The unprecedented magnitude of the 2017 dengue outbreak in Sri Lanka provides lessons for future mosquito-borne infection control and prevention

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6 authors, including:

Shahid Ali
University of Swat

Abdul Waheed Khan
Università degli Studi di Torino

Shahana Malik
Kyung Hee University

Saba Gul
The university of agriculture,peshawer pakistan

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Discussion paper

The unprecedented magnitude of the 2017 dengue outbreak in Sri Lanka provides lessons for future mosquito-borne infection control and prevention

Shahid Ali [a,1], Abdul Waheed Khan [b,*,1], Andrew W. Taylor-Robinson [c], Muhammad Adnan [d], Shahana Malik [d], Saba Gul [e]

[a] *Center for Biotechnology and Microbiology, University of Swat, Kanju, Pakistan*
[b] *Medical Genetics Unit, Department of Medicine and Surgery, University of Insubria, Varese, Italy*
[c] *School of Health, Medical & Applied Sciences, Central Queensland University, Brisbane, QLD, Australia*
[d] *Institute of Biotechnology and Genetic Engineering, The University of Agriculture, Peshawar, Pakistan*
[e] *Laboratory of Malaria Research, Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, Brazil*

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KEYWORDS
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Abstract *Background:* The outbreak of dengue during 2017 in Sri Lanka is the worst incidence of this mosquito-borne virus infection in the South Asian country since records began.
Methods: In this retrospective study, up to the end of December 2017 over 185,000 clinical cases were reported from all regions of the island nation.
Results: This crisis placed an overwhelming burden on Sri Lanka's public health system and also had a significant negative impact on its economy.
Conclusions: The unsurpassed level of morbidity and mortality has highlighted the pressing need for an effective operational plan to both manage the existing outbreak and to reduce the threat of a future episode of disease. This should involve an integrated nationwide program of vector surveillance and control, tertiary care of severely affected individuals and the implementation of measures to prevent future infectio ns, including widespread vaccination.

Highlights

- Since the start of 2017 Sri Lanka has been confronted by a devastating dengue outbreak.
- The outbreak has broken national records for morbidity from dengue infection.

* *Corresponding author.*
E-mail address: khan_ibge@yahoo.com (A.W. Khan).
[1] Share equal contribution.

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- An environment conducive to mosquito population growth is escalating the crisis.
- Establishment of an effective control strategy is a major public health need.

Introduction

Dengue is an arboviral infection of humans that often causes febrile illness and influenza-like symptoms as well as, in a minority of clinical cases, severe complications such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). In this century, dengue outbreaks have escalated enormously, posing serious hazards to public health and impacting significantly on the global economy. According to a recent estimate from the World Health Organization (WHO), over 70% of the world's dengue-vulnerable population lives in the Asia-Pacific region, thereby earmarking countries in this geographical location as the epicentre of dengue outbreaks [1].

The causative agent of dengue infection is Dengue virus (DENV), a member of the genus *Flavivirus* and family Flaviviridae. DENV has four authoritatively recognized antigenically distinct serotypes (DENV 1—4). The transmission of DENV is facilitated by vector mosquitoes of the day-biting *Aedes* genus. As the major invasive species that flourish in urban and peri-urban settings in tropical and subtropical climatic conditions *Aedes aegypti* and *Ae. albopictus* are the principal vectors of dengue transmission between humans [2].

The 2017 dengue outbreak

The Indian subcontinent is one of the major regions confronted with DENV infection every year. Since the start of year 2017, Sri Lanka is facing a fresh outbreak of DENV that is spreading across the island nation of 21 million people [3]. According to data released by the country's Ministry of Health, over 185,688 clinical cases have been notified from the start of the year till the end of December 2017 (Fig. 1). The level of morbidity is extremely high compared to figures for recent previous years (Fig. 2) [4]. Data related to the age group of infected individuals show that many of the patients are young people (Fig. 3) [5]. According to a report released by the WHO, the present outbreak is thought to be responsible for at least 250 fatalities [6].

Although Sri Lanka is endemic for DENV, a possible reason for the escalated morbidity and mortality in the 2017 outbreak may be a change in the virus strain, i.e. dengue serotype, which is acting as the etiological agent of disease [7]. The preliminary findings of the present outbreak indicate DENV-2 as the causative serotype [6]. According to reports, DENV-2 is not common in Sri Lanka and hitherto had been detected only infrequently over the preceding decade [7]. Therefore, local inhabitants may well lack exposure to, and hence not show immunity to, this serotype; indeed, those who have a history of previous dengue infection (due to a different serotype) might be more vulnerable to dengue-associated complications due to antibody-dependent enhancement of infection [8]. This phenomenon occurs when pre-existing antibodies present in a person's body from a primary DENV infection bind to an infecting DENV virion during a subsequent infection with a different dengue serotype. The antibodies from the primary infection cannot neutralize each virus particle. Instead, the antibody-virus complex attaches to Fcγ receptors on circulating monocytes. By so doing the antibodies inadvertently help virions to infect monocytes more efficiently. The outcome is an increase in the overall replication of the virus, leading to a higher viremia and a greater risk of severe dengue.

