zoonotic disease caused by RNA virus belonging to family flaviviridae [5]. Mosquito *Aedes aegypti* and *Aedes albopictus* are main JE virus transmission vectors. These mosquitoes breed in large numbers in fresh water habitat and through blood feeding bites transmitting different JE virus genotypes among different hosts. These new genotypes or mutant variants are circulating in human population and have established themselves in different epidemiological locations i.e. endemic to epidemic area, in separate forms. Due to high frequency of occasional bites by overlapping population of infected mosquitoes mutant variants are interchanging its hosts. These mutant variants/new genotypes have been detected in the blood samples of local population which re-circulate before arrival of rains and filling of water reservoirs with the rain water. This is the main reason of induction of high sero-conversion rate in patients. In Northern India a novel mutation (S227T) is domain II of the envelope gene of Japanese encephalitis virus circulating in North India [7]. Though virus also affects and reservoir hosts but human is the main target group.

In India, in the last 10 years JE incidences have been alarmingly increased due to rising vector and vertebrate host population in paddy growing areas. Another valid reason behind increase in infectivity is invasion of infant population by new mutant variants /strains of JEV. This is one of the leading causes of high mortality and morbidity cases in rural and sub-urban areas. Further, local environment such as high annual precipitation cycles, frequent human travels, demographic clustering, and insecticide resistance in target mosquito species has increased the endemic area. Other factors are poor economic and socio cultural environment and lack of timely therapeutics. In addition, presence of revertants epidemiology in the endemic area has created an alarming situation.

So far researches have been done ten stable temperature-sensitive mutants of Japanese encephalitis virus have been artificially generated by mutagenesis. These flavivirus mutants are cloned wild-type virus and generated in the presence of the nucleic acid precursor analogs 5-fluorouracil and 5-azacytidine. These are inefficient, nonreciprocal, and show complementation. But interference between mutants is causing mixed infections. Few complementing mutants synthesize virus-specific RNA at the non-permissive temperature, while other complementation groups display an RNA+ phenotype. Two other groups of mutants synthesize only low levels of virus-specific proteins at the higher temperature [8]. Mutants in the remaining two groups did not produce detectable levels of proteins under non-permissive conditions. Few important mutants rJEV(nEB1-M41) propagated in N18 cells as Beijing-1. Envelope protein mutations L107F and E138K are important for neurovirulence attenuation for Japanese encephalitis virus SA14-14-2 strain (Table 2).

These m mutants show low virulence but induce high immunity in mice after vaccination in a single intraperitoneal injection. A high virus yield was obtained from the m mutant in tissue culture, with titers of about 10(9.5) TCD(50) per ml. These m mutant can be used for the preparation of inactivated tissue culture vaccine, but before exploration of its genetic stability it remains a fiction

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Table 2. major virus generated human diseases

Virus causing diseases	Pathogen source/site/symptom	Vector/Source	Host reservoir	Mutants reported
Japanese encephalitis	Blood and CNS neurovirulence	Mosquitoes	Birds and pigs	Four genotypes, rJEV(nEB1-M41), Envelope protein *mutations* L107F and E138K
Dengue	Low blood platelet counts, failure of the circulatory system and shock	mosquitoes *Aedes aegypti* and *Aedes albopictus*	Mammals	Recombinant dengue virus type 1 (DV1) strains possess $NS3_{hel}$ protein (L435S or L480S
Hepatitis	Jaundice, weakness	Dirty water	No vector	Envelope protein (HBsAg) and C gene, HBeAg, procure mutant
Severe acute respiratory syndrome (SARS	Lungs, GI tract, liver kidney and upper respiratory tract Oxygen deficiency and ASRD, Sepsis	Respiratory droplets Man to man, Bats, palm, civets	Micro aerosols suspend and virus, Mammalian laboratory species	Double mutants E484Q and L452R, deletion of two amino acids (H146del and Y145del), E484K and D614G variants in spike protein, RBD mutations in L452R and E484Q, Triple mutant B1.168 and AP N440
MERS	Sepsis and neurotropic effect Nasal and eye discharge, blood, ticks, tissue	Rodents	Domestic ruminants	Single, double and triple mutants
Influenza	Aerosols, feces (birds), influenza A (H1N1) and H2N2, (H3N2). H1 N2, H2N1, H3N1, H2N3	Water bird, ducks	Mammals, poultry, bastard, falcons, quail, stone curlew, pigeon, dromedaries	Transmission of triple re-assortant H3N2 influenza A viruses
Rotaviruses	Rotaviruses	Fouling fruit juice drinking, ice creams, and drinking water	House fly	VP4, NSP1, and NSP4 genes cause virulence
West Nile Virus	Neuroinvasive disease and febrile illness	Man to man through blood transfusions and organ transplants	Mossquito bite	Substitution mutation in amino acid in the prM protein
Zika virus	High fever	mosquito-borne	Nonhuman primates	Mutation in viral envelope gene (E-V473M)
Rabies	Mammals including humans	Wild and stray dogs cats, wolves, and, cattle, horses, goats and sheep	Dogs and cats	Antigenic mutation in two amino acid substitutions in the ectodomain of the glycoprotein.
Rubella virus	Mammals including humans	Stuffy nose and swollen lymph nodes		Substitution of serine at Cys82 or deletion of amino acids in hydrophobic domain
RVF Rift Valley fever	Blood, liver, spleen Mammals including humans	Buffalo, spring duck, Midges, mosquitoes, direct or indirect contact with the blood or organs of infected animals	Lamb, goat, bovine, calves, dromedary, cattle, sheep, camels and goats	ZH548 and MP-12-specific mutations,
AHF	Blood feces, nasal discharges	Ticks	Sheep, dromedary and others	Mutation in envelope protein
Poliomyelitis	Paralysis of limbs, nerve dysfunction	Air and feces	Air and feces	Neurovirulent PV-1 Mahoney strain by 55 nucleotide mutations
Mumps virus	Meningitis and inflammation of testicles.	Obstruct cellular STAT proteins	Air	Mutations in V protein, E95D, show defective STAT3 targeting
HIV Human immunodeficiency virus type 1 (HIV-1) and HIV-2	Acquired immune deficiency syndrome Man	Blood, semen, vaginal fluids, and breast milk.	From HIV infected person or by blood transfusion	HIV-1 mutants resistant to NNRTIs, CCR5-delta 32
Hantavirus	Rodent aerosols, excreta	Rodents, cats, foxes, coyotes, Hantavirus Pulmonary Syndrome, lungs and kidney	Rodents	I532K/S1094L mutations
Marburg/Ebola	Reuse of unsterile needles and syringes	Green monkey, bats	Human	Mutation in soluble glycoprotein (sGP or GP)
Enterovirus D68	Acute flaccid myelitis, affect nervous system, spinal cord gray matter	Air, and direct contact	Young children	Mutation in untranslated region (UTR) at amino acid position 88 in VP3; 1, 148, 282 and 283 in VP1; 22 in 2A; 47 in 3A.
Yellow fever	Flavivirus, Fever, headache, hemorrhagic	Mosquito bites,	Monkey and human	No Live attenuated vaccine
Chikungunya	F togoviridae	Mosquito bite A aegypti	Arthralgias, hemorrhages	No vaccine avoid mosquito bite

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[9]. Though vaccines against JE are available, but there is a need to develop a live, attenuated Japanese encephalitis vaccine, that can work against its all there genotypes.

2.2 Dengue Hemorrhagic Fever

Dengue is a mosquito-borne *Aedes aegypti* and *Aedes albopictus* disease caused by dengue virus (DENV). It has spread throughout the world and causes hemorrhagic fever that continues from 2 to 7 days. As fever declines, warning signs may develop and smallest blood vessels or capillaries become excessively permeable and large volumes of fluid come out from the blood vessels and seep into the peritoneum. Viral fever causes low platelet count, arise tendency to bruise easily and skin hemorrhages and pleural effusions in cavity. Patent also display fearful symptoms i.e. severe abdominal pain with persistent vomiting, red spots or patches on the skin, black, tarry stools (feces, excrement), drowsiness or irritability. Patient face difficulty in breathing, profusely bleeds from nose or gums, and internal bleeding also occurs This may lead to failure of the circulation of blood and initiate shock, and possibly death without prompt, and an appropriate treatment. Patient should provide analgesics (pain relievers) with acetaminophen and avoid those containing ibuprofen, naproxen, aspirin, or aspirin-containing drugs. They should also rest, drink plenty of fluids to prevent dehydration, avoid mosquito bites while febrile and consult a physician.

The main reason of infectivity and uncontrolled dengue is nonstructural protein 1 (NS1). It is a monomer and a cells surface dimer, but it is secreted as hexamer into the blood stream. This protein play key role in the viral life cycle, mainly assist in RNA replication and immune evasion of the complement pathway. It exerts direct action on the vascular endothelium and triggering release of vasoactive cytokines from immune cells. It results in endothelial hyper permeability and vascular leak and generates severe pathogenesis [10]. In current time four serotypes of dengue virus are circulating and keeping half of the human population at risk of infection. This is astonishing that all four dengue virus serotypes have mutations and are causing a serious problem to body's immune defense, as vaccine or antibodies prepared against one serotype could not work against second serotype or a different serotype. Therefore, alternative vaccine strategies should be considered long-term safety. Therefore, a composite vaccine is being required that can generate ample adaptive immune response by inducing production of neutralizing antibodies to non-structural protein 1, and reduce the level of pathogenesis [11]. A dengue virus vaccine named CYD-TDV is available in the market, but it is less efficacious and offers a limited coverage.

