<u>Review</u>

Dengue control in Sri Lanka – challenges and prospects for improving current strategies

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Sri Lankan Journal of Infectious Diseases 2016 Vol.6 (1):2-16 DOI: http://dx.doi.org/10.4038/sljid.v6i1.8107

Abstract

Dengue is an acute viral or viral haemorrhagic fever caused by a flavivirus of four well-known serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Aedes aegypti and Aedes albopictus mosquitoes transmit DENV, which causes symptomatic dengue in some infected individuals and asymptomatic infection in others. Although Sri Lanka has been experiencing dengue outbreaks since 1960, the disease burden and severity has increased in the last two decades, contributing to significant morbidity and mortality in the island. Innovative strategic methods must be planned and implemented for effective dengue control, targeting dengue vectors via multiple methods. Some recent developments in vector control include the use of insecticide-treated long lasting mosquito nets, lethal ovitraps, spatial repellents, genetically modified mosquitoes and Wolbachia-infected Aedes. Some of these new methods might play an important role in the longterm prevention and control of dengue. The current review highlights the importance of pooling existing knowledge and resources to work on capacity building using all available human and financial resources to optimize the vector control programme. These efforts would facilitate and improve regional cooperation, foster networking and encourage sustainable co-ordination to retain effective control methods. Motivated staff working on vector control, prediction models such as geographic information systems (GIS) to detect future dengue outbreaks and coordination of control methods in risk areas within a country or implementing country-wide specific strategic control measures will be crucial to reduce the existing dengue burden.

Keywords: Capacity building, dengue control, environmental and climatic factors, integrated mosquito control

Introduction

Dengue is one of the rapidly spreading mosquito-borne viral infections throughout tropical and sub-tropical regions of the world. The cost associated with dengue fever (DF) is not only counted in the pain, suffering and deaths due to severe dengue, but also in the stringent disease management imposing a burden on developing economies of dengue endemic countries. The global incidence of dengue has increased more than 30-fold in the past 50 years and currently the disease is endemic in 128 countries, putting more than 2.05-3.74 billion people at risk.¹ At least

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Received 18 February 2016 and the revised version accepted 25 April 2016

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500,000 people a year are admitted to hospitals with severe dengue with a mortality rate of 25,000 every year.² Prevention of dengue using effective and sustainable vector control will contribute to reduce the disease burden and associated cost on developing economies in Asia and other dengue endemic regions in the world.

In the past, dengue control programmes focused on the following 3 aspects: ³

- 1. Surveillance for planning and response;
- 2. Reducing the disease burden;
- 3. Inculcating attitudinal changes in the public to improve and contribute to vector control efforts.

However, in recent times, strategic dengue control approaches have been revised. Current approaches focus on *A. aegypti* eradication using ultra-low volume insecticide application, regulation of air travel, development and use of dengue detection methods and vaccines.⁴

Although these newer approaches are used and encouraged in dengue endemic regions, some elements of older strategies such as inculcating attitudinal changes in the public arena to improve and contribute to vector control cannot be totally forgotten as these are major steps in societal contribution and ownership of disease control and are also being promoted for noncommunicable diseases.

A. aegypti and *A. albopictus* mosquitoes are the most important dengue vectors.⁵ *A. aegypti* originated in Africa but has established its existence worldwide in the last 5 decades.⁶ *A. albopictus* originated in South East Asia but in the past 30 years has spread to Africa and the Western hemisphere.⁷ Globalization, increasing urbanization and climate change are among the major factors favouring the expansion of these vectors and facilitating the spread of dengue.⁸

Progress has been made in many areas of dengue prevention and control, including better diagnostic facilities, improved clinical management, integrated vector control and ongoing vaccine trials.⁸ The advancement in the development and introduction of the dengue vaccines have, however, created hope for all those affected by dengue. The first dengue vaccine named Dengvaxia (CYD-TDV) was introduced late last year by Sanofi Pasteur's vaccine manufacturers in France. The vaccine was first registered for use in Mexico. Dengvaxia is a live recombinant tetravalent vaccine given in 3 doses to people between 9-45 years of age.^{9,10} This vaccine launch has allowed dengue to be considered a vaccine preventable disease if the vaccine produces immunity as expected. Clinical trials are planned to be started in Sri Lanka in late 2016 with Inviragen, a product of Takeda vaccine manufacturers, Japan.¹¹ Inviragen was developed by chimerization of DENV-2 and PDK53 virus and the resultant chimera attenuated by cell passaging in order to use the chimera as a vaccine.^{10,11} Although forthcoming vaccine trials have raised slight hopes on dengue prevention, growing loss of faith in the effectiveness of vector control is creating fear among the public. There is thus a need to develop new insecticides or develop 'strategic' vector control strategies, using existing knowledge on currently used tools and re-evaluate older strategies that have failed or are considered unsustainable.

