MULTI AGENT BASED SIMULATION FOR TYPHOID FEVER WITH COMPLICATIONS: AN EPIDEMIC ANALYSIS.

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ABSTRACT

The purpose of this paper is to describe an epidemic modeling and simulation of the spreading Typhoid disease and the possibility to become complications, and assess its in one population. Typhoid disease was implemented inside the NetLogo modeling epidemic. The aim of design is to present a percentage of Typhoid disease outbreak and likelihood complications. The concept of phenomena—that is, how patterns in spreading Typhoid infection result from the interactions of many people in one population. The Typhoid epidemic modeling provides the epidemiologist with the opportunity to observe and explore these interactions in simulated epidemic that enable them to analyze the outbreak of this disease. As known that Typhoid Fever is an infection disease that can spread from human to human through the social interactions in the bad of hygiene and sanitation circumstances. Typhoid Fever is caused by Salmonella typhi and occurs sporadically in every year in Indonesia. The NetLogo programming epidemic allows epidemiologists to build computer models of infected human to healthy human interactions in one population and visualize agent (person) of healthy, typhoid infected, typhoid complications in the populations. These models are able to illustrate how if there are 10 Typhoid infectious persons in one population can spread to the healthy persons and then the Typhoid patients may become complicated. The results of this simulation can be viewed in monitor and graph plots.
KEYWORDS: Epidemic agent based modeling, Outbreak, Typhoid fever, Netlogo.

INTRODUCTION

Typhoid fever is a communicable disease, found only in man and occurs due to systemic infection mainly by *Salmonella typhi* organism. It is an acute generalized infection of the reticuloendothelial system, intestinal lymphoid tissue, and the gall bladder. Incubation period usually 10-14 days but it may be as short as 3 days or as long as 21 days depending upon the dose of the inoculums. Mode of transmission is transmitted by feco-oral route or urine-oral route, either directly through hands soiled with feces or urine of cases or carriers or indirectly by ingestion of contaminated water, milk, food or through flies (Singh 2001).

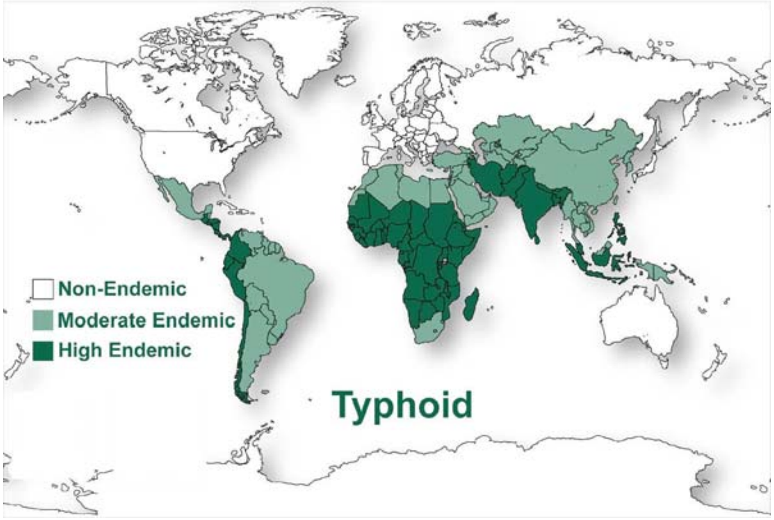
Many of them perish within 48 hours but some may survive for about 7 days. Survival can be up to a month in ice and ice cream and up to 70 days in the soil irrigated with sewage. Typhoid bacilli grow in milk without altering its taste and appearance. Vegetables grown in sewage farms or washed in contaminated water are a health hazard. These factors are compounded by social factors such as drinking water supplies, open air defecation and urination, low standards of food and personal hygiene and also health ignorance.

Typhoid fever also means a disease of poor environmental sanitation and hence occurs in parts of the world where water supply is unsafe and sanitation is substandard. It is still remains the important public health problems in many developing countries (including Indonesia) of the world. Although, it is difficult to estimate its real global impact due to problems related to the clinical and laboratory diagnosis. The socioeconomic impact of the disease is significant because most of the time, several months are necessary for the patients to recover completely and resume normal work again (Singh 2001).

