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Review

Evolution of dengue in Sri Lanka—changes in the virus, vector, and climate

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SUMMARY

Despite the presence of dengue in Sri Lanka since the early 1960s, dengue has become a major public health issue, with a high morbidity and mortality. *Aedes aegypti* and *Aedes albopictus* are the vectors responsible for the transmission of dengue viruses (DENV). The four DENV serotypes (1, 2, 3, and 4) have been co-circulating in Sri Lanka for more than 30 years. The new genotype of DENV-1 has replaced an old genotype, and new clades of DENV-3 genotype III have replaced older clades. The emergence of new clades of DENV-3 in the recent past coincided with an abrupt increase in the number of dengue fever (DF)/dengue hemorrhagic fever (DHF) cases, implicating this serotype in severe epidemics. Climatic factors play a pivotal role in the epidemiological pattern of DF/DHF in terms of the number of cases, severity of illness, shifts in affected age groups, and the expansion of spread from urban to rural areas. There is a regular incidence of DF/DHF throughout the year, with the highest incidence during the rainy months. To reduce the morbidity and mortality associated with DF/DHF, it is important to implement effective vector control programs in the country. The economic impact of DF/DHF results from the expenditure on DF/DHF critical care units in several hospitals and the cost of case management.

1. Introduction

Dengue viruses (DENV) are mosquito-borne flaviviruses that have plagued humans for centuries. Urbanization and human population growth in the tropical regions of the world have produced favorable conditions for DENV transmission. Moreover, changes due to urbanization and human population growth have led to the current global dengue pandemic, characterized by a dramatic increase in DENV infections and an expanding geographic distribution of both DENV and the mosquito vectors,[1] *Aedes aegypti* and *Aedes albopictus*, which transmit DENV among humans.[2]

In Sri Lanka, 48 Aedes species belonging to 11 subgenera have been reported to date. The subgenera are Aedimorphus, Cancraedes, Christophersiomyia, Diceromyia, Finlaya, Mucidus, Neomelaniconion, Paraedes, Rhinoskusea, Stegomyia, and Verrallina. The established DENV vectors A. aegypti and A. albopictus belong to the subgenus Stegomyia.[3,4] However, nothing is known about the role of the remaining 46 Aedes species in DENV carriage and transmission, an area that might shed some light on how DENV survive the intra-epidemic periods.

Sri Lanka has been affected by dengue fever (DF)/dengue hemorrhagic fever (DHF) epidemics for over two decades. DENV infections have been endemic in Sri Lanka since the mid 1960s. DF was serologically confirmed in the island in 1962.[5] The presence of DF in all of the major towns situated below 1200 m elevation was confirmed in 1966 and in 1976–1978.[6]

In Sri Lanka, DF control efforts have been targeted at the disease and vector, including laboratory surveillance for DENV infections in patients and vectors, vector control, social mobilization, clinical management of DF/DHF patients, and the emergency response during outbreaks in terms of accelerated vector control and public awareness through the media. A national-level multidisciplinary task force on DF/DHF has been established to govern the DF/DHF control activities. Furthermore, there are provincial and district-level DF/DHF control activities in place. Training clinicians on clinical management has been carried out continually in an attempt to bring the DF/DHF mortality to zero, or to a minimum level. It is hoped that with the implementation of collective control programs in collaboration with other governmental and non-governmental organizations, with maximum cooperation from the community, the morbidity and mortality of DF/DHF will be reduced in the near future.[5]

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2. The virus

DENV is a flavivirus transmitted by *Aedes spp* mosquitoes. There are four antigenically distinct DENV serotypes, DENV 1–4. Infection with a single DENV serotype leads to long-term protective immunity against that particular serotype, but not against the other serotypes.[7] Thus prior infection with a single serotype of DENV only provides a homotypic protection.

The origin of DENV has been reported to be African, with the distribution of DENV around the world occurring as a result of the slave trade.[8,9] Conversely, it is believed that DENV may have originated in a forest cycle involving lower primates and canopy-dwelling mosquitoes in the Malay Peninsula.[9,10] It is possible that different DENV serotypes evolved in taxonomically related mosquito species in different geographical regions. All four DENV serotypes have been documented in a forest cycle in Asia, while only one (DENV-2) has been documented in Africa.[10] It is currently thought that DENV probably had an Asian origin, which is supported by serosurveys conducted in rural communities of Malaysia in the early 1950s.[9]

Biologically, DENV are highly adapted to their mosquito host and are maintained in the mosquito species responsible for forest cycles, with periodic amplification in lower primates.[10] In the past, due to the clearing of forests and the development of human settlements, DENV has moved out of the jungle and rural environment from where they were and still are transmitted to humans by mosquitoes. Due to the migration of people and commerce, DENV have ultimately moved into the villages, towns, and cities of tropical Asia, where these viruses are most likely to be transmitted sporadically by *A. albopictus* and other closely related peri-domestic *Stegomyia* species.[1]

The four serotypes of DENV have been co-circulating in Sri Lanka for more than three decades and their distribution has not changed drastically in the last 30 years. Although the Sri Lankan population had been exposed to DENV for a long time, the severe forms of DENV infection (DHF and dengue shock syndrome (DSS)) were rare before 1989. Studies have shown the existence of more than one DENV serotype in many parts of the country. There was an island-wide epidemic of DF associated with DENV serotypes 1 and 2 from 1965 to 1968. This epidemic caused 51 DHF cases and 15 deaths.[5] DENV-1 and DENV-2 were isolated from the outbreaks in 1965 and 1966.[11]

A study conducted using mosquito pools in the Western and North-Western provinces of Sri Lanka, including the districts of Colombo, Gampaha, and Kurunegala, has indicated the circulation of multiple DENV serotypes within close proximity to each other.[12] Mosquito pools from Kurunegala district were positive for both DENV-2 and DENV-4, while mosquito pools from Gampaha and Colombo districts had DENV-2 and DENV-4. Higher numbers of positive pools of DENV-1 and DENV-4 have been reported in Kurunegala.[12]

The results of another study performed between 2003 and 2006, indicate the circulation of the DENV-1 serotype in the Colombo district of Sri Lanka.[13] However, this study showed a change in the genetic characteristics of the DENV-1 serotype during the study period. The two isolates of DENV-1 serotype from Sri Lanka obtained in 1983 and 1984 belonged to the South Pacific genotype, and it is believed that some time during the period 1984–1997, the Africa/America genotype of the DENV-1 serotype became established in Sri Lanka; this new genotype of the DENV-1 serotype continued to circulate through 2004. Moreover, the South Pacific genotype of the DENV-1 serotype has not been detected during the past 8 years in Sri Lanka.

In 2009, the largest epidemic of DF/DHF occurred in Sri Lanka (35 008 reported cases, 170 cases/100 000 population, and 346 deaths) and that outbreak was found to have been caused by a new strain of the DENV-1 serotype.[14] Results from DENV nucleic acid detection by reverse transcription (