Assessment of past Rift Valley fever outbreak using Modeling, Risk analysis and decision tree in Sudan

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Abstract

Background

 A retrospective study was performed in selected states of the Sudan that include Gezira state, White Nile, Blue Nile, Khartoum, River Nile and Sennar states in order to determine the seroprevalence of Rift Valley Fever (RVF) and associated risk factors as well as an attempt was made to apply mapping, risk analysis tool to investigate the disease .Those epidemiological tools were used for purpose of good management strategies and policy makers as well. The source of data was epidemiological reports and archives from the Federal Ministry of Animal resources, universities and Non Governmental Organizations for outbreaks of RVF also and laboratory reports of serum samples tested by ELISA. The test performance characteristics were 99% test sensitivity and 99% test specificity.A total of 3393from, sheep, goats and cattle were sampled and selected to be examined. Estimated Seroprevalence of RVF was 0.15% (n=905) in sheep, 0.20 %(n=776) in goats and 0.13 %(n=638) in cattle respectively. Also information gathered was used to determine the distribution of the disease, transmission and recovery rate of infection over point in time.

Method

 This study was retrospective survey designed to investigate previous outbreaks of RVF. The method used was risk analysis, modeling and decision tree to explain the distribution of chronology of the disease.

Result

The current study was carried out quantitative risk analysis to investigate RVF. Risk analysis revealed that RVF is likely to occur in the Sudan, and vaccination was estimated with highest rollback to reduce the seroprevalence of RVF to be unlikely with expected value of $ US 4368789. A frequency of 0.12%, 0.12% and 0.1% from cattle, goats and sheep population were entered in SIR model respectively. The adjustable parameters were susceptible, infected, recovery rate and death rate; the result concluded that the curve of susceptible(S) was declining, infected (I) was increasing; while recovered(R) was increasing. A total of 2487 mosquitoes were pooled, represented by 600 mosquitoes in the final model, recovery rate of mosquito overtime was 0.22 which is statistically not significant, (P-value =0.9825), and rate of infection was 0.83 %. In the current study, the Basic reproductive number (R0) was estimated by one. Uncertainty for RVF model was ranged between 0.01 to 610.65 with confidence of 95%. This study concluded that RVF is endemic in the Sudan.

Conclusion

Rift Valley Fever (RVF) is arthropod-borne viral zoonosis disease. It affects small ruminants, sheep and goats, and large ruminants like cattle and camel, and also can affect human. Rift Valley Fever virus (RVFV) belongs to the family *Bunyviridae*, genus *Phlebovirus*. The first isolation of RVFV was done in Kenya (4). RVFV is a negative sense RNA virus. RVFV genome is structured from three partites, small, medium and large. It is peracute or acute febrile disease that is characterized by numerous abortions in

female and high mortality among young animals and humans. Mosquitoe is the principle vector of the disease. It is transmitted by direct contact with infected tissues or organs of animals and ingestion of uncooked or row milk (1). The study was carried out to investigate the risk related to RVF seroepidemiology and distribution of the disease among livestock and to determine the most efficient policies in management of RVF outbreak by using retrospective data, however more further serosurveillances were required to thoroughly understand the epidemiology of the disease.

Introduction

Rift Valley Fever (RVF) is arthropod-borne viral zoonosis disease. It affects small ruminants, sheep and goats, and large ruminants like cattle and camel, and also can affect human. Rift Valley Fever virus (RVFV) belongs to the family *Bunyviridae*, genus *Phlebovirus*. The first isolation of RVFV was done in Kenya (4).RVFV is a negative sense RNA virus. It is peracute or acute febrile disease that is characterized by numerous abortions in female and high mortality among young animals and humans. Mosquitoe is the principle vector of the disease. It is transmitted by direct contact with infected tissues or organs of animals and ingestion of uncooked or row milk(1).

Objectives

This paper is to understand epidemiology of Rift Valley fever in the study by using Risk analysis tools.

Materials And Methods

RVF statistical model

Statistical model was analyzed based on data and information given during RVF outbreak. Model for RVF was mathematical or compartment model which referred to S (susceptible), I (infected) and R (recovered) from the study population (Fig. 1). It is used to investigate the distribution of disease in the population. It has been built on SIR Model template adopted for *influenza virus* by (6). The parameters for host and vector models were obtained from literature (5),(15). The study assumed that population was homogenous. The model was comprised from a system of three coupled non-linear differential equations (Tables 1 and 2).

$$\acute{S}= \beta SI \quad (1.1a)$$

$$\acute{I}=\beta SI\gamma I \quad (1.2b)$$

$$\acute{R}=\gamma I \quad (1.3c)$$

Where, $\acute{S}$ is susceptible, $\acute{I}$ is infected and $\acute{R}$ is recovered or and immunized individuals, β is transmission rate, γ is recovery rate and denote the derivatives with respective to time t. N denotes for population size.

$N = S + I + R,$

$$\acute{N} = \acute{S} + \acute{I} + \acute{R} = 0$$

Applying phase plane analysis to the equation set

$$\acute{S} = \beta SI = 0, \quad (1.2a)$$

and $\acute{I} = \beta SI\gamma I = 0 \quad (1.2b)$

therefore, S-nullclines were

$$S = 0, \quad (1.3a)$$

$$I = 0; \quad (1.3b)$$

and the I-nullclines were

$$S = \gamma \div \beta, \quad (1.4a)$$

$$I = 0 \quad (1.4b)$$

The three nullclines form a triangle with vertices $(0, 0)$, $(N,0)$, and $(0,N)$ on the SI −plane. This triangle was invariant region of steady state. The trajectory always starts from the line $S + I = N$, since $R(0) = 0$. A point was an equilibrium point if and only if $\acute{S} = \acute{I} = \acute{R} = 0$, thus any trajectory was converge to a point $(S,0)$ where $0 \le S \le N$.

