

Bioinformatics-base and Determinants of the Spatiotemporal Variations of Emerging and Re-emerging Infectious Diseases

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Abstract

Emerging and re-emerging infectious diseases pose grave threats to all countries. The emergence and re-emergence of infectious diseases invariably constitute significant health dilemma globally. The risk of parasitosis following emerging and re-emerging infectious diseases varies spatiotemporally within disparate environments and seasons. A proper understanding and elucidation of the spatial and temporal trajectories in infectious disease risk and the determinants during the variations are significant for the adequate presentation of interactions and interventions to harness and curb the deleterious impact of the emergence and re-emergence of infectious diseases and concomitant sequelae. Models are pertinent to explicate associations between the epidemiology and spatiotemporal distribution of the vectors and parasitoses regarding the risk profile of endemic regions. The role of policy makers and researchers are relevant per the modalities of the transmission and dissemination of infectious diseases and parasitoses as well as exotic bias of infectious diseases.

Keywords: Emergence; Re-emergence; Parasitoses; Models; Tropical neglected diseases

Introduction

Infectious diseases constitute one of the global mortality significant agents impacting on health and security challenges. In 2009, Novel Swine-origin Influenza A (H1N1) virus (S-DIV) was detected in specimens from two epidemiologically detached subjects in the United States of America, with the same strain observed in other places including Canada and Mexico [1]. Emerging infectious diseases including the re-appearance of erstwhile controlled diseases, such as lassa fever, ebola, malaria, and tuberculosis constitute major epidemiological and public health issues and concern, challenges in the determination of transmission and etiological parameters. Dynamic features impacting on the dissemination of infectious diseases and parasitoses encompass globalization, environmental alterations, population increase and antibiotic resistance [2]. In the long-term, environmental parameters, such as climate metamorphosis, air pollution, ecosystem derangement, and biodiversity dissipation are crucial to understand, elucidate and control infectious disease dissemination. In varied instances, deforestation is inextricably linked to changing patterns, trajectories and modalities of malaria and schistosomiasis, thus depicting climate change impacts on zoonotic transmission of cryptosporidium, as the parasite is easily transmitted *via* the environment, particularly aquatic environment, and cryptosporidiosis seasonal trends. These are also extrapolated to considerable resultant impact on infant mortality, socioeconomic factors and air pollution [3,4]. Infection disease diffusion at population level is of critical concern in the awareness, prevention, management and control of emerging and reemerging infectious diseases through space and time [5]. A vast majority of these infectious diseases are sensitive to climatic factors as 1°C elevation in average temperature significantly correlates with 0.4% and 2% augmentation in risk of diarrhea, dengue, influenza, malaria, mumps, shigellosis and rabies

[6,7]. The impact of socioeconomic attributes on communicable disease risk is principally governed by population density more than other variants or variables.

Numerous ecological processes culminate in significant spatial patterns or variations in disease risk or incidence whereby pathogen dissemination could be increasingly localized, with spatial restriction of vectors or reservoirs for pathogens, and clumping of susceptible or vulnerable hosts [8]. The elevation of worldwide terrestrial temperature is predictive of climate alterations may directly influence certain infectious disease transmission [9]. An expected temperature elevation under climatic alteration is liable to induce increased number of insects and an augmented infectious probability of the parasite that elicits Chagas disease transmission. Nutrient deficiencies and intercurrent disorders are likely indicators and inducers of parasitism [10]. On a global scale, infectious diseases are a principal healthcare dilemma resulting in grave and expansive mortality. For the development of effective and efficient control as well as regulatory modalities, it is pertinent that reliable computational procedures and tools are employed to understand and elucidate the dynamics of diseases for the prediction of emerging and re-emerging cases, whereby the computational and predictive tools are applicable by policymakers and healthcare administrators in informed and constitutive sustainable decision-making. Numerous emerging and reemerging infectious diseases are etiologically defined by generalist pathogens which infect and transmit by means of multiple hosts with diverse dissemination trajectories, thus obfuscating the important elucidation of pathways and trajectories of pathogens [11].

The Emblem of Infectious Diseases

The emergence and re-emergence of the pathogens in all populations are mostly inextricably linked with global modifications, such as anthropogenic socioeconomic attributes, climate or biodiversity alterations *via* the invasion and colonization in novel

ecological niches, and thereby modifying the characteristics of transmission pathways which are amenable to prevalence of the pathogen in the ambient with resultant emergence and re-emergence of infectious disorders and parasitoses [11]. Parasitoses are widely disseminated in the animal kingdom and plants. They cause widespread pathologic effects ranging from commensalism to severe, even fatal illnesses. Several parasitic infections cause considerable suffering and impact economically on human health, livestock and crop production. The deleterious impact of many parasitic infections necessitates their control as regards health, environment and economy [12,13]. Emerging infections are perspicuously infections which newly become salient in a population, or are accelerating their incidence or broadening their geographic scope [14-16]. Re-emerging infectious diseases are those previously in decline but have now resurfaced with a more expansive impact. These involve the entrance and eventual dissemination of a virus into a human community or population, particularly from a zoonotic reservoir or source to a previously isolated virus to new hosts.