But there is hope that a cell culture based vaccine can be generated by using human monocyte‐derived DCs (mdDCs) infected with recombinant dengue virus type 1 (DV1) strains. These display a single point mutation in the $NS3_{hel}$ protein (L435S or L480S). Both mutated viruses infect and replicate more efficiently and produce more viral progeny in infected mdDCs compared with the parental, non‐mutated virus (vBACDV1) [12]. Few single point mutations in subdomain 2 have important implications for adenosine triphosphatase (ATPase) activity of DV1‐$NS3_{hel}$ [12]. More specially, there is an utmost need of a live attenuated dengue vaccine that is suitable for all age groups. It provides a long-term safety covering against all infection causing dengue serotypes when injected in healthy person [13] (Table 2).

2.3 Hepatitis

Hepatitis is the inflammation of liver it is caused different types of viruses named A, B, C, D and E. Disease is supported by bacterial infections, or continuous exposure to alcohol, drugs, or toxic chemicals, aerosol and paint thinners or due to an auto-immune disorder. The main symptoms of hepatitis are jaundice (yellowing of skin and eyes that occurs when the liver fails to break-down excess yellow-colored bile pigments in the blood. Hepatitis results in either damage or reduction in the livers' ability to perform life-preserving functions, including filtering harmful, infectious agents from blood, storing blood sugar and converting it into usable energy forms, and producing many proteins necessary for life. There are five different Hepatitis disease types with different symptoms.

Hepatitis A

Hepatitis A is a self-limiting disease that is found all across the world. It is usually transmitted through oral ingestion of infected material (mainly water), but sometimes transmitted parenterally; infection causes symptoms of a mild flu attack and jaundice.

Hepatitis B

Hepatitis B is an acute viral disease. It primarily spreads parenterally, its main mode of spread is intimate contact and from mother to the new born. Patient shows mild fever, anorexia, nausea and, vomiting. Later on feverish condition give rise to severe jaundice, urticarial skin lesions, arthritis, etc. Some patients become carriers or even remain chronically ill, even though most patients recover in about three to four months.

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Hepatitis C

It usually occurs after transfusion or parenteral drug abuse. It frequently progresses to a chronic form that is usually asymptomatic, but may involve liver cirrhosis.

Hepatitis D

Hepatitis D usually occurs as a super infection in case of Hepatitis B, with much increased severity.

Hepatitis E

This disease is transmitted by the oral fecal route; usually by contaminated water. Chronic infection does not occur but acute infection may be fatal in pregnant women.

The Hepatitis B virus contains S, P, C, and X genes. Among which gene P is largest that codes for synthesis of DNA polymerase. Gene S codes synthesis of envelope protein (HBsAg) and C gene codes for HBeAg and HBcAg [14]. The C gene has a precore and regulates synthesis of HBcAg protein product. This is a marker protein assisting in replication and infectivity. A pre-core mutant of hepatitis B virus can not replicate and does not produce e antigen i.e. HBeAg [14]. All these HBV mutants are dreadful and infection caused by these viruses is very difficult to treat [15]. Its infection persists for prolonged duration and gives rise liver cirrhosis [16]. Hepatitis B viral mutants have been emerged in patients due to selection pressure from either immune response or treatment options. Mutations that occur within the immunodominant epitopes of hepatitis B surface antigen (HBsAg) allow mutant virus to propagate in the presence of a neutralizing immune response [17]. (Table 2).

2.4 Rotavirus

Rotaviruses are highly pathogenic and cause life-threatening dehydrating gastroenteritis in children and animals. Virus contains several genes which regulate formation of viral structural proteins V4, VP6, VP7 and non structural proteins NSP1, NSP2, NSP3, NSP4 and NSP5 [18] (Table 2). Virus possesses one nonstructural protein, NSP4 is a trans-membrane, and endoplasmic reticulum-specific glycoprotein is encoded by gene 10. This protein is responsible for virulence as it under goes mutations. In addition, mutations in three genes i.e. VP4, NSP1, and NSP4 are responsible for hike in virulence. Adult diarrhea rotavirus (ADRV) strain is detected in eastern U.P. that infests larger population due to fowling fruit juice drinking, ice creams, and drinking water and routing fruits. The re-emergence of human group B rotavirus (HuGBR) in India is a fast growing rotavirus that causes infection very fast [18] (Table 2).

2.5 West Nile Virus

West Nile virus (WNV) is a notable cause of neuro-invasive disease and febrile illness.WNV is transmitted to humans and animals through a mosquito bite. Over 60 species of mosquitoes have been reported transmission vectors of West Nile virus. Mosquitoes become infected when they feed on infected birds. Human-to-human transmission of WNV does not occur, but it spreads in through blood transfusions and organ transplants. Several subtypes of WNV lineage 1 have been phylogenetically identified in mosquitoes in Israel [19]. From amino sequencing WNV virus shows lineage 1 that is identified an amino acid mutation in the prM protein sequence. This mutations mostly occurs between day 19 and day 28 of persistent viremia and viruria in a person with confirmed WNV encephalitis [20] (Table 2). A gene substitution mutation in of a key amino acid of prM protein has converted mild forms of the West Nile virus into a highly virulent strain. It is more deadly disease detected in American crows. WNV is endemic in Israel and its outbreaks have been reported in recent years [21]. WNV is detected in urine and serum of the affected patient with low-level of neutralizing antibodies. Most of these patients are immunocompetent in which infection persists for longer time due to its active replication of virus. WNV generates low viremia levels during infection [22].

2.6 Zika Virus

Zika virus spreads through infected *Aedes* species mosquito (*Ae. aegypti* and *Ae. albopictus*). Name of the virus is derived as, it was first reported from Ziika Forest of Uganda, in 1947. Its maternal-to-fetal transmission also occurs during pregnancy. Virus also viremia in non-human primates that causes urban transmission of Zika virus and the main reason behind its recent emergence [23]. Virus shows close similarity to dengue, yellow fever, and Japanese encephalitis and West Nile viruses. Virus take patients in grip of fever, develop rash, joint pain and red eyes and paralysis. Virus spread to lymph nodes and reach to the bloodstream. Virus also attack pregnant women, and generates birth defects in new born babies. Since 1950s, virus invaded equatorial belt from Africa to Asia. During 2007 to 2016 it was spread eastward, across the Pacific Ocean to the Americas, leading to the 2015 -2016 Zika virus epidemic. Recently ZIKV virus has acquired mutation in its envelope gene (E-V473M) that is responsible for an increase in virulence, infectivity and mortality (Table 2).

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2.7 Rabies

Rabies is a zoonotic disease spread by infected stray mammals dogs and cats, wolves and other animal species [24]. Its person-to-person spread transmission is very rare (Table 2). But virus is transmitted to humans and other animals through close contact with saliva from infected animals through bites, scratches, licks on broken skin and mucous membranes. Rabies is caused by rabies virus (RABV) which challenge central nervous system function very severely.

For RABV pathogenicity a G protein is responsible. In experiments through mutagenesis G protein mutations have been studies in virulent strain. However, replacement of Gly_{349} was replaced by Glu_{349} in G did not significantly influence viral growth but is enhancing the immunogenicity of GD-SH-01 in periphery and induced more expression of interferon alpha (IFN-α) in the brain in mice. This site G349 in G proteins also leads to attenuation of pathogenicity of RABV [24].

However, an antigenic double mutant of rabies virus CVS strain (challenge virus standard) is used for generation of monoclonal antibodies. However, two neutralizing anti-glycoprotein monoclonal antibodies, both specific for antigenic site III were generated for therapeutic purposes [25]. In these double mutants two amino acid substitutions have been done in the ectodomain of the glycoprotein and lysine in position 330 and the arginine in position 333 were replaced by asparagine and methionine respectively. This double mutant virus could not penetrate the nervous system, more specially sensory or motor neurons, while single mutants infect and target motoneurons in the spinal cord and sensory neurons in the dorsal root ganglia of man. These double mutant were isolated from infected BHK cells, neuroblastoma cells in vitro experiments [26]. However, genetic and/or antigenic differences found in Rabies virus and vaccine strains could be used to generate potentially more efficacious rabies vaccines [27]. For instant control of Rabies keep away children from the reach of stray dogs, even pats and livestock and vaccinate pats and stray for primary prevention of Rabies [27] (Table 2).