In Indonesia, Typhoid fever can be found every year. The disease is being apart of the transmitted disease according to the government regulations no. 6, on 1962 in term of outbreak. However, Typhoid fever cases occur in Indonesia by sporadically, not epidemically in normal circumstances. Many complications might be occur such as intestinal bleeding, intestinal perforation, illeus paralytic, myocarditis typhosa, thrombosis, thrombophlebitis, hemolytic anemia, thrombocytopenia, disseminated intravascular coagulopaty, pneumonia, empyema, pleuritis, hepatitis, cholecystitis, glomerulonephritis, pyelonephritis, osteomyelitis, periostitis, toxic encephalopathy, meningitis and pyelonephritis perifer (Sutiono 1999).

In this epidemic simulation, we have developed computer models using a programmable modeling environment, NetLogo, to visualize how the typhoid people might infect to the others based on typhoid infectiousness, recover level and duration. Inside NetLogo, ‘patches’ are like environment which consist of population, land, area and geographic background. The patches can be assigned as variables to define the components that needed in side the environment and also a state of a patch can be altered based on interactions among agent to agent or agent to environment or environment to environment.

NetLogo programming language is consist of specific functions for epidemic simulation of Typhoid fever. The agents called ‘turtles’ are able to simulate person interactions in this environment. The users can give command from hundreds to thousands of agents. This software makes epidemic problems possible to be explored and analyzed in populations and the patterns that make interaction of many agents (people). We would like to discuss about our models can make contribution to understanding typhoid epidemic pattern.



Source: http://www.iol.ie/~tmb/Diseases/Typhoid.htm

Fig. 1 Typhoid Epidemic in the world

MODELS OF EPIDEMIC PROCESS

The pattern of epidemic typhoid fever become typhoid complications will begin in the first 3^{rd} – 4^{th} weeks after *Salmonella typhii* infection and has been confirmed positive *Salmonella* on blood, urine, stools test by increasing fever gradually. Differential diagnosis fevers within 2 weeks are varies. Before laboratory examination of S*almonella typhii* confirmed positive we can not exclude Typhoid fever. Otherwise in this model infected person means that have already positive *Salmonella typhi.* This infected people are able to infect the other people in population.

As in the real population, this model using NetLogo, can create the agent or person become infected, get typhoid complications, recover and die. In population commonly there is new born and die due to getting old or illness. New born means in a family may have a new baby and in this model we limited only maximum 2 children might be born. Die due to illness in this simulation is caused by whether or not complications of typhoid fever.

The patches in NetLogo also can be programmed as what we need. Patches in this simulation is an area where the people are living in. They are moving and get interaction on patches. Like environment, patches may influence the people who living in, but in this epidemic model we perform patches as normal environment which means may not give impact on the agent itself.

The NetLogo language is possible in epidemic simulations to help epidemiologist and decision maker understand how the epidemic problem occur in society. Interactions among person agents can result in observable patterns at the interface. Usually, in a traditional method, these epidemic patterns are done as direct observation and asking to the person by person like epidemiologist have been done to collect the information and database for epidemic analysis.

In epidemic simulation environments, epidemiologist can control the behavior of hundreds or thousands of typhoid infected, typhoid complications, healthy person "agents." By exploring the relationship between the agents rules of behavior and the patterns that emerge as a result of these rules, epidemiologist are able to eliminate many ineffectiveness that are generated by time, human resources, fund and others.