This review is based on the global and Sri Lankan literature and databases on dengue and dengue control strategies. Overall, the current review discusses the importance of pooling existing

knowledge on various dengue control strategies as a means to incorporate certain elements of success in different countries to improve the existing control efforts in Sri Lanka.

Changes in dengue risks and integrated vector control in Sri Lanka

Sri Lanka is a tropical country with two monsoons, the northeast monsoon (December to March) and the southwest monsoon (May-September). The average annual temperature for the country ranges from 28 to 30 °C. Humidity in Sri Lanka ranges from 60%-90% during different seasons and in the different regions of the country.¹² Two annual peaks have been identified in the occurrence of dengue cases in the country in association with the monsoon rains (Figure 1). The first peak occurs in May/July that coincides with the south-western monsoon which commences in late April. The second peak occurs at the end of the year and is associated with the north-eastern monsoon rains that prevail from December-March.¹³ Sri Lanka has been experiencing dengue outbreaks of varying magnitude since 1960 with a massive outbreak in 2009/2010.¹⁴ In 2014, 47502 clinically diagnosed dengue cases were reported to the Epidemiology Unit of Sri Lanka. At present DF and dengue haemorrhagic fever (DHF) are a big economic burden on the country⁷ and the number of DF/DHF cases are increasing every year (Figure 1).^{13,15,16}

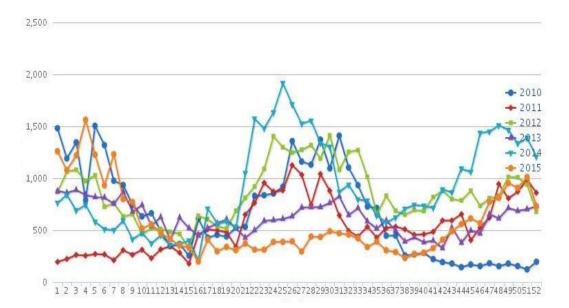


Figure 1. Distribution of DF/DHF cases in Sri Lanka from 2010-2015. The Figure was adapted using data from the Epidemiology Unit, Ministry of Healthcare and Nutrition.

All four DENV serotypes have been circulating in the country for several decades and the *Aedes* vectors are also well established in the island.¹⁴ In the 1965 to 1968 outbreaks, DENV-1 and DENV-2 serotypes dominated in the country.¹⁷ However, the 1978 epidemic was due to DENV-4.¹⁸ From 1980 to 1990, DENV-3 (IIIA) dominated^{18,19} and in 1992, DENV-4 reappeared.¹⁸ Subsequently, from 1993 to 1997, DENV-3 (IIIB) dominated. In 2003, both DENV-3 (IIIB) and DENV-4 dominated. However, the serotypic trend of DENV changed in 2004 and DENV-1 started to appear with DENV-3 (IIIB)²⁰ and DENV-4. In the 2006, 2009 and 2010 outbreaks, DENV-1 was the dominant serotype.^{18,21} From 2011-2015, DENV-1 and DENV-4 have been the

most common serotypes circulating in the Western (Sirisena and Noordeen Unpublished data; Tissera Unpublished data), Central²² and Northern (Muruganathan and Noordeen Unpublished data) Provinces of Sri Lanka. Moreover, mixed infections of two or more DENV serotypes were also detected in DF/DHF patients in these provinces (Sirisena, Senaratne, Murugananthan and Noordeen Unpublished data).

Despite the extensive vector control efforts, dengue outbreaks continue to occur in the island. The risk increases with time and outbreaks occur due to increasing population density, changes in rainfall and abundance of vector breeding habitats.^{23,24} Moreover, increase in the incidence of dengue continues with large-scale agriculture and improperly managed wastewater and solid disposal systems in most of the dengue endemic world including Sri Lanka.⁸ The Sri Lankan government uses integrated vector control strategies including environmental management, biological control, chemical control and use of personal protection methods in order to reduce the dengue burden.²⁵

Environmental management measures

Environmental approaches for dengue control in Sri Lanka include environmental management, modification and manipulation.²⁵ Environmental management methods include minimizing vector breeding and/or vector destruction. Environmental modifications include long lasting physical transformation of vector habitats, such as proper waste disposal and removal systems in cities, townships and suburbs. Environmental manipulation includes facing-down water storage containers, using mosquito proof overhead tanks and gutters and properly designed cisterns and any other underground water reservoirs. In general, environmental management, modification and manipulation for effective vector control without harming or producing residual deleterious effects to the ecology and such methods would include avoiding mosquito human contact by vector proofing windows in tropical houses with screens on doors and windows.²⁵

Biological vector control

Biological vector control uses predators, parasites or pathogens to reduce mosquito larvae and is often combined with environmental management.