2.8 Rift Valley Fever

Rift Valley fever (RVF) is a zoonotic spread by bites of infected mosquitoes to humans (Table 2). RVF virus is not transmitted from person to person but there are reports about its transmission through blood transfusion or infected organs of donors. Human is also infected with RVF by ingesting the unpasteurized or uncooked milk of infected animals. Human infections have also resulted from the bites of infected mosquitoes, most commonly the *Aedes* and *Culex* mosquitoes and the transmission of RVF virus by hematophagous (blood-feeding) flies is also possible. The virus can be transmitted to humans through the handling of animal tissue during slaughtering or butchering and disposal of carcasses or fetuses. Persons who take care of livestock, conducting veterinary services infected easily. In addition, occupational groups such as herders, farmers, slaughterhouse workers, and veterinarians higher risk of infection. Virus directly transfers from infected mice to working man or through contact with broken skin, or through inhalation of aerosols produced during the slaughter of infected animals.

RVF varies virus has a short incubation period of 2 to 6 days. Disease starts with a mild fever, which after 4 days suddenly changes in flu-like fever, muscle pain, joint pain and headache. Some patients develop neck stiffness, sensitivity to light, loss of appetite and vomiting. RVF virus causes ocular (eye) disease (0.5 -2% of patients), meningoencephalitis (less than 1% of patients) and hemorrhagic fever (less than 1% of patients). RVF patients also face hemorrhagic fever, encephalitis, and sometimes blindness.

RVF virus has acquired mutations (4 and 2) in M and L segments of MP-12 reported in ZH548 subpopulations. These subpopulations homology in nucleotides at the mutation site in the Egyptian strains [28]. Other strains of this virus isolated are ZH501, ZH1776, and ZS6365. A recombinant rMP-12 is also prepared and it contains very low numbers of viral subpopulations.

RVF can be controlled by animal vaccination that should be done before an outbreak. Larvicides must be used to kill mosquito larvae in breeding sites. People should avoid raw milk and meat, and they should be well cooked before eating. In addition, RVF outbreak also occurs due to climatic impact. In East Africa disease spreads only after heavy rainfall that occurs during the warm phase of the El Niño -Southern Oscillation (ENSO) phenomenon.

2.9 Rubella Virus

German measles is also known as rubella, this virus spread with air and causes a red rash on the body. About two to three weeks after exposure patient feel mild fever and headache, fever, muscle pain, headache, runny or stuffy nose and swollen lymph nodes. In pregnant females Rubella virus causes congenital rubella syndrome and disrupt the development of the baby and give rise to serious birth defects, such as heart abnormalities, deafness, and brain damage. This is a highly contagious virus spreads through close contact or through the air. It may pass from person to person due to exhaled tiny drops of fluid from the nose and throat after sneezing and coughing.

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Rubella virus (RV) virions contain two glycosylated membrane proteins, E1 and E2, which exist as a heterodimer and form the viral spike complexes on the virion surface. This E1-E2 heterodimer ensures transportation of E1 out of the endoplasmic reticulum lumen to the Golgi apparatus and plasma membrane. Hence, substitution of serine at Cys82 (mutant C82S) or deletion hydrophobic domain (mutant dt) of E1 destroy its conformational structure. Thereby it cell surface expression of both E1 and E2. Similarly, substitution of either aspartic acid at Gly93 (G93D) or glycine at Pro104 (P104G) is never required for E1-E2 heterodimer formation and not for transport of E1 and E2 at the cell surface [29]. Besides this, 13 different mutations were found in the nonstructural protein open reading frame (NSP-ORF), five in the structural protein open reading frame (SP-ORF) and three in the untranslated regions (UTRs) (one in each three UTRs). These mutations also occur in amino acid substitutions at ten residues. TO-336 vaccine strain (TO-336vac) of rubella virus and its wild progenitor virus (TO-336wt) genome sequences showed 21 differences in the nucleotide sequences between the TO-336vac and the TO-336wt. Mutations M33 (wild viruses), and RA27/3 and Cendehill (vaccine viruses) mutations responsible for attenuation of vaccine strain [30] (Table 2). Rubella Children having an age between 1 to 6 year of age should vaccinate (Table 2).

2.10 Alkhurma Hemorrhagic Fever

Alkhurma hemorrhagic fever virus is a Flavivirus (AHFV) (CDC 2017). It causes hemorrhagic fever through tick bites. In beginning FHV infected person shows simple symptoms i.e. chill, mild fever, headache, joint and muscle pain, vomiting, and loss of appetite. But after 8 days patient faces neurologic, central nervous system, and hemorrhagic problems. Patient feels heavy discomfort, epitasis, hallucinations, disorientation, convulsions, and features of life-threatening epistaxis [31]. Virus infection elevated liver enzymes, leukopenia, proteinuria and thrombocytopenia, which leads to hemorrhagic fever and encephalitis (Table 2). First time this virus was initially isolated in 1995 from a patient in Saudi Arabia.

2.11 Yellow Fever

Yellow fever is transmitted by infected by Aedes aegypti, throughout the tropics and subtropics. Due to illness causes jaundice that is why it named as yellow fever. Patient feels fever, headache, jaundice, muscle pain, nausea, vomiting, fatigue and acute hemorrhage. For control of yellow fever, mosquito vector population must be controlled in the area regularly. Vaccination is used for prophylaxis mainly day visitors, field workers and travelers those who move in infected areas (Table 2).

Yellow fever virus belongs to genus Flavivirus. This is an enveloped positive-, single-stranded virus of 40 -50 nm in width and contains 10.862 nucleotides [32]. Virus possess a single open reading frame encoding a poly-protein which is disintegrated into three structural (C, prM, E) and seven nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5) by host proteases [33]. This arrangement is also found same in the protein coding genes in the genome. [33] Yellow fever virus (YFV) 3'UTR region is required for stalling of the host 5'-3' exonuclease XRN1. The sfRNAs also form from incomplete degradation of the viral genome by the exonuclease that is responsible for viral pathogenesis [34].

2.12 Ebola Virus Disease

EVD (Ebola virus disease) is a rare and deadly disease in people and nonhuman primates. EVD mainly occurs in sub-Saharan Africa and it is a viral hemorrhagic fever of humans and other primates caused by ebolaviruses [35]. Fruit bats are believed to be the carrier and transmission vectors of this virus. Virus is also transmitted through breast milk, blood and semen. Infected people carry this virus for several weeks to months even after his/her recovery (WHO 2014) [35]. Normal symptoms of disease appear after two days and three weeks after receiving the virus [36]. EV causes fever, sore throat, muscular pain, and headaches and severe bleeding, and organ failure mainly liver and kidneys. Severely affected patient begins bleeding both internally and externally that causes their death. This is sudden shock occurs due to loss of fluid from blood and plasma [37].

Ebola virus (EBOV) virus has acquired dominant mutations which are responsible for enhanced virulence or tropism. Ebola virus shows mutations in the glycoprotein [GP], nucleoprotein [NP], or RNA-dependent RNA polymerase [L]. Its EBOV variants carry A82V in the glycoprotein (GP), R111C in the nucleoprotein (NP), or D759G in the RNA-dependent RNA polymerase (L) [38]. Both NP and L mutants showed replication in monkey Vero E6, human A549, and insectivorous bat Tb1 cells. Its L mutant is less virulent whereas the GP mutation shows a slight increase in virulence but mainly impacts viral tropism. A single substitution mutation inEBV gene impacts its pathogenicity while amino acid replacement in EBOV severely affect host immune system as it obstructs activity of interferon-alpha, interferon-beta, and interferon gamma. There is a need to rational design of efficacious antiviral therapies against EBO virus generated infections (Table 2).

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2.13 Chikungunya Virus

Chikungunya virus (CHIKV) belongs to genus alphavirus. It causes epidemic fever, rash and polyarthralgia in Africa and Asia. Both *Aedes aegypti* and *Aedes albopictus* are transmitting vectors. Two outbreaks Chikungunya have been reported so far, first is reported from in Malaysia, in Klang, Selangor (1998) and another Bagan Panchor, Perak (2006). Symptoms appear two to twelve days after initial exposure to virus. Patient shows problems like headache, muscle pain, joint swelling and a rash and chronic arthritis. Due to similarities in clinical presentation with dengue, CHIKV is probably often under-diagnosed or misdiagnosed as dengue. Till date no vaccine or antiviral therapy is being available for prevention and control of this. But medical treatment with few antibiotics and vector control is only tools to check the disease. CHIKV is epidemiologically linked to other virus generated ongoing local or international outbreaks in endemic areas [39].

2.14 Poliomyelitus

Poliomyelitis virus is transmitted through air and feces of infected patients. Virus causes paralysis of limbs. Recently few cases of drug resistant and vaccines derived virus strains have been detected in clinical samples collected from four African countries. Here, just after polio vaccination, more children were found paralyzed by attack of vaccine-derived virus. There were three natural or "wild" type polioviruses from which type 2 was eradicated in 2015. Since more than 20 years, no mutant viruses derived from the type 2 polio vaccine (OPV2) have been identified. Vaccination with OPV2 is currently the only available method to induce immunity and prevent transmission among children. OPV2 risks seeding more of the mutated poliovirus mainly *d* (delayed) mutants. The *d* character is evolved when virus is cultured under gradual decrease of acid agar to recognize the susceptibility of the host cells to *d* virus. The optimal growth conditions were a narrow pH range that results in reduced neuropathogenicity [40]. The attenuated Sabin strain of poliovirus type 1 (PV-1) differs from the neurovirulent PV-1 Mahoney strain by 55 nucleotide mutations. Only one of these mutations (A-480---G), in the 5' noncoding (5' NC) region of the genome, showed strong attenuating effect. In the past 11 mutations in this region of the Sabin 1 genome, and in particular a mutation in the polymerase gene (U-6203--C, Tyr-73-*His), were found to be involved in the attenuation of PV-1. A new mouse-adapted PV-1/PV-2 chimeric strain v510 has been prepared by mutagenesis of locus 6203. This new hybrid v510/Sabin 1 (C-6203--U) carrying the downstream 1,840 nucleotides of the Sabin 1 genome including the 3D"" and 3' NC regions [41] (Table 2).

