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Simulation of the use of *Yersinia pestis* as a Biological Weapon in Nigeria

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Abstract. A simulation study using the Spatiotemporal Epidemiological Modeler was carried out on the potential usage of *Yersinia pestis*, the causative agent of plague ('black death'), as a biological weapon of terror. The study revealed widespread infections, incidences and deaths due to the infection all over Nigeria with bioweapon attacks originating from 2 Nigerian cities. Instituting an effective intervention program against the infection could save as many as 3.6 million lives within 10 days of the onset of the intervention program. Intervention programs could include social distancing policies and the use of antibiotics in addition to controlling the rodents and fleas vector population. Because of the relative ease of development of bioweapons and the desperation by terrorists to use any weapon at their disposal to achieve terror, there is an urgent need for an effective preparedness plan that can stop or limit the use of this category **A** bio-agent for biowarfare.

Key words: Simulation, *Yersinia pestis*, bioweapon, preparedness, Nigeria.

1. Introduction

Biological weapons are microorganisms that can be used to kill or incapacitate humans, animals and plants as an act of war. The potentials of the use of certain microorganisms as biological weapons is a cause of concern and worry for many nations of the world [1]. Different organisms have been used in the past for attacks and many have been contemplated as potential biological weapons for attack [2]. Biological warfare is as old as recorded history and some early records date back to 490 BC or earlier when Scythian archers used arrows that they dipped in blood, manure and decomposing bodies which they then shot at their vulnerable enemies with devastating casualties [1].

Yersinia pestis is a gram negative, non-motile, non-sporulating bacterium and belongs to the family enterobacteriaceae of γ-Proteobacteria of which it is a biochemically unreactive member [3,4]. It is the aetiological agent of perhaps the most well documented and devastating epidemic ever known to man called plague ("bubonic plague", "pneumonic plague", "septicaemic plague", "black death") which is a dreaded killer of humans and animals that still persists and is endemic in some countries across the globe [5,6]. Over 200 species of mammals are susceptible to infection by this agent [7] and it has been credited with the death of about 200 million people in human history [8]. It belongs to the highest class of bioterrorism agents being classified as a category A bioterror agent by the Centre for Disease Control, Atlanta, U.S.A. [1,9–11].

The clinical presentations of plague in humans depend on which of its main 3 major forms is in manifestation after primary infection from animal sources, mostly rodents. The bubonic plague form presents as fever, painful bubo from flea bite, chills and headache [12,13]. The septicaemic form presents with bacteraemia symptoms of fever, chills, malaise and headache and is almost always fatal if treatment is delayed [7,9]. The pneumonic form usually involves the respiratory system and presents with pneumonic signs and is a frequent deadly presentation of plague [2,7,9].

People who live close to wild animals especially rodents, live in rural areas with poor sanitation, handle wild rodents, have infected people close to them and laboratory workers are at high risk of infection with the disease [14–16]. In the realm of biological warfare the elite infamous Japanese 731 unit was said to have used fleas deliberately infected with *Yersinia pestis* and dropped from planes in rice food bags and food containers in China that led to a plague epidemic that claimed many lives [17].

There are currently no approved and recommended vaccines for use in humans for plague but capsular antigen F1 and virulent antigen V have shown promising results in producing a recombinant vaccine for plague from plant sources that may prove very useful in the future against plague [13]. In the past the killed whole cell plague vaccine has been used and a live attenuated vaccine is also available with varying results [18].There are also various preparations of

vaccines available and being tested for different types of animals and some have proved potent and efficacious [19–21].

Plague has been reported and documented in 26 countries in Africa including Nigeria which have experienced at least one human plague case between 1887 and 2009 [12]. With the eradication of Rinderpest cattle plague world-wide [22] from animals many countries especially African countries still have another more devastating animal and human plague to contend with and preparedness will be key to successful control of any threat posed by *Y. pestis* [1,2,7].

Few models have been done to alert on the seriousness of potential agents of bioterror especially *Y. pestis* in developing countries especially of African origin and yet agents of bioterror are easy and relatively cheap to develop and possess [5,6,11,14,17]. Nigeria has been reported to have experienced plague infection but very little is known about the Nigerian situation and little has been studied on this potential agent of bioterror [12,23]. This simulation study was carried out to alert on the potentials of a biological weapon attack on nations especially developing countries, with Nigeria as a case study, and awaken the need for a preparedness plan for prevention and control in the event of such a sudden attack. Because time is of the essence in biowarfare, timely and accurate implementation of intervention measures in the face of biowarfare will ensure adequate control of agents of bioterror. This study reports the incidence, infection and deaths resulting from a simulation scenario of a potential bioterrorist attack on Nigeria and underscores the need for the development of rapid prophylactic measures against possible *Y. pestis* bioterrorist attacks.

2. Materials and Method

2.1. Model parameters

The IBM Spatiotemporal Epidemiological Modeler (STEM®) version 1.2.3 was used for the simulation with a Deterministic SEIR disease model. The following parameters were used for the disease model:

1. Time period(TP)= 86400000 ms
2. Reference population density=100PM/SQKM
3. Road.Net.Inf.proportion=0.01 fraction per road

4. Characteristic mixing distance=2.25km
5. Transmission rate(ß)=3.0
6. Non-linearity coefficient=1.0
7. Infectious recovery rate(γ)=0.2 PM/TP
8. Infectious mortality rate(μ_i)=0.4 PM/TP
9. Immunity loss rate(σ)=0.05 PM/TP
10. Incubation period(φ)=0.2 PM/TP

2.2. Scenario

Two scenarios were set up. In the first scenario two STEM "infectors" were used; one in Abaji in the FCT and the other in Maiduguri, Borno state using rodents and fleas infected with lethal doses of *Y. pestis* capable of infecting about 8.4% of the population initially with primary pneumonic plague and then secondary pneumonic plague follows [24]. A sequencer was added to the scenario capable of making the simulation go on for 6 months but the cut off data was taken at 40 days. With the CSV loggers set on, the simulation was allowed to run and the data generated collected from the CSV files in the STEM work space. In the second scenario all former parameters were maintained but there were modifications and additions. Two control graphs to isolate 0.3 fraction of the population infected at Abaji-FCT and Maiduguri, Borno state were introduced one for each location. A modifier from the existing disease model was created to modify the transmission rate down from 3.0 to 0.7 and the infectious mortality rate from 0.4 to 0.1 PM/TP. This modification was assumed to be due to isolation of sick and exposed individuals (social distancing policy), treatment with antibiotics, spraying of fleas with insecticides and control of the suspected rodent population with rodenticides in addition to mounting enlightenment campaigns against the infection. A predicate was created to make the modifier start working only after 30 days of the start of the infection. The Modifier and predicate were added into a trigger and introduced into the second scenario and it was executed till at least after 40 days of the simulation of the deliberate bioterrorism attack. Data generated were collected from the CSV files in the STEM work space.