If $S(0) = S0 < \gamma \div \beta$, both $S(t)$ ant $I(t)$ decreased and converged to a point on the S-axis; There is no outbreak. If $S0 > \gamma \div \beta$, $I(t)$ first increased in the region $(\gamma \div \beta, I)$ and then decreased to 0; in this instance outbreak occurs. In conclusion, there was a threshold value $\gamma \div \beta$. Define as the basic reproduction number $(R0)$.

$$R0 = N\beta \div \gamma \approx S0\beta \div \gamma \quad (1.5)$$

Then

$$S0 > \gamma \div \beta \leftrightarrow R0 > 1, \quad (1.6)$$

and $S0 < \gamma \div \beta \leftrightarrow R0 < 1, \quad (1.7)$

If $R0 < 1$, RVF epidemic dies out, when $R0 > 1$ a RVF outbreak is possible, (17). The final model has been calculated by disease- euler-quad model which as follow

R0*= r (n) + ((1-d)*r*I (n))*C + 0.5((1-d)*r*(k*S (n)*I (n)-r*I (n)))*C^2 (1.7)

Where, s(n) was susceptible, I(n) was infected, r(n) was recovered, K was transmission rate, r was recovery rate, d was death rate, C was constant

Table 1
Adjustable parameters of Rift Valley Fever model in ruminant

Parameter* (adjusted)	Description	Symbol	Value	Reference
Susceptible	Susceptible with RVF from animal sampled	(S0)	49990	Estimated
Infected	Infected with RVF from animal sampled	(I0)	10	Estimated
Total in population	population of study (ruminant)	(N)	50000	Estimated
Transmission rate	Transmission rate of RVF from S0 to I0	(k)	0.000004	Estimated
Recovery rate	Recovery duration (year)	(R)	8/365	(16)
Death rate	Natural death rate in ruminant(year $^{-1}$)	(d)	1/5.7	(18)
Total sick &not died		(Rfinal)	16500	Estimated
Total deaths		(Tfinal)	15000	Estimated
Number never sick		(Sfinal)	33500	Estimated
Max sick at one time		(Imax)	7000	Estimated
Max prop(of S0)sick		(ofS0)	0.140028	Estimated
Max prop(of N)sick	Probability of infection in ruminants	(ofN)	0.14	(19)
Mosquito infection rate	Proportion of infected mosquitoes from vertical transmission			

*Parameters entered in SIR model were adjusted from different publications to understand the proportion of Suspected, Infected and Recovered livestock in relation to RVF. Also, it is estimated when there is no reference cited. These parameters were used to calculate the model to investigate the distribution of RVF among study population.

Table 2
Adjusted parameter for RVF vector model

Parameter* (adjusted)	Description	Symbol	Value	Reference
Mosquito infection rate	Proportion of infected mosquito from vertical transmission	(k)	0.000005	(20)
Recovery rate	Mosquito recovery rate from RVF infection	(r)	0.021918	Estimated
Death rate	Death rate of mosquito due RVF	(d)	63.84	(21)
Susceptible	RVF susceptible mosquito population	(S0)	59990	Estimated
Infected	Infected population of mosquitoes by RVF	(I0)	10	Estimated
Total population	Total population of mosquitoes	(N)	2487	Estimated

This parameter were used to calculate the model for Mosquitoe vector and understand the distribution and circulation of the virus among vector of the disease, and can be used to generate models for infectious disease.

Table 3
Rift Valley Fever risk groups and risk assessment and management

RVF Risk group (category)	RVF (risk assessment &management)			
Risk	Likelihood	Impact	Risk score	Treatment/action
RVF incidence (index case)	33.3% probability to produce secondary case	Presence of IgM Abs in free area	Acceptable level of risk e.g. development of a RVF foci	Treatment of infected cases or and / quarantine of index case
RVF foci	33.3% probability to produce an outbreak	Presence of IgM&IgG Abs in endemic area	Unacceptable level of risk e.g. development of RVF outbreak	Buffer vaccination around a foci or/ and restricted movement
RVF outbreak	33.3% probability to produce a pandemic	Presensce of IgM&IgG Abs both in free and endemic areas	Unacceptable level of risk e.g. spread of RVF through trade route	Official notification & reporting of disease status, vaccination, vector control, quarantine and trade ban

Statistical analysis

Mathematical or statistical model was adopted by using SIR model used in Microsoft Excel, version 2007 and Decision tree were analyzed by Solution tree version.

Results

SIR Model in host

A total of 50000 hosts were entered in SIR model over time, to explain the trend of the disease. Population structure was 58.8% susceptible, 3.9% infected and 37.3% recovered. The model was found that at 0.18% of the herd seroprevalence of sheep flocks has shown only one positive case could be detected in order to consider that the herd was positive for RVF, While at 0.56% herd seroprevalence of goat flocks only one positive case could be detected in order to consider that the herd was positive for RVF and at 0.73% herd seroprevalence of cattle only one positive case could be detected in order to consider the herd was positive for Rift Valley Fever (Figs. 2,3 and 4).

A 0.12% of cattle populations were enforced in the model. The adjustable parameters for the final model were 49990 susceptible, 10 infected for 50,000 animal hosts, 0.000004 was transmission rate, 0.021918 was recovery rate and 0.3 death rate. The curve of susceptible population were declining at 500000, curve for infected were increasing and reached the peak at 30500, while recovered had gotten plateau at 40000 (Fig. 2).The sheep populations were 50390000, and the goat populations were 42756000 with density of 20.11 and 17.06 respectively. A 0.1and 0.12% from sheep and goats were entered in RVF Model, respectively. The parameters were a susceptible (S0), 49990susceptible, 10 infected for50000, 0.000004 transmission rates, 0.02 recovery rates and 0.03 death rates. The curve for susceptible sheep and goat were declining at 30500, curve for infected were reached 20500, whereas recover get plateau at 50000 (Fig. 3and 4).

