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Review Article

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Emerging and re–emerging diseases: A narrative review

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ABSTRACT

Infectious diseases remain a serious concern all over the world due to its significant impact on public health and economic stability. About 30 new causative organisms have been discovered over the past few decades, most of which are zoonotic in origins. Thus, infectious diseases are now posing a never-ending challenge to human civilisation. As a result, constant awareness along with adoption of effective strategies to control infectious disease spread has now become crucial. This review gives valuable information on diseases that emerge and re-emerge every now and then. The paper also highlights challenges related to tackling of infectious diseases in present scenario and significance of employing strategies for effective control in near future against various deadly infectious diseases like COVID-19.

KEYWORDS: Emerging and re-emerging; Infectious diseases; Zoonotic; Public health; COVID-19

1. Introduction

Impairment of the normal functioning of a body organ or system in an organism has been referred to as "disease". Specific internal or external signs and symptoms causing infection tends to interfere with the normal functioning of the organ or system of the organism. Internal factors lie inside the body of the organism and arise due to genetic disorder affecting the normal functioning of the body such like sickle cell anaemia. On the other hand, external factors lie outside the organism that get transmitted when the organism comes in contact with an agent from outside being referred to as "vector". An example of it is the female *Anopheles* mosquito which transmits *Plasmodium*, the causative agent of malaria. Such illnesses that occur due to invasion of foreign organisms that harm or impair the normal functioning of the body or system have been regarded as infectious diseases[1–3]. It has been reported by WHO that about one-third, *i.e.*, 20 million deaths, occurring worldwide have been attributed to infectious diseases[4,5]. These diseases occur predominantly by microorganisms that upon entering the organism, damage the organ/organ system. Entries of microbe inside the organism mainly occur from mouth, eyes, genital openings, nose and skin while organ system disruption due to microbial growth causes release of toxins or enzymes that hamper the normal functioning of the body[6]. The emergence of infectious diseases in human population occurs at specific point of time in a specific environment. The methods for fighting, preventing and controlling the diseases get developed after understanding of the disease dynamics along with means of contracting them[2,7,8]. There are certain pathogens causing infectious diseases which after a certain period of time exhibit properties that enable them to re-infect the organism/host in unusually high numbers. Such pathogens of infectious diseases have been referred as re-emerging pathogens. The concept of disease emergence dates long back around 5th century B.C., and has been well explained by Charles Nicolle in 1920 during his talk about "Life and Death of Infectious Diseases" which shed light on the risk of infectious diseases[2,9].

In 1987 Joshua Lederberg, Robert B. Shope, and Mary Wilson coined the term "emerging and re-emerging diseases"[10], which signifies those illnesses in humans whose incidence had either

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increased within the past two decades or is threatening to increase in the near future. Several of them are zoonotic in their origin. Over 70% of emerging infectious diseases among humans for the last 30 years have been found to be zoonotic[11,12]. Zoonotic infectious diseases are those that get transmitted naturally from vertebrate animals to humans and *vice versa*. Infectious diseases of zoonotic origin are caused due to bacteria, parasites, fungi, viruses and prions. However, the greatest threat of repeatedly occurring zoonotic diseases is mainly attributed to viruses accounting to two-thirds of the infectious disease burden and being characterized with very high epidemicity such as like Filoviruses, Ebola and Marburg[13,14].

2. Transmission of emerging infectious diseases

Numerous factors, including global urbanisation, rising population density, poverty, social unrest, travel, land clearing, farming, hunting, keeping domestic pets, deforestation, climate change, and other human activities that destroy the microbial habitat, have been related with the invasion of infectious agents on humans[15,16]. The chance of contracting new pathogen(s) also increases with human activities that interfere with ecological and environmental conditions, and are transmitted *via* intermediate animal hosts like rodents due to increased contact of rodent with humans because of environmental and human behavioural factors[1,17]. The transmission of emerging diseases (EIDs) in humans involve a reservoir host that might make contact with a native host, such as a person or animal. Certain level of host behaviour, pathogen changes, and environmental factors along with contact or spill over between reservoir specimens and the native host are some of the factors responsible for transmission of EIDs in humans[2,18]. Sustained insusceptible host or secondary host transmission of pathogens have resulted in emergence of epidemics in pandemic proportions leading to failure to initiating cross-species infection or generating secondary infections that interrupt the emergence process[6]. Emerging infections apart from Human immunodeficiency virus (HIV) are mainly zoonotic because they are transmitted from animals to humans. HIV transmission occurs mainly among humans due to sexual behaviour. Socioeconomic factors are the major contributor causing bulk of the infections in the developing world[19–21]. In 2014 West Africa Ebola Virus Disease (EVD) outbreak, combination of several factors triggered the disease emergence. The EVD outbreak occurred in Meliandou, Guinea. Meliandou is the forest region encompassing Guinea, Sierra Leone, and Liberia[22,23]. It has been reported that destruction of the forest caused bat species, the natural reservoir for the virus, to come in contact with human settlements[24,25]. Lastly, the transmission of EIDs is also linked with conditions of extreme poverty, weakened healthcare system along with certain local customs such as washing the dead body before burial[26,27].