2.15 Mumps Virus

Mumps virus is transmitted through air; it causes meningitis and inflammation of testicles in adults. Mumps virus, possesses one unique V protein that can assemble a ubiquitin ligase complex from cellular components. It causes destruction of cellular signal transducer and activator of transcription (STAT) proteins. V proteins target the interferon-activated STAT1 or STAT2 protein and STAT3 proteins. It causes ubiquitin modification and proteasome-mediated degradation. If single amino acid substitution is being made in the mumps virus V protein, E95D, it results in defective STAT3 targeting, but the ability to target STAT1 remains intact. E95D mutation disrupts the ability of the V protein to associate with STAT3 [42]. For treatment of mumps affected pregnant women hyperimmune globulin are provided. It instantly works against virus that is displayed in reduction of symptoms (Table 2).

2.16 AIDS

AIDS, the Acquired Immune Deficiency Syndrome is a sexually transmitted disease caused by the human immunodeficiency virus (HIV). HIV transmits from one person to another through bodily fluids such as blood, semen, vaginal fluids, and breast milk. It spreads carelessly by unprotected sex with an HIV infected person or directly from receiving of HIV-infected blood or sharing infected injection syringes, needles, and other clinical equipment. It is also transmitted through open wounds, or mucous membranes of eyes, mouth, rectum, and vagina. The risk of HIV infection from any single sexual exposure is generally low, but receptive anal intercourse is the highest risky sexual activity, followed by receptive vaginal intercourse. Oral sex is very low risk, and HIV cannot be transmitted through saliva, sweat, or tears.

Approximately more than 1.2 million American people are infected with HIV, and almost a fifth (18.1%) of HIV infected Americans are unaware of their status. There is a large percentage of ethnic Americans which have HIV but never tested for the disease that is too risky to map the population. According to World Health Organization (WHO) estimates there are more than 70 million people infected with HIV from which 35 million people have died of AIDS since the beginning of the pandemic. The most infected group is 0.8% of adults between 15 and 49 years of age are living with HIV worldwide. Sub-Saharan Africa continues to be the most affected region, reporting an average of 1 in 20 adults living with HIV. In the United

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States the number of HIV survivors because of availability of medications that treat HIV, but in under developed countries people are facing severe morbidities and dying of the disease.

Recently three mutants of human immunodeficiency virus type 1 (HIV-1) (reverse transcriptase V106A, V179D, and Y181C) have been identified in clinical isolates. These show resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs). More specially, abnormalities were noted in RNase H cleavages which are common characteristics of HIV-1 mutants resistant to NNRTIs. These DNA 3′-end- and RNA 5′-end-directed cleavages are associated with significant reductions in the replication fitness of HIV-1 [43]. CCR5-delta 32 mutation is responsible for the two types of HIV resistance. This mutation provides ability to HIV to infiltrate immune cells. This mutation also slightly changes CCR5 co-receptor on the outside of cells to develop smaller than usual and no longer sit outside of the cell. It is true that not all human immunodeficiency virus (HIV)-1 -specific immune responses are equally effective in controlling HIV-1 replication.

From multiple immune-driven sequence polymorphisms HIV-1 Gag region of transmitted viruses found highly conserved, it is associated with reduced viral replication in newly infected humans. These conserved viral regions can be used to develop an effective HIV-1 vaccine [44]. There is a need of large scale clinical investigations on infectivity of HIV, mutations and pathogenicity caused by HIV. Similarly, detection of immunological abnormalities associated with HIV, can disclose major reasons of morbidities and mortalities in rural, suburban clusters and urban population. A world level immune surveillance be needed to find out HIV infected groups, and clinical status and deaths occurred. It will also help in display of symptoms, treatment, public awareness and socio-economic reasons of disease (Table 1 and 2).

Both chlamydia and gonorrhea are AIDS associated with bacterial infections and treatable by drug therapies, treated with medication. In women, Chlamydia in women causes pelvic inflammatory disease (PID), that results in infertility, chronic pelvic pain, or tubal pregnancies. In males it appears in form of urethral infection with swollen testicles or upper genital tract. Especially gonorrhea is seen in both male and female partners having HIV infection. There is a third opportunistic i.e. syphilis caused by bacteria in STD patients. Common symptoms of syphilis are ulcer or chancre, mild fever, fatigue, headache, or rash. Bacterial infection also causes mental illness, blindness and death. Syphilis is treatable with antibiotics. Syphilis is an incubating disease that left untreated can cause mental illness, blindness and death. There are many other STDs including: genital warts, human papillomavirus (HPV), and genital herpes.

2.17 Hantavirus Infection

Hantavirus infection is a viral disease that transmitted from rodents *Apodemus agrarius* mice and carried by *Rattus norvegicus* rats to people. This virus causes severe infections in lungs and generates cough and shortness of breath. It also affects kidneys cause rash and abdominal pain [45]. Hantavirus causes pulmonary syndrome (HPS) cause fatal, respiratory disease in humans. Hanta virus generated renal syndrome (HFRS) is a serious public health problem in the People's Republic of China. Till date7 sero/genotypes of Hantaviruses have been isolated from rodents. Hantavirus seek I532K/S1094L mutations in DOBV Gn/Gc. However, incorporation of these mutations into hantaviral Gn/Gc proteins generate rVSVs a robust replication-competent that could be used for preparation of new vaccines [46] (Table 2). Hanta virus infection is vaccine preventable.

2.18 Enterovirus D68

Enterovirus D68 (EV-D68) was first isolated in California in 1962 and again in 2014 in U.S. outbreak. Since then this virus has spread worldwide in the current century. Previously, it was suspected as a polio-like disorder called acute flaccid myelitis. Just after beginning of infection patient displays common symptoms like cold, runny nose, sore throat, cough, and fever, variable rashes, abdominal pain and soft stools. After completion of 5 days it causes respiratory problems and generates flu-like symptom [47]. Patients feel difficulty in breathing as pneumonia rises. It increases the dehydration of body and concentrated the urine. Now virus affects the nervous system, specifically spinal cord gray matter, muscles and disturb reflexes in the body.

EV-D68 virus has acquired six kinds of gene mutation, M291T, V341A, T860N, D297N, S1108G, and R2005K in a distinct clade B1 of EV-D68 strains from U.S. [50]. These mutations have increased the neurovirulence of EV-D68. Till the date no vaccine, and specific drug regimen is available to treat the EV-D68 disease. People recover naturally but few need hospitalization. But only symptomatic patients are provided antiviral drug pleconaril [49]. (Table 2). EV-D68 generated paralysis cases are treated with steroids, intravenous immunoglobulin and/or plasma exchange. EV-D68 generated paralysis cases are treated with steroids, intravenous immunoglobulin and/or plasma exchange. But in some cases even after treatment no recovery of motor function was observed [48].

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2.19 Influenza

Influenza is an acute respiratory tract infection caused by influenza virus. It's three strains A, B and C have been detected, among which influenza A strains cause pandemic. Influenza outbreak occurs repetitively is virtually every year, but at few places its incidence rate gets increased. This also reality influenza epidemics occur at intervals of two to three years, and pandemics at intervals of about 10 to 15 years. Disease exists all over the world and affects millions of people. First pandemic was seen last century in 1918-19, and affected approximately 500 million people and more than 20 million deaths. In India alone, over six million people died during this pandemic. The transmission of influenza virus occurs from reservoir hosts like pigs, horses, birds but latent infection or continuous transfer also occurs from one person to another. H3N2 influenza A viruses are re-assorted due to mutations and show inter-specific and intra-species transmission [51] (Table 2).

In year 1957-58 pandemic caused by a new strain of virus influenza A (H2N2) and again repeated 1968 but causative agent was H3N2 strain of influenza A virus. Type C virus also causes influenza but it is not so severe and occurs sporadically. Influenza A (H2N2) suddenly evokes and spreads very rapidly in human population. Virus has a very short incubation period. In a short span of time a large section of human society get infected, and virus over throw the patient immunity.

