

Mathematical Modeling on Communicable Disease- A Review

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Abstract

Mathematical modelling on the spread of communicable/infectious diseases is used as an important tool to investigate the transmission and propagation of the diseases. Mathematicians along with researchers from health departments are working on the control measures of these diseases by incorporating different factors in the models. This helps us to know about the timely interventions and measures to be taken to control the disease.

Introduction

Study of factors that determine the frequency and influence of a disease or other health related problems, their cause to prevent the further spread of disease by making preventive strategies, establishing programmes in a defined human population is known as Epidemiology. It can be categorized as

- Descriptive Epidemiology
- Analytic Epidemiology.
- The first one is the stage in which the disease occurred is examined by taking into account the time, place where it has occurred and symptoms of the person affected are considered. Hypothesis regarding the cause of disease are made in this stage. In the second one, the hypothesis made above are tested. The diseases can be categorized in two groups:
 - Communicable diseases
 - Non-communicable diseases

Communicable disease are those diseases which pass from one person to another by direct transmission or indirect transmission and can be caused by bacteria, fungus, yeast, viruses and parasites. These infectious/communicable diseases can spread through by water, air and direct/ indirect contact. For example syphilis, gonorrhoea, AIDS are sexually transmitted diseases. Nosocomial infections, Rhinovirus cold, Brucellosis (slaughter house contact), Hepatitis B virus are few examples of infections by contact. Cholera, Giardiasis, Listeriotic, Campylobacter are few examples of food/ water borne infections. Airborne infections give rise to Tuberculosis, Influenza, Measles, Mumps, rubella, pertussis (childhood disease) para influenza and many more types of diseases. Some vector borne infections are malaria, Dengue, Yellow Fever, Rocky mountain spotted fever and other. The infectious diseases can be transmitted through human, animal, soil and water reservoirs. AIDS, Syphilis, shigellosis, fever, herpes simplex virus take human as reservoirs. Rabies, Plague, anthrax etc. are examples of diseases with animals as reservoirs. Tetanus, Botulism, Histoplasmosis travel through soil as reservoir. Some infections with water as reservoir are UIT, hot tub folliculitis etc. The other category of disease is non-communicable which is also known as chronic. Cardiovascular diseases, non-infectious diseases of respiratory track, diabetes, cancer are four types of non-communicable diseases. Unhealthy diet, smoking, lack of exercise and abuse of alcohol are few important causes of this type of diseases. Cervical cancer is caused human papilloma virus conveying that there is a thin line separating communicable and non-communicable diseases. Communicable disease or infectious diseases have been important part of history because there were epidemics that have attacked populations, causing deaths very often, then disappearing to reoccur after certain times, possibly in decreasing severity as people develop immunity against them. For example, Black deaths (bubonic plague) in fourteenth century propagated in many

waves from Asia to Europe and almost one third of population died in that. There are many diseases which become endemic causing many deaths. In developing countries many diseases like measles, diarrhoea, respiratory infections and many other which can be treated easily claim millions of people. Diseases like cholera, sleeping sickness, malaria are endemic in many parts of world. Effects of high mortality on average life span and disease burden on economy of countries is considerable.

The aim of studying infectious disease through mathematical modelling is to control and eradicate the infection from the given population by knowing the values of R_0 and understanding the disease dynamics. There may be many factors associated with disease transmission like human behaviour, temperature, geographical conditions and contact rate of susceptible with infective, availability of control measures like vaccination and their frequency. Different researchers are working to help the world to control and prevent these diseases using mathematical modelling.

To study population level dynamics, two parameters are required.

- 1) The basic reproduction number i.e. the average number of secondary infections from single individual in a susceptible population.
- 2) The other parameter is time scale of infection i.e. the infectious period and exposed time period in SEIR models.

The above two factors have huge variability in Epidemiological modeling. E.g. childhood diseases like rubella, measles or chickenpox (SEIR models) very high R_0 [1]. The pioneer of study of infectious disease was John Graunt (1620-1674) who analysed various causes of deaths. The first model in mathematical epidemiology was given by Daniel Bernoulli (1700-1782) which was inoculation against small pox known as variolation to produce lifelong immunity against the disease. In 1855, John snow gave the knowledge that disease like cholera is transmitted by water. In 1873, William Budd explained the transmission for epidemiology with compartmental modeling was given by Sir R.A. Ross, Meachandrick, Kermack and Hamer in 1902, Ross demonstrated the dynamics of malaria transmission through compartmental modelling. The development of compartmental modelling for infectious disease helped mathematicians and health professionals in different ways as their goals being better understanding of diseases transmission and practical procedures for management of disease. It is better for both of them if the effects of disease transmission on human population and human behaviour can be embedded in mathematical models [2]. There are so many diseases in the list of infectious diseases like yellow fever, chikungunya, rotavirus diarrhoea and many more.