Advances in technology which permit microbial identification, the pathologic and immunologic alterations induced are essential in the nomenclature of a disease and the characterization of the clinical scope and epidemiology. The etiologic agent of cat scratch disease was previously assumed to be a microbe carried by cats but with the development of more powerful diagnostic technologies, the agent was identified or elucidated in cats and humans as well as associated with grossly distinct pathologic process namely, bacillary angiomatosis in AIDS patients [17]. Alterations in environmental conditions caused by anthropogenic activities are frequently responsible for microbial or viral traffic. Anthropogenic activities such as, environmental perturbation, agriculture, population migration, rural urbanization and rural-urban drift currently have expansive latitude for the spread of infectious routes and natural hosts or vectors which had been previously isolated geographically, thereby augmenting opportunities for nascent infections [15,16]. Early warning systems by means of networks for surveillance of infections are essential [14-16,18], effective and efficient defense, prevention and treatment regarding emerging and re-emerging infections and diseases with their sequelae. Diseases resulting from plant pathogens are a major constraint to agricultural production. The etiological agents include spiroplasmas, mycoplasmas, bacteria, fungi, viruses and viroids. Amongst the plant pathogens, viruses rank second only to fungi regarding crop and yield losses [19]. Latin America is currently battling with intricately complex alterations in agricultural environments which impact on both export and domestic staple commodities but unfavorably is deficient in adequate human and financial resources to mitigate these problems [20].

These require the investigation of systems of increasing complexity using models. Global gross alterations in our lifestyle potentiate the spread of certain infections and the ascertainment of more previously confounding infections will be ascertained [21]. Since parasites exhibit heterogeneity as regards distribution patterns, the area size (size of areas of their occurrence is extremely variable and may be influenced by environmental or inanimate environmental factors), area shape (areas of their occurrence vary with emphasis placed on continuous and disjunctive distribution), variance (whereby closely related parasitic forms occupy separate areas), and prognosis (qualitative predictions regarding human parasitoses) are emphasized as they relate to global regions, countries or peoples. A variety of these diseases and infections are the neglected diseases which constitute a medically diverse group of tropical infections particularly endemic in

low-income populations in developing regions of Africa, Asia, and the Americas. This paper tends to fundamentally predict, assess and reduce human and environmental susceptibility and risks associated with diverse factors in infectious diseases as they impact on our economy and quality of life.

Modalities for Dissemination of Infectious Diseases

A two-step process has been described for the emergence or re-emergence of microbial disease, the "viral trafficking" of microbes from one species or locale to another, and subsequently microbe dissemination [16]. In addition, a microbe could circulate within human populations for generations unobserved and then culminate in an amplification episode of outbreak or epidemic which results in the increase of microbial population through an apparently trivial or latent homeostatic host interaction to a significant host infection of greater magnitude and microbial dissemination [22]. Environmental and social factors potentiate complex modes such as, routine exposure to available raw human waste by enteric microbes; in increased high density households by respiratory microbes; expansive intravenous drug abuse *via* blood-borne microbes; and sexually transmitted agents between *Homo sapiens*. Amplification may easily be prevented or mitigated easier in a medical or healthcare setting where there are extant sustainable modalities to control human disease and its sequelae.

Microbes which rely on the human host for survival become adapted to the social and biological ambient or niche created by that host. Microbes often undergo mutation, recombination, genetic shift and drift as variants break away from vaccine-induced immunity [23]. There are several factors which are amenable to disease recognition such as spatiotemporal clustering of cases [24], prevalence increase, distinctive symptoms and signs, laboratory findings, short incubation, rapid progression, high mortality, appearance in a new population or geographic site, presence in a high visibility or affluent population. Several factors govern the vulnerability of plant, animal and human populations to morbidity and mortality. These include ageing population, immunosuppression from HIV/AIDS and medical interventions such as, chemotherapy, nosocomial and iatrogenic modalities, prosthetic valves and joints, dialysis, overcrowding, environmental pollution, social upheaval and mobility into new habitats and lesser genetic diversity [24-27]. In protecting public facilities, modern technology may also cause damage to the system or contamination occurs resulting in massive outbreak of cryptosporidiosis [28]. Evaluation of baseline data is important for the identification of changes in such a system. Infectious diseases are caused by pathogens and exposure of vulnerable individuals or populations to pathogens. Thus, the reduction of vulnerability and exposure constitute main preparatory feature for new disease threats, prediction, detection, rapid response and prevention in a sustainable cohesive modality that must be inculcated spatiotemporally in every economic and technological development structure. Infectious diseases have continued to constitute an enigma for elimination, and remain the leading cause of global mortality and a leading cause of death in the United States [29]. With changes in technology, society and environment, it is pellucid that pathogens evolve or disseminate and alter the infectious disease spectrum. Emerging infectious diseases such as prolonged diarrheal illness from water-borne *Cryptosporidium* [30], hemorrhagic colitis and renal failure due to food-borne *E. coli* 0157:H7, and rodent-borne hantavirus pulmonary syndrome, tuberculosis, pertussis, ebola, HIV/AIDS and cholera evidentially

elucidate that the global population remains increasingly vulnerable to the microorganisms present and saddled with us in our environment. It becomes necessary to have improved surveillance for emerging and re-emerging infections to: (a) strengthen or undergird national notifiable disease system; (b) establish population-based emerging and re-emerging disease programmes; (c) establish seasonal surveillance networks; (d) develop a system for enhanced global surveillance; (e) employ newfangled tools and strategies to surveillance [31].

