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Review

Enhanced surveillance and response approaches for pilgrims and local Saudi populations against emerging Nipah, Zika and Ebola viral diseases outbreaks threats

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SUMMARY

Increasing emergence and spread of Nipah, ZIKV and Ebola case and potential outbreaks threats have been reported in several regions around the globe. Yet, emerging Nipah, Ebola and Zika viral diseases outbreaks have been indirectly linked to substantially globalization of trade and travel, climate change and intense urbanization impact, healthcare and socioeconomic inequities as well in affected community settings. Although no case has been documented in Saudi Arabia, there is a great risk of sudden emergence of any of these viruses and others via introducing among pilgrims coming from endemic regions during ritual ceremonies of mass gatherings. Consequently, promoting and investing on new and sensitive proven effective and innovative surveillance and monitoring approaches, including enhanced risk communication, improved integrated vectors surveillance in addition to improved sustainable highly pathogenic surveillance control programs to human motility and environmental sanitation strategies all represent 'One Health' approach implementation strategic core. Initiation, development and implementation led by Saudi government and international stakeholders' of new partnership, coordinated response leadership and resource mobilization for multidisciplinary and intersectorial advocacy on emerging viral disease outbreaks, accompanied with R&D roadmap and taskforce is crucial. More efforts in epidemiological and laboratory early screening and surveillance of highly pathogenic germs/microbes, and confirmation of asymptomatic and syndromic cases amongst suspected Hajj and Umrah pilgrims, local vulnerable populations and expatriate workers is vital in generating reliable data and data sharing platform for timely risk communication and tourist information update, appropriate immunization campaigns or safe and efficacious care delivery implementation. Moreover, increase Hajj/Umrah mass gathering emergency outbreak preparedness, pilgrims health education and engagement outreach, pre-, during and post programs coverage and effectiveness is needed through One Health approach integration in attaining pilgrims and local population health safety and security, in advancing Saudi sustainable health development goals.

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Abbreviations: WHO, World Health Organization; PHEIC, Public Health Emergency of International Concern; AMR, Antimicrobial resistance; NiV, Nipah virus; HeV, henipavirus; R&D, Research and Development; ZIKV, Zika virus; EDV, Ebola virus.

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Introduction

Globalizing health challenges and health solutions are no longer a luxury but an urgency and joint venture of both developed and developing countries [1]. The growing interest and popularity around more collaborative and co-productive way of formulating evidence translation decision making policy and interventions about health problems affecting countries around the world, including emerging diseases with the potential to harm millions [1,2]. However, there is very scanty, coordinated and coherent local/national and internal evidence-based programs or projects based on the grouped specific health or disease epidemics nature, extend of threats and impacts. Quality evidence-based decisions and strategies are critical and valuable tools in strengthening health systems policies, strategic priorities action plans and comprehensive care delivery management [2]. However the occurrence and incidence of sporadic cases and sometimes cluster outbreaks of MERS-CoV, Influenza and Dengue to antimicrobial resistance been reported in most endemics countries worldwide including Saudi Arabia [1,2].

Ample and sustained investment in research and development preparedness is needed to detect, prevent and control potential dangerous virus in host or reservoir (bird, bat, monkey, rat, cattle, camels, etc.), environment and human being outbreaks and emerging pandemics threats pilgrims and citizenry protection, diseases prevention and control in Saudi Arabia and worldwide [1,2]. Early recognition and infectious case confirmation, rapid surveillance tracing and safety measures to case management interventions implementation are necessary for building quality data and database of viruses ecological and adaptation context for appropriate emergency protection and response measures. Strengthening strict local and nationwide infection prevention and control guidelines and measures implementation is core toward interruption of the virus transmission and containment likely to cause severe outbreaks in the near future. Building and maintaining new, proactive and productive partnerships and collaboration to public health needs and demands require new momentum and leadership commitments and investments efforts, which is currently poorly advocated and neglected by governments, policy-makers and programs implementers [1–3].

The paper provides an update of the trend of emerging Nipah, Ebola and Zika viral diseases outbreaks in affected countries in order to improve integrated robust and sustainable surveillance and monitoring systems, investing in context-specific research and development preparedness and rapid response approaches and tools for prevention and control guidelines and countermeasures amongst perennial pilgrims and local populations in Saudi Arabia.