Mathematical modeling on Yellow fever

Infectious disease like Yellow fever is transmitted through virus from mosquitoes to human and humans to mosquitoes. Yellow fever is viral haemorrhagic fever caused by biting of a mosquito *Aedes aegypti*, a YF vector of the urban cycle of the disease. After incubation period of 3 to 6 days, the disease becomes symptomatic with symptoms like mild fever, jaundice, vomiting, muscle pain and the disease may aggravate to death in some cases. Regarding its epidemiology, it occurs in tropical South America and Sub-Saharan Africa where it is otherwise endemic and intermittently epidemic. The first outbreak of yellow fever occurred in 1647 in Islands of Caribbean and afterwards at least 25 major America. In 1793, more than 9% of total population died in Philadelphia. In 1878 epidemic in Mississippi river valley claimed 20,000 people and many more to mention. The risk of acquiring yellow fever is determined by many factors like immunization status, location of travel, season, duration of exposure, activities during travel, and rate of virus transmission. It has been largely controlled by widespread vaccination programmes in which a live attenuated vaccine is administered in single shot [3]. Inwang (1967) studied mathematical formulae for two things one out of which is resistance potential to DDT i.e. the inherited genetic capacity of *A. aegypti* or other insects (if applicable) to develop resistance when they are subjected to some insecticide with target of 80-90% mortality. It was also studied that number of generations which must be subjected to insecticide to attain DDT resistance yellow fever mosquitos i.e. *Aedes aegypti*. Experimental data from only one generation was used in studying these formulae [7]. Monath et al. (2001) studied the underlying cause of yellow fever infection to the travellers travelling to tropics. It was suggested that travellers should be aware about the yellow fever endemic areas. Along with the risk of yellow fever while travelling, the risk YF17D vaccine has been assessed by the author

after some serious and adverse cases have been seen. It is being observed that there is shortage of YF vaccine and we need more vaccines in case epidemic occurs, the vaccine requirement will exceed its production [8]. SAGE working group worked on use of yellow fever vaccine to update the 2003 SAGE review. They worked on many factors like need of booster dose against yellow fever after every 10 years, vaccine safety in elderly people with age >60, vaccine safety in HIV infected persons, in persons with other immune compromising situations, pregnant women, lactating women, whether the injection can be co-administered with other vaccines, routine vaccination and epidemic outbreak strategies [9]. A model to control *Aedes aegypti* mosquito by the sterile insect technique was introduced by Esteva et al. in (2005). It is a method in which normal insects/ mosquitoes are radiated with gamma rays to make them sterile. It was observed that effectiveness of SIT depends on two factors (1) mating competitiveness of sterile mates (2) to make sure that sterile mosquitos are dispersed near breeding site so that they can have fair chance of mating. Stability analysis was performed and value of $R_0 > 1$ predicts that SIT control programmes will be effective depending upon the relation to sterile mosquitoes release and displacement of natural mosquitos in the environment, effect of immigration of females who already have laid fertile eggs and nullified the sterile releases [10]. Johansson et al. (2010) studied the yellow fever dynamics through incubation period of the virus in mosquitoes through which the virus travels to host i.e. humans. The external incubation period that is period of yellow fever virus in *Aedes Aegypti* and its dependence on temperature has been studied [11]. The outbreak of yellow fever in Asuncion in 2008 was studied by Johansson et al. (2012). Values of R_0 were calculated considering various factors like mosquito (Vector) biting rate, human transmission, vector density, hospitable environment. The simulation resulted in R_0 values 0.42 and 90 with lower and higher end estimates. The calculation of probabilities of introduction of YF epidemic and autochthonous transmission is be done efficiently by considering factors rates of travel, number of persons infected, values of R_0 and vaccinations coverage rates [12]. Monath (2012) studied the risks and benefits of yellow fever vaccines. The only vaccine available for YF is live attenuated vaccine in 17D lineage, which is mainly used to protect not only population in endemic areas but also persons travelling to those areas. It was suggested by the author that some safer alternative to live attenuated 17D vaccine should be there for travellers and population groups [13]. The estimate of disease burden in Africa was estimated by Garske et al. in 2014. Based on the data of yellow fever occurrence by improving estimation methods. The analysis in the paper incorporated spatial and temporal distribution of yellow fever in the continent. It is evident in the paper that the estimates of severe cases of yellow fever annually in Africa match with previous global estimates. The factors affecting the estimates regarding burden of disease are uncertainty in demographic data, uncertainty regarding spatial distribution of yellow fever, its occurrence in different countries [14]. The yellow fever vaccination outbreak in Sao Paulo, Brazil in 2009 was studied by Ribeiro et al. (2015). Their model helps in finding the areas to be vaccinated and proportion of people to be vaccinated in order to minimize the deaths. The paper gives an idea of vaccination strategy to minimize the number of vaccine induced mortality [15]. Bonin et al. (2018) worked on mathematical computational model of immune response to yellow fever vaccine. Their model simulations were done in four scenarios [16]. Sakamoto (2018) studied the risk of yellow fever in travellers visiting Brazil thereby importing the infection of yellow fever to different international destinations. In June 2018, 1257 confirmed cases and death of 394 persons were reported after the outbreak and it confirmed 12 imported cases from Brazil to 8 different countries since December 2017. Their study advised that the travellers should be well informed about the area of infection transmission. Secondly, if they cannot avoid going to these destination, then prior vaccination should be strongly advised to prevent infection [17]. Wilder Smith et al. (2018) estimated the number of Chinese worker who were not vaccinated against yellow fever during outbreak in Angola in 2016. It was suggested that yellow fever vaccination should be ensured to the persons travelling to infected areas in order to prevent the international spread of disease. Border controls should be tightened and proof of yellow fever vaccine should be produced at arrival from yellow fever endemic countries [18]. Shi Zhao (2018) studied the outbreak in Luanda and Angola through mathematical modeling. To identify the process of epidemic in Anglola in 2015-2016 and the study the vaccination campaign, mathematical modelling was used. The factors like role of mosquito vectors, R_0 , the climate and human behaviour were included in the model. The model helped to find that vaccination saved 5.1 fold more people from death and 5.6 fold people from illness out of 941 observed cases. Their modeling includes host and