Vector model

This study had revealed that Mosquito as a principle vector to transmit RVF in the Sudan, *Aedes* spp was a primary vector to cause RVF according to its biology which renders RVFV to survive for longer period during dry season in Dambos "land depression". This feature (transovarian transmission) was to preserve RVFV in mosquito's egg; when flooding comes, infected eggs hatch and flare up and disseminate RVFV to susceptible population depending on mosquitoes vector density. *Culex*s pp has found to have a secondary role in transmission of RVFV in the Study area from 1973 to 2007 (Table 2).

A total of 60000 sample of mosquitoes were entered in SIR model after pooling with 95% confidence limit (CL), transmission rate was 0.000005, death rate was 63.8% and RVF recovery rate of mosquito was 0.02 (Fig. 5), (Table 4).

Vector Model is referred to suspected (s) is decreasing at 30 individual, infected(I) was increasing at 50 individual and recovered (R) was increasing at 95 individual with 100 time iteration. This was development of epidemic curve in vector at a point in time. This to explain distribution of RVFV in mosquitoe vector population by dividing it into three parts.

Table 4
Identification of RVF mosquito vectors in Sudan from 1973 to 2007

Country	RVF outbreak	Vector	Reference
Sudan	1973	Culexspp, Aedesspp	(25), (26)
	1997 to 1998	Not defined	(27), (28)
	2003 to 2006	Not defined	(27) (28)
	2007 to 2008	Aedesspp, culexspp	(29),(30)
*Parameters entered in Vector Model were adjusted from different publications to understand the proportion of Suspected, Infected and Recovered Mosquito vector in relation to RVF. Also, it is estimated when there is no reference cited.			

Decision tree model

The current study has built model for RVF control measures by solution tree with 21 nodes, total probability of 31% and expected value of $ 78,774,726.09. Four decision branches, sixteen chance branches and twelve end points had been produced. Assumptions for the scenario had been analyzed with 0.5% Probability or likelihood distribution with 95% confidence. The expected or pay off value of vaccination, vector control and expert opinions were estimated by $78,774,726, $7,217,056 and$24,056,798, respectively. The model has resulted in 37.5% chance of success for vaccination, whereas vector control and expert opinion have 18.75% chance of success as countermeasures for RVF outbreak. Vaccination was estimated with highest rollback value of $69,900,624. It has resulted in decreasing of RVF prevalence to be unlikely or negligible with expected value of $4368789(Fig. 6).

Uncertainty analysis of RVF model

Uncertainty was analyzed to estimate the fitness of RVF model with 95% confidence interval (CI) to simulate the occurrence of the disease in the real life. Uncertainty for RVF Model was ranged between 0.01 to 610.65 with confidence of 95%. Five parameters were entered and analyzed in the model for sheep, goats, cattle and vector. Uncertainty for average of contact were124.65, susceptiblewas610.65, infected were 401.94, while uncertainty for duration of infectionness was 0.72. Lower quantile for susceptible, infected, transmissibility, rate of contact and duration of infectionness were estimated by 152.6, 100.4, 0.002, 31.1, 0.18, while upper quantile were estimated by 457.9, 301.4, 0.006, 93.4 and 0.54 respectively. Also, uncertainty was estimated by measuring homogeneity and representativeness, of parameters taken against day of time (Fig. 7).

Discussion

In this study, SIR Model had analyzed dynamic and epidemiology of RVF in study population. The populations at risk were estimated over 30,000 heads for sheep, goat and cattle, whereas study host was more exposed to RVFV (Fig. 2,3and 4), with uncertainty analysis that ranges from 0.01 to 610.65, with

confidence of 95%, although there is lack of information and data available for the disease during study, which is important to know the dynamics of the disease when it occurs. Clustering had been reported in Gizera state, where foci or pockets of the disease were present; this had come into agreement with research done by (8), where clustering can estimate the incidence of RVF in study area for a certain period of time which provides understanding for the spatial distribution and epidemiology of RVF. Frequency of annual temperature and annual rain fall were been analyzed to understand its relatioship with RVF outbreaks in study area.Environmental risk factors like ElNioSouthern Oscilliation, Average Annual precipitation and Elevation Map had significant and important role to play as predisposing factors to occurrence of RVF by increasing of rainfall which improve multiplication of RVF insect vectors to dissemenate the virus to susceptible hosts. Studying the climate and ecosystem, RVF was found to be correlated with weather anamolies and Elino phenomenon in Eastern Africa by (22), which was leading to up-average rainfalls that prefer replication and increased mosquito density. This has important role in tramission cycle of RVFV to exposed host, when the virus can survive in egg of pregnant mosquites which could be dormant in dambos or land depression for long peroid of time specially in interepidemic peroid and when rainfall come, it flared up and dissmenated the virus to suspected hosts, this is has been significantly important observation in East of Africa. Also, it had explained that parameters of deterministic models(2) is analyzing the multiplication rate of the disease and rate of infection in a given geographical zone .Vector model had analyzed more than 80% of mosquito to carry RVFV to the vector, given that susceptible hosts were exposed to the vector, RVF outbreak is likely to occur with 95% confidence. In addition, entomological survey had shown that *Aedes vexans* and *Culex quinquefasciatus* were positive to RVF virus (13).Therefore, epidemiological model for RVF in this study was carried out analysis of SIR model, vector model, spatial mapping model and risk factors associated with RVF seroprevalence. Epidemiological model for this study had manifested probability distribution of RVF on study population and different degree of statistical differences and association for host population, environmental risk factors with RVF seroprevalence, this agreed with the effect of environmental risk factors and disease dynamics on population by(23), whereas models is build up on availability of information and report about the disease; Although it is also important to improve the knowledge about disease by analyzing available information by using disease models. RVF is mainly endemic in Africa and these are involving several regions and countries in the same time. Also, it had occurred outside African continent in Arabian Peninsula and some Indian Ocean islands. It was associated with periodic cycle and heavy rain falls and flooding which usually occurred after interval which prefers mosquito proliferation. RVFV was first reported in Sub-Saharan Africa and southern Africa (3).Although the virus had been found outside Sub-Saharan Africa to Egypt (Gerdes,2004), Saudi Arabia and Yemen (24). In 1973, RVF outbreak was erupted in Southern Africa where human deaths were reported (12). A 958 human causalities in1977 and 200 human deaths in 1978 were occurred due RVF epidemic in Egypt. In Kenya and Somalia, RVF caused 478 human deaths in 1997(14). In 2000, RVF outbreak was confirmed in Saudi Arabia and Yemen with 882 confirmed cases and 124 deaths (11). In the Sudan, serological evidence of RVF was reported in 1936 which revealed 6.7% of 164 human sera by using precipitating antibodies (7). In addition, reporting of cases of RVF, diagnosis and treatment capability and raising awareness of the disease epidemiology, training of medical cadres and research and development is