The disastrous floods that affected most of the island during 2017 [9], combined with the heavy monsoon rains that left behind standing water, created ample opportunities for mosquitoes to breed and therefore for the *Aedes* vector population to flourish [9]. Moreover, municipal authorities in Sri Lanka failed to tackle the rain-soaked heaps of garbage that built up as a result of floods and rains in urban and suburban areas, which worsened the situation still further [10]. As a consequence of the unprecedentedly high incidence of dengue infection in 2017 the already overstretched healthcare system of the country faced an overwhelming burden of clinical cases. Hence, due to limited or absent appropriate medical resources, lack of adequate health infrastructure and delay in delivery of mandatory services, an unexpectedly high death toll has resulted [11]. The greatest number of dengue-related mortalities has been recorded in Western province (128), followed sequentially in descending order by Eastern province (24), Sabaragamuwa province (22), Southern province (17), North Western province (15), Central province (15), North Central province (8), Uva province (5) and Northern province (2). Being the most intense outbreak of dengue in the history of Sri Lanka (Fig. 2), incidence of infection was not confined to a specific area, rather it spread actively to all major cities throughout the country (Fig. 1).

History of dengue in Sri Lanka

Dengue outbreaks in Sri Lanka date back to 1962, when DENV was identified for the first time [12]. It is evident from molecular genotyping of past outbreaks that all four serotypes of DENV have remained prevalent in the country to the present day (Table 1). Many outbreaks manifested as co-circulation of multiple serotypes. Record keeping reveals that DENV is highly endemic on the island. Among the various reasons that may facilitate the spread of infection, a combination of the island's conducive climatic conditions and the lack of an effective control strategy are notable.

Climate-related reasons for increased dengue incidence

In recent decades there has been a global surge in the number and extent of dengue outbreaks. According to the

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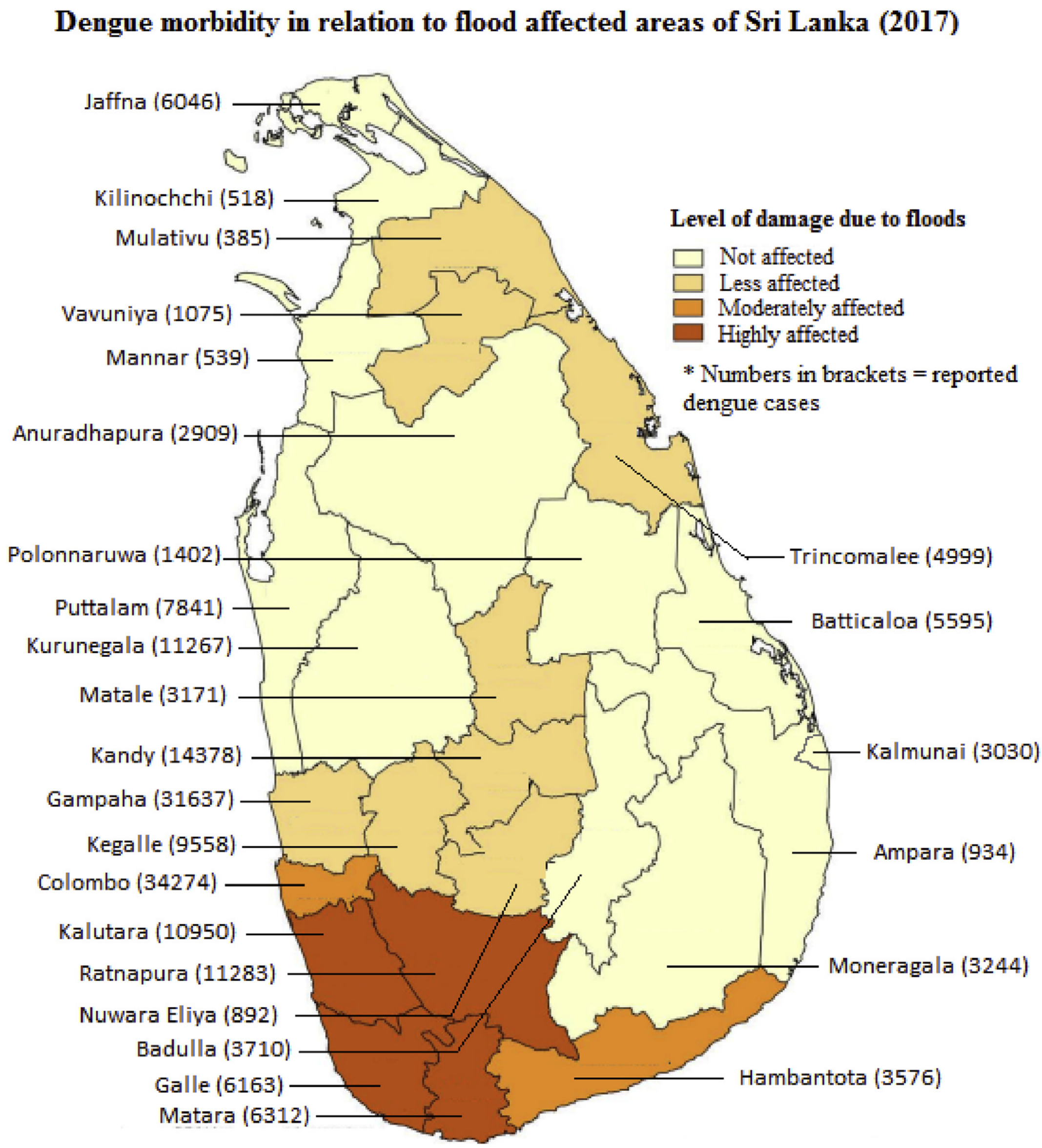