vector population as well as asymptotic and severe proportions of host population. It has been simulated with different vaccination schemes [19].

Mathematical modeling on Chikungunya virus

Chikungunya is a vector borne viral diseases transmitted from human to human by mosquito *Aedes albopictus* also known as Asian Tiger. *Aedes aegypti* belongs to the same family which also transmits chikungunya as well as dengue. The name of the disease is derived from Makonde word which means “that which bends up” as it cause joint pains mainly ankles and wrist pains causing the person to bend which can prolong for months. This virus was firstly identified in 1953. Firstly, it was considered as a tropical disease but now the disease poses threat to the public health globally. So there is need to target the control measures to eradicate the disease or to avoid epidemic. Many researchers have worked on the control of this virus.

Dumont et al. (2008) worked on the outbreaks of chikungunya in Reunion Island in 2005 and 2006 with the help of mathematical modeling. Compartmental models for humans as well as mosquitoes were studied using set of differential equations. Calculation of basic reproduction number predicted that there will be disease free equilibrium for $R_0 < 1$. Conditions for global asymptotic stability were also discussed numerical simulations revealed that values of R_0 changed from < 1 to > 1 which is in agreement with the situation that there is no outbreak in 2005 and almost one third of population got affected in 2006. Values of reproduction number calculated revealed that force of infection varies from place to place which can be controlled by destruction of breeding sites of mosquitoes. Parameters like temperature, weather and humidity can be incorporated in the model to study in case of *Aedes aegypti* mosquito but not *Aedes albopictus* which are both vectors for chikungunya [20]. Moulay et al. (2010) studied the transmission of chikungunya virus to human population with two models. One is on mosquitoes and the other one on humans [21]. Dumont et al. (2010) studied the outbreak in Reunion Island in 2006 with the perspective to stop the chikungunya episode through mosquito control tools. Simulations result predicted $R_0 < 1$ for 2005 because of which the outbreak was not of as much amplitude as in 2006. One of the main reasons of 2006 outbreak was formulated by Vazelle et al [22]. Dumont et al. (2011) studied sterile insect technique for the eradication and preventions of *Aedes Albopictus* mosquito causing chikungunya. Numerical simulations discussing various equilibrium points, values of R_0 indicate that the SIT techniques are useful if rather than large and rare releases of sterile mosquitoes, small and frequent releases are more efficient if the timing of release is taken into consideration [23]. Poletti et al. (2011) studied chikungunya virus transmission potential and its control measures for outbreak in Italy 2007 [24]. Moreno et al. (2012) studied chikungunya virus introduction to United States [25]. Fischer et al. (2013) studied the effect of climate change on chikungunya virus in Europe [26]. Liu et al. (2014) studied the control strategies to seasonal model of chikungunya disease. Switching parameters like mechanical control of breeding sites, reduction of contact between mosquitoes and pulse vaccination with vaccine future are considered. Numerical simulation were used to find the efficacy of control schemes [27]. Robinson et al (2014) studied a model for the outbreak of chikungunya in Rural Cambodia in which outbreak in village of Trapeang Roka Kampong spece province in March 2012 with 44% of biologically confirmed cases [28].