2.3 Population and maps

The 2006 population figure and maps found in STEM version 1.2.3 were utilized for the purpose of this study. It was assumed that spread of infection will be enhanced through road travels and air travels that will bring more infectious people in contact with the susceptible population and expose them to the infection.

2.4 Analysis

The data collected were opened with Excel to check accuracy and consistency and imported into IBM SPSS® version 20 for data analysis and creation of bar charts. Other charts of disease were generated and copied from STEM. The data were checked for normality using Kolmogorov-Smirnov, Shapiro-Wilks, Kurtosis and Skewness tests. Related samples Wilcoxon signed ranked test was used to elucidate any differences in the infection, incidence and deaths recorded between the 2 scenarios at 99% confidence level [25].

3. Results

The results of the simulations shows the data for infection (I1 and I2), Incidence of the infection (Incidence1 and Incidence2), Deaths recorded as a result of the plague (Deaths1 and Deaths2) for pre and post intervention periods respectively with more infection, more incidence and deaths recorded during the pre-intervention period (Table 1). The intervention introduced at day 30, within 10 days, reduced the number of deaths from 9552090 to 5922317 which are about 3629773 lives saved within 10 days of intervention (Table 1). Similarly the infectious people and incidence reduced from 1964337 to 1290929 and from 2068247 to 399221 respectively. There was a statistically significant difference between the 2 scenarios of "without any intervention" and "with intervention" in terms of number of people infected/infectious, incidence and number of deaths due to plague (Table 2). The mean incidence of plague in the different states in Nigeria without any intervention at day 40 (Figure 1) and with some form of intervention beginning on day 30 and stopping at day 40 (Figure 2) is shown with the highest incidences at Lagos and Yobe states respectively. The mean number of infectious people of plague in the different states in Nigeria without any intervention at day 40 (Figure 3) and with some form of intervention

beginning on day 30 and stopping at day 40 (Figure 4) is shown with the highest Infections at Lagos and Borno states respectively. The mean number of deaths due to plague in the different states in Nigeria without any intervention at day 40 (Figure 5) and with some form of intervention beginning on day 30 and stopping at day 40 (Figure 6) is shown with the highest deaths at Borno and the FCT for both scenario. The commencement of the bioterror attack with *Y. pestis* simultaneously at Maiduguri, Borno State and Abaji in the FCT is shown (Figure 7). The spread of the infection round the country by day 40 without intervention is shown (Figure 8) and the restrictive value of intervention is shown (Figure 9). The time series spread of plague based on the disease model simulated is shown for the FCT (Figure 10).

Table 1.Overall Descriptive Statistics in Nigeria during simulation

	N	Minimum	Maximum	Sum	Mean	Std. Deviation	Variance
I1	538	.0000	95625.7082	1964337.9515	3651.185783	9290.0664256	86305334.192
I2	538	.0000	57656.2942	1290929.5766	2399.497354	7175.1728148	51483104.923
INCIDENCE1	538	.0000	173843.5762	2068247.8706	3844.326897	10879.4880315	118363259.828
INCIDENCE2	538	.0000	17238.3843	399221.3194	742.047062	2075.7920871	4308912.789
DEATHS1	538	.0000	1151468.1942	9552090.5042	17754.815064	72432.1778140	5246420382.882
DEATHS2	538	.0000	1089368.3283	5922317.2560	11008.024639	62153.2650926	3863028361.669
POP1	538	8553.00	2162567.87	121378715.38	225610.9951	176060.17712	30997185966.975
POP2	538	8553.00	2247853.93	125009125.02	232358.9684	178101.22990	31720048090.153
Towns	538						

Key: I1=Infection before Intervention; I2=Infection after Intervention; Incidence 1=Incidence before Intervention; Incidence2=Incidence after Intervention; Deaths1=Deaths before Intervention; Deaths2=Deaths after Intervention; POP1=Population count before Intervention; POP2=Population count after Intervention; Towns=Total number of Nigerian towns studied.

Table 2. Statistical comparison of before and after Intervention Scenario data

Variables	Test	Sig. (P)
Incidence 1 Vs Incidence 2	Related sample Wilcoxon Signed Rank Test	0.0001
Infection 1 Vs Infection 2	Related sample Wilcoxon Signed Rank Test	0.0001
Deaths 1 Vs Deaths 2	Related sample Wilcoxon Signed Rank Test	0.0001