Conduits of Infectious Diseases

Notwithstanding the advances in diagnosis an infectious diseases control of non-human primates in the laboratory setting, certain infectious agents increasingly plague colonies. For instance, the Measles virus and *Mycobacterium tuberculosis* cause sporadic outbreaks circumventing well-established biosecurity protocols; and others, such as retroperitoneal fibromatosis-associated Herpesvirus, have only recently appeared, usually as a result of immunosuppressive experimental manipulation. Due to the peculiar social housing requirements of non-human primates, importation of foreign-bred animals, and deficiency of antemortem diagnostic assays for several new diseases, eradication of these disease agents is often intricately complex. Parasitoses, emerging and re-emerging infectious diseases are widely disseminated in flora and fauna, and cause considerable morbidity and mortality. Alteration in environmental conditions caused by anthropogenic activities is frequently responsible for microbial or viral traffic [32]. Although, there have been advances in medical research and treatment in recent decades and for centuries, infectious diseases have ranked with wars and famine as major challenges to human development, progress and survival; and they constitute one of the leading causes of global morbidity and mortality. The world's microbial life is varied, versatile and expansive thus, novel associations with humans are inevitable. Certain organisms are bound to become dissipated, and nascent ones will surface [32]. These are liable to become aetiological factors for new disease syndromes in populations or individuals with distinct genetic make-up or associate with other microbial life or environmental influences in the creation of newfangled disease or trajectories. About eighty percent of disease outbreaks reported are due to waterborne organisms such as cryptosporidiosis and cholera or emanate from a waterborne source as in legionellosis.

Environmental stresses, perturbations and conditions are direct contributors to these diseases. From the 1960s to 1990, the average yearly Documented Water Disease Outbreaks (WBDOs) in the United States quadrupled with *Giardia* being the most identifiable, but advanced techniques unraveled *Cryptosporidium* in increasing episodes [33]. Also, the abundant number of cases of acute gastroenteritis due to waterborne organisms, although of undecipherable etiology are putatively of viral origin [34]. Inasmuch as the presence of WBDOs in industrialized countries are traceable to negligence of treatment systems or leakages within distribution networks, an expansive number of outbreaks are resistance to frequently applied disinfectant concentrations. The perspicuous instances are the cysts which enable protozoa such as *Giardia* and *Cryptosporidium* to survive in treated water networks. Also, algae in freshwater ecosystems absorb chlorine to form hazardous chlorinated hydrocarbons, thereby reducing free chlorine. There is increasing public health issue not currently adequately discussed and dealt with in water quality criteria.

Global phytoplankton blooms have been evidenced [35]. Less than fifty are realized to be toxic from circa five thousand phytoplankton species. Established toxic or nuisance blooms persist due to either their depletion of available nutrients and resources, or toxins accumulate and become inhibitory factors to other phytoplankton or reduce zooplankton grazing pressure [36]. The deleterious impact of phytoplankton blooms is expansive. The dissipation of human life and health perturbation are of primary concern. The proximate or neighboring economies undergo hardships and are disproportionately affected due to the toxicity of the shellfish which culminates in declining environmental quality and dissipation of finfish. Marine mammal mortality is inextricably linked to the phytotoxin concentrations in marine food chains [37], and the effect of phytoplankton toxicity on non-commercial species may be enormous. The more debilitating impact of climate change on toxic marine phytoplankton may be envisaged in developing nations and in isolated islands, thus impeding rapid prevention, detection and assistance due to lack of specific areas of interest [38], decided plan on harmful algae and marine biotoxins [39], and absence of computerized databases [40]. Climate metamorphoses and increased anthropogenic activities are apparently contributory factors to phytoplankton growth. The predictability of potential toxicity are amenable to early bloom detection, remote sensing [41,42], and specific identification of toxic phytoplankton [43,44] and public alert of potential hazards [45-47] as well as adoptions of other actions and management policies.