Swine influenza is caused by Swine influenza virus or swine-origin influenza virus (S-OIV). The important reservoirs Swine influenza virus are pigs and virus commonly house in pig populations worldwide. influenza, swine flu, hog flu and pig flu is an infection caused by any one of several types of swine influenza virus. Both Swine influenza virus (SIV) or swine-origin influenza virus (S-OIV) strain of the influenza virus are endemic in pigs. In year 2009 and onwards disease was spread by influenza C and various serotypes of influenza A virus i.e. H1N1, H1 N2, H2N1, H3N1, H3N2, and H2N3. Thus Swine flu is zoonotic rather than simple influenza. People with regular exposure to pigs are at increased risk of swine flu infection. These strains of swine flu rarely pass from human to human. Symptoms of zoonotic swine flu in humans are similar to influenza and of influenza-like illness, namely chills, fever, sore throat, muscle pain, severe headache, coughing, weakness and general discomfort.

Influenza A virus (IAV), is highly infectious respiratory pathogen it is causing threat to global public health. Influenza virus genes evolve two to three times faster than the corresponding genes in B viruses [52]. It is reported that NS gene of influenza A virus A/WSN/33(H1N1) (WSN) display 1.5×10^{-5} mutations per nucleotide per infectious cycle [53]. Virus has acquired significant modifications. Virus has attained significant modifications in the receptor-binding specificity due to changes at gene level and its concerned protein [54] (Table 2). This remarkable mutation in surface proteins (HA (hemagglutinin) and NA (neuraminidase) give rise antigenic drift that is the main problem in generation of vaccine.

3. Acute Respiratory Disease

Severe acute respiratory syndrome (SARS) is a zoonotic disease. It is caused by SARS coronavirus (SARS-CoV). First time it was evoked in November 2002 and July 2003, in southern China with 8,096 reported cases of infected and 774 deaths. Majority of cases were reported from Hong Kong with 9.6% fatality rates. From Hong Kong SARS spread to 37 countries in early 2003 and affected millions of people. Aagin disease is remerged in November 2019 in China from where is spread whole of Europe, African countries, U.S.A, Canada, Brazil, Australia and heavily attacked South-East Asian countries and Russia as well. Covid-19 viral infections alone posed a significant global health challenge in the present time. It has affected millions of people worldwide, and showing its high aggression in Europe, America, China, Brazil and India after making millions of fatalities. Virus specially targeting young people age between 15 to 45 years of age. It is also affecting children and old age people both. India is also on war path and fighting against the second wave of corona virus generated by various mutant strains. As nature of viruses, this corona virus assumed mutation by its own, but it cannot be denied a rapid lethal mutation is only possible in laboratory. Now this is much speculated that this virus might have spilled out from some defense laboratory. Un-imaginable Covid-19 is spread worldwide within 120 days and has gripped whole of world in its fatal clutches. Virus has been imposing a serious public health threat and making heavy economic losses to human society mainly to world economy.

Covid-19 is more disastrous as it is causing high infectivity and large numbers of deaths that have been reported round the globe [55]. Coronavirus grows in upper respiratory tract and is released in open air through sneezing and coughing by patient. Thousands of micro aerosols or small droplets suspend and virus live for two three hours in air and enter inside next host human body through inhalation of air [56] (Table 1). Seasonal climatic changes like humidity and temperature enhance the impact of virus. Because ambient humidity present in atmosphere raise the respiratory droplet size and its stability as water content evaporates. Two physical changes occur

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in sneezed air. First droplet size gets increase with down pouring rain drops that quickly come to the ground. Small humidified aerosols remain suspended in air for longer time after evaporation. People on road by accident inhale these influenza virus loaded aerosols with respiratory air. Few eco-climatic factors such as relative humidity assist in formation of water- droplets in atmosphere, when they come down increasing the settling of large droplets on the ground and virus get inactivated. Torrent rains also assist in removal of infection with rain water, and largely influences viral transmission. First rains though help in washing of suspended air droplets of infectious agents but humidity in soil increases the stability, transportation and natural spread of virus from human spits, faces, drainages and wastes cannot be denied. Thus sudden change in weather or climatic factors other than precipitation also affects seasonal infection rates. Areas where no air pollution is available and fouling air is least they remain devoid of any infection. Mainly in open climate of villages and single storey housing pattern and spatial separation of one village to the other decreases virus transmission mainly, but ill habits of smoking, spitting, and tobacco chewing and open drainages provide space and stay to this deadly virus and add risk to transmission (Table 1) [57]. In urban areas due to high density of population amount of contagious air increases in air, less wind movements, close air circuits enhance the transmissibility of viruses. If foul smell released from stacked toilets in multistoried buildings due to pipe leakage it mixes in air currents flowing through indoor spaces. It spreads in nearby spaces with the virus particles suspended in air. With this population inter-mixing in crowded places will increase the passive transmission of this virus that may prove more fatal.

Coronavirus is a highly mutable virus and can attain both negative and positive mutations according to changing physical climatic factors mainly seasonal variation in temperature, relative humidity, rainfall, wind velocity, day light, altitude and gravity. Besides, environmental factors, non-environmental factors such as human behavior, interaction, family and social structures show proximity and lack of social distancing increase the intensity of virus infection [58].

However, in response to climatic changes virus has increased its genetic susceptibility by acquiring important mutational changes in genes and proteins. Recently mutations two mutations have been reported in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus in comparison to Wuhan-Hu1 or USA-WA1/2020 [59]. SARS-CoV virus replicase polyprotein ORF1b has undergone towards negative selection that has given rise significant changes in spike protein gene [60]. Besides this two key mutations to the outer spike portion of the virus have been observed in B.1.617 variant. In addition, its new variants have been detected in the United Kingdom, Brazil and South Africa with much enhanced threat level. The Indian variant has been isolated from Maharashtra where it is causing high infectivity and mortality. This variant is climate induced and displaying a high infection rate. This variant has overpowered the prior immunity of patients within initial days of infection and causes high mortality.

It is amazing that in a short period of less than two years SARS-CoV-2 virus has mutated thrice and its different variants have been evolved. These new environmentally induced mutant variants of SARS-CoV-2 are very rapidly circulating in the population mainly in urban areas. Due to spread of these mutant variants both infectivity and mortality of COVID-19 have been significantly increased [61]. These also have acquired resistance to existing treatment options both drugs and vaccines. Changes in the viral genome can result in changes to viral proteins and, therefore, can also impact the performance of an antigen or serology test. Genetic variants of SARS-CoV-2 due to change in antigen escaping are challenging immunodiagnostic tests and samples are tested as false negative results.

About SARS-CoV-2 mutations no one can emphatically say that how many times virus will mutate. But it can be presumed that re-infection by mutated strains will increase the infectivity and transmission very rapidly and human population is going towards herd immunity [62]. It will become possible only when a large portion of a community becomes immune to a disease through vaccination or through the mass spread of the disease. Though, it will keep vulnerable people at risk of severe disease, since the virus can move through the herd to reach them.

These double i.e. variant B.1.617 [63] and triple mutants variant B.1.618 are circulating in Indian states; Delhi, Maharashtra and some other places and are responsible for sudden origin and rapid hike of second wave of COVID-19. Recently, variant B.1.618 was reported from West Bengal that has shown much increased transmissibility and ability to diffuse and weaken the immune response generated by host body. The double mutant in India carried two mutations—E484Q and L452R—in the crucial spike protein part of the pathogen. Both the E484Q mutation (reported in both UK and South African variants) and L452R mutation (found in the California strain) have been associated with much greater binding and antibody escape capabilities. Virus is acquiring capability to more severely challenge human immune system and overpowering prior immunity. More especially deletion of two amino acids (H146del and Y145del), E484K

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Table 3. showing various lineages of corona virus, mutations in spike protein genes, its impact on transmissibility, lethality, neurovirulence and vaccine efficacy.

Lineage	Former identification	Detected in country	Effect of mutation on transmission	Effect on lethality, virulence and vaccine efficacy
Lineage B.1.1.7 / Variant of Concern 20DEC-01	Lineage B.1.1.7 or 20I/501Y. V1 (formerly 20B/501Y.V1).	First detected in United Kingdom in October 2020	40% -80% increased transmissibility	Increase in lethality, but no evidence of increase in virulence
Variant of Concern	VOC-202102/02,	Public Health England (PHE) as "B.1.1.7 with E484K	B.1.1.7 with E484K mutations, increased 15-20% transmission	Increase in lethality
Lineage B.1.1.207	Similar to UK's Lineage B.1.1.7.	Reported from Nigeria in August 2020 in Nigeria, and 16 more countries	Variant shows 40% -80% increase in transmission	Increase in lethality
Lineage B.1.1.317	Not an VOC	Brisbane, Australia	Rapid spread in human population	Increase in lethality, but no evidence of increase in virulence
Lineage B.1.1.318	VUI (VUI-21FEB-04, VUI-202102/04	Reported in UK	Rapid spread in human population	Increase in lethality, but no evidence of increase in virulence
Lineage B.1.351	501.V2 variant, (501.V2, 20H/501Y.V2 (formerly 20C/501Y.V2), VOC-20DEC-02 (formerly VOC-202012/02),	Three mutations in spike glycoprotein of the virus: N501Y, K417N, and E484K. The N501Y is reported from U.K. United Kingdom and African countries	Targeting young people	Responsible for second wave of the COVID-19 epidemic in the country
Lineage B.1.429 / CAL.20C	CAL.20C in California, the variant	Five mutations i.e. I4205V and D1183Y in the ORF1ab-gene, and S13I, W152C, L452R in the spike proteins S-gene	Acquired ~20% increase in viral transmissibility, B.1.429 is possibly more transmissible,	Challenging vaccine/ antibody neutralization efficacy
Lineage B.1.525	Previous VUI-202102/03	E484K-mutation in P.1, P.2, and 501. V2 variants, deletion of the amino acids histidine and valine at positions 69 and 70. UK and Denmark	Increase in transmission	Variant under investigation
Lineage B.1.526	B.1.526	U.S. states and 18 countries.	Acquired a ~20% increase in infectivity	Challenging vaccine/ antibody neutralization efficacy
Lineage B.1.617	B.1.617 or VUI-21APR-01	Mutations in spike protein D111D (synonymous), G142D, P681R, E484Q and L452R, India	Escape from antibodies	'Variant under investigation
Lineage B.1.618	CoV-Lineages	Mutation E484K, reported in West Bengal, India and eight other countries	Acquired increase in infectivity	'Variant under investigation
Lineage P.1	Previous VOC-202101/02	Mutation in spike protein, mutations: N501Y, E484K and K417T. England	Acquired increase in infectivity	P.1 variant
Lineage P.3	VUI-21MAR-02	Mutations in spike protein, reported in U.K. Philippines, Malaysia	Transmissibility is yet to be ascertained.	P.3 variant