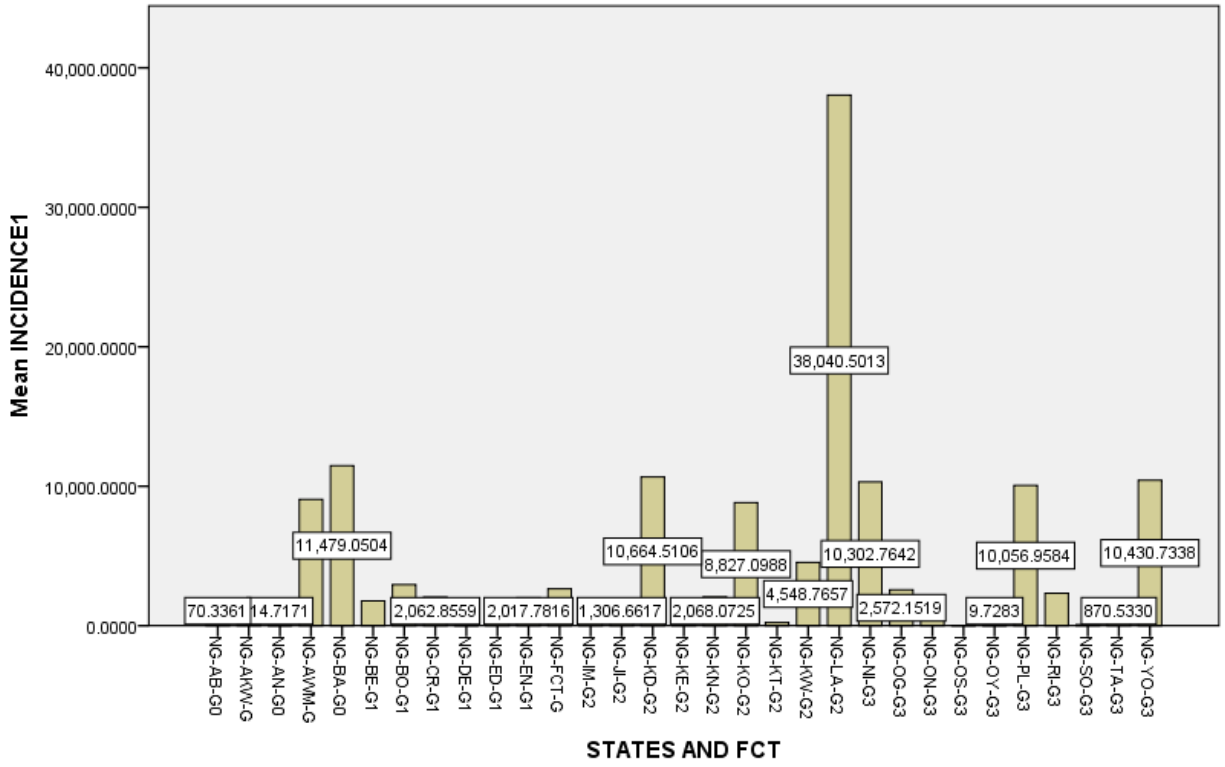

Figure 1. Bar chart showing Mean Incidence without Intervention at Day 40

Key: NG-AB-G0=Abia State; NG-AKW-G=Akwa Ibom State; NG-AN-G0=Anambra State; NG-AWM-G=Adamawa State; NG-BA-G0=Bauchi State; NG-BE-G1=Benue State; NG-BO-G1=Borno State; NG-CR-G1=Cross River State; NG-DE-G1=Delta State; NG-ED-G1=Edo State; NG-EN-G1=Enugu State; NG-FCT-G1=Federal Capital Territory; NG-IM-G2=Imo State; NG-JI-G2=Jigawa State; NG-KD-G2=Kaduna State; NG-KE-G2=Kebbi State; NG-KN-G2=Kano State; NG-KO-G2=Kogi State; NG-KT-G2=Katsina State; NG-KW-G2=Kwara State; NG-LA-G2=Lagos State; NG-NI-G3=Niger State; NG-OG-G3=Ogun State; NG-ON-G3=Ondo State; NG-OS-G3=Osun State; NG-OY-G3=Oyo State; NG-PL-G3=Plateau State; NG-RI-G3=Rivers State; NG-SO-G3=Sokoto State; NG-TA-G3=Taraba State; NG-YO-G3=Yobe State