Predatory copepods (Copepoda: Cyclopoidea), small fresh water crustaceans, have proved effective in specific container habitats.²⁵ Larvivorous fish species used for dengue mosquito larval control are top minnow or 'Nalahandaya''(*Aplocheilus* species) which are efficient in clean water, Guppy (*Poecilia reticulata*), which can be used successfully even in organically polluted water and Tilapia species (*Orechromis mossambicus* and *O. nilotius*), juvenile stages of which are highly voracious and very effective in larval control.²⁵ *Toxorhynchites splendens* has been found in Sri Lanka, the larvae of which suppress *A. aegypti* and *A. albopictus* larvae when they are in the same breeding containers (MRI Unpublished data).

Entomopathogenic bacilli, *Bacillus thuringiensis var israelensis* and *B. sphaericus* are considered the most potent organisms to be used in field control programmes.²⁶ The former has been used in Sri Lanka as a larvicide in the Western Province of Sri Lanka. However, no reports are available on the outcomes of these field control programmes.

Chemical vector control methods

Chemical dengue vector control includes indoor and outdoor spraying with insecticides and displaying larvicide treated ovi-traps in most dengue endemic countries.⁸ Dichloro-diphenyl-trichloroethane (DDT) was one of the first chemical control measures used to target adult stages of *Aedes* mosquitoes. DDT spraying reduced the vector populations significantly, but resistance to DDT was one of the key factors that contributed to the re-emergence of dengue since the 1960s.²⁷ To control the adult stages of *Aedes*, insecticides such as oil and sulfur fumigation are used in some countries. However, the most frequently used chemicals have been formulations containing temephos, malathion, fenitrothion and pyrethroids.²⁸ Temephos was used for treating water containers targeting the larval/pupal stages. Malathion and fenitrothion were used for indoor and outdoor spraying targeting the adults.²⁶ Pyriproxyfen, an insect juvenile-hormone analogue, sub-lethally affecting adult mosquitoes by decreasing fecundity or fertility has also been introduced in certain countries.¹⁴ Pyriproxyfen contaminated adult females can transfer effective doses of this hormone analogue to any breeding site she subsequently visits.²⁶

Insecticide-treated materials have proven effective in preventing diseases transmitted by nocturnally active mosquitoes and the effects of these are being tested against *A. aegypti.*²⁹ Trials in Latin America show the impact of insecticide-treated window curtains and/or insecticide-treated domestic-water container covers in reducing *A. aegypti.*²⁹

The insecticide-treated ovi-trap or ovi-position trap was first recommended by WHO for surveillance of *Aedes* vectors and then to kill adults or larvae. Lethal ovi-traps with deltamethrin-treated ovi-strips killed 89% of *A. aegypti* adults and were shown to produce more than 99% larval mortality during a one month trial in Brazil.³⁰

New knowledge on vector control used by other countries

Several new biological vector control principles have been developed in the recent past using different biological agents such as densoviruses. These could be developed as biological control agents against *A. aegypti* larvae,³¹ by releasing insects carrying dominant lethal mutations (RIDL) designed to reduce or eliminate mosquito populations infected with DENV.^{32,33} Moreover, synthetic transposable elements aim to modify vector populations by introgression of genes that remove vector competence.^{34,35,36}

Another strategy has been to infect *Aedes* with a bacterium – *Wolbachia* which prevents the replication of the DENV in mosquito tissues, reduces egg production and possibly prevents the eggs from hatching.³⁷ Release of *Wolbachia* infected mosquitoes to areas with dengue transmission could reduce the ability of the vectors to transmit DENV and *Wolbachia* based dengue control systems are being studied. However, there are concerns that, mosquitoes could become resistant to a particular strain of *Wolbachia* by increasing the effective dose or restricting tissue distribution of *Wolbachia*. Field trials on this mode of control are under way in Vietnam.³⁷ However, *Aedes* vectors may evade *Wolbachia*-based control with time.¹⁴

New studies indicate a high efficacy of pyriproxyfen, an insect juvenile-hormone analogue, for effective dengue control.²⁶ However, these developments need safety assurance and evidence of effective control for implementation.

Loopholes in the current vector control programmes

Despite actions taken by most countries, many factors, including failure to collect waste by local bodies, have led to the breeding of mosquitoes. A study done in the northern part of Sri Lanka shows the breeding of *Aedes* mosquitoes in polluted and brackish water which complicates vector control efforts in island nations like Sri Lanka.³⁸ Fumigation of insecticide only during an outbreak and the inability to sustain vector control throughout the year is another drawback. Conversely, failure to harness public support has always been an impediment for effective vector control in many townships and villages. Many Asian, African and Latin American countries store rain water because of the unreliable water supply and/or distaste of the tap water. In Vietnam, the contribution of poorly designed water tanks to *A. aegypti* proliferation is a well recognized fact.³⁹ In addition, some villagers prefer to use uncovered water containers and at times the state funded supplies become insufficient to cover all outdoor containers.

In Sri Lanka, most of the urban councils use cost-recovery basis for water consumption through meter controlled water supplies. Collection and storage of rain water as a roof catchment has become a cheaper alternative to obtain water and this has caused continued use of storage containers which provide breeding habitats for mosquitoes.²⁵ Traditional water storage, either from a common well or rain also continues in certain parts of the country even when reliable piped water is available for consumption. Thus it would be necessary to educate public through effective communications using local paper based and broadcasting media to discourage traditional water storage practices that provide breeding conditions for *Aedes* vectors.