**P.1 and P.3 variants are evolved from the lineage B.1.1.28,*

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and D614G variants in spike protein have acquired higher infectivity and lethality.

From phylogenetic analysis of genome sequence a predominant clade of SARS-CoV-2 was found, and named as lineage B.1.617. It displays common signature mutations D111D, G142D, L452R, E484Q, D614G and P681R, in the spike protein including within the receptor binding domain (RBD). More specifically, mutations are also seen on residue positions 452, 484 and 681 in other globally circulating lineages. In addition, SARS-CoV-2 is making substitutions per nucleotide per cell infection i.e. 10−6 to 10−4 s/n/c [64]. This has led to increase the of copying of virus genome per cell and thereby enhanced per cell infection. Finally, RBD mutations L452R and E484Q along with P681R in the furin cleavage site, has increased ACE2 binding and rate of S1-S2 cleavage that give rise better transmissibility. These two mutations have decreased monoclonal antibodies (mAbs) binding and affecting their neutralization potential and challenging both therapeutics and immunodiagnostics [65]. For over spread and rapid spillover in transmission of SARS-CoV-2 fast gene recombination is responsible [66] (Table 3).

4. Factors Responsible for Disease Occurrence

In the last twenty years series of viruses generated infectious diseases have been emerged and remerged [6]. The zoonotic microbes are continuously evolving and acquiring adaptations, and showing high infectivity and mortality at global level. Severity and risks of communicable diseases have been increased due to human movement, trade, recreation activities and dense population structures. Presence of pathogens in human community and its easy exposure is providing new hosts while eco-climatic conditions favoring microbial growth, transmission and infectivity. Further, evolution of new mutant variants of these pathogens have acquired high infectivity and generating catastrophic effects in human population. There are rising incidences of virus generated disease, flu, dengue, hepatitis, chikungunya, Rabies, polio, gastroenteritis and encephalitis throughout the globe.

There are external factors which support disease occurrence, among them few important factors are heavy rains, water logging, high humidity, temperature difference, urbanization, deforestation, and human migration, settlement of slums, relief camps, and nomadic movements. There is a lack of clean drinking water, cooking and washing. Lack of sanitation, presence of disease vectors and contaminated food and waste disposal are responsible for spread of communicable diseases. Among non communicable diseases diabetes is one of the important diseases that kill roughly 30 million people per year worldwide. Three major challenges are i.e. development of insecticidal resistance in insects/vectors of potential communicable diseases, drug resistance in microbes and parasites. Cases of lung infection, liver, kidney and gastrointestinal tract, child diarrhea are rapidly increasing in developing countries [67]. Besides, this incidence of child diarrhea [68], neonatal jaundice [69,70], and helminthes parasitic infections are spreading in developing and in third world countries.

Due to climatic effect and drug resistance and new mutations in pathogens disease burden has been exacerbated enormously at global level. In all cases helminthes, protozoan's, fungi, bacteria, virus pathogens and parasites available drug structure seem to be failed or their usefulness has been much reduced due to evolution of new mutant variants with multiple drug resistance. There are serious failures at the level of operation, management and control of disease. The utmost failure is due to lack of appropriate vaccine, drug regimens, clinical care and awareness among people. These are major reasons that are why diseases become uncontrolled and unmanageable. Year after year new mutant variants or climate induced microbial pathogen genotypes are emerging; these are not only challenging existing drugs but also challenging vaccine efficacy. This disastrous situation can be overcome by having new potential drug structures, control strategies and methods. For finding quick solutions all biomedical researches should arrange drug repurposing, testing, diagnosis and treatment methods with a focus on major human parasitic and microbial diseases. In this article major zoonotic infections/communicable diseases have been explained with their specific etiology, transmission and epidemiology and control/preventive measures. More specifically effect of climate on disease occurrence, vector population, drug and insecticide resistance and generation of new genotypes of microbial pathogens and parasites have been described.

5. Management Issues and Failures

Three mutants of human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (V106A, V179D, and Y181C), which occur in clinical isolates and confer resistance to nonnucleoside reverse transcriptase inhibitors (NNRTIs), were analyzed for RNA- and DNA-dependent DNA polymerization and RNase H cleavage. All mutants demonstrated processivities of polymerization that were indistinguishable from wild-type enzyme under conditions in which deoxynucleoside triphosphates were not limiting. The V106A reverse transcriptase demonstrated a three- to fourfold slowing of both DNA 3′-end-directed and RNA

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5′-end-directed RNase H cleavage relative to both wild-type and V179D enzymes, similar to what was observed for P236L in a previously published study (P. Gerondelis et al., J. Virol. 73:5803 -5813, 1999). In contrast, the Y181C reverse transcriptase demonstrated a selective acceleration of the secondary RNase H cleavage step during both modes of RNase H cleavage. The relative replication fitness of these mutants in H9 cells was assessed in parallel infections as well as in growth competition experiments. Of the NNRTI-resistant mutants, V179D was more fit than Y181C, and both of these mutants were more fit than V106A, which demonstrated the greatest reduction in RNase H cleavage. These findings, in combination with results from previous work, suggest that abnormalities in RNase H cleavage are a common characteristic of HIV-1 mutants resistant to NNRTIs and that combined reductions in the rates of DNA 3′-end- and RNA 5′-end-directed cleavages are associated with significant reductions in the replication fitness of HIV-1.

5.1 Malnutrition

Other than climatic factors the major factor is malnutrition. It is a condition generated due to intake of either nutrient deficient diet or some components in excess, or in wrong proportion. According to World Bank published report, India has a large number of children suffering from malnutrition and ranked first among the list of other countries. In India Uttar Pradeh has the highest number of malnourished or under nutrition children and comes at fourth number from the bottom on child nutrition rates. This is falling behind Bihar, Andhra Pradesh and Daman and Diu. In many states of Indian children in rural areas are facing protein and iron deficiency in food. This Protein-energy malnutrition and iron deficiency is seemed in form of nutritional anemia, due to which children remain less productive and weak. Similarly, vitamin A deficient food results in either blindness or a weakened immune system. In addition, iodine deficiency, causes serious mental or physical complications. Therefore, to finish problem readymade therapeutic food should supplied for treatment of severe acute malnutrition in children from six months to five years of age [71]. Due to folic acid scarcity in diet lead to insufficient birth weight or congenital anomalies such as spina bifida. Hence, specially formulated foods should give to feed children with moderate acute malnutrition in low- and middle-income countries [72]. This eastern part of India has bowl shaped landscape, due to which huge water collection takes place in pools & high humidity in rainy season. This region has high population density, malnutrition, poor sanitary conditions, contaminated water, poverty, illiteracy and almost every alternate year several serious diseases are occurring. Entire area is very poor in maintaining sanitation, irregular supply of safe drinking water and problem of wages, education and employability.

5.2 Lack of Sanitation Facilities and Equipment

At global level management of child and women health, is not good and conditions of third world countries is worst. Even in few developing countries sanitation conditions are not so good. Meanwhile, their urban sites are full of scattered slums with lots of garbage, filths, solid waste, and open water pools of dirty water, which are epicenters of mosquito breeding and other insect vectors. There is no authority to look after sanitation conditions, drainages and vector control only for slums. If these are available, most of them are either non-functional, low budgetary bodies or do not have required number of trained workers. Poor sanitation conditions are also responsible for spread of communicable diseases in rural and urban areas. In many poor countries large numbers of households in rural areas do not have toilet facility, or non speticc tank attached latrines, hence, people are forced to defecate in open that is contaminating fresh water, underground water and river water sources of that area and chances of communicable disease remain fair. In these areas flavivirus generated zoonotic diseases are very common of easy transmission due to fouling smell and presence of vectors [73]. These also attract insect vectors to breed. Open air defecation leads to the spread of disease both parasitic, bacterial and viral infections [73].