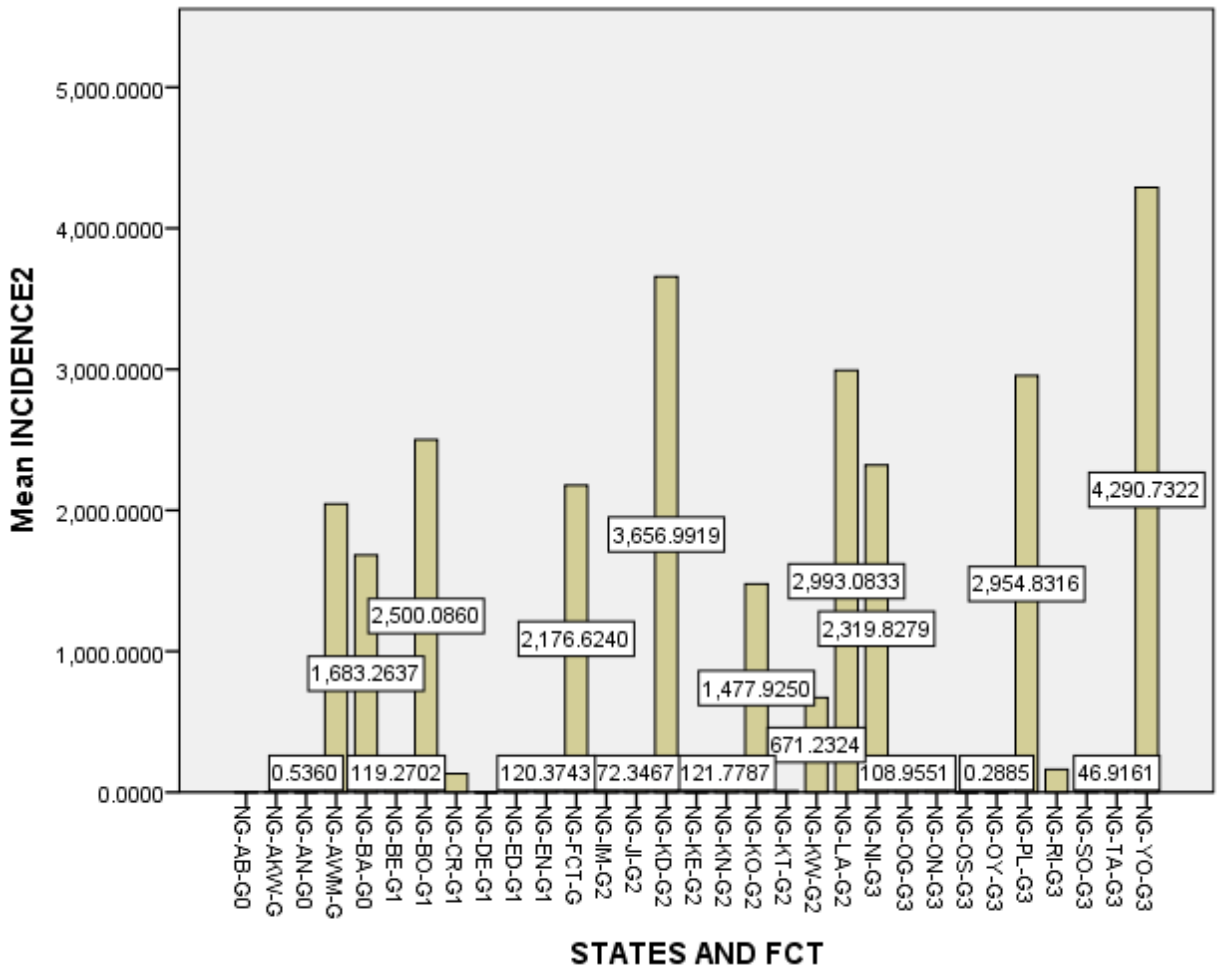

Figure 2. Bar chart showing Mean Incidence after 10 Days Intervention at Day 40

Key: NG-AB-G0=Abia State; NG-AKW-G=Akwa Ibom State; NG-AN-G0=Anambra State; NG-AWM-G=Adamawa State; NG-BA-G0=Bauchi State; NG-BE-G1=Benue State; NG-BO-G1=Borno State; NG-CR-G1=Cross River State; NG-DE-G1=Delta State; NG-ED-G1=Edo State; NG-EN-G1=Enugu State; NG-FCT-G1=Federal Capital Territory; NG-IM-G2=Imo State; NG-JI-G2=Jigawa State; NG-KD-G2=Kaduna State; NG-KE-G2=Kebbi State; NG-KN-G2=Kano State; NG-KO-G2=Kogi State; NG-KT-G2=Katsina State; NG-KW-G2=Kwara State; NG-LA-G2=Lagos State; NG-NI-G3=Niger State; NG-OG-G3=Ogun State; NG-ON-G3=Ondo State; NG-OS-G3=Osun State; NG-OY-G3=Oyo State; NG-PL-G3=Plateau State; NG-RI-G3=Rivers State; NG-SO-G3=Sokoto State; NG-TA-G3=Taraba State; NG-YO-G3=Yobe State

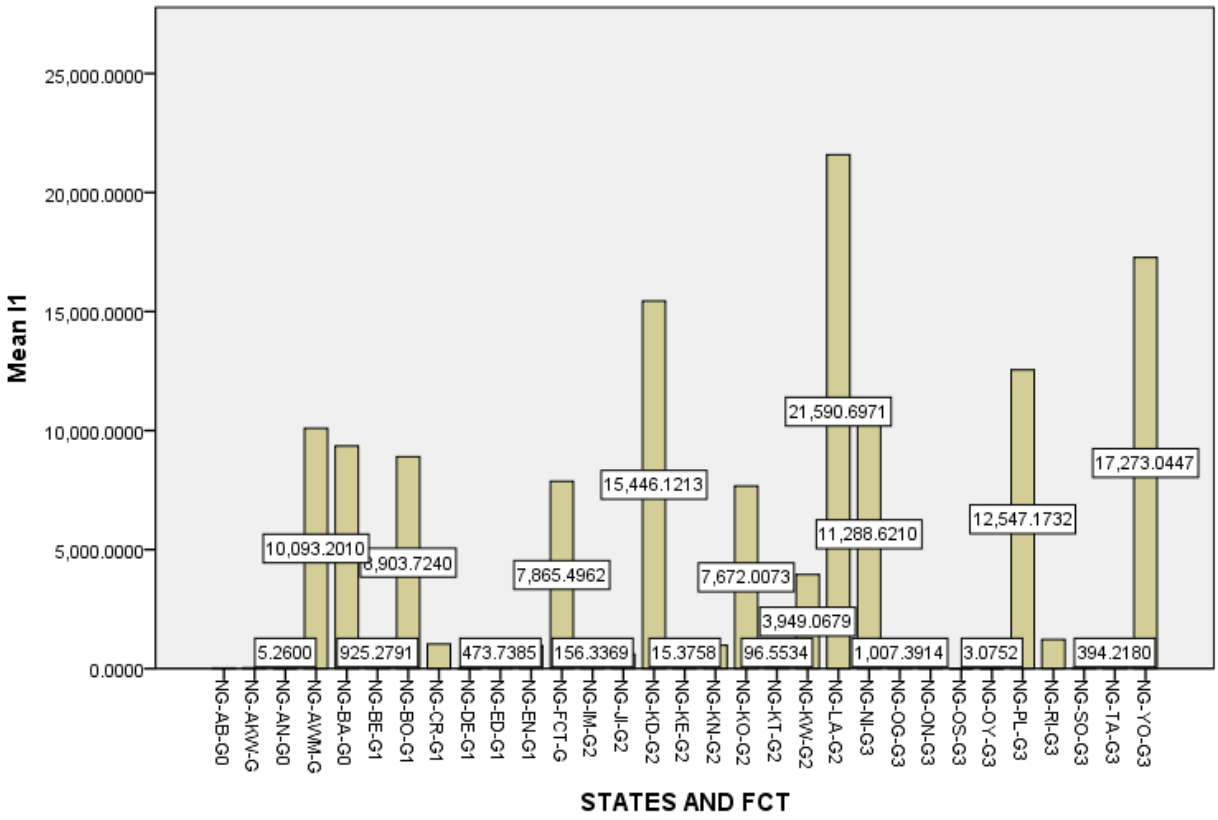

Figure 3. Bar chart showing Mean Infection without Intervention at Day 40

Key: NG-AB-G0=Abia State; NG-AKW-G=Akwa Ibom State; NG-AN-G0=Anambra State; NG-AWM-G=Adamawa State; NG-BA-G0=Bauchi State; NG-BE-G1=Benue State; NG-BO-G1=Borno State; NG-CR-G1=Cross River State; NG-DE-G1=Delta State; NG-ED-G1=Edo State; NG-EN-G1=Enugu State; NG-FCT-G1=Federal Capital Territory; NG-IM-G2=Imo State; NG-JI-G2=Jigawa State; NG-KD-G2=Kaduna State; NG-KE-G2=Kebbi State; NG-KN-G2=Kano State; NG-KO-G2=Kogi State; NG-KT-G2=Katsina State; NG-KW-G2=Kwara State; NG-LA-G2=Lagos State; NG-NI-G3=Niger State; NG-OG-G3=Ogun State; NG-ON-G3=Ondo State; NG-OS-G3=Osun State; NG-OY-G3=Oyo State; NG-PL-G3=Plateau State; NG-RI-G3=Rivers State; NG-SO-G3=Sokoto State; NG-TA-G3=Taraba State; NG-YO-G3=Yobe State