Challenges in implementing/sustaining effective vector control

A key challenge in the control of *A. aegypti* is identifying and treating the diverse breeding sites such as natural and artificial containers. *A. aegypti* can also breed in small gaps between the lid and the base of the cement jars covered with incompatible aluminum lids which allows the authorities to miss hidden breeding places.²⁵

Chemical control is restricted due to its potential toxicity, death of non-target organisms, insecticide resistance and other environmental impacts.³⁹

Biological control methods also have their fair share of problems. The life cycle of the predators needs to be well adopted or fitted harmoniously with the requirement of the prey. Hence, mass rearing and release of the predators or parasites is expensive and difficult to practice.

Although awareness on dengue prevention is universal, various challenges still remain unanswered. Inadequate funding, limited resources, particularly in the villages and some suburban areas and the lack of an implementable and sustainable strategy to respond to the problem in an expanding geography of dengue are continuing problems faced by the authorities despite the many efforts made in the past.

Feasible methods for dengue control in resource limited settings

Integrated vector control is a combination of chemical, biological and environmental means to reduce or eliminate vectors (Figure 2).

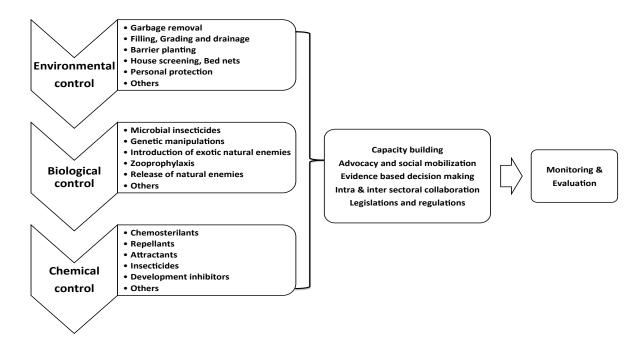


Figure 2. Proposed integrated vector control approach.

Source reduction by elimination of breeding places and chemical and biological control must be carried out objectively in conjunction with vector surveillance indices.^{11,24} It is important to have a pre-planned response strategy by governments through environmental management and other technologies for larval and adult *Aedes* control using novel insecticides and repellents during an outbreak.

In order to reduce larval habitats, regular street cleaning systems must be in place to remove discarded water-bearing and dry containers. Cleaning drains must be done regularly to avoid water stagnation to prevent *Aedes* breeding in all townships.

Encouraging the community to use proper waste disposal systems plays a major role in vector control. Containers that can be recycled for profit in small and large-scale businesses need to be promoted. As accumulation of waste creates breeding habitats for the vector mosquitoes, active promotion of the use of proper solid waste disposal systems and using waste for compost making is a profitable way to handle the household organic waste and to control vector breeding.

Publicity should be given to methods which provide personal protection. These include the use of mosquito protective screens on doors, windows and other openings in houses, application of mosquito repellents and the use of anti-mosquito coils and mats. The latter are among the most

popular and widely used insecticide vaporizers because they are easy to use and not very expensive. Light coloured thick clothing can offer additional protection from mosquito bites. All such feasible measures should be encouraged.⁴⁰

Vector surveillance must be an essential step in planning, monitoring and evaluation of control methods. Regular surveys are also necessary for studying the ecology and distribution of vectors as well as to predict outbreaks. Since vector density has a positive correlation with climatic factors,¹⁴ it is necessary to forecast future outbreaks in relation to local climate and vector density patterns. Hence, incorporation of rainfall and entomological data would help to predict future outbreaks and map high-risk areas for effective control. With the help of resource rich countries, resource limited countries can make biophysical models of climate–animal interactions to make decisions in relation to climate change and vector control.⁴¹ Biological vector control methods such as use of predators, parasites or bacteria are feasible for resource poor countries. On the other hand, multi-level human involvement especially through sociological approaches must be incorporated to the existing vector control strategies in Sri Lanka for better outcomes.

Transfer of knowledge and capacity building at various levels

Organization of vector control

Singapore has achieved success in vector control. The main elements of their control programme include virus surveillance and characterization, risk analysis, preventive checks before local periods of peak transmission, encouraging greater community participation and increasing resources for control and community education.⁴²

Although very well planned systems are in place in Sri Lanka, strong intra and inter-sectoral collaborations and continuous monitoring and evaluations require to be strengthened. To resolve this issue, in 2010, a Presidential Task Force was initiated to strengthen multi-sectoral collaboration and implementation of strategies to control dengue at the national, provincial and district levels, including regular removal of possible mosquito breeding sites from the environment which resulted in reduction of mosquito breeding sites and thus reduction in mortality and morbidity in 2013 and 2015.