Through NetLogo, we can make predictions about the behavior of the model under varying model parameters then test their predictions by exploring model outcomes as they manipulate variables in a simple graphical user interface (Nigel G & Klaus GT, 2005)

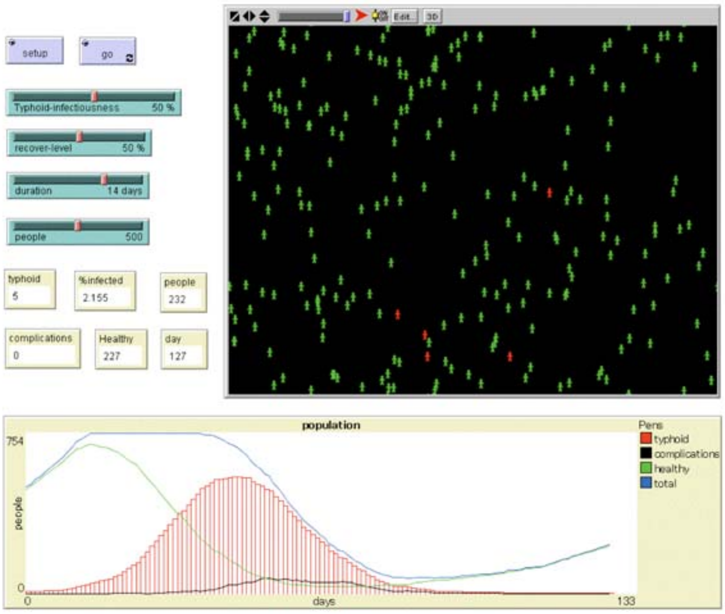


Fig. 2 User Interface NetLogo

On Fig. 2 epidemiologist are able to observe through user interface NetLogo. Behind the interface there are procedures of “setup” and “go” button, slider of Typhoid infectiousness, recover level, duration and number of people. Setup button is like reset button before simulation begins. It will arrange the number of population according to the number of people slider chosen and then prepare the typhoid infectiousness and recover level as sliders shown. In this epidemic simulation we make 10 people who had been infected typhoid fever and then make a contact to the other people. The spreading of the disease depends on the typhoid infectiousness which means the infectious level may have correlation with the how is seriousness the infection on *Salmonella typhii* in human being. Furthermore the infected people may become recovers and healthy again or maybe become Typhoid complications.

Monitor interface will show the number of population, typhoid patient, typhoid complications, healthy people days of epidemic event and infections percentage. Beside that to make an easy observation, graph plot can be seen on NetLogo interface. Each line represents the number of each items that are healthy, typhoid infected, typhoid complications and total populations. In this model, although we perform the same setting on number of population, typhoid infectiousness, recover level and duration but after pressing “setup” button and then run the simulation by press “go” button, the result of simulation may be different in every running of simulation. By these differences we can analyze the probability of spreading typhoid epidemic simulation by compare and estimate the number of simulations.

We concentrate on the likelihood of complications in one population. How many people will get complications after typhoid infections and how many days this complications will appear. Most of typhoid patients in hospitals usually get serious complications on the 2^{nd} and 3^{rd} weeks post *Salmonella typhi* invasion or approximately 10-14 days but it may be as short as 3 days or as long as 21 days depending upon the dose of the inoculum (Singh 2001).

Typhoid infectiousness can be arranged by slider and may assume that if the people who live in this environment have level of awareness of hygiene, sanitation or other circumstances which related with the possibility of water borne transmitted disease like typhoid are low, it means that the typhoid infectiousness will increase. The recover level may represent the condition of health facilities, the time when the patients get treatment from doctor as soon as possible, so that the faster to go to the health facilities and get the treatment, the recover level will also increase.

ANALYSIS OF TYPHOID EPIDEMIC MODEL

On graph plot (Fig. 3), the spreading of typhoid fever had been starting around 2^{nd} weeks and increased on 3^{rd} weeks as shown by red bar chart, meanwhile the complications had already happened as shown by black line on 3^{rd} weeks. The green line is showing the healthy people. If the percentage of typhoid fever people increase, the healthy people will decrease. In epidemiology, when we collect data it can begin to characterize an outbreak by time, place and person. Characterizing an outbreak by these variables is called descriptive epidemiology, because it describes what has occurred in the population under study (Richard Dicker & Nancy C. Gathany, 2007)