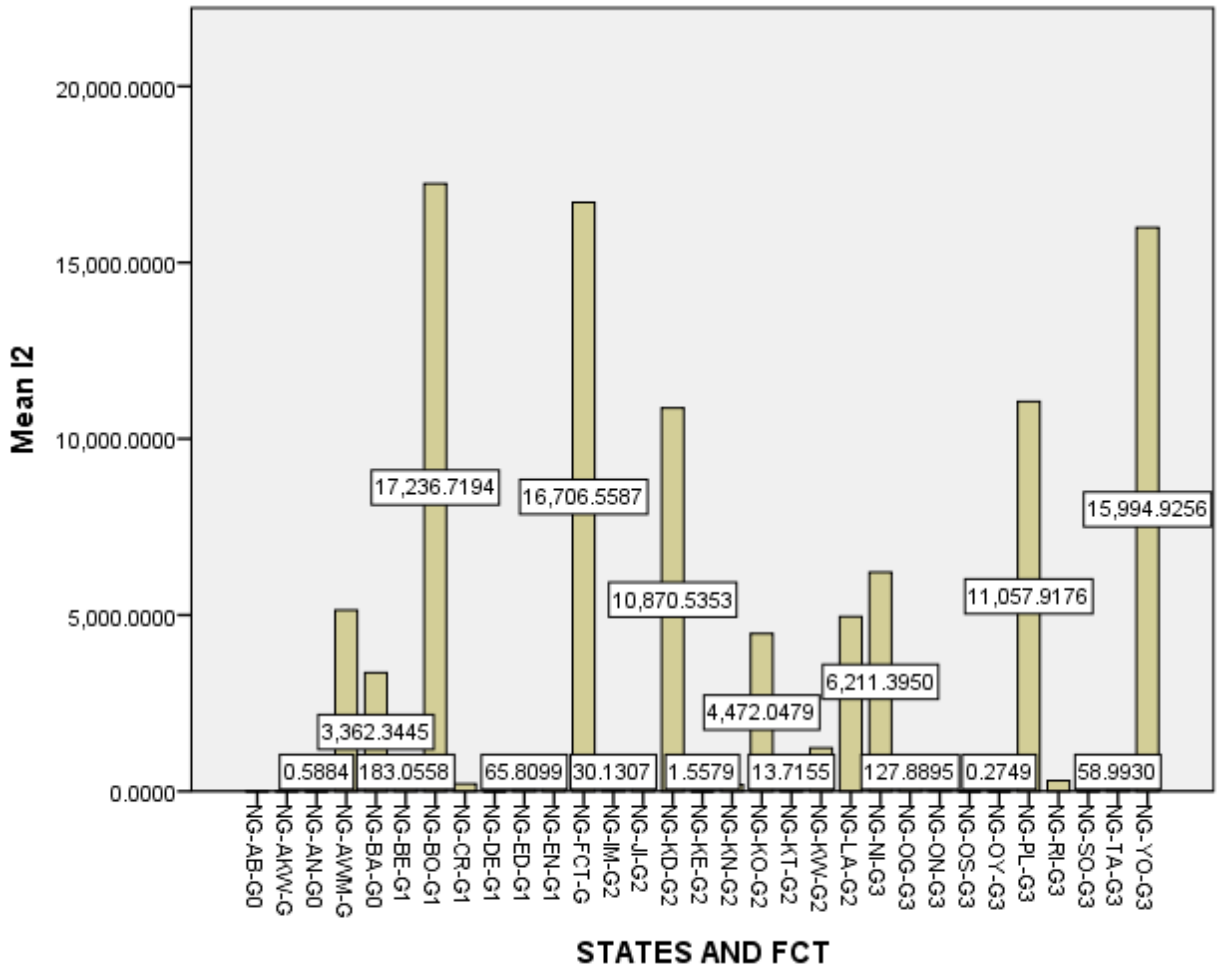

Figure 4. Bar chart showing Mean Infection after 10 Days of Intervention at Day 40

Key: NG-AB-G0=Abia State; NG-AKW-G=Akwa Ibom State; NG-AN-G0=Anambra State; NG-AWM-G=Adamawa State; NG-BA-G0=Bauchi State; NG-BE-G1=Benue State; NG-BO-G1=Borno State; NG-CR-G1=Cross River State; NG-DE-G1=Delta State; NG-ED-G1=Edo State; NG-EN-G1=Enugu State; NG-FCT-G1=Federal Capital Territory; NG-IM-G2=Imo State; NG-JI-G2=Jigawa State; NG-KD-G2=Kaduna State; NG-KE-G2=Kebbi State; NG-KN-G2=Kano State; NG-KO-G2=Kogi State; NG-KT-G2=Katsina State; NG-KW-G2=Kwara State; NG-LA-G2=Lagos State; NG-NI-G3=Niger State; NG-OG-G3=Ogun State; NG-ON-G3=Ondo State; NG-OS-G3=Osun State; NG-OY-G3=Oyo State; NG-PL-G3=Plateau State; NG-RI-G3=Rivers State; NG-SO-G3=Sokoto State; NG-TA-G3=Taraba State; NG-YO-G3=Yobe State