In 2014, six sub-committees comprising of experts in clinical management, vector control, virology and vaccine development, social mobilization, legislative enactments and co-ordination of research on DF/DHF were established in Sri Lanka. This initiative is now showing some promising results. Due to the collective efforts made by all these parties, Sri Lanka has achieved a greater success with less number of DF/DHF cases and reduced mortality in 2015.

Workers in dengue control teams are well trained due to ongoing educational programmes and training in certain provinces of the country. There is, however, a need to build and strengthen capacities of employees working on vector control with limited training and expertise in the country. Trained workers can be used to transfer knowledge and expertise in a planned manner to improve worker capacity on the task throughout the country.

Designing houses without gutters was included in the legislation on prevention of mosquito breeding in Sri Lanka in 2007.²⁵ Examining and monitoring the houses built after this legislation in 2007 for the requirements to eliminate mosquito breeding is not in place. Thus a special team has to be appointed to examine the new plans for special requirements and post-building examination and these will help to implement the 2007 legislation to facilitate vector control.

Mobilization of the community for vector control

Social mobilization and communication have increased awareness and improved practices by the public on vector control. The success of such measures depends on the support and motivation of staff and volunteers, accurate applications of chemicals and having early case warning systems in place.⁴³ Wherever the vector control efforts have worked, intensive community engagement has been identified as an integral component for success and thus community awareness, education and support must be made as the key elements in sustainable multi-sectoral vector control efforts through knowledge transfer in Sri Lanka

Indonesia has started moves on promoting changes in human behaviour to revitalize the National Working Group on Dengue by having programmes in partnerships with the educational sector to create and strengthen political commitment, which helps the country to achieve new targets in vector control.⁴⁴ Cambodian community and school-based education on the negative impact of dengue on their developing economy shows reductions in the number of breeding sites.⁴³

Similar methods have been implemented in Sri Lanka by establishing the National Dengue Control Unit in 2005. Mosquito larvae surveillance programmes are carried out by the National Dengue Control Unit, Anti-Malaria and Anti-Filariasis Campaigns and the Medical Research Institute with the help of the Regional Medical Officer or Entomologist. Currently, 107 entomological teams are deployed for entomological surveillance at central and district levels and these teams are responsible for planning, implementation, monitoring and evaluation of entomological surveillance.¹⁷

In order to sustain a successful vector control programme, it is essential to focus on the involvement of hospitals, non-health sector departments including schools/colleges or municipal councils of local governments, local religious bodies, non-governmental organizations (NGO) and local health clubs and nature societies.² These groups should be provided with information on all aspects of DF including the role of the vectors in disease transmission, common vector breeding/resting sites and the methods of control. Moreover, the groups must work together with local vector control authorities to maximize the control efforts.

A government implemented control programme targeting housewives, school principals, teachers and traders was also introduced under social mobilization to enhance the community participation for sustainable DF/DHF control and prevention is also showing good results.⁴⁵

Public and social media could be used to effectively transfer information and mobilize the community for vector control efforts.

Sri Lanka is a highly literate country among other Asian countries, having a literacy rate of over $95.6 \ \%^{46}$, a positive feature to educate and encourage the public to gain knowledge on vector

control to reduce the dengue burden. However, certain attitudinal and cultural factors can derange vector control through non-acceptance of control strategies by certain members of the community. Resistance to change their normal practices by local residents when chemical or biological control methods are introduced to water sources is an impediment to control efforts.

Some of the major drawbacks for vector control require improvements in housing, waste disposal and management of public spaces. Living in semi-permanent (17.6%) and improvised houses $(0.7\%)^{46}$, modifications of both private and public building designs to reduce vector breeding sites and rapid repair of property including drains to minimize entry of mosquitoes require both community and individual effort. Similarly, improved waste management is a major priority which needs national and local authority inputs and community collaboration. Solid waste disposal in the country is still unsatisfactory with ~ 46.9% of households burning waste, disposal within the premises by 23.5% and composting by 7.8%. Thus only 20.4% of the solid waste is being collected by the authorities.⁴⁶

Special campaigns through mass media including local vernacular newspapers, magazines, radio and TV, especially using local cable networks as well as outdoor publicity like hoardings, drum beating, forum theatres and rallies in villages to educate the people may be useful to effect such changes.

Health education materials should be developed and disseminated in the form of posters, pamphlets, handbills and hoardings. Inter-personal communication through group meetings, traditional or folk media could be organized in villages and townships to suit the local preferences.

Figure 2 provides a framework summarizing an integration of all the possible measures available for vector control.

Vector and virus epidemiology

Data on vector and virus epidemiology will help to make accurate predictions on vector activity and disease outbreaks. Most importantly, the ability of well-resourced and functioning public health services to counter outbreaks need recognition and emphasis, not only to help produce more practical models, but also to provide evidence to support initiatives to control the disease in areas where the morbidity and mortality are high.