importantly significant to exceed the planning and policy to contingency and preparedness against RVF and reducing its spreading in suspected countries.

Conclusion

Rift Valley Fever (RVF) is arthropod-borne viral zoonosis disease. It affects small ruminants, sheep and goats, and large ruminants like cattle and camel, and also can affect human. Rift Valley Fever virus (RVFV) belongs to the family *Bunyviridae*, genus *Phlebovirus*. The first isolation of RVFV was done in Kenya (4). RVFV is a negative sense RNA virus. RVFV genome is structured from three partites, small, medium and large. It is peracute or acute febrile disease that is characterized by numerous abortions in female and high mortality among young animals and humans. Mosquitoe is the principle vector of the disease. It is transmitted by direct contact with infected tissues or organs of animals and ingestion of uncooked or row milk (1). The study was carried out to investigate the risk related to RVF seroepidemiology and distribution of the disease among livestock and to determine the most efficient policies in management of RVF outbreak by using retrospective data, however more further serosurveillances were required to thoroughly understand the epidemiology of the disease.

Abbreviation

CDC center of Disease control

CI confidence interval

CL confidence limit

ELISA Enzyme Linked Immunosorbent assay

R0 Basic Reproduction number

RNA Ribonucleic acid

RVF Rift Valley Fever

RVFV Rift Valley Fever Virus

SIR Suspected, infected and recovered

Declarations

This to declare that this research work is to fulfill partial requirement of doctoral degree

Ethical Approval and Consent to participate

It is not in human data (retrospectively registered)

Consent for publication

All authors have agreed to publish this manuscript

Availability of data and materials

Yes

Competing interests

There is no conflict of interest from any of authors of this manuscript

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Authors' contributions

The manuscript is written and statistically analyzed by Mohammed E.Ahmed[1], Maximilian the project coordinated by PO Baumann2 the statistical analysis was revisioned by Thomas Selhorst[3] the bench work and data availability for project was supplied by Tamador M. Abdellah[1, 2] The manuscript was revision and designed for writing by, Atif A Abdelgadir[4]