Nipah virus (NiV) outbreak

The ongoing re-emerging Nipah virus (NiV) outbreak also called “mystery disease” led to 12 deaths including 3 laboratory confirmed cases, and over 25 suspected cases in Kerala, India [4]. Nipah virus causes severe disease in both humans and animals with reported

the fatality rate up to 40–75% in previous outbreaks. Nipah virus (NiV) is a newly emerging virus caused a zoonotic virus of the henipavirus (HeV) genus that is normally hosted by fruit bats (natural hosts of the virus) to other species, which gets transferred from animals to humans, and it causes severe disease in both animals as well as humans [5]. The natural host of the virus is fruit bats of the “Pteropodidae Family, Pteropus genus”. It is often carried by fruit bats to humans, infected bat secretions can also spread to domestic and wildlife animals notably pigs, human-to-human close contact with infected patients, blood or body fluid samples and contaminated raw food products and cause disease pathophysiology in vulnerable populations [5–7]. It was first identified during and reported a 1998 outbreak among pig farmers from Kampung Sungai Nipah in Malaysia and spread to Singapore with more than 100 deaths and nearly 300 human infected cases cumulatively [4–6,8]. Previous two reported NiV outbreaks in 2001 and 2007 outbreaks claimed 50 lives in India alone, whereas Bangladesh has borne the brunt of Nipah viral disease in recent years, with more than 100 deaths out of over 600 reported human cases between 1998 and 2015 since its first outbreak reported in 2001 [5,9–11]. The identified virus source in 2004 was reported from humans became infected with Nipah after eating date palm sap contaminated by infected fruit bats [5,12]. So far, no case has been reported in Saudi Arabia, although some studies have revealed the presence of trace or variable species in pilgrims pre and post Hajj and Umrah [9–11], but still no documented local case nationwide in Saudi Arabia.

Zika virus outbreak

Zika virus infection has emerged as a major public health issue in the Americas. Zika virus (ZIKV) is an emerging arbovirus of the Flaviviridae family and is related to dengue, Chikungunya, West Nile, yellow fever, and Japanese encephalitis viruses. Hajj is among the global travel gatherings, drawing between 2 and 3.5 million Muslims from 183 nations annually to perform pilgrimage in Mecca, Saudi Arabia [3]. The broad geographical range of the vector and the emerging complications of the ZIKV infection have made this flavivirus a growing global concern. This calls for constant epidemiological surveillance and a strategic response plan. Zika virus (ZIKV) is an emergent arthropod-borne flavivirus associated with neurologic complications [1]. The first reports of human disease were described in Uganda and Tanzania during an outbreak in 1952 [1,3,13]. On February 2016, the World Health Organization (WHO) declared Zika virus infection a Public Health Emergency of International Concern (PHEIC) due to the increasing number of cases and its associated complications. Currently, ZIKV is responsible for the ongoing outbreaks in the Caribbean and South America following the initial outbreak in Brazil [2]. The primary route of human ZIKV transmission is through the bite of mosquitoes *Aedes aegypti* and *Ae. Albopictus* in tropical and temperate regions [13–15]. ZIKV is also transmitted via transfusion of blood products, organ transplantation and congenitally, laboratory exposure, sexual and, vertical maternal–fetal transmission [16,17]. After an incubation period of 2–14days, patients develop an acute febrile syndrome asso-

ciated with unspecific symptoms such as headaches, arthralgia, pruritic rash, no purulent conjunctivitis, myalgia, anorexia, asthenia, dysesthesia and retro-orbital pain [1,15,17,18]. Despite the low frequency of fatalities and hospitalization due to severe disease, ZIKV infection is associated with a high frequency of neurologic complications such as congenital microcephaly and Guillain–Barre syndrome.