It is pertinent to prevent or mitigate the impact of vector-borne disease agents by identifying peculiar characteristics which enhance their emergence, re-emergence and distribution. Vector-borne pathogens have the frequent tendency to be genetically stable than disease carrying agents which cycle through a specific host because few principal variants are liable to thrive in the competitive and demanding requirements of an alternating cascades of differential hosts or reservoirs. A successful variant must find adaptation to both an arthropod as a vector and a vertebrate as the reservoir host. Emergence is amenable to environmental change that enhances vector abundance or an alteration in the density or admixture of non-human vertebrates. Outbreaks of vector-borne infections tend to emerge radically due to their expansive communicability [48]. Of extreme importance in the multifactorial features of vector-borne diseases are the anthropogenic influences, especially debilitating environmental alterations. This is typical in the passage of an exotic vector. With the movement of *Aedes albopictus* from Asia into the Americas in the mid-1980s, *Aedes aegypti* mosquito was capable to transmit not less than five distinct viruses such as, dengue fever and enteric equine encephalitis which are endemic to the Americas with re-emergence of dengue and Dengue Hemorrhagic Fever in Latin America. These are the resultant effects of complex economic changes which enhance accumulation of non-disposed accumulation of wastes in the proximity of households in an increased population density [49]. In 1930, there existed just three arthropod-borne virus (Arbovirus) human diseases, yellow fever, pappataci fever and dengue fever [50]. Nowadays, an excess of hundred Arboviruses are human pathogens [51]. Humans are normally accidental hosts and usually do not suffer morbidity and, infections are latent. Arbovirus disease is seasonal and, is thus, influenced by climate (temperature, rainfall), prevalence due to vector competence, duration of extrinsic and intrinsic incubation, vector density and mobility or transport to distant locations as well as level of vertebrate immunity in the population. Arbovirus disease invariably becomes apparent, old diseases appear in new geographical

locations, and there are also diseases to correlate with orphan viruses [52].

Ixodes and *Borelia* that transmits two zoonoses which emerged in Europe and North America in the 1970s has continued to impact on human health [53]. A spirochetosis caused by *Borelia burgdiferi* named Lyme disease produces a debilitating chronic sickness that affects diverse organ systems. Human babesiosis that sometimes constitutes fatal malarial infection from *Babesia microti* may occur alone or as an adjunct to Lyme disease. In Eurasia, tick-borne encephalitis, an arboviral infection is co-transmissible with Lyme disease. Clinical findings are not easily amenable to interpretation because a single *Ixodes* tick is unilaterally capable of transmitting each pathogen or in combination with diverse pathogens with concomitant human disease that is diversified in incubation [period, clinical signs and symptoms]. The distribution pattern of Lyme disease and its interacting vectors in Europe and the Northeastern United States emanates from the recent proliferation of deer resulting from the reforestation process throughout the global North temperate zone. Human residential development apparently promotes small tree-enclosed meadows with admixture of woodland strips, an interspersed measure favorable to prized deer, mice and humans. The resultant effect is that an increasing population reside where risk of Lyme disease and babesiosis is grave. The infectious agents which were previously enzootically transmitted by a distinct rodent-feeding vector reverted to zoonotic agents [53]. In Massachusetts in the United States, the 20th century emergence of zoonotic eastern encephalitis has been due to environmental alteration [54]. *Cs. melanura*, the principal mosquito vector of the infection was seldom observable in eastern North America before the 1930s. Its relative absence was due to the destruction of the swamps which had been lumbered or drained for agricultural purposes in the 18th and 19th centuries. With the resultant maturation of the swamps in the early 1900s, the formation of subsurface pools of water underneath grown and mature trees probably augmented the accessibility of mosquito breeding sites. Transmission is liable to have increased by simultaneous proliferation of wetland-roosting robins and the extinction of vagile birds like the passenger pigeon. The severity of the initial major outbreak of equine sleeping sickness in 1938 was probably precipitated by the scarcity of herd immunity in an expansively proliferating reservoir bird population. These relate that recent landscape, floral and faunal alterations led to zoonotic equine encephalitis emerging in Massachusetts after a century's decline. By application of basic epidemiological and ecological data, the Rift Valley Epidemic along the River Senegal at the foreclosure of the Dialmo dam was predicted over a decade antecedent to its occurrence [55,56]. Prospective investigations of emerging RVF necessitates surveillance and prompt coordination within varied networks employing rapid, informed decisions and interventions at locations of RVF emergence.

Microsporidia are ubiquitous, obligate intracellular protozoan parasites increasingly detected as opportunistic pathogens in AIDS patients. These parasites have been associated with chronic and fatal intractable large-volume diarrheas, hepatitis, cholangitis, pancreatitis, enteritis, keratoconjunctivitis, and peritonitis in either homosexual or heterosexual individuals. Optimum diagnostic and therapeutic measures of these pathogens still elude both clinicians and researchers. The most essential function of an adequately equipped laboratory for optimum clinical management of a patient presenting with microsporidiosis is the performance of genus-level diagnosis to distinguish the different microsporidial agents. Since *microsporidia* have been recognized as ubiquitous organisms which cause

opportunistic infections, more cases of microsporidiosis will emerge as the number of patients with AIDS and HIV infections increase. The sources of human microsporidial infection and modes of transmission still remain unknown. In efforts to present features identical to infections observed in immunodeficient patients, animal models have been developed. Further study is required to elucidate the exact prevalence and clinical characteristics of microsporidia [57]. *Acanthamoeba* has been designated an emerging environmental, public health and clinical problem. It is an uncommon, but increasingly prevalent infection liable to cause perturbative ocular damage, particularly in frequent contact lens wearers. The clinical course, specificities in ophthalmologic and parasitologic diagnosis, drug and surgical treatment of *Acanthamoeba* keratitis pose a difficulty to both clinicians and researchers. New insights have been provided with respect to the risk factors, incidence and pathogenesis of contact lens-associated infectious keratitis. *Acanthamoeba* keratitis may be associated with poor outcome, even with intensive treatment, especially in the latter clinical course of the disease with its distinct characteristic features which are perturbative in our environment [58]. The Eastern Mediterranean Region, EMR remains a hotspot for the emergence and re-emergence of infectious diseases, with the concern and necessity for the prevention, detection, and response to any infectious disease threat to global and communal health security being a major challenge or priority. MERS-CoV emergence in 2012 accompanied by its persistent transmission presents an expansive perturbation. With regard to the increasing frequency, duration and magnitude of disease manifestations, WHO has functioned closely with member states in the arenas of public health improvement, preparedness, awareness, surveillance systems, outbreak response, and other externalities, challenges and constraints [59].