2.1. Some of the major EIDs affecting humans

2.1.1. Cholera

The bacterium *Vibrio cholerae* causes cholera that leads to severe watery diarrhea along with dehydration and even death if untreated. This disease commonly occurs in poor and underdeveloped nations that lack proper hygiene and sanitation facilities. It has been reported that cholera gets contracted by 3-5 million people worldwide in a year and among them 28 800 to 130 000 deaths are registered during the year[28,29]. Cholera was first described to occur in the European literature during the year 1642 by a Dutch physician named Jakob de Bondt in his book called De Medicina Indorum[30]. In India, the first case of cholera pandemic was reported from 1817-1824 in Kolkata, which later got spread to other countries *via* trade route[31]. The outbreak of cholera in the Indian sub-continent had been believed to occur due to poor living conditions along with the presence of pools of still water which provided ideal conditions for the cholera bacterium to thrive[32].

2.1.2. Plague

Yersinia pestis, a Gram-negative, rod-shaped bacterium, is the causative agent for plague. It is a facultative anaerobe that can infect both humans and other animals. The disease gets transmitted to humans from rodents, which are the primary carriers of the pathogen Yersinia pestis. Plague usually occurs in the tropical and sub-tropical latitudes, and in the warmer parts of the temperate latitudes around the globe, between the parallels 55° North and 40° South[33]. The occurrence of plague pandemic dates back to several centuries ago and its first incidence being reported was the Plague of Justinian which emerged in Egypt and then got spread to Europe along with Asia Minor during the year 541 and the wave of the pandemic continued till the year 767[34,35]. Since then, plague has re-emerged several times and, in several places, claiming huge number of lives. Out of several incidences of plague outbreak, the most severe outbreak that occurred was the “third plague pandemic” which emerged in Yunnan of China in the year 1855 and later got spread to India causing 12 million deaths, with about 10 million being killed in India alone[36,37]. In 1994 also, a minor plague attack occurred in India between August 26 to October 5, claiming around 56 lives[38].

2.1.3. Swine flu

Swine flu occurs due to swine influenza viruses, which are influenza family of viruses being endemic in pigs such as H1N1, H1N2, H2N1 etc[39]. The first outbreak of swine flu due to H1N1 viral strain occurred in humans in United States during the year 1918, claiming about 50 to 100 million lives[40,41]. In India, the first case of swine flu was reported from Hyderabad[42]. The transmission of swine flu infection occurs mainly among people who do pig farming, as reported in a case study been conducted at university of lowa during the year 2004[43].

2.1.4. Smallpox

Smallpox is caused by variola virus, a member of the Orthopoxvirus genus of the family Poxviridae. The history of smallpox emerging in human population dates back to about 10 000 BC[44]. It was reported that smallpox was responsible for 300-500 million deaths during the 20th century[45–47]. A research article published during 1983 also reported that during 1967, approximately 15 million people got infected with smallpox and among them nearly two million people lost their lives[48]. The first emergence of smallpox in India occurred during the year 1974, claiming 15 000 lives. It has been reported that 61 482 cases of smallpox were recorded in India during the year 1974 which accounted for 86% of the world's smallpox cases of 1974[49]. The disease again re-emerged in October 1977, bringing along with it the last case of smallpox infection recorded, afterwards WHO certified the global eradication of the disease in 1980[50].