Figure 1 Map of Sri Lanka showing the incidence of clinical cases during the 2017 dengue outbreak [3] in relation to the distribution of flood-affected areas [9].

statistics of WHO, the global burden of dengue has increased for 2.2 million cases in 2010 to 3.2 million in 2015 [13]. The most probable factors that contribute toward this heightened incidence of infection include increased globalization, trade and travel, which together facilitate the dissemination of vector mosquitoes. Further, global warming and adaptation of the transmission vector to a range of environmental and climatic conditions have combined to enable the advance of dengue into areas which in the past remained free from dengue [2,12]. Global warming can prolong the disease transmission season, decrease the duration of the female mosquito's gonotrophic cycle and shorten the period required for ingested viruses to transform into infective stages inside the mosquito [14]. These factors aid the propagation efficiency of arboviral diseases, including dengue, that are spread by mosquitoes of the *Aedes* genus [14]. Ambient air temperature is crucial in regulating the seasonality of dengue outbreaks in sub-tropical and temperate regions, affecting vector distribution, vector blood feeding activity and DENV incubation period [15]. In addition, the availability of substantial water resources, primarily due to sufficient precipitation in the tropics and subtropics, best supports the propagation of vector mosquito species [12]. In the Indian subcontinent a rise in temperature during the northern hemisphere summer month, starting in May, is accompanied by increased precipitation due to the developing monsoon season that typically extends till the end of October. This drives an elevation in vector activity that consequently promotes a rise in dengue morbidity.

Measures for control and prevention

In the context of the 2017 outbreak in Sri Lanka, the escalation in clinical cases was observed to continue for several months. The favorable conditions on the island as a

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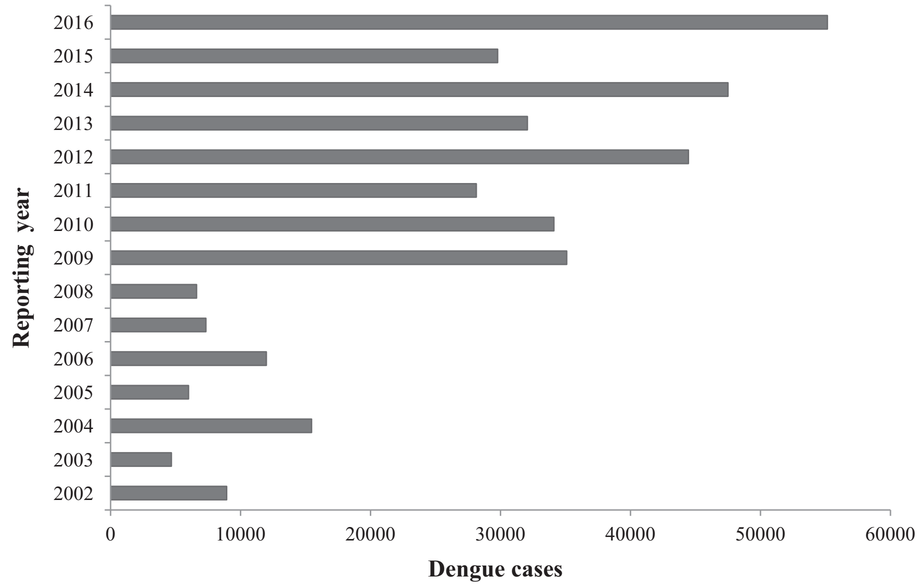

Figure 2 Total number of recorded dengue cases in Sri Lanka annually from 2002 to 2016 [4].