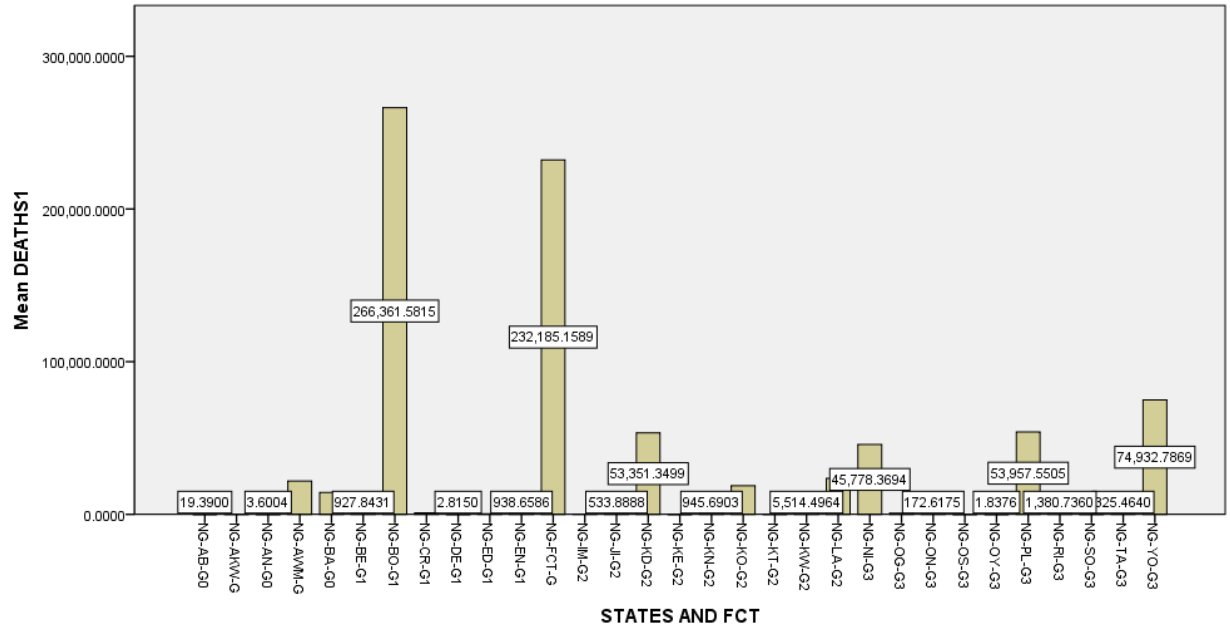

Figure 5. Bar chart showing Mean Deaths without Intervention at Day 40

Key: NG-AB-G0=Abia State; NG-AKW-G=Akwa Ibom State; NG-AN-G0=Anambra State; NG-AWM-G=Adamawa State; NG-BA-G0=Bauchi State; NG-BE-G1=Benue State; NG-BO-G1=Borno State; NG-CR-G1=Cross River State; NG-DE-G1=Delta State; NG-ED-G1=Edo State; NG-EN-G1=Enugu State; NG-FCT-G1=Federal Capital Territory; NG-IM-G2=Imo State; NG-JI-G2=Jigawa State; NG-KD-G2=Kaduna State; NG-KE-G2=Kebbi State; NG-KN-G2=Kano State; NG-KO-G2=Kogi State; NG-KT-G2=Katsina State; NG-KW-G2=Kwara State; NG-LA-G2=Lagos State; NG-NI-G3=Niger State; NG-OG-G3=Ogun State; NG-ON-G3=Ondo State; NG-OS-G3=Osun State; NG-OY-G3=Oyo State; NG-PL-G3=Plateau State; NG-RI-G3=Rivers State; NG-SO-G3=Sokoto State; NG-TA-G3=Taraba State; NG-YO-G3=Yobe State

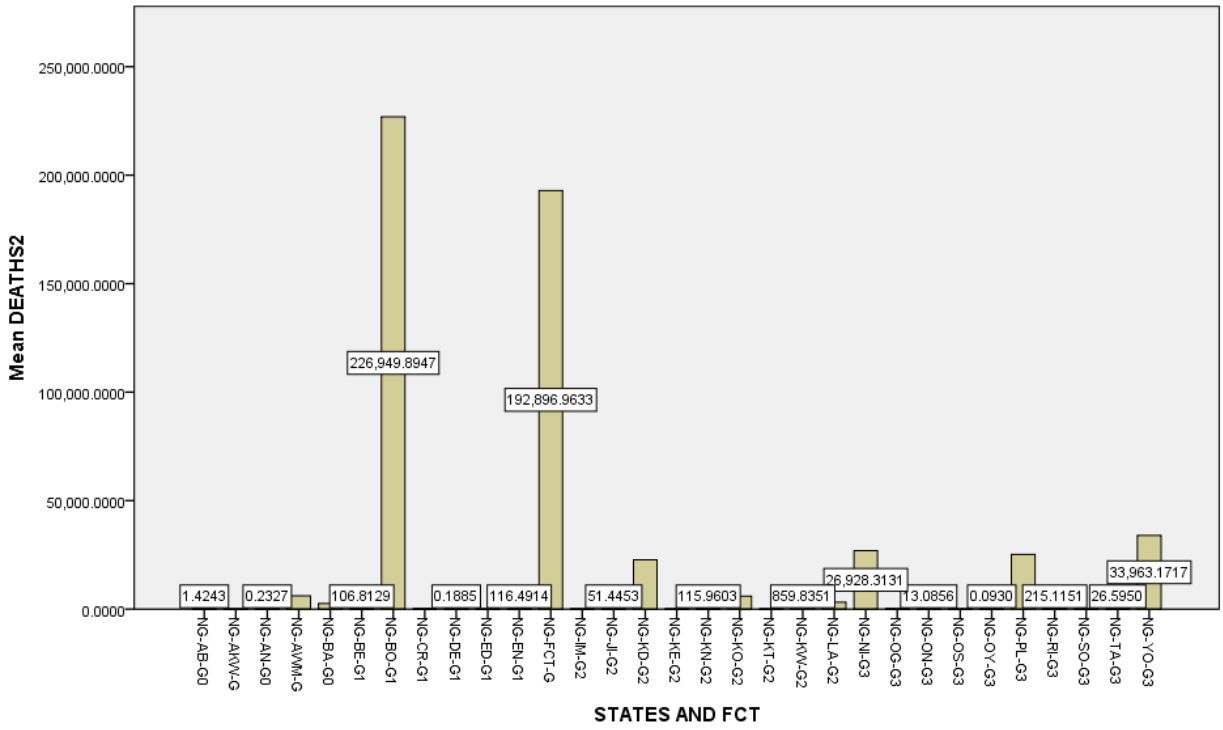

Figure 6. Bar chart showing Mean Deaths after 10 Days of Intervention at Day 40

Key: NG-AB-G0=Abia State; NG-AKW-G=Akwa Ibom State; NG-AN-G0=Anambra State; NG-AWM-G=Adamawa State; NG-BA-G0=Bauchi State; NG-BE-G1=Benue State; NG-BO-G1=Borno State; NG-CR-G1=Cross River State; NG-DE-G1=Delta State; NG-ED-G1=Edo State; NG-EN-G1=Enugu State; NG-FCT-G1=Federal Capital Territory; NG-IM-G2=Imo State; NG-JI-G2=Jigawa State; NG-KD-G2=Kaduna State; NG-KE-G2=Kebbi State; NG-KN-G2=Kano State; NG-KO-G2=Kogi State; NG-KT-G2=Katsina State; NG-KW-G2=Kwara State; NG-LA-G2=Lagos State; NG-NI-G3=Niger State; NG-OG-G3=Ogun State; NG-ON-G3=Ondo State; NG-OS-G3=Osun State; NG-OY-G3=Oyo State; NG-PL-G3=Plateau State; NG-RI-G3=Rivers State; NG-SO-G3=Sokoto State; NG-TA-G3=Taraba State; NG-YO-G3=Yobe State