Exoticized Perspectives of Infectious Diseases

Cultural factors related to the distribution of parasitoses include customs, traditions, and habits as well as other anthropogenic activities. They include agricultural practices and the construction of irrigation systems to develop agricultural areas, dam construction for artificial irrigation and/or for energy supply. Also, pertinent cultural factors include different eating habits, prehistoric, and prevailing migratory habits of human. Certain development programs enhance the acquisition of parasitic diseases. For instance, a major problem associated with dam construction or mining operations [60] and certain human activities/development projects [61] is the need for the assemblage of several people within a short span of time. This relates that prior endemic but clinically unimportant diseases become a mass phenomenon in the construction area; with subsequent introduction of non-autochthonous parasites. These have been established to occur for the pathogenic organisms associated with inter alia malaria [62], onchocerciasis, schistosomiasis [63], dracunculiasis and trypanosomiasis [64] and protozoan parasites [65]. Usually prostitutes do profound business at construction sites with the frequent introduction of sexually transmitted diseases, such as trichomoniasis and HIV. This is also applicable for the whole of society with increased or augmenting promiscuity. The increased number of persons living together in a limited space on construction sites is amenable to high water pollution with resultant convenient breeding places for *Culex quinque fasciatus*, an important vector of *Wuchereria bancrofti*. Reduced water flow/velocity above a dam results in unsuitable water usage due to breeding of blackflies, *Anopheles* spp., *Culex* spp., and intermediate hosts such as, snails and other cyclopides. A major important factor for the occurrence of parasitosis is eating and

drinking habits. The consumption of raw/unprocessed or insufficiently cooked animal food may result in infection. Also, the drinking of guinea worm-contaminated pond water has resulted in severe suffering and decreased livelihood in many parts of the developing world. Human customs and habits of an extremely different sort instigate or enhance [66] the occurrence of parasitic diseases. Examples include the use of domesticated dogs to lick up the vomit and feces of infants and toddlers, as well as cleaning up children by licking their faces and anuses. Carnivores and cannibals are also infected by the consumption of the dead. Human behavior is also substantiated by religious practices, whereby trichinosis is absent in some populations. This, however, limits *Trichinella spiralis* in human and not in animals in this select group. Emerging infections such as HIV/AIDS make us realize how lethal infections culminate irrespective of adequate nutritional status, healthcare provision, therapy and high living standards. Recent projections of the global demographic impact of AIDS indicate that under the current trajectory of transmission and fatality, the HIV is liable to cause premature mortality of a vast majority of future generations [67].

Africa presents unenviable and untoward challenges regarding the double burden of infectious diseases and non-communicable diseases with accelerated progression in the continent [68]. Just Ebola is a hemorrhagic fever of the *filovirus* family with a 50-90% case fatality rate. There is currently no effective treatment for Ebola excepting the euphemistically profiled “supportive therapy” [69]. The virus is disseminated through contact with infected fluids, particularly blood, and immediately it has infected a new patient, it quickly attacks the internal organs and connective tissue, causing severe bleeding, vomiting, aches, mental impairment and dementia, and in grave cases, grand mal seizures. The frequent cause of death is multi-organ system failure [70]. The global community initially became aware of Ebola in 1976, when the disease broke out in Yambuku, Zaire (now the Democratic Republic of the Congo) and N’zara, Sudan [71]. During these eruptions, most of the international community paid cursory attention to the new disease; legionellosis was identified following the outbreak of pneumonia among persons in a conference in Philadelphia, USA [72]. Ebola has been exoticized, linked with “traditional” practices, local customs, and cultural “beliefs” as well as stigmatized to be due to African ignorance and backwardness. Indeed, reified culture is reconfigured into a “risk-factor,” invariably linking the outbreak of the disease to practices such as burial traditions or consumption of bushmeat. Ultimately, the specific subtype that had proven fatal to the monkeys was discovered to be harmless in humans [69]; however, viral phobia had been triggered by the episode and only increased spatiotemporally [73].