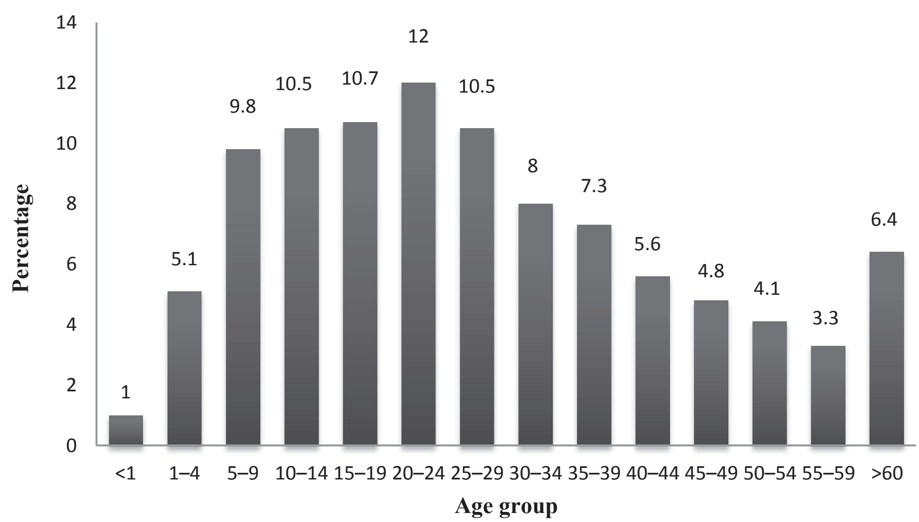

Figure 3 Distribution of 2017 Sri Lankan dengue outbreak-affected individuals on the basis of age [5].

result of floods and rains provided safe havens for the nurturing of vector mosquitoes. Hence, preventive measures should be considered as a public health priority. These include personal use of mosquito repellents and insecticide-impregnated safety nets, fumigation of houses and closely surrounding areas, and draining of water-filled ditches and other mosquito breeding sites incorporating the efficient disposal of household waste well away from residential areas. This is in furtherance of inhibiting the nurturing of mosquitoes, particularly the predominant dengue vector species *Ae. aegypti* that has a noted predilection for inhabiting household environments [2]. In order to safeguard against the prospect of future outbreaks an effective surveillance system that is equipped to monitor dengue vector activity is an urgent public health need.

Taking a holistic approach, it is imperative to devise consensus criteria on a global scale, not just individual countries such as Sri Lanka, which involve stake holders representing all currently affected and at-risk nations to address the issue of dengue control. The recently launched dengue vaccine Dengvaxia® is at present recommended for use only under certain conditions in endemic countries because of contra-indications that in all but the highest transmission settings vaccination may lead to an increase in the risk of hospitalization for dengue in seronegative recipients (those who have not been previously infected, typically young children) [16]. Hence, the present version of Dengvaxia® is not considered a general purpose vaccine for mass immunization [13,16]. The latest WHO position paper recommends it only for persons between ages 9–45 [16]. Made by Sanofi Pasteur, Dengvaxia® has been used in limited countries for anti-dengue immunization and Sri Lanka is reported to be among the list of nations that remain reluctant to administer the vaccine due to

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Table 1 Chronological identification of dengue serotypes circulating in Sri Lanka.

Reporting year	Dengue serotype	Reference
1965	DENV-1, DENV-2	[14,27]
1968	DENV-1, DENV-2	[14,27]
1978	DENV-4	[28]
1980	DENV (IIIA)	[29,30]
1990	DENV (IIIA)	[28–30]
1992	DENV-4	[28]
1993	DENV (IIIB)	[31]
1997	DENV (IIIB)	[31]
2003	DENV (IIIB), DENV-4	[28]
2004	DENV-1, DENV (IIIB), DENV-4	[28]
2006	DENV-1	[28]
2009	DENV-1	[32]
2017	DENV-2	[5,6]

apprehensions regarding its perceived low efficacy and possible side effects [17].