5.3 Problem of Safe Drinking Water

There is an utmost need to improve water supplies for controlling *Aedes* vectors, especially *Ae. aegypti.* Clean water supply and use of filters in houses and water treatment can ensure reduction in water borne communicable diseases. Central water supply unit should provide clean, well treated and filtered drinking water to all households. For this purpose, water is drawn by pumps, from underground borings or wells, and filled in central over hand tank by standpipes; from it is supplied to the community. Due to lowering in underground water table due to high extraction of water, for water supply rooftop catchments and other water-storage systems are also used. To complete un-interrupted water supply, rain water harvesting can be done for collection of water in tanks, and recharging of wells. For, provide water supply at low subsidized cost in urban areas per unit/gallon charges are to be levied for cost-recovery and maintenance of other expenditures. Therefore, for fair supply of water to all, gauze-meter

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reading boxes are to used to ensure water supply to every consumer of the area. To manage low cost water supply household collection and storage of roof catchment rainwater must be encouraged by making underground water harvesting chambers. Households should clean or drain water-storage containers to stop larval culture in tires, drums, overhead plastic or concrete tanks.

Due to supply of contaminated drinking water large number young age infants, juveniles, sub-adults become victims of diarrhea, cholera, dysentery, and hepatitis. In rural areas diseases like hepatitis A, enteric fever, intestinal worm infections, and fungal infections of skin and eye flu occur due to fouling, lack of sanitation, poor hygiene and unsafe drinking water. People also use water from wells, rivers, or ponds where decontamination of water never done. People are using unsafe contaminated drinking water in rural areas, and common water sources are local mark taps which drain contaminated water collected in upper underground water table. Due to extraction of large portion of groundwater for irrigation local pumps, wells, and taps become non-functional. Insufficient maintenance of the environment around water sources, groundwater pollution, excessive arsenic and fluoride in drinking water pose a major threat to India's health.

5.4 Vector Control

Without controlling disease transmission vectors, control of communicable diseases is impossible. For instant control of malaria, dengue fever, Japanese encephalitis and other pathogenic diseases mosquito control must be ensured by using variety of strategies i.e. using repellents, insecticides, fumigation are used to control adult mosquitoes. Deterrent or repellent treated mosquito nets, door nets, window mosquito mesh covers, killing of larvae in home outlets can cut down transmission of mosquito borne diseases. Infected birds, bats, dogs and other canine either treated with vaccine or finish by any method to control SARS, bird flu and Rabies. It is also possible through environmental management. By changing and cleaning the local environment minimize vector population can be minimized, with reduction human contact and bites. For vector control houses are regularly sprayed with low toxic pesticides and fumigants can be used in morning as well as in evening time. Larval habitats must be treated by using bio-insecticides, oils and soap water for dengue vector control. For improvement of cultural environment kill mosquito larvae in vector breeding habitats, keep vessels, bottles, buckets, coolers empty, clean them by scrubbing, fumigation of houses, spray of garden plants, waste disposal, and cleaning of gutters and drainages are highly essential. For complete check on mosquito breeding community water supply should be provided through distribution pipes by connecting them with household connections.

To ensure regular improvement in cultural environment street drains must be treated by low toxic insecticides to kill developing mosquito *Aedes. aegypti* larvae in stagnant water. Both household, medical and garden pests must be controlled. There is a need to keep low level of chlorine treatment in treating drinking-water to avoid dosages, it is highly to humans. Label instructions when using insecticides. There must be cultural and social feeling to maintain local environment clean healthy. However to combat spread and infectivity of flaviviruses vector control, epidemiology and immune surveillance and other safety measures must be ensured [74]. By vector control both disease transmission and pathogenesis can be controlled instantly [75].

5.5 Solid Waste Management

Mosquitoes breeding sites are mostly in solid waste sites where dirty water is filled in plastics. Solid waste is non-biodegradable garbage that attracts pigs, mosquitoes, flies, cockroaches and other organisms. By applying many of the basic principles population of *Aedes aegypti* larval habitats can be controlled. For environmental cleaning reduce, reuse, recycle of waste is highly important. For safe disposal of community waste proper storage, collection and disposal of waste are must. Integrated *Aedes aegypti* control with waste management can provide greater success in disease control.

5.6 Urban Hygiene and Health

For urban hygiene and health, before construction of buildings and other housing infrastructures should circulation of fresh air, housing water discharges from outlets should be kept in mind. Roof top rain water should be collected in overhead tanks and treated with to reduce disease vectors, including *Ae. aegypti, Culex quinquefasciatus* and *An. stephensi*. For this purpose, policy framework for creation of housing structures allows under legislation and rules of housing boards and municipalities. Face of building must be East to West so that fresh air can circulate easily through corridors and balconies.

5.7 Drainage and Irrigation Systems

In Tarai areas major water supply is through canals; that alternatively provides surface to mosquito vectors to breed. To stop breeding of mosquitoes subsurface drainage systems will prove more beneficial in control. There should be regulated irrigation of crop lands to control the

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vector breeding. In alkaline soil conditions heavy watering of crop lands through soil, keep salts accumulating in the root zone and making the soil unproductive. After spring season all these areas become filthy and full of vector population therefore, water drainage and irrigation systems must be well planned to drain out water or restore irrigation by using drip method or through pipeline to avoid staying and breeding of mosquitoes. Municipalities should set up a drainage pipe system that carries the water off the roof and safely away from home [76]. Water collected from rainwater harvesting can be used for irrigating lawn and garden plants, cleaning of clothes and utensils.

5.8 Lack of Knowledge and Social Awareness

For better management of epidemics or pandemic people should be abided by the importance of social distancing and other preventive measures. This is the duty of government and concerned public bodies to make people aware about the severity and devastation caused by pandemics. Only following rules, norms, and value of restrictions and support of protective measures with a positive attitude can reduce the intensity of pandemics. People must make aware about the presence of virus, its transmission and common symptoms and prevention. They essentially follow, lockdown, and maintain social distancing. For increasing awareness, social interactions, discussions and community level display are required. There is a need to design awareness programs to ensure participation of local people and thereby implement community-based disease or disaster management in their area. Social enterprises must aware about real time situations and remain in search, how to have saved themselves during disasters, pandemics and forest fires. United Nations ESCAP has issued directives for social enterprises to provide employment marginalized and vulnerable human communities and fulfill Sustainable Development Goals [77].

6. Issues Related to Health Management

6.1 Insurance-cooperative Community Health Services

For fighting communicable diseases cooperative-health insurance policy is required to provide medical treatment cover and remit clinical care expenditure. It must be essentially owned by the people. It should be formed of mutual insurance that may ensure all hospital entry and make clinical easy and mandatory to all the patients. It should be both publicly funded and single-payer healthcare insurance organization. President Obama suggested that all future health insurance cooperatives would run by their own, and receive a partial investment the government and would then handed over to non-profit organization [77]. Farm Security Administration (FSA) was running many rural health cooperatives. Un-irrupted health care is possible through on premium insurance plans with high benefits.

6.2 Female and Child Health Issues

In developing countries child mortality is high. The main reason behind it is mal-nutrition. Problems are child marriage, delayed marriage, obesity and other physiological ailments. Most of the mother-child health care centers in rural areas do not have skilled birth attendants and lack of quality emergency maternal care. One of the most severe and increasing problems among women in India, resulting in higher mortality rates due to malnutrition, breast cancer, and stroke, delivery and post pregnancy deaths. Vitamin, protein, iron and folate deficiency are responsible for child mortality. The main cause of female malnutrition in India is the traditional foods and social practices. Due to obesity and overage in females polycystic ovarian diseases are increasing the infertility rate in females. This condition causes many small cysts to form in the ovaries, which can negatively affect a woman's ability to conceive Child marriage is a curse and making the life of young couples hell, because most of them are unemployed, and facing physical and physiological illness. In India maternal mortality rates in rural areas are one of the highest in the world [78].

6.3 Rural Health

In developing and under developed countries 50-60% of total population is living in rural areas and half of all residents of rural areas live below the poverty line, struggling for better and easy access to health care and services. Rural areas of many countries also have local health issues evolved due to communicable diseases i.e. influenza, dengue, filarial, rubella, Ebola and malaria. Rural people are also facing illness caused by life style diseases such as diabetes, blood pressure, obesity, cardiovascular problems, cancer with heavy trauma of communicable diseases. Malnutrition, loss of habitat, cultural and social detachment are serious problems in resource-poor rural areas. Thus, demographic, local climatic changes and invasion by disease pathogens are causing high maternal mortality particularly in rural India. Both malnourished mother and child need instant care and medical aids.