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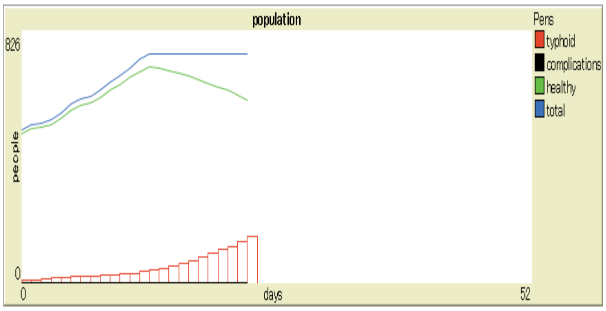

Fig. 3 Graph plot typhoid simulation

This step is critical for several reasons. First, by looking at the data carefully, it will become familiar with them. We can learn what information is reliable and informative (such as if many cases report the same unusual exposure) and learn what may not be as reliable (for example, many missing or “don’t know” responses to a particular question). Second, we can provide a comprehensive description of an outbreak by portraying its trend over time, its geographic extent (place), and the populations (persons) affected by the disease. We can assess our description of the outbreak in light of what is known about the disease (usual source, mode of transmission, risk factors and populations affected, etc.) to develop causal hypotheses. We can, in turn, test these hypotheses using the techniques of analytic epidemiology.

Before begin simulation, 84 patients of Typhoid fever with complications were analyzed by multiple regression using SPSS. As we know that multiple regressions is used to account for (predict) the variance in an interval dependent, based on linear combinations of interval, dichotomous, or dummy independent variables. Multiple regression can establish that a set of independent variables explains a proportion of the variance in a dependent variable at a significant level (through a significance test of R^2), and can establish the relative predictive importance of the independent variables (by comparing beta weights). The database like gender, age classification, education level, nutritional status, symptoms (anorexia, headache, abdominal discomfort) can be added as independent variables to explore curvilinear effects with Typhoid complications as dependent variable. And the multiple regression typhoid with complications equation takes the form:

$$\{S,NS\} = \int_{Di} \{G, A, EL, Nut, Anx, Ha, Abd\}$$

Where:

{S, NS}= Serious and non seriousness typhoid complications (dependent variable)

as independent variables are:

G	= Gender
A	= Age
EL	= Educational Level
Nut	= Nutritional status
Anx	= Anorexia
Ha	= Headache
Abd	= Abdominal disconfort

Furthermore the database should be coded for regression analysis. The dependent variable typhoid fever was classify into serious complications = 1 and non serious = 0, and also independent variables, that, gender, age, education level, nutritional status, symptoms (anorexia, headache and abdominal discomfort) has been coded. The equation for linier regression is:

$$Y\ (\text{typhoid}) = B_1X_{gender} + B_2X_{age} + B_3X_{EL} + B_4X_{Nut} + B_5X_{Anx} + B_6X_{Ha} + B_7X_{Abd} + C$$

The B's are the regression coefficients of each independent variable of typhoid complications, representing the amount the dependent variable y changes when the corresponding independent changes 1 unit. The c is the constant, where the regression line intercepts the y axis, representing the amount the dependent y will be when all the independent variables are 0. The standardized version B coefficient are the beta weights, and the ratio of the beta coefficients is the ratio of the relative predictive power of the independent variables. Associated with multiple regressions is R^2, multiple correlation, which is the percent of variance in the dependent variable explained collectively by all of the independent variables. The results of educational level and symptom headache have significant value 0.001 and 0.000 meanwhile the other independent variables have no significance, that, gender = 0.534; age = 0.538; nutritional status = 0.816; Anorexia = 0.078; abdominal discomfort = 0.902, and C = 1.067 as B constant coefficient regression. By this statistical analysis we conclude that only independent variable educational level and symptoms headache which significant with typhoid complications. Actually the educational level can represent the social background of the typhoid patients but it needs more details investigations. The symptom headache on this analysis may give influence significantly and may refer to the level of typhoid infectiousness on the model. Otherwise this two of significant independent variable must be broken down for further analysis.