It has not yet been documented in highly endemic *Aedes* settings in Saudi Arabia, Africa and elsewhere and requires urgent investigations [19,20]. Although high throughput sequencing revealed the presence or circulation of flavivirus linked diseases in Saudi Arabia. ZIKV infection during pregnancy can cause a set of fetal developmental complications, known as the congenital Zika virus syndrome or complications particularly microcephaly in newborn babies with ZIKV infected pregnant mothers [18,20]. Along with this syndrome, ZIKV is also associated with a higher rate of pregnancy loss and stillbirths among infected women. Congenital ZIKV syndrome may include microcephaly, ventriculomegaly, intracranial calcifications, extra-axial fluid, decreased brain parenchymal volume, lissencephaly, cerebellar hypoplasia, impairment of normal brain development in the fetus, delayed myelination and hypoplasia of the corpus callosum [21–23]. Fetus to newborns of infected mothers can develop cardiac anomalies with septum defects, hearing loss, seizures due to the underlying brain malformations, neuromotor abnormalities such as spasticity and feeding difficulties and ocular abnormalities requires population-based screening and identification of asymptomatic infected or susceptible individuals [2,3,24,25].

Recognizing that the risk of vertical transmission and congenital ZIKV syndrome exists for both symptomatic and asymptomatic mothers or ZIKV exposure risk three times during pregnancy even if they are asymptomatic, ZIKV infection of pregnant women can also cause pregnancy losses and congenital malformations such as cardiac defects and craniosynostosis [16,18,26]. This may cause bias when estimating the risk of congenital ZIKV syndrome among women older than 35 years old, significantly increased risk of spontaneous abortion/stillbirth [18]. Moreover, the frequency of birth defects resulting from vertical transmission of ZIKV is not well established as the risk of developing the congenital ZIKV syndrome is higher during the first and second trimester, even though severe fetal or newborn sequelae can also occur within the third-trimester infection [3,18,21].

Ebola outbreak

The new and recurring Ebola virus outbreak in Ituri, Kivu and Bikoro communities in North-West, DR Congo has led to the declaration of national health emergency with over 1500 deaths from 8th May 2018 to date. Interestingly, nearly 141,000 people have been vaccinated in the affected eastern DRC provinces of Ituri and North Kivu, Epicenters. Humanitarian emergency responses and aid assistance have hampered by protracted violence and militia activity in Ituri and North Kivu as well as hostility local community to medical teams and Ebola vaccination resistance. Ebola virus infection is a highly contagious and severe infection that is directly or indirectly spread contact with infected bodily fluids or sexual intercourse may progress causing hemorrhagic bleeding and multiple organ failure [2,27]. The slow and late emergency response to the 2014 West Africa Ebola outbreak crisis (Guinea, Sierra Leone and Liberia) led to more than 11,325 deaths and 28,600 cases with immense socio-economic havoc alarm around the world in the impoverished West African countries [1,2,28]. The lack of remote and hard to reach community emergency preparedness and limited rapid response capacity may underscore the reduced return of immunization benefits to vulnerable communities from

the huge natural resources mining and exploitation documented over decades in DR Congo; This remains a regional and global public health and sanitary concern [1,2,29]. Timely and effective coordination and resource mobilization in providing and maintaining resilient logistics in frontline are urgent needed, in supporting the DR Congo Ministry of Health and related intersectorial stakeholders, to closely evaluate and monitor emergency operation's needs [27,28]. The DRC government together with WHO regional Office is taken all necessary measures to respond promptly and effectively to this new Ebola epidemic as \$1 million Emergency fund has been released coupled with 50 experts to work in tracking and safe EVD ring vaccine immunization program roll out in prevention and containment of further spread [28].

In Saudi Arabia, there has not reported case of imported and local Ebola virus in the Kingdom. Yet there is a high risk of transmission and spread of Ebola and other emerging diseases due to Hajj and Umrah pilgrims' residents from endemic settings, overcrowding and aged populations [30]. A recent study showed that healthcare providers (physicians and nurses) had sufficient knowledge, skills, and best practices about the etiology, mode of transmission, signs and symptoms, and treatment of EVD [29,31]. Hence, building robust and sustained surveillance (clinical and laboratory) capacity, strict standard infection control and precautionary measures adherence and implementation requires further strengthening coupled with regular hand sanitation and hygiene. Increasing sustained access to and use of personal protective equipment and community preparedness and participation at all levels for pilgrims and citizenry safety and wellbeing is crucial [28,32].