6.4 Vaccination Drives

Vaccine is only way to artificially raise body's natural defenses so that immune system can recognize and fight

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off the viruses and other pathogens. A vaccine essentially contains an antigen or a gene that synthesize antigen that can generate a significant level of immune response after administration. But it is tje greatest challenge in present time as new variants/mutants of viruses are evolving, and these are responsible for enhancement of neurovirulence, anti-genicity, host immune responses and disease transmission in endemic areas [79]. It has led to decrease the vaccine efficacy. Till the date thousand of vaccines have been generated against various diseases under W.H.O. banner under licensing. Vaccination needs pre and post vaccination surveillance to adjudge the successfulness of vaccination drive. Vaccination drives against virus and bacterial infections were found successful as the efficacy was noted between 90-97% in a few cases. After vaccination, if the body is later exposed to those disease-causing germs, the body is immediately ready to destroy them, preventing illness. Such vaccine is considered to be efficacious and shows success rate around 90%. It is great truth that vaccines save millions of lives each year [80].

In the present time vaccines are only hoped in the battle against COVID-19. There is a huge demand to vaccinate every person; hence there is an utmost need to speed up the production of safe and effective vaccines against COVID-19. For large scale immunization in India as well as in other countries manufacturing capabilities are to be enhanced, license and duty policy should be elasticized. Further, at the global level governments and manufacturers must ensure to have fair and equitable allocation of the vaccines for all countries. But for fast control of disease there must be some change in vaccine policy. It must be de-licensed so that its manufacturing could be increased and cost comes lower down. If we want to defeat recently merged pandemic no patents are to be given and open licensing will increase manufacturing level, it will speed up vaccination process. Now greater questions are there are three categories of people in current time unvaccinated healthy, first dose takers and people recovered from Covid-19 infection. If people who have administered first dose, if they will not be provided booster dose then vaccination has no meaning. Now, for greater success all age groups should be vaccinated within six months before third wave, and it is seeing impossible. There should be a broader plate form, and a group of scientists collaborators and manufactures to generate vaccines 4-5 million doses per week to collectively save lives and to end this pandemic. For control of invasion of retroviruses anti-retroviral therapy could be provided. Similarly, few viral diseases could be treated by using anti-viral drugs, if they are used after consultation with a physician in initial phase of disease [81].

Since the pandemic began, in India mark of infected has been reached beyond 30 million cases. It has also reported more than 200,000 deaths. About 150 million shots have been given, equivalent to 11.5% of India's 1.3 billion people. India started its Covid-19 vaccination program in mid-January. Initially chances of success looked high. Though, government has formed the vaccination policy and categorizes the various age groups to vaccinate. But by seeing population size it will need more than two billion doses for one primary vaccination and for a second dose as a booster. India has fully vaccinated less than 2% of its 1.3 billion huge population. Therefore, rate of vaccine production and its administration should be increased. Production of vaccine at current rate is not sufficient for immunization of whole country. Though, India is self reliant in vaccine production but it will need huge infrastructure to give tough fight to corona pandemic. Indian government has set the new rules to make "pricing, procurement, eligibility and administration of vaccines open and flexible." The nation is now the main hotspot of the pandemic, despite being home to the world's largest vaccine manufacturer. The vaccination program is highly essential to vaccinate the people to reduce the selective pressure for emergence of new strains. A much faster vaccine drive could end this pandemic much faster. Not just that, India is also helping out many countries with vaccines. Due to shortage of vaccine inoculation centers across the country are running short of doses. Before, finishing of second wave all age groups in India must be vaccinated. Despite being the world's biggest producer of vaccines, the country is suffering an internal shortage and has placed a temporary hold on all exports of AstraZeneca to meet domestic demand.

India has been using two vaccines - the Oxford-AstraZeneca jab (known locally as Covishield) and another (Covaxin) is made by Indian firm Bharat Biotech and Serum Institute of India Ltd. Recently, Russian-made Sputnik V vaccine has been confirmed its production in India by end of July this year.. All these vaccines are well tested and passed through a double blind, randomized clinical trial of immunogenicity and safety on a dose-response study [82]. Vaccination in India is going on with few "18904 adverse events" including 180 deaths following immunization. These adverse events were "minor" and happened due to anxiety, vertigo, giddiness, dizziness, fever, and pain. All such patients had recovered, the government said. More deaths were observed due to underlying conditions or persons facing any life style disease including heart problems, high blood pressure and diabetes.

There are several reasons of vaccine failure, it occurs at the level of antigen purification, instability or poor stabili-

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ty of antigen, production and manufacturing time, storage, transport and immunization [83]. The biggest challenge to current vaccination is to protect the immune-compromised patients and the elderly, with severe lower respiratory tract infections. Vaccination is only way to manage respiratory failure and ARDS; septic shock; prevention of other physiological. Vaccination is safe and provides protection shield against Covid-19. Besides success few China made vaccines were found un-reliable and totally failed the main reason behind is de-naturation or instability of antigen. There are two important questions how long current vaccines will work against array of mutants that may come in future. Because low antigenic homology in surface proteins both vaccine and circulating strain will differ always. It will affect the efficacy of vaccine and remain insufficient to viral antigen load in the vaccine. Among important reasons of vaccine failures are mutations in epitopic regions of viruses, poor antigenecity and low neutralization power. In the past several attenuated vaccines have been failed due to low reactogenicity and immunogenicity to newly formed viral strains mainly new mutant variants [84]. Total failure of vaccine is loss of efficacy of immune protection and generation of level of antibodies after immunization.

The main problem in control and prevention of communicable disease is poor economic condition of people. They are not in a condition to pay heavy expenditure occur in treatment, hence they never reach to hospitals. These solely depends on government hospitals and on international disease eradication programmes launched by W.H.O. Due unemployment and low availability of resource people are struggling for better and easy access to treatment and health care. Rural population in so many countries has severe health issues that will need social networking for proper clinical care. To finish disease it is essentially required to bring together people with education-technology and knowledge dissemination on a single platform. There is no institution which can hear problems of slum residents, poor farmers and residents of Tarai region of eastern part of India.

7. Conclusions

There are several causes of outbreak of communicable diseases. Among all reasons arthropod life cycles are more frequent which consequently responsible for dispersal of various categories of viruses i.e. arboviruses and flaviviruses. These areas also have to transmit vectors and reservoir hosts both in the area, at the same time and in same season. Mosquito vectors are transmitting pathogens between various vertebrate hosts. Due to heavy rains in low land areas flood water collected speedily full of garbage, human and animal wastes, fertilizers and other chemicals. This large area of flood water, support large vegetation cover, huge plankton and fish population attracts migratory birds. In addition, increase in water surface area in hundreds of wetlands and adjoining paddy fields provide a broad base to mosquitoes breeding. It occurs very fast because with supported supplementation of different fertilizers. In addition, new migrants received by the water reservoirs provide blood feeding to mosquito population, thus transfer of pathogen between hosts becomes easy. It is responsible for virus multiplication and transmission. Once there are rains, a rapid increase occurs in vector population, amplifying hosts and migratory birds are seen. These ecological and landscape factors are responsible for emergence/re-emergence of virus diseases with other associating complex factors, such as viral recombination and mutation, leading to more virulent and adaptive strains. Furthermore, urbanization and human activities are creating more permissive environment for vector-host interaction, and increased air travel and commerce. To fight against the rising JE, malaria, dengue, and SARS-COV-2 geographic, demographic, vector and host biology and climatic studies are highly important. For an effective control of communicable diseases, vector control, improvement of local environment, social awareness, clinical care and vaccination are important steps. Disease management is only possible after management; it will not only control diseases but stop its outbreak but check conversion of endemic diseases into pandemic. Contrary to this, Covid-19 is spreading beyond the limits of demographic and geographical locations. Virus is equally showing mortality rate in temperate and tropical and subtropical regions.

Among important reasons of outbreak of communicable disease are high annual precipitation cycles, frequent human travels, demographic clustering, and insecticide resistance. Due to filth and garbage ditches mosquito's larvae get adapted to chemical pesticides, from which insecticide resistant adult population emerged. It leads to transmission of disease pathogens in human population. Further, poor economy, socio cultural environment and lack of clinical care and therapeutics increase the number of affected people. On other side microbial pathogens are also developing resistance to drug structures and new mutant variants or revertants of many viruses are increasing infectivity and mortality in the epidemiological area. Other complex factors related to human activities like deforestation, dam construction, open irrigation, and climatic changes brought on by EI Nino-related events such as droughts, forest fires and severe haze, environmental gases changing the effecting the precipitation cycle. Due to monoculture economic crops, composite fish farming,

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hatcheries, and mixed agro-pig farming practices are providing base to viruses, because both vectors and reservoir hosts remain in exposure to this fowling environment, hence, communicable disease pathogens easily generate their progenies and spillovers of the virus take place from wildlife reservoir hosts into pig population. Pig farming between the human habitations should be ceased immediately and these should be shifted far away from human habitations. Furthermore, ecology, global warming and rising vector population have significantly increased the potential for disease emergence and its spread. For overall health management both surveillance and diagnosis are equally needed. For combating Covid -19 pandemic all the reasons of virus generated epidemics, virus genetics, host immune status, fast and earlier diagnosis, clinical care, long term safer immunization, vector control and socio-clinical management of communicable diseases be required in affected areas.

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Conflict of Interest

The authors declare no competing financial interests.

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