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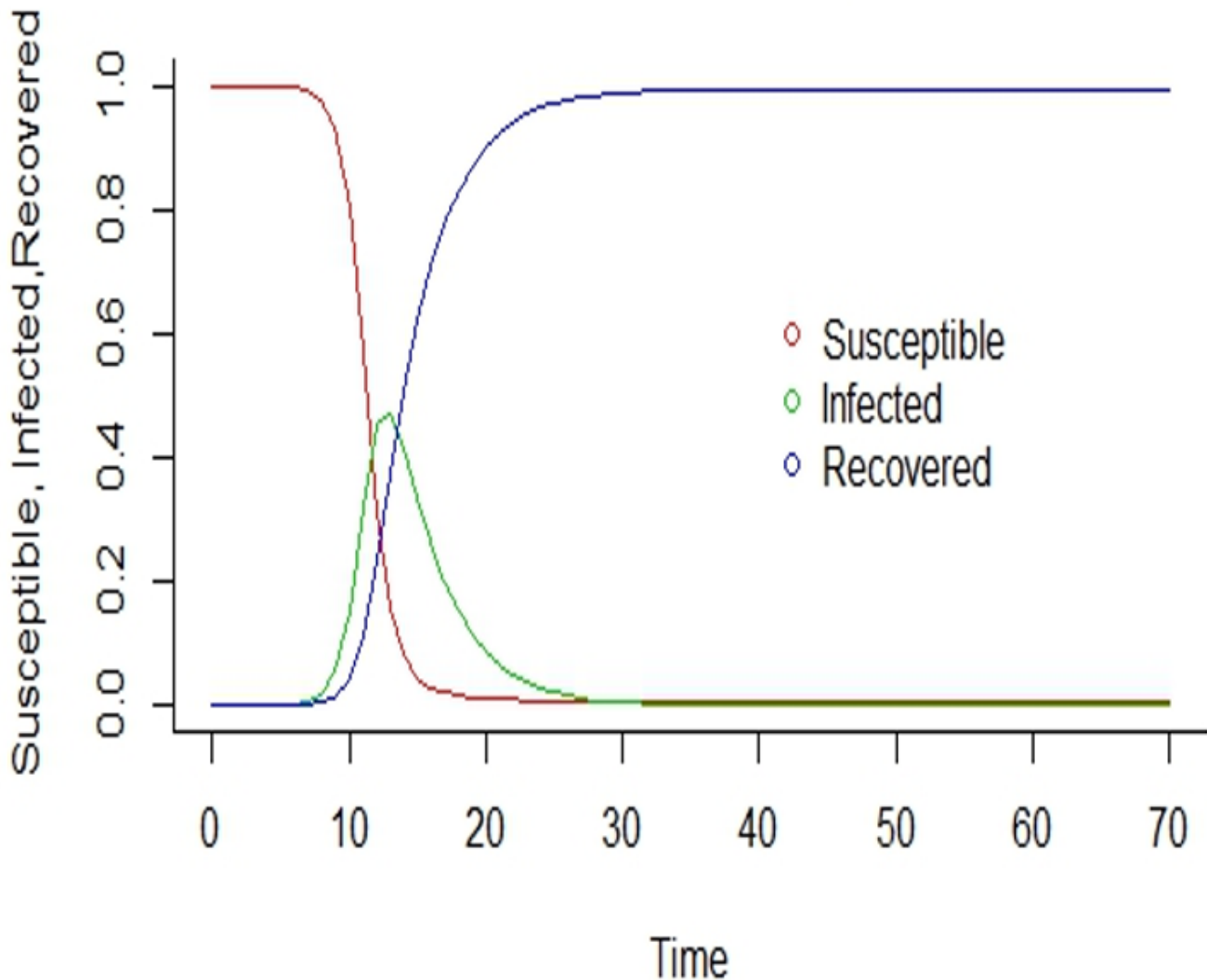
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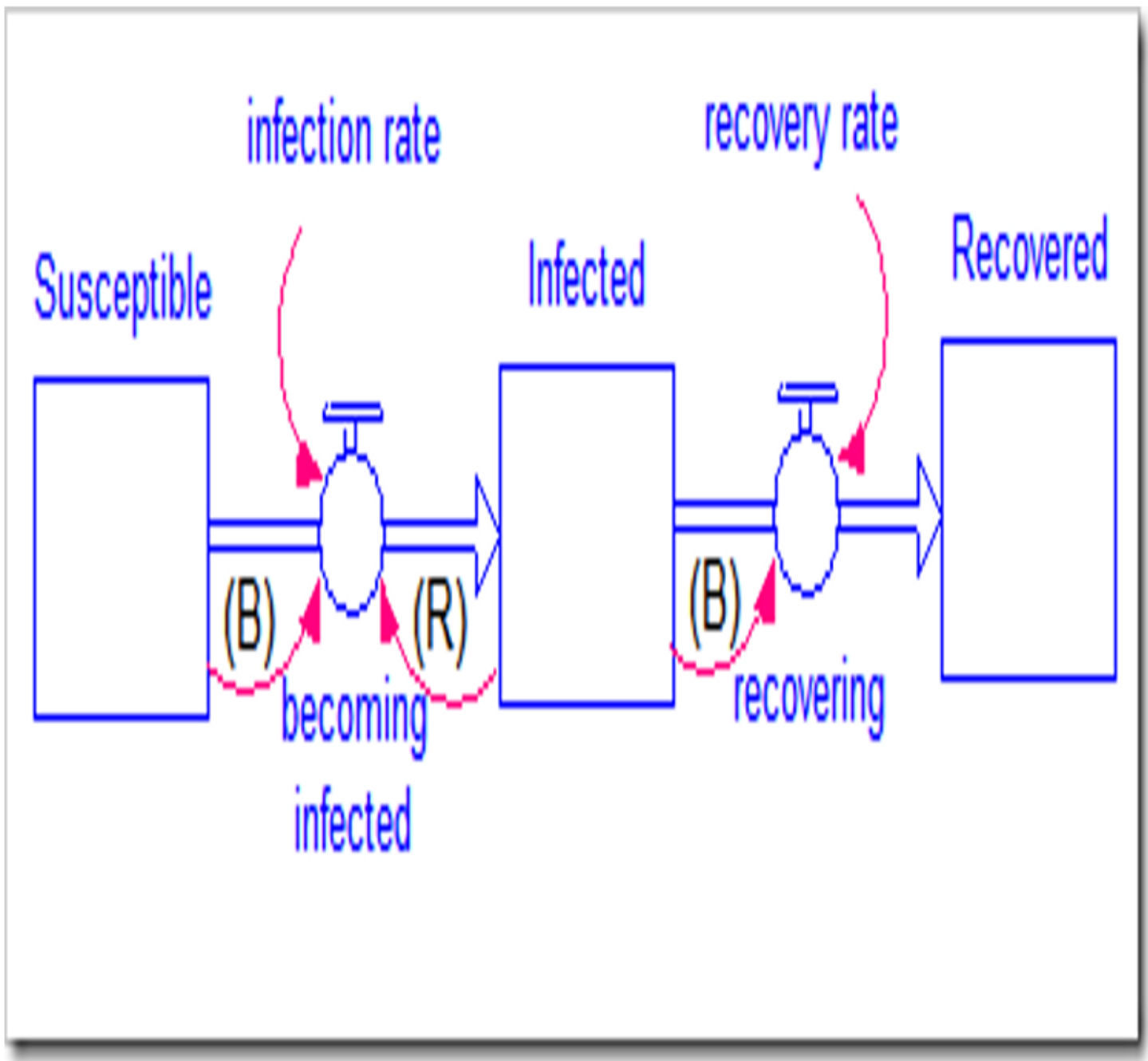
Figure 1