At first, this simulation is setup on 50% typhoid infectiousness, 50% recover level, 14 days duration of probability to become complications or recover and 500 people in population. As a result, before the simulation start on “go” button, 2% population has been infected as source of infection which can be transmitted to the other one. After running simulation, on day 14^{th} – 21^{st} begins appear the increasing of typhoid cases and also may look the complications in this population. On 2^{nd} weeks there are 3 persons (2.94%) who become complications from 102 typhoid patients and total population 750. At the beginning, number populations are 500 by slider, due to we programmed the agent on simulation can get married and have 2 children so that they can growth, meanwhile some of them can die due to typhoid or getting old with maximum age 100. The maximum populations are also setup on 750 people.

The most serious complication of typhoid fever is intestinal bleeding or perforation that may develop in the third week of illness. About 5 percent of people with typhoid fever experience this complication (Mayo 2006). The 2 most common complications of typhoid fever are intestinal hemorrhage (12% in one British series) and perforation (3-4.6% of hospitalized patients) which happened on 2^{nd} – 3^{rd} weeks. From 1884-1909 (ie, preantibiotic era), the mortality rate in patients with intestinal perforation in typhoid fever was 66-90%_(Brusch. 2006). In Hasan Sadikin University of Padjadjaran Hospital Bandung Indonesia from 1995 - 1997, Typhoid complications were 84 patients (23%) of 354 typhoid patients_and 14% complications began on 1^{st} weeks hospitalization. This number was high because of the patients came to this referred hospital with severe conditions.

The likelihood of a human becoming infected with typhoid is a function of the likelihood of a human being contact with typhoid patient and the amount of time an individual would spend contacting at that moment, so both of these conditions are a direct function of typhoid infection. These functions are represented by typhoid infectiousness slider.

In the real world, one of the most exciting and challenging tasks facing an epidemiologist working in a public health department is investigating an outbreak. Frequently, the cause and source of the outbreak are unknown. Sometimes large numbers of people are affected. Often, the people in the community are concerned because they fear more people, including themselves, may be stricken unless the cause is found soon. There may be hostilities and defensiveness if an individual, product, or company has been accused of being the cause. Into this pressure-packed situation comes the epidemiologist, sometimes from the local health department, more often from “the outside.” In this setting the epidemiologist must remain calm, professional, and scientifically objective. Fortunately, epidemiology provides the scientific basis, the systematic approach, and the population and prevention orientations that are needed. Later on epidemiologists try to find the solution for epidemic analysis by using agent based modeling. This is possible to reduce the time and fund while investigating the outbreak. As long as the role of disease is the same and database can be used as the first statistical analysis, furthermore the epidemic agent based modeling can be used as epidemic analysis tools. Computer models are easy to program for any kind of spreading disease. So that the intervention as preventive actions can be done before the outbreak happened. In Indonesia, epidemic agent based modeling will be useful due to the source of fund are limited for investigation.

SUMMARY AND FUTURE RESEARCH

An Epidemic Agent Based Modeling for simulating the dynamics of typhoid caused by *Salmonella typhi* transmission has been developed by using the NetLogo development turtles (agent/people), patches (environment) and observer (graph). The model simulates the spreading typhoid fever disease, behaviors, and population dynamics of people contact, and it simulates the interactions among these healthy person and typhoid patients in one population.

It is important to point out that the current simulation is not a predictive model. It is a tool for epidemiology researchers to use as a virtual environment laboratory to uncover the dynamic behaviors of the system as a result of the interactions among individual agents in the system. The accuracy and usefulness of the model depend heavily on the quantitative definitions of the behaviors of, and interactions among, the individual agents in the model. For an epidemic agent based modeling of this type, extensive field research data are needed in order to calibrate it. Using these kinds of data for calibration is an important next step for this research.

Fig. 4 Post tsunami in Banda Aceh, Indonesia

The current implementation of the model includes only three types of representative typhoid patients as the source of infection, typhoid patients who become complicated and healthy people as target of new typhoid patients or not. In the next phase of our research, we will expand the model to allow for multiple agents, with complex situation, as well as the probability of epidemic process on disaster area in Indonesia like tsunami, earthquake or other natural disasters.

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