Mathematical modeling on Rotavirus

Rotavirus is the main cause of diarrhoea and severe gastroenteritis in children aged < 5 years. Almost 95% of children get infected by rotavirus before reaching the 5 years age with peak incidence between 4 to 36 months. It got its name from word ‘rota’ which means wheel as it resembles wheel under microscope. The symptoms are watery diarrhoea, fever, vomiting, and nausea. Its incubation period is two days. It has been observed that children having two natural infections had complete protection against infections as each infection confers immunity. It is being seen that rotavirus claims 20% of diarrhoea death under 5 years in developing countries. So far, there is no specific cure of the infection, thereby controlling being just by preventing dehydration. It was suggested by WHO June 2009 recommendation that its vaccine should be included in vaccine chart of every country as its economic burden being considerable. Rotavirus infection has claimed so many young children in developing countries as compared to the countries where mortality rate are low.

Bishop et al. (1983) worked on the immunity conferred by rotavirus infection in new born babies. It was concluded that neonatal rotavirus infection does not grant/ confer immunity for subsequent infections but

protect against several clinically severe diseases during reinfection [29]. The dynamics of rotavirus infection through mathematical modeling by incorporating the factors seasonality, breastfeeding and control of infection through vaccination was studied by Shim et al. (2005) in [30]. It is being discussed in the paper that different vaccines like Rotashield (1998, USA), RRV-TV i.e. Rhesus Rotavirus tetravalent, Rotrix, Rotateq are effective. In 2007, Jit et al estimated the number of death due to rotavirus infection by using two methods and gave estimates of 3.8 and 3.2 deaths per year in England and Wales [31]. The concept of herd immunity in rotavirus infection is studied by Effelterre et al. in 2009 by employing a mathematical transmission model. This model helped in studying the impact of vaccination programmes for RV infection and disease for five countries France, Germany, Italy, Spain and UK of European Union. It is being calculated with the values R_0 and model that when vaccination coverage is 70%, 90%, 95%, herd immunity along with direct effects of vaccination help by introducing the RV- related gastroenteritis incidence by 25%, 22% and 20% respectively. In the paper it is being assumed that vaccination mimics natural RV infection which wanes from 100% to 0.1% from birth to age of 6 months [32]. Zaleta et al. (2010) worked on modeling of nosocomial transmission of rotavirus in hospitals in paediatric wards. Set of differential equations were analysed quantitatively and qualitatively for calculation of basic reproduction number of $R_0 = 0.870$ from the parameters estimated from Ringenbergs et al. (1989) was obtained [33]. Palam et al. (2010) evaluated the effects of national introduction of monovalent rotavirus vaccine and assessed its impact on diarrhoea in children with age less than two years in El Salvador, America, from January 2007 to June 2009. It was observed that dose of vaccine was 51% (26% to 67%) effective as hospital admission under age five declined by 40% in 2008 and by 51% in 2009 after vaccination in 2006 [34]. Lopman et al. (2012) considered low socio Economic settings (SES) to study reduced effects of Rotavirus vaccine. It was observed that rotavirus vaccine efficacy ranges from 50% in low SES to >90% in high socio-economic settings [35].

The co-infection of rotavirus and malaria is discussed by Omondi et al. in 2018 after a study conducted in Ghana which showed that 11.8% of 243 children examined were found to be infected by both [36]. Vaccination as one of the factors in a mathematical model was considered by Omondi et al. (2018). It was suggested that disease being endemic in population should be controlled by preventive measures like vaccination, safe drinking water and maintaining hygiene. It is being recommended that all the new born should be vaccinated in order to control rotavirus infection effectively [37].

The main aim of studying these models is to gain knowledge of transmission of these communicable/infectious diseases. Models can help us in optimisation of resources to target control measures in the direction of eradicating the disease from the population.

Conclusion

Infectious diseases are leading cause of death worldwide. Different researchers are working to help the world to control and prevent these diseases using mathematical modeling using non-linear differential equations. Factors associated with disease transmission like human behaviour, temperature, geographical conditions and contact rate, availability of control measures like vaccination are included in the models and analysed by using stability theory. This analysis help in making some control strategies based on reproduction number as it can predict whether a disease will die out or turn into an epidemic. Vaccination strategies and timely interventions can be recommended through the models.

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