SIR Model represents Susceptible, Infected and Recovered compartments of study population with infection and recovery rates. The explain the distribution of RVF among study population by dividing it into three parts
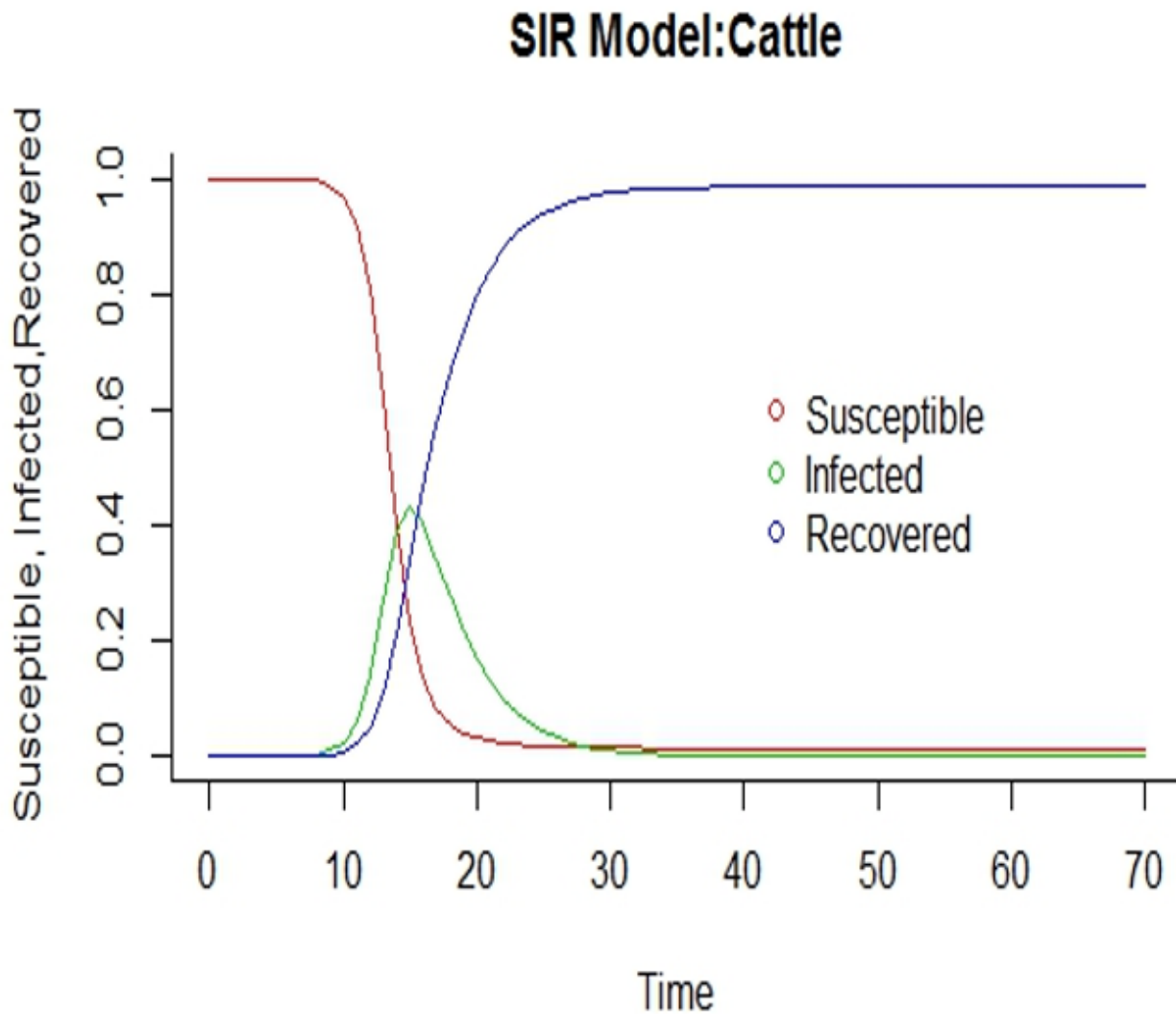
Figure 2

SIR Model for RVF in Cattle population in Sudan from 1973 to 2007. SIR Model is referred to as suspected(S) was decreasing at 95 individual, infected(I) was increasing at 80 individual and Recovered(R) was in increasing with continuous growth at 200 individual with 100 times (iteration) multiplication .Also this to explain the distribution and trend of RVF in population by dividing it three parts.
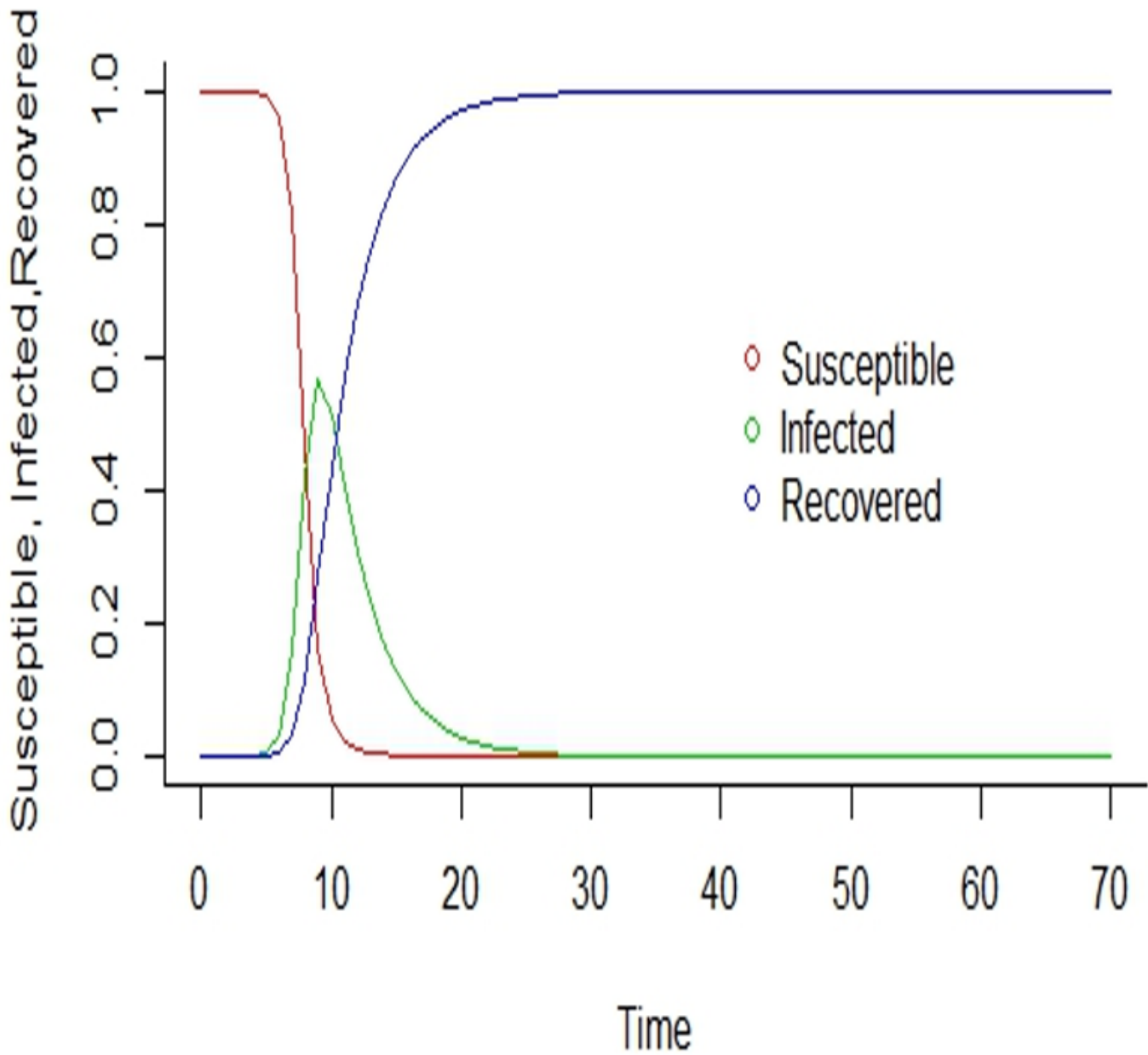
SIR Model:Sheep