In 2014, the eruption of Ebola in Guinea, Liberia, Sierra Leone and Nigeria and patches of Europe and the United States triggered several mortality and morbidity cases, stigmatization and prevention of the affected countries to participate in international sociocultural activities and sports. A total number of 15,351 confirmed, probable and suspected cases of Ebola Virus Disease (EVD) was reported in six countries (Guinea, Liberia, Mali, Sierra Leone, Spain, and the United States of America) and two formerly affected countries (Nigeria, Senegal) until 18 November 2014. There were 5459 reported deaths. Based on the WHO Ebola Response Roadmap structure, country reports are placed in two categories: (a) countries with widespread and intense transmission (Guinea, Liberia, and Sierra Leone); and (b) countries presenting with or which have had an initial case or cases, or with localized transmission (Mali, Nigeria, Senegal, Spain, and the United States of America). A distinct, unrelated outbreak of EVD in

the Democratic Republic of the Congo was declared as vanquished [74]. Since the natural reservoir of Ebola virus has not been clearly elucidated and that human disease outbreaks manifest sporadically within an expansive region, predicting the spatiotemporal characteristics of Ebola spillovers presents an increasingly urgent public health concern for targeted surveillance [75].

Mathematical modeling constitutes an essential procedure to elucidate the dynamics of the spatiotemporal dissemination of infectious diseases ostensibly emanating from natural outbreak or anthropogenic activities due to the deliberate release of pathogenic biochemical agents. Researchers, decision- and policy-makers equipped with strategies and modalities to harness and curb diseases, epidemics and threats have to be equipped with adequate and accurate computational tools and procedures undergirded by mathematical modeling [76] and bioinformatics in these intricately complex conditions exemplified in three real cases of Ebola Haemorrhagic fever in Uganda, Gabon and Guinea, respectively in 2000, 2001 and 2014. The development of a computational framework reliant on Gaussian processes for spatiotemporal prediction of infectious diseases explores the particular structure of identical matrices in the formulation to present a formidable implementation for the prediction of scenarios for public health policymakers [77].

Lassa fever is an acute viral illness found in West Africa; and was discovered in Lassa, Borno State, Nigeria in 1969 whereupon two missionary nurses died. It is a zoonotic single-stranded RNA virus of the family *Arenaviridae*. Lassa fever is endemic in Guinea, Liberia, Nigeria and Sierra Leone; other neighbouring countries are at risk, though. The “multimammate rat” (*Mastomys natalensis*) is the animal vector for Lassa virus, and it is distributed throughout the region [78]. The first case from Mali was reported in a traveler residing in Southern Mali in 2009. Towards the end of 2011, Ghana reported its first case. Also, Cote d’Ivoire and Burkina Faso reported isolated cases, with serologic evidence of Lassa virus infection in Benin and Togo. It is estimated that there are 100,000 to 300,000 Lassa virus infections and 5,000 deaths annually in West Africa. These numbers are of heuristic value because the case surveillance for the disease is not uniformly carried out [79,80]. It has been documented that 10%-16% of persons admitted annually to hospitals present with Lassa fever in certain areas of Liberia and Sierra Leone; thus, indicating the severe impact of the disease in the region. In 2014, the CDC and the Minnesota Department of Health confirmed a diagnosis of Lassa fever in an individual who returned to the United States from West Africa [81]. The Minnesota event was the seventh case reported of Lassa fever for travelers coming back to the United States, while the last known case was detected in 2010 in Pennsylvania [81,82].

More than thirty new infectious agents have been revealed globally in the last three decades; 60 per cent of which are of zoonotic origin [83]. Developing nations such as India disproportionately suffer because of the burden of infectious diseases given the confluence of extant environmental, socio-economic, and demographic factors. In the recent past, India has witnessed eruptions of eight organisms of emerging and re-emerging diseases in diverse sections of the country, six of these being zoonotic in origin. To prevent and control emerging infectious diseases will increasingly necessitate the application of sophisticated epidemiologic and molecular biologic techniques, human behavioral changes, as well as a national policy to early detect and rapidly respond to emerging infections and a plan of action. It is becoming evident that an admixture of complex changes in European societies is rapidly creating new opportunities for the emergence of

new infections. These are inter alia (a) globalization and environmental change (climate change, habitat destruction, migration, long distance travel, global trade (b) demographic and social forces (population senescence, social inequality and unmitigated urbanization), (c) public health system influencers (antimicrobial resistance, health care capacity, animal control), and (d) new influenza virus variants, new pathogenic microbes, especially those transmitted from animals, resurgent infections such as TB, resistance to antimicrobial drugs and bioterrorism threat [84].

The communal perspective of living and training environments, as well as suboptimal hygiene and stressors in the field, place military personnel at higher risk of contracting emerging infectious diseases. Some of these diseases rapidly spread within ranks leading to expansive outbreaks; and personnel deployed are frequently immunologically ignorant to otherwise uncommonly-encountered pathogens. Also, the opportunity of offensive biological agents being employed in conventional warfare or otherwise remains a realistic, albeit often concealed, threat. However, such challenges also provide the latitude for the enhancement of preventive and therapeutic military medicine, some of which are later adapted to civilian settings [85]. These include enhanced surveillance, new vaccines and drugs, improved public health interventions and inter-agency co-operations. The legacy of successful management of infectious diseases is reminiscent of the importance to sustain efforts and ensure a safer environment for both military and the community at large. Emerging and re-emerging infectious diseases are threats which military establishments have to guard against, as they constitute potential and substantial impacts to operations and training. These diseases may emanate from within the military community, as spill-over from proximal civilian populace, or during military operations and deployments. Biological warfare and bioterrorism are additional possibilities which militaries need to be in preparedness [85].