2.1.5. HIV–AIDS

HIV belongs to the family of retroviruses which causes acquired immune deficiency syndrome (AIDS) in humans[51,52]. HIV was first reported in USA during the year 1981 while the term AIDS caused by HIV infection was officially given by Centre for Disease Control during September 1982[53,54]. The disease again re-emerged during 1991 in Spain where 4 322 AIDS cases were notified corresponding to a rate of 11 per 100 000 population[55]. HIV was first reported in India during the year 1986 among female sex workers of Chennai and today India accounts for second largest population of people being infected with HIV with an estimated 5 million infections[56,57]. Recently in 2015, an outbreak of HIV was identified among drug addict people of Glasgow and Clyde area of Scotland because of using infected needles and syringes for drug administration into the body[58].

2.1.6. Rotavirus infection

It is a double-stranded RNA virus of family Reoviridae which causes diarrhea among infants and young children[59]. As one of the major causes of gastrointestinal illness among children, rotavirus was responsible for 453 000 deaths of children worldwide in 2008[60]. Rotavirus was first identified in humans in 1973 and since then several cases of rotavirus associated diarrhea among infants have been reported from different parts of the world[61,62]. It has also been reported that every child with $\leqslant$5 year of age has been infected by rotavirus at least once[63]. The emergence of rotavirus associated diarrhea among children has been extensively studied in China from 1994 to 2013[64].

2.1.7. SARS

Severe acute respiratory syndrome (SARS) is caused by certain group of viruses being referred to as coronavirus. SARS emerged in late 2002 as a global epidemic with 8 000 confirmed infections and around 800 deaths. The duration of SARS outbreak was from the year 2002 to 2004 after which no further report related to re-emergence of SARS infection was recorded[65].

3. Current threat of COVID–19 Pandemic: Emergence of a new strain of coronavirus (SARS–CoV–2)

Coronaviruses are single-stranded RNA viruses which can infect both animals and humans causing respiratory, gastrointestinal, hepatic, and neurologic diseases[66]. Emergence of new coronavirus strain is attributed to a variety of factors like high prevalence and wide distribution, large genetic diversity and frequent recombination of genomes along with increasing human-animal interface activity [67,68]. In Wuhan, Hubei province of China, during late December 2019, several local health authorities reported many cases of pneumonia of unknown origin, which were epidemiologically linked to a seafood market[68]. This virus was later recognised to be novel coronavirus (SARS-CoV-2) by surveillance mechanism for "pneumonia of unknown etiology" which was established in the wake of 2003 SARS outbreak with the aim of allowing timely identification of novel pathogens[68,69]. WHO, on 30th January, 2020, declared COVID-19 as "public-health emergency of international concern" while COVID-19 was declared to be a pandemic by WHO on 11th of March 2020 since it got spread to most of the countries and because there were more than one hundred thousand patients affected by COVID-19 in more than 114 nations[70,71]. Since 2020, COVID-19 Pandemic has spread very rapidly all across the world affecting millions of people till date. Due to constant genetic mutation and lack of adequate information regarding the designing of accurate vaccine for eliminating the virus, it has become very difficult to tackle the infection rate, thereby accounting for huge morbidity and significant mortality.

3.1. Mode of transmission of SARS–CoV–2

The natural reservoir/host in transmitting various viruses like Ebola, Nipah along with coronavirus are wild animals and bats[67,72]. SARS-CoV-2, a beta-CoV is the seventh member of the family of coronaviruses with about 70% genetic similarity to SARS-nCoV[73]. It has been recently reported that the virus is 96% identical at the whole genome level to a bat coronavirus, which means bats are the most possible host of the SARS-CoV-2[74,75]. Likewise, minks and pangolins have been found to be potential intermediate host to SARS-CoV-2, but in general there may be multiple intermediate hosts linked to SARS-CoV-2 transmission [73,76].

3.2. Symptoms associated with COVID–19 and treatment

COVID-19 symptoms are non-specific and the disease presentation can range from no symptoms (asymptomatic) to severe pneumonia and death. It has been reported from a study on 41 patients that the

common symptoms of COVID-19 were fever, cough and myalgia/fatigue while atypical symptoms included sputum, headache, haemoptysis and diarrhea[77]. In another study it was found that the most common symptoms of COVID-19 were fever, cough, diarrhea and vomiting[78].