Conducting ongoing mosquito larvae surveillance and evaluation of larval populations that produce mosquitoes capable of migrating into populated areas will also be helpful in dengue control. Continuous evaluation of dengue transmission dynamics, vector adaptability and insecticide resistance is required, with regular monitoring of data from mosquito traps, taking action on complaints and reports from the public to correlate with seasonal records on climatic data, all of which will assist the evaluation of current and future trends.²⁵ Together with these new approaches, monitoring larval and adult mosquito distribution, accurately identifying, mapping and monitoring areas that might facilitate breeding of mosquitoes will have to be made part of an accelerated control effort.

Another important tool in dengue epidemiological surveillance is to monitor virus activity and genetic changes in DENV types and strains, which in turn has been demonstrated to be an important factor in determining the magnitude and severity of epidemics. Over the years DENV serotypes have been evolving in the country¹⁴ and little is known about the mutations and the new strains responsible for continuous outbreaks. Investments should aim to strengthen the technical and operational capability of health services and laboratories that conduct DENV-vector research to expand the existing knowledge in the area.¹¹ Monitoring DENV infection levels using sero-prevalence data in the adult Sri Lankan population may help avoid massive outbreaks in the future.

An interesting dilemma was faced by Singapore when the country faced a massive dengue outbreak in 2013/2014. It is believed that low exposure rate to DENV in the population had led to this outbreak. The possibility that populations with low exposure rate are more susceptible has been pointed to the importance of sustaining vector control.⁴⁷

More research is needed to develop novel effective methods to eliminate vector eggs and winged forms and to remove more sensitive entomological risk indicators like plants with water holding leaves, cracks and crevices that can hold water and mass collections of small plastic containers and discarded automobile tyres.

Comprehensive research on different areas of vector biology, entomology, virology, chemical ecology and specific epidemiology of dengue as shown in Figure 3 in Sri Lanka is needed to control and sustain vector control efforts.

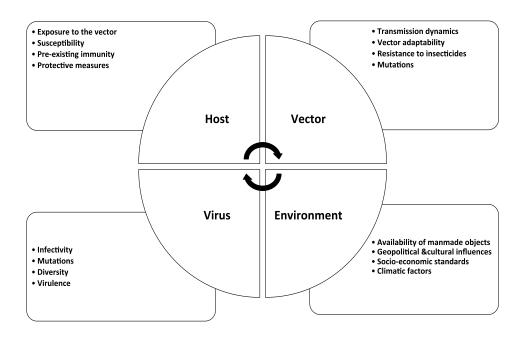


Figure 3. Host, vector, virus and environmental factors for effective dengue control.

Conclusion

Currently prevention of dengue is mainly based on vector control in Sri Lanka, although initiatives have been taken to start the vaccine trials. Vector control strategies show variable success in different areas of the country and thus policy makers await effective and sustainable alternatives. Community participation plays a major role in sustaining control measures. Comprehensive approaches including surveillance and integrated management of the *Aedes* mosquitoes through biological and chemical control measures that are safe, cost effective and gained success regionally or globally must be implemented step by step. Environmental management, legislations and action at community levels will help to minimize the dengue burden on developing economies like Sri Lanka. Overall, various parties acting together using the pooled knowledge will determine the effectiveness of future control efforts by contributing positively to the existing dengue control methods in the country.

Acknowledgments

We would like to acknowledge the National Research Council of Sri Lanka for funding through a startup grant, RG/NRC/11/129 to Dr. F. Noordeen.

Ethics

This review on dengue control is written by pooling the existing knowledge from the literature and databases. The publication therefore does not require ethical approval.

References

- 1. Brady OJ., Gething PW., Bhatt S., et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. *PLoS Negl Trop Dis* 2012; 6:e1760. *http://dx.doi.org/10.1371/journal.pntd.0001760*
- 2. WHO Dengue and severe dengue, Fact sheet. URL:http://www.who.int/mediacentre/factsheets/fs117/en/
- 3. Gubler DJ., Meltzer M. Impact of dengue/dengue hemorrhagic fever on the developing world. *Adv. Virus Res* 1999; 53:35-70. *http://dx.doi.org/10.1016/S0065-3527(08)60342-5*
- 4. CDC Prevention guidelines database (Archive).URL:http://wonder.cdc.gov/wonder/prevguid/p0000010/p0000010.asp#head00100200 0000000
- 5. Watts DM., Burke DS., Harrison BA., et al. Effect of temperature on the vector efficiency of *Aedes aegypti* for dengue 2 virus. *Am J Trop Med Hyg*1987; 36(1):143-52. *No doi*
- 6. Rodhain F., Rosen L. Mosquito vectors and dengue virus-vector relationships. In dengue and dengue hemorrhagic fever. Edited by Gubler DJ, Kuno G. Cambridge, MA: *CABI Publishing*, 1997
- 7. MG Guzman., SB Halstead., HArtsob., et al. Dengue: a continuing global threat. *Nature Reviews Microbiology* 2010; 8:S7-S16. *http://dx.doi.org/10.1038/nrmicro2460*
- 8. Global strategy for dengue prevention and control 2012-2020. URL:*http://apps.who.int/iris/bitstream/10665/75303/1/9789241504034_eng.pdf?ua=1*
- 9. World Health Organization- Dengue vaccine research, 2015. URL:http://www.who.int/immunization/research/development/dengue_vaccines/en/