Formulating Modalities to Explicate/Elucidate Infectious Diseases

At the emergence of a disease, a litany of molecular, immunological, physiological and epidemiological techniques are present in developed economies, but not so readily in certain deteriorated economies without supported internal health programs. The alarming rate presented by emerging diseases both in floral and human populations necessitates development, promotion and research in integrated disease epidemiology. Newly emergent vector-borne pathogens are likely to sustain increased virulence than those which undergo direct transmission, but both types of pathogens are amenable to non-virulence [86]. Evolution in microbial pathogens is dependent on similar principles of variation and selection evidenced in higher organisms; and these implicate multiple interactions within variables in species communities and health system interventions [87]. Epidemics are conceptualized as both biological and sociological occurrences. Anthropology conceptualizes human health and disease in furtherance of the conventional epidemiological model of host-pathogen-environment interactions or inextricable linkage; thus emerging disease is observed as mutual interactions of organic, inorganic and cultural milieu [88]. Research on emergent and reemerging diseases are beneficial to develop intricate disciplinary linkages between biomedical, social sciences and their diverse subdisciplines. The emergence and global dissemination of new and resurgent infectious diseases such as HIV/AIDS, malaria, cholera, tuberculosis and Ebola virus are contributory factors to the complexity

of health patterns and their impact on the predictability of dominant health-transition strategies. These strategies are undergirded by demographic postulations on long-term health sequelae of ageing populations based principally on morbidity and mortality indicators. The pertinent advances in technology and, financial consequences of noninfectious chronic and degenerative disorders affecting an increasingly older population have been the major foci for investigative research. These stem from varied interactions of an expansive range of risk factors which are not completely comprehended [89]. New and resurgent infectious diseases are perspicuously compounding the predictability of extant health-transition models. Political and social dimensions such as inter alia equity, labour market structure, land use, education and environmental protection need to be incorporated into the framework for sustainable health ecosystem strategies.

Discussion

Although, there have been advances in medical research and treatment in recent decades and for centuries, infectious diseases have ranked with wars and famine as major challenges to human development, progress and survival; and they constitute one of the leading causes of global morbidity and mortality. Epidemics of new and old infectious diseases emerge periodically, and intractable infectious diseases persist increasing the worldwide burden of infections. Investigations of these emerging infections elucidate the evolutionary properties of pathogenic microorganisms and the dynamic interactions between microorganisms, their hosts and the environment [90,91]. In the past two decades, innovative research, improved diagnostic and detection techniques have exposed erstwhile unnoticed human pathogens. For instance, chronic gastric ulcers, which were previously assumed to be due to stress or the diet have been linked to infection by the bacterium *Helicobacter pylori*. There is need to recognize that actions and policies towards other countries, policies, agricultural subsidies, and geopolitical struggles are liable to have deleterious consequences for global health outcomes. Policymakers and citizens need to recognize the internationalized effects of their actions, transcend from cultural to structural factors in Ebola epidemics, and thrive to mitigate inequality and poverty rather than altering a reified "culture" in the evaluation and implementation of outbreak control efforts. Historically, neglected tropical infectious diseases have lacked adequate attention in global public health efforts, thus resulting in inadequate prevention and treatment alternatives. The subset of infectious tropical diseases disproportionately impacts the world's economically disadvantaged, and represents a significant and underappreciated global disease burden, and is a major constraint to development efforts for the alleviation of poverty and human health improvement [92].

Increased commercial activities in exotic animals for pets and as food sources have enhanced the opportunity for pathogens to traffic from animal reservoirs to humans. Exotic rodents imported to the United States as pets were discovered to be the origin of the recent U.S. outbreak of monkeypox; and consumption of exotic civet cats in China was found to be the route of the SARS coronavirus transition from animal to human hosts. Several factors allow for the emergence and re-emergence of new infectious pathogens [92]. Natural genetic variations, recombinations and adaptations permit new strains of documented pathogens to occur to which the immune system has not been previously exposed, and thus, not primed to recognize (e.g., influenza). Increased abuse of antimicrobial drugs and pesticides has resulted in the development of resistant pathogens, paving way for

many diseases which were previously treatable with drugs to revert to their infectious status (e.g., tuberculosis, malaria, nosocomial, and food-borne infections). Also, decreased compliance with vaccination policy has culminated in the re-emergence of diseases such as measles and pertussis which were formerly under control. The application of deadly pathogens, such as smallpox or anthrax, as agents of bioterrorism is an increasingly documented threat to the global population. Furthermore, several significant infectious diseases have never been adequately controlled on either the national or international level. Infectious diseases which are continuous health problems in certain countries are re-emerging elsewhere, such as food- and waterborne infections, dengue, West Nile Virus [91]. The benefits of basic research include HIV protease inhibitors development by researchers funded by NIH and others. These drugs, when used in combination with other anti-HIV drugs contributed to the remarkable decline in mortality from AIDS in the United States [93].