Challenges to control and prevention

A major hurdle to the robust tackling of future potential outbreaks of dengue in Sri Lanka is the lack of a highly effective vaccine. In fact, substantial numbers of susceptible individuals will already be affected by the ongoing outbreak by the time, if and when, a targeted reactive vaccination program is implemented. Furthermore, the phenomenon of antibody-dependent enhancement of DENV infection presents a hindrance to utilizing therapeutic antibodies as the basis of an alternative treatment [8]. As complimentary components of an integrated dengue control program, it is essential to promote vector control and surveillance alongside public vaccination schemes. This requires the cooperation of numerous stakeholders at local, regional and national levels.

Transforming global dengue control experience into the Sri Lankan scenario

Globally, the conventional chemical control strategies, especially the widespread use of the organophosphate larvicide temephos, have proved reasonably effective in treating mosquito-infested standing water. Various South East Asian nations including Cambodia, Malaysia and Thailand continue to apply temephos to successfully restrict the breeding of *Ae. aegypti* in water receptacles and storage tanks [18,19]. Nowadays, an emerging debate surrounds the introduction of innovative biological control technology involving the Gram-negative bacterium *Wolbachia* to reduce the virus-receptive capacity of *Aedes* mosquitoes and the onward transmission of DENV to healthy humans [20]. Along similar lines, OXI53A transgenic refractory *Ae. aegypti*, designed to reduce the population by passing a lethal gene to their offspring, are undergoing trials in a dengue-endemic location in Brazil [21]. Most recently, testing of the application of predaceous copepods in synergy with nanoscale-formulated biopesticides against *Ae. aegypti* larvae suggested substantial control of the larval population in response to the combined treatment [22]. Similarly, other innovative vector control strategies, discussed in detail previously [20], are under evaluation.

With the ongoing rapid advancement in information sciences and computer technology, many methods have been proposed for warning, surveillance and awareness regarding dengue outbreaks that may be applied specifically in a Sri Lankan context. One such method, called "Mo-Buzz", involves the utilization of mobile phones and the internet for the aforementioned purposes [23]. The Mo-Buzz surveillance and education system is comprised of three main components that focus on predictive surveillance, civic engagement and health communication. The predictive surveillance component uses computer software to alert health authorities, other official bodies and the general public about future outbreak threats. The civic engagement component provides a means of interaction between health authorities and the general public to utilize social media tools to assist in the surveillance process by reporting issues of potential concern, such as symptoms, mosquito bites and breeding sites, using smartphone technologies. The health communication component aims to exploit the useful information extracted from the data gathered from the first two components and to communicate appropriate health awareness alerts to promote safety and precautionary measures among citizens. Preliminary surveys have been carried out recently relating to the implementation and refinement of this system. One study [24], focused on the feedback of users regarding the suitability of Mo-Buzz, revealed that the predictive surveillance and civic engagement elements were highly appreciated by the general public, who perceived them to be useful. Similarly, two separate studies [25,26] were conducted to identify gaps in Mo-Buzz that could be useful in devising strategies to enhance and improve the system for better outcomes.

Overall, the positive outcome of pilot scale wet laboratory experiments [18–22] and the web based computer programs [25,26] against control of dengue infection is sufficient testimony to their effective implementation and points to their potential for extensive roll-out. Therefore, with the long term goal of eradication of dengue and other arboviral infections in mind the time is ripe to consider a multidisciplinary approach that involves a wide range of tools and methods to further develop dengue infection control strategies in harness with research on vaccine refinement. This combination plan is projected to play a critical role in curtailing the ongoing public health burden of DENV outbreaks such as that currently experienced in Sri Lanka.

Conclusion

The 2017 dengue outbreak in Sri Lanka was the greatest in the island's history. Record levels of morbidity and hundreds of deaths have been attributed to DENV infection. Following on from this, ongoing public health care is required urgently in order to prevent escalation into a full-scale humanitarian crisis. Consolidated measures for vector control and disease prevention should be imposed to

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reduce the risk, scale and impact of any future outbreaks of DENV in Sri Lanka.

Ethical considerations

Ethical approval was not required or obtained for this study.

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Authorship statement

All authors have made substantial contributions to the final version of the article. SA and AWK conceptualized the study. AWK and AWTR contributed significantly to writing the manuscript. AWK, SA, MA, SM and SG carried out data collection and analysis. AWK, AWTR and SG revised the manuscript. "AWK is PhD student enrolled in the Life Sciences and Biotechnology program of XXXIII cycle at the University of Insubria, Varese, Italy. All authors approved the final version".

Conflict of interest

The authors declare that they have no competing interest.

Provenance and peer review

Not commissioned; externally peer reviewed.

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