- 10. Subedi D., Taylor-Robinson AW. Development of a dengue vaccine in humans: So near, yet so far. *SOJ Vaccine Res* 2015; 1(1):7. *No doi*.
- 11. Epidemiology Unit, Sri Lanka 2016. Dengue to stem the tide. URL:http://conference.epid.gov.lk/images/Abstract_Book/Dengue_Conference_Book2016.pdf
- 12. Meteorology Data, Department of Meteorology, Sri Lanka. URL:http://www.meteo.gov.lk/index.php?option=com_content&view=article&id=13&Itemid=13 2&lang=en.
- 13. Epidemiology Data. Epidemiology Unit, Ministry of Healthcare and Nutrition, Sri Lanka. URL:http://www.dengue.health.gov.lk/index.php/information-on-dengue,
- 14. Sirisena PDNN., Noordeen F. Evolution of dengue in Sri Lanka-changes in the virus, vector, and climate. *Int J of Infect Dis* 2014; 19:6-12. *http://dx.doi.org/10.1016/j.ijid.2013.10.012*
- 15. Manouri PS., Sankha SKJ., Dishni SW., et al. Economic cost of hospitalized non-fatal paediatric dengue at the Lady Ridgeway Hospital for Children in Sri Lanka. *Sri Lankan J of Child Health* 2014; 43(4), 205-207. *http://dx.doi.org/10.4038/sljch.v43i4.7762*
- 16. The dilemma of dengue and the health economics of it. URL:http://www.ft.lk/2014/08/18/the-dilemma-of-dengue-and-the-health-economics-ofit/#sthash.QCR3LIHw.dpuf
- 17. Vitarana T., Jayakuru WS. Historical account to dengue haemorrhagic fever in Sri Lanka. WHO/SEARO. *Dengue Bull.* 1997; 21:117-118. *No doi*
- 18. Kanakaratne N., Wahala MP., Messer WB., et al. Severe dengue epidemics in Sri Lanka 2003-2006. *Emerg Infect Dis* 2009; 15:192-199. *http://dx.doi.org/10.3201/eid1502.080926*
- 19. Messer WB., Vitarana UT., Sivananthan K., et al. Epidemiology of dengue in Sri Lanka before and after the emergence ofepidemic dengue hemorrhagic fever. *Am J Trop Med Hyg* 2002; 66:765-773. *No doi*
- 20. Malavige GN., Fernando S., Aaskov J., et al. Sero-prevalence of anti-dengue virus antibodies in children in the Colombo District, Sri Lanka. *Dengue Bull* 2006; 30:68-71. *No doi*
- 21. Tissera HA., Ooi EE., Gubler DJ., et al. New dengue virus type 1 genotype in Colombo, Sri Lanka. *Emerg Infect Dis* 2011; 17:2053-2055. *http://dx.doi.org/10.3201/eid1711.101893*
- 22. Senaratne T., Wimalaratne H., Alahakoon DGS., et al. Characterization of dengue virus infection in a sample of patients suggests unique clinical, immunological and virological profiles that impact on the diagnosis of dengue and dengue hemorrahagic fever. *J Med Virol* 2016; 1-7. *http://dx.doi.org/10.1002/jmv.24525*
- 23. Wai KT., ArunachalamN., Tana S., et al. Estimating dengue vector abundance in the wet and dry season: implications for targeted vector control in urban and peri-urban Asia. *Pathog Glob Health* 2012; 106 (8): 436-445. *http://dx.doi.org/10.1179/2047773212Y.000000063*.
- 24. Weeraratne TC., Perera MDB., Mansoor MACM, et al. Prevalence and breeding habitats of the dengue vectors *Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae) in the semi-urban areas of two different climatic zones in Sri Lanka. *Inter J of Trop Insect Science* 2013; (4):1-11. *http://dx.doi.org/10.1017/S174275841300026X*.
- 25. Epidemiology Data. Epidemiology Unit, Sri Lanka. URL:http://www.dengue.health.gov.lk/index.php/activities-services-eng/integrated-vectormanagement
- 26. Gammon K., Jones GW., Hope SJ. Conjugal transfer of toxin-coding megaplasmid from *Bacillus thuringiensis* subs. *israelensis* to mosquitocidal strains of *Bacillus sphaericus*.