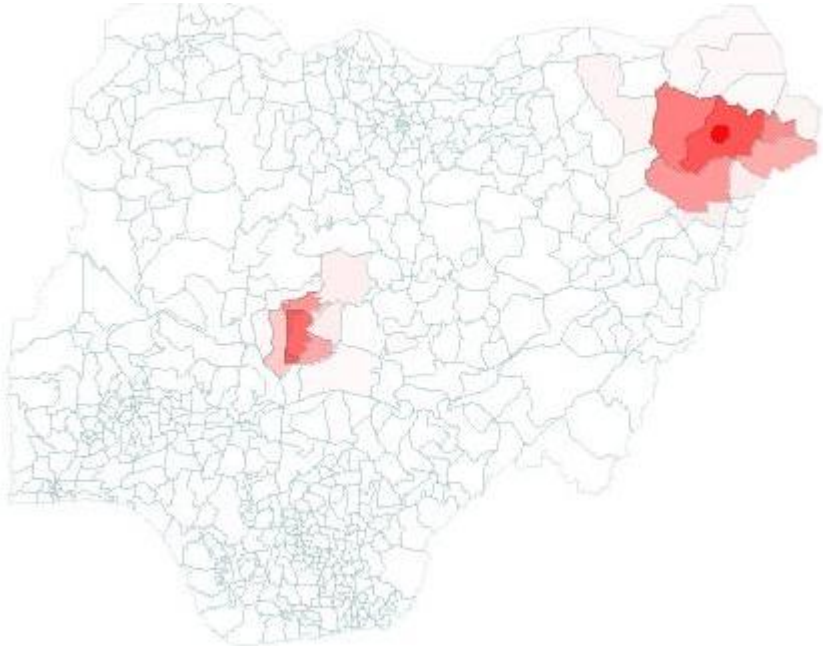

Figure 7. A bioterror attack originating from Abaji(Abuja-FCT) and Maiduguri(Borno State) Simultaneously(Red colour)

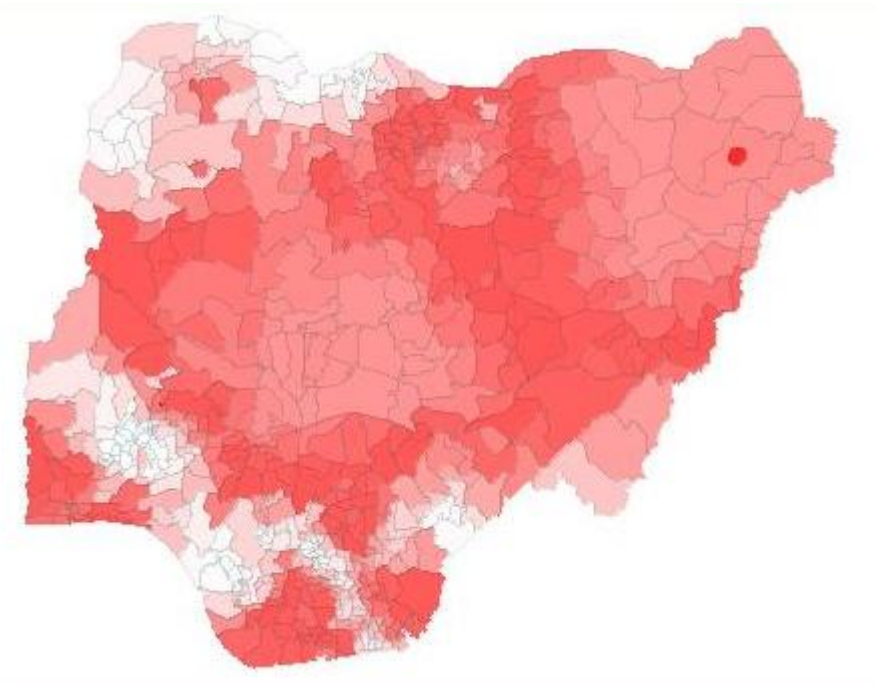

Figure 8. About Day 40 infection has spread without intervention to almost all states