There is need to recognize that actions and policies towards other countries, policies, agricultural subsidies, and geopolitical struggles are liable to have deleterious consequences for global health outcomes. It is pertinent to prevent or mitigate the impact of vector-borne disease agents by identifying peculiar characteristics which enhance their evolutionary capacity, emergence, re-emergence and distribution. A variety of these diseases and infections are the neglected diseases which constitute a medically diverse group of tropical infections particularly endemic in low-income populations in developing regions of Africa, Asia, and the Americas [94]. These require the investigation of systems of increasing complexity using models. The obligation of national and world governments is to respond and fully inform their constituencies but frequently the constituencies are incapable of grasping the nature and consequences of parasitoses, emerging and re-emerging infectious diseases and, may not be able to accept the magnitude of change needed to face them. Detection and recognition of these diseases are imperative due to their confounding effects on experimental data, consequence on colony health, and potential for zoonotic transmission. Emerging and re-emerging pathogens are a threat to laboratory-reared non-human primates (NHPs); as these animals are critical to certain biomedical research programs; and are applied extensively in drug discovery and development. In contrast to those of other laboratory animal species, infectious diseases have proven cumbersome to eradicate from primate colonies, and diverse pathogens may impact on animal and colony health. Despite remarkable advances in infectious diseases diagnosis, unrecognized or adventitious pathogens are common in NHPs and possess the potential to confound experimental work [94].

Conclusion

This study portends to develop and improve the welfare and well-being of vulnerable populations in the interactions or co-morbidities or co-occurrence of emerging and re-emerging infectious diseases in contextually, socioeconomic milieu and provide newfangled healthcare research modalities and techniques to vulnerable populations globally; develop and promote evidence-based strategies to mitigate or eradicate health development challenges *via* inter alia providing innovative research funding to curb inequitable gender norms, perceived internalized stigma, validate a measure of rights-based access to healthcare in prevalent emerging and re-emerging infectious diseases with minimal costs or prices within populations. Regarding socioeconomic status and income as facilitator, it is pertinent that public health and national economy modify the allocation of

healthcare expenditures to presenting social programs [95]. One major constraint is that a vast majority of the data on the epidemiology of the interface between emerging and re-emerging infectious diseases with undergirding socioeconomic factors emerge from developed countries, whereas the population at risk is in LMICs. A profound analysis of the pharmaceutical conduit portends drug development augmentation for tropical ailment. The program impact is not equitably distributed with tuberculosis and malaria, for instance, thus presenting marked novel development whereas numerous other diseases are devoid of novel drug offers, benefits and beneficiaries [96].

The questions arise if government and the public should take anticipatory measures for environmental protection before the emergence of problems or their impacts are felt; or if environmental and developmental problems be viewed exclusively of the social, political and economic patterns which beget them? These must not be treated in isolation. Policy must require concurrent attention to the sources, channels and multiple effects of infectious diseases. The sources are presumably social conditions giving rise to specific habits, for instance demographic and sociocultural forces. The unanticipated untoward impacts of several large-scale development projects in developing countries have shocked many economists and environmentalists [97,98]. Economic planners have to adapt to new patterns of reasoning for the effective handling of the complex interplay of issues. We need a future with in-depth adjustments in environmental and macroeconomic policies both domestically and globally to effectively manage these situations [99]. Research plans and priorities include [93]: (a) To strengthen basic and applied research on the pathogen, host, and environmental factors which influence emergence and re-emergence of disease; (b) application of the understanding of pathogen, host, and environmental interactions to develop and augment the ability to predict and prevent conditions which lead to plant, animal and human disease; (c) institutional and governmental support to develop diagnostics, vaccines, and therapies important for the detection and control infectious diseases; (d) to develop and supporting sequencing and post-genomics research of emerging and re-emerging as well as resistant infectious disease agents and animal vectors and elucidate genetic basis for microbial/vector evolutionary process, adaptation, and pathogenicity; (e) developing new strategies to control diseases which are re-emerging due to drug or insecticide resistance; (f) identify and develop better control strategies for intractable infectious diseases that continue to challenge global health; and (g) to develop and have maintained sustenance of domestic and global scientific acumen necessary to rapidly respond to presenting and future health threats through the support of research and training programs.

Policy makers, development aid agencies and concerned citizens hold more general types of social responsibility on behalf of the general public welfare to re prevent, retard or report incidences of infectious diseases together with cultural factors which promote them in any specific area. The remedy of sociocultural and health perturbations requires political action. In as much as the magnitude of the political intervention is likely to be controversial, the social and health concerns of the public must be a crucial responsibility of policy makers in lieu of monetary gains. In several instances, prevention of an untoward social and health outcome is achievable by behavioral change in the general public based on proper public education. Education of the public creates opportune expansive and domestically effective action. Research should be initiated and encouraged into the sociocultural, environmental and developmental impact of infectious diseases. Active research programs supported by government or other institutions in

these areas are virtually absent in developing economies and deteriorated societies. These and other traditional social and environmental health research need to be incorporated into public policy in both developed and developing countries [99] to inter alia regulate viral trafficking issues [100].

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