Appl Environ Micro 2006; 72:1766-1770. *http://dx.doi.org/10.1128/AEM.72.3.1766-1770.2006.*

- Endersby NM., Hoffmann AA. Effect of Wolbachia on insecticide susceptibility in lines of Aedes aegypti. Bull of Entomol Res 2013; 103:269-277. http://dx.doi.org/10.1017/S0007485312000673
- Dorta DM., Vasuki V., Rajave A. Evaluation of organophosphorus and synthetic pyrethroid insecticides against six vector mosquitoe species. *Rev. Saúde Pública* 1993; 27 (6):391-7. *http://dx.doi.org/10.1590/S0034-89101993000600001*
- 29. Kroeger., Lenhart A., Ochoa M., et al. Effective dengue vector control with curtains and water container covers treated with insecticide in Mexico and Venezuela: cluster randomized trials. *BMJ*2006; 332:1247-1250. *http://dx.doi.org/10.1136/bmj.332.7552.1247*
- 30. Zeichner BC., Perich MJ. Laboratory testing of a lethal ovitrap for Aedes aegypti. Medical and Vet Ento1999;13:234-238. http://dx.doi.org/10.1046/j.1365-2915.1999.00192.x
- 31. Buchatsky LP. Densonucleosis of bloodsucking mosquitoes. *Dis Aquat Organ* 1989; 6:145-150. *http://dx.doi.org/10.3354/dao006145*
- Heinrich JC., Scott MJ. A repressible female-specific lethal genetic system for making transgenic insect strains suitable for a sterile-release program. *PNAS* 2000; 97(15):8229-8232. http://dx.doi.org/10.1073/pnas.140142697
- 33. Horn C., Wimmer EA. A versatile vector set for animal transgenesis. *Dev Genes Evol* 2000; 210:630-637. *http://dx.doi.org/10.1007/s004270000110*
- 34. Adelman ZN., Jasinskiene N., James AA. Development and applications of transgenesis in the yellow fever mosquito, *Aedes aegypti. Mol Biochem Parasitol* 2002; 121:1-10. *http://dx.doi.org/10.1016/S0166-6851(02)00028-2*
- 35. Mori A., Dave DC., Douglas H., et al. Reinvestigation of an endogeneous meiotic drive system in the mosquito, *Aedes aegypti* (Diptera: Culicidae). *J of MediEnto*2004; 41:1027-1033. http://dx.doi.org/10.1603/0022-2585-41.6.1027
- 36. Davis S., Bax N., Grewe P. Engineered under-dominance allows efficient and economical introgression of traits into pest populations. J Theor Biol 2001; 212:83-98. http://dx.doi.org/10.1006/jtbi.2001.2357
- 37. Elizabeth AM., O'Neill SL. Beyond insecticides: new thinking on an ancient problem. *Nature Revi Microbiol* 2013; 11:181-193. *http://dx.doi.org/10.1038/nrmicro2968*
- 38. Ramasamy R., Surendran SN., Jude JP., et al. Larval development of Aedesaegypti and Aedesalbopictus in peri-urban brackish water and its implications for transmission of arboviral diseases. PLoS Negl Trop Dis 2011; 5:1369-1377. http://dx.doi.org/10.1371/journal.pntd.0001369
- Nguyen Thi Kim Tien., Do Quang Ha., Tran Khanh Tien., Luong Chan Quang Predictive indicators for forecasting epidemics of dengue/dengue haemorrhagic fever through epidemiological, virological and entomological surveillance. *Den Bull* 1999; 23:34-39. *No doi*
- 40. Dengue fever. URL:https://www.townsville.qld.gov.au/__data/assets/pdf_file/0009/3213/Dengue-Fever.pdf
- 41. Megan R., Valdez W., Nimmo D., et al. Genetic elimination of dengue vector mosquitoes. *PNAS* 2011; 108: 4772-4775. *http://dx.doi.org/10.1073/pnas.1019295108*
- 42. Chan KL. A report on the pilot control scheme in mosquito eradication at the Geylang-Tanjong Rhu area in Singapore. *Sing Pub Health Bull* 1967; 1:52-72. *No doi*

- 43. Chang MS, Christophel EM, Gopinath D, et al. Challenges and future perspective for dengue vector control in the Western Pacific Region. *West Pacific Surveill and Respo J* 2011; 2(2):9-16. *http://dx.doi.org/10.5365/wpsar.2010.1.1.012*
- 44. Eduardo AU, Yara AH, Donald SS. Use of expansion factors to estimate the burden of dengue in Southeast Asia: A systematic analysis. *PLoS Negl Trop Dis* 2013; 7(2):1-15. *http://dx.doi.org/10.1371/journal.pntd.0002056*
- 45. Social mobilization. URL:http://www.dengue.health.gov.lk/index.php/activities-services-eng/social-moblization
- 46. Census and statistics data. Department of Census and Statistics, Ministry of Finance 2012. URL:http://www.statistics.gov.lk/PopHouSat/CPH2011/Pages/Activities/Reports/FinalReport/Fin alReport.pdf .Census of population and housing
- 47. Fact sheet on managing Singapore's dengue outbreak. URL:http://www.nea.gov.sg/docs/ default-source/corporate/COS-2014/managing-singapore's-dengue-outbreak.pdf