Figure 3

SIR Model for RVF in sheep population in Sudan from 1973 to 2007. SIR Model is referred to as suspected(S) was decreasing at 90 individual, infected (I) was increasing at 85 individual and Recovered (R) in increasing at 195 at 100 time (iteration) multiplication . This was development of point curve of RVF, when it occurred at point in time. The figure was illustrating the Susceptible, Infected and Recoved model for Rift Valley fever in animal population over time and their percentages were 58.8%, 3.9% and 37.3% respectively. This means to simulate the rate of occurrence of RVF to understand the occurrence in real life. Also this to explain the distribution and trend of RVF in population by dividing it to three parts.

SIR Model:Goats

Figure 4

SIR Model for RVF in goat's population in Sudan from 1973 to 2007. SIR model is referred to as Susceptible, Infected and Recovered for goats population. Susceptible was decreasing, infected was increasing and Recovered was increasing for 70 days. It represents the basic SIR model for an epidemic at a time. Also this to explain the distribution and trend of RVF in population by dividing it into three parts.
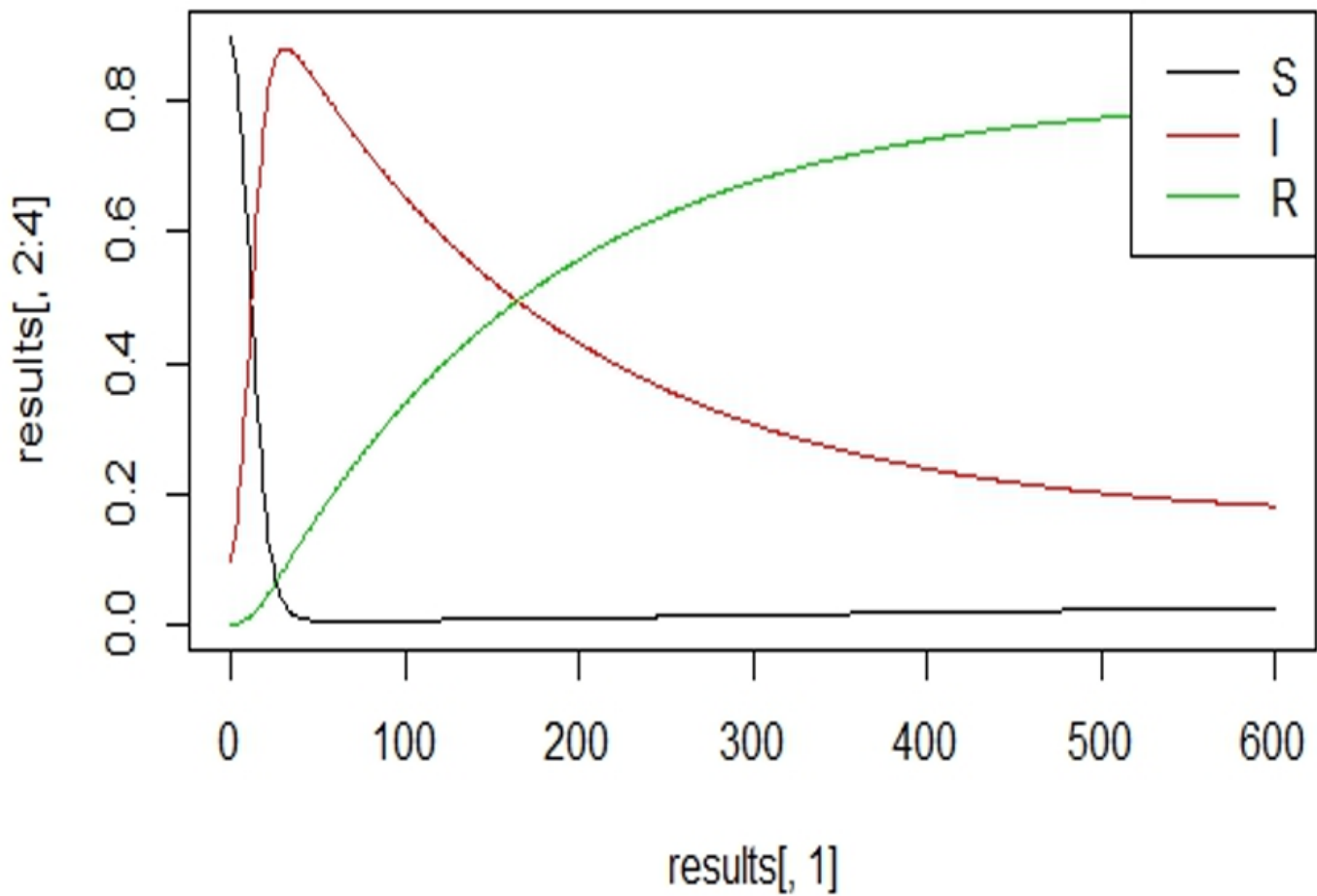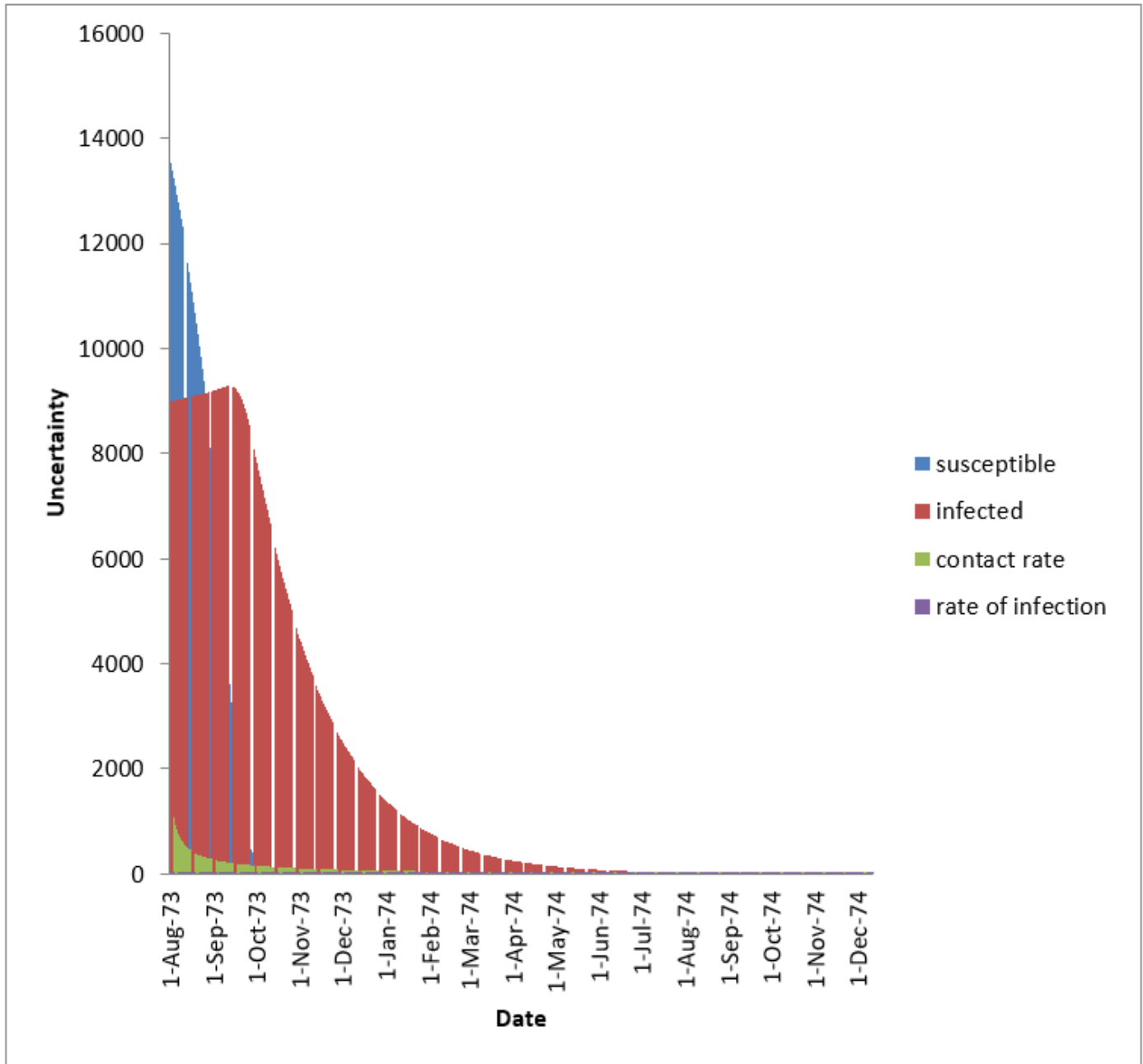
Figure 5

Vector model. Vector Model is referred to suspected (s) is decreasing at 30 individual, infected(I) was increasing at 50 individual and recovered (R) was increasing at 95 individual with 100 time iteration. This was development of epidemic curve in vector at a point in time. This to explain distribution of RVFV in mosquitoe vector population by dividing it into three parts.

Figure 6

Decision tree model for RVF outbreak explaining probability and expected values of branches and cost-effectiveness for RVF control. Decision tree has explained the probability distribution from the nodes and branches of decision analysis of three options to control RVF which are vaccination, vector control and expert opinions to estimate what is more rational path to be considered . This method is one of the decision supporting tools that have role in policy for prevention and control of infectious diseases. This diagram explains also the percentage of most important tool for control of RVF with less economic cost.

Figure 7

Uncertainty analysis for SIR model. Uncertainty was obtained by estimating the standard error (SE) of sample (SE mean was 26.6 for suspected, 139.3 for rate of contact and 0.15 for duration of infectionness) with 95% confidence interval. It was measuring the degree of goodness of fit for the model with optimization of assumed parameters to be simulated at SIR model. This analysis is to investigate the accuracy of disease model that has be studies in this research.