Presently, several vaccines like Covishield and Covaxin are available for fighting against the COVID-19 Pandemic. Moreover, drugs like Remdesivir, steroids, tocilizumab, favipiravir, and ivermectin are also administered to COVID patients for treatment.

3.3. Challenges related to tackling of EIDs and the future ahead

Several EIDs are now posing very severe and never-ending challenge to human civilisation due to their periodic re-emergence. Infectious diseases have killed several millions of people each year for the past two decades. Several virulent pathogens are continuing to emerge and re-emerge every now and then. Several factors have accounted for the increase of infectious diseases which include Human, Social, Political, environmental, technological, microbial along with ecological factors[79]. For combating EIDs successfully, several techniques need to be improved and updated.

3.3.1. Genetic variation

Genetic alterations in pathogenic microorganisms encode for new phenotypic traits that adapt infectious agents to new or old host(s), which may be favoured by altering host and environmental conditions. This only causes emergence and re-emergence of infectious diseases leading to new pandemics. A classic example of emerging and re-emerging infectious agent(s) are the influenza viruses by their ability to undergo multiple genetic changes and evolve in response to changing host and environmental conditions[2,80–82]. So, emergence of infectious diseases will continue as long as pathogens undergo genetic changes along with pathogen adaptation for causing infection due to human and environmental activities.

3.3.2. Antimicrobial resistance

Resistance to drugs is another major problem which has arisen due to genetic changes[83]. The phenomena of antimicrobial resistance has been observed in case of HIV infection whereby due to drug-drug interaction and toxic side effects, drug resistance has evolved from drug pressure coupled with high rate of genomic variation (during viral replication) leading to treatment failure and necessitating regimen switches[84,85]. The problem of antimicrobial resistance along with emergence of drug resistant microbes encompasses several bacterial infectious agents like *Escherichia coli*, *Pneumococcus*, *Neisseria gonorrhoeae*, and *Staphylococcus aureus*. The problem of antimicrobial resistance has thus necessitated continued development of new antiviral and antimicrobial products.

3.3.3. Surveillance

EIDs have genuinely called for the need of constant surveillance and timely intervention. Vaccines and drugs need to be deployed effectively among desired places and there is also a need for necessary infrastructure and skilled personnel to support prompt diagnosis and a need for ongoing research to aid development of effective countermeasures. However, effective surveillance and control of EIDs is a significant public health challenge owing to extensive distribution of pathogens[86–88], making prediction of events related to zoonotic disease emergence a subject requiring persistent scientific exploration.

Past epidemics have greatly enhanced our knowledge about unpredictable and devastating nature of infectious diseases, and EIDs have shown their capacity to emerge and spread rapidly by any possible means across borders along with exhibiting high pathogenic potential and evolve or mutate to resist drug attack. So, there is need for proper and constant surveillance to strengthen the capacity for identification of microbial agents with epidemic potential so as to prevent their emergence. Special attention is needed on situations that promote disease emergence, which can be achieved by monitoring human activities that degrade environment and alter ecological conditions, which thereby increases animal(s) contact with humans.

4. Conclusions

Emerging and re-emerging infectious disease are major public health threats that have serious social, political, and economic effects. The problem of pandemic has worsened the living of humans in every way possible, which arise by a variety of factors relating to human behaviour and activities, pathogen evolution, poverty, and changes in the environment as well as dynamic human interactions with animals. Some pandemics such as like cholera occur from time to time repeatedly causing extensive damage to society. Likewise, the virus causing COVID-19 pandemic is evolving rapidly due to frequent genetic mutations due to which no vaccine is effective enough for fighting against the disease. The development of herd immunity among the population is the only solution to this problem. Lastly, for addressing this issue of emerging and re-emerging diseases, intensive research collaboration amidst national and international organizations, proper networking, appropriate financial support for public health infrastructure along with poverty reduction are very crucial.

Conflict of interest statement

The authors claim there is no conflict of interest.

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Data availability statement

The data supporting the findings of this study are available from the corresponding author upon request.

Authors' contributions

Biswas S and Khuntia HKcontributed to conception and designing of the manuscript. Critical revision of the manuscript along with supplementing materials for preparing the manuscript thoroughly was done by Ranjit M. The work of completing the manuscript was equally assisted by Bal M as well as by Pati S. All the authors agree with the content of the manuscript.

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