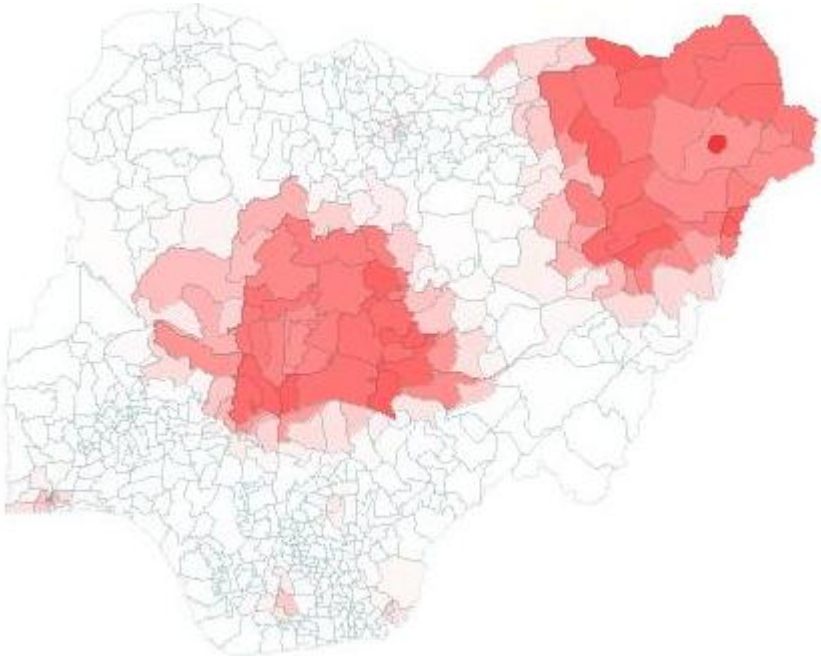

Figure 9. About Day 40 Intervention is restricting spread of Infection

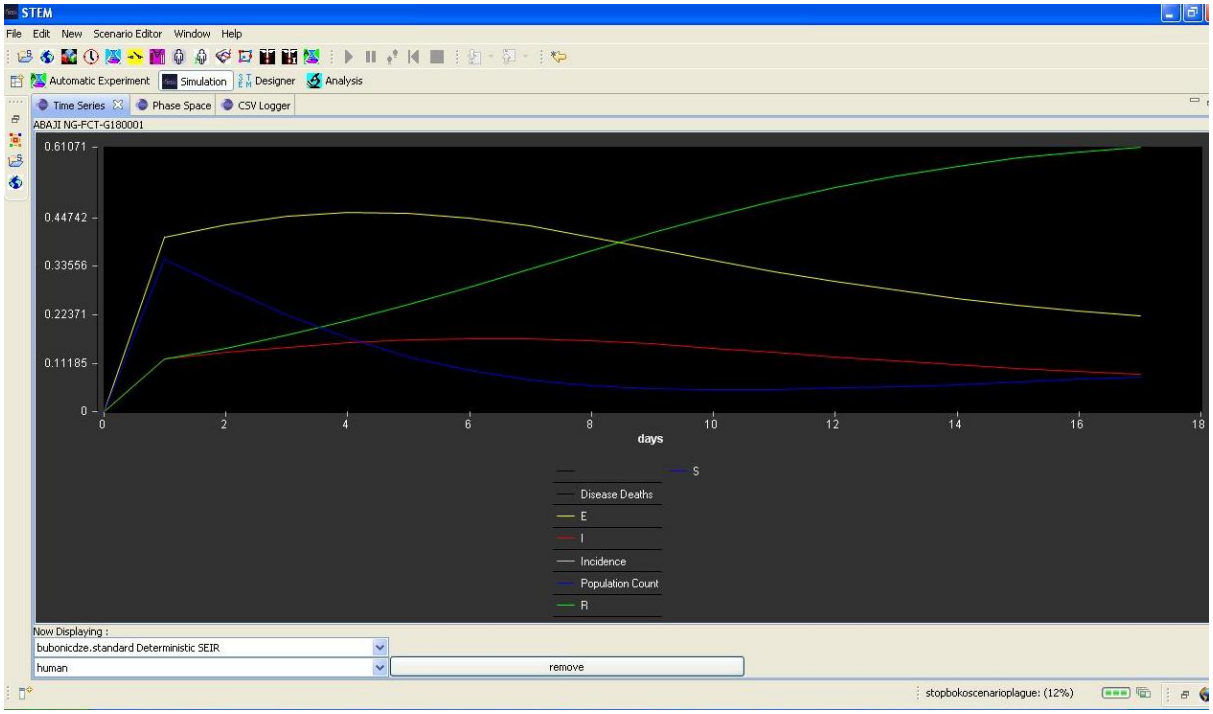

Figure 10. Time series showing the disease spread progression using different colour lines

4. Discussion

Plague is a rapidly progressing bacterial infection if left untreated with an incubation period as short as 1 or 2 days but also longer [24,26]. Our study

reveals increase infections, incidences and deaths as result of plague when left to spread without any form of intervention. The spread was so rapid that within 40 days 9.5 million people were death. This is not surprising for a notoriously deadly infection that has claimed 200 million lives in documented history and attempted to wipe out a third of Europe during the 'black death' around 1346 A.D. [1]. If diagnosis of plague is delayed and treatment is not instituted on time many lives will be lost with rapid spread of infection all over the country, and even beyond, since infections can spread easily now worldwide through global travel [27]. Some of the challenges that would cause delay in responding to a bio-threat will be financial implications which have hampered the control of animal diseases in developing countries [28]and human diseases in developing countries like Nigeria [29].

Social distancing policies such as isolation of infected individuals and effective chemotherapy and chemoprophylaxis will certainly reduce the number of incidence, infections and deaths arising from plague [24]. In an outbreak in Madagascar patients were treated with streptomycin antibiotic: 0.5g every 3hours for 2 days, 0.5g every 4 hours for 2 days and 1g twice a day for 4 days and chemoprophylaxis consisted of sulphadoxine at 2g per adult [24]. Since plague is primarily carried by wild rodents such as squirrels, gerbils, marmots, meadow voles and pikas and passed on to humans by fleas, controlling these group of animals will enhance reduction in the transmission of the infection and reduce subsequent deaths that might result [9]. Fleas who are the vectors of *Y. pestis* to humans are a very important connection line that should be destroyed for effective control and prevention of plague in a population [30].

After primary infection with plague especially the pneumonic form, secondary pneumonic plague is spread by infected individuals who infect those who come in contact with them. Our study shows that at day 40 cities and states that are heavily crowded and with high insanitary conditions encouraging high contact rates within humans like Lagos had higher incidences and infection rates of the disease. Cities and states also close to the original infector locations such as Yobe state that was close to Maiduguri also had high incidences of the infection. Studies have shown that close contact among humans due to overcrowding and

high interaction with rodents in insanitary conditions are predisposing factors for plague to occur and spread [31]. The locations from where the infections first started in this study (FCT and Borno State) experienced the highest number of deaths due to a concentration of the infection within the locality and delay in intervention to control the infection and limit its spread. Research has indicated that the highest casualties are usually not too far from the point of origin of the original infectious individuals [1,24,32] but deliberate infections as in this case will also lead to more widespread infections that are difficult to control [1,17,24]. In the period of the black death as people were running away from the plague and war and moving from one part of Europe to another they carried the disease along with them leading to the death of about a third of the population of Europe then [1]. This is why early detection and isolation of infectious individuals and treatment of the exposed population is very crucial to limiting the spread of the infection.

5. Conclusion

Plague can be very devastating if not adequately controlled. Effective control can only be done if there is early diagnosis of the infection and treatment is promptly instituted. Social distancing policies in combination with chemotherapy and chemoprophylaxis will ensure minimum level of destruction by the deadly plague infection. It will be worthwhile to have a stock-pile of potential antibiotics that can be used for therapy and chemoprophylaxis of the exposed population. Medical personnel and paramedical personnel should be trained on what to do in case of a sudden attack. In a world where terrorists can use any means at their disposal to wreak havoc on the human race it is very important to re-awaken to the possibilities of biological weapon attack. Preparedness is the key word to ensure prevention of such attacks and effective control in the face of inevitable attacks.

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