Major weaknesses and challenges of emerging and re-emerging Ebola virus outbreaks in most affected countries mainly in sub Saharan Africa include shortage of skilled health workforce and gross unpreparedness to prevent, detect and contain outbreaks of highly pathogenic nature at source. Frontline health workers were few, lacked skills and logistic support to handle infected cases, making them 21–30 times at higher risk of being infected than the general adult population⁶. Poor infrastructure impeded transport of cases and samples, while porous borders made cross-border contact tracing difficult [1,2,27–29]. Fear and superstition among affected populations, and lack of understanding community perceptions, customs and practices, impeded implementation of effective disease containment policies including safe burial practices [2]. More, lacking the 'One Health' approach creates poor linkage between the animal, wildlife and environmental health surveillance systems [29]. Therefore, routine information and alert warning signals do not exist and not share, delaying effective response coupled with limited or lack of financing of routine surveillance and preventive actions, also weak existing capacities to reactive response [2,29,33].

Strengthening community participation and provide training on syndromic surveillance for real time reporting, as well as integrating the animal and human health workers teams and building community trust pre, during and post public health emergency at local community and country and global levels [1,2,29,33]. Local and provincial financing targets through a public private partnership strengthening collaboration, coordination and linkage of disease prevention strategies and surveillance efforts among the environment, wildlife, domestic animals and human health sectors benefits, not only from the private sectors' resources, but also from their capacities and best practices [29,33–35]. This is pivotal to updating contingency plans, and strengthening preparedness and response capacities of the wildlife, domestic and human health systems for early risk detection and analysis of human and animal cases followed by prompt reporting to national health authorities, humanitarian organizations and the World Health Organization [1,2,35,36]. Intensifying community social mobilization, health education and awareness outreach in variety of social media

and local oral/mass media communication tools to foster robust community participation in all necessary emergency response strategies and measures to prevent and contain the deadly and contagious viruses (e.g. direct contact or indirect infected objects between humans and animals), while dispelling any fear, miscommunication and ill-perceptions through joined citizenry and governments engagement and responsibilities [1,2,28,33,35,36].

Moving forward

Although no case of recent emerging diseases threat has been reported in Saudi Arabia, rapid and coordinated leadership for resource mobilization and financing of (Hajj and Umrah) pilgrims and populations' maintenance of disease preventive capacities are behind these successes. Population -based surveillance and response implementation is needed against emerging viral diseases outbreaks. The coherent and sustainable emerging outbreak preparedness and response system development and establishment is core to increase awareness, re-enforcement of individual pilgrim and host community preventative and precautionary measures. Increasing advocacy on emerging viral disease R&D roadmap taskforce development and implementation of outbreaks countermeasures (diagnostics, therapeutics and vaccines) that are most needed by affected and prone countries through national and international multidisciplinary and intersectorial stakeholders' partnership is crucial to promote early diagnosis, timely treatment, and vaccination programs implementation. Strengthening routine diagnostic and surveillance port of entry and hospitals and community-health centers including private clinics and treatment standards best practice adherence in upholding infection emergence and spread prevention and control. The absence of accessible and available safe drug and vaccine, sensitive and point of care accurate diagnostic tools and timely safe drugs Nipah and Zika or Ebola remain a major challenge for scale mass administration and immunization programs in most endemic areas and worldwide. Implementing integrated "One Health" and AntiMicrobial Resistance (AMR) stewardship platforms and data sharing to coordinate multi-sectoral emerging pandemic threat collaboration and coordination at national level is a must opportunity to leverage their efforts, by institutionalizing key structures and capacity, and not a choice. It is still unclear and challenging to quantify and ascertain the spread and impact improvements in emerging epidemics and epidemics training, and to ensure the likelihood and sustainable development. and disbursement to prevent further spread, fast-track an understanding contextual risk factors, and contain the deadly remote rural and urban outbreak transmission dynamics and losses can be averted, prevent and contain through proven effective and innovative approaches, and sustainable strategies. In addition, community alertness and empowerment is needed to reduce and minimize contact with infected bats, pigs and raw food products which may have been contaminated sources and host reservoirs diversity. Likewise, comprehensive fruits bats/population migration, phylogenetic mapping of the global Ebola, Zika and NiV/HeV strains genetic variability and evolutionary data and enhanced capacity for data sharing and sequence data analysis for forecasting and modeling to support collaborative clinical research, including methods and standards.

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Competing interests

Author has no competing interest.

Authors' contributions

ET conceived the idea and conceptual framework. ET and AGED collected and analyzed the data. Authors revised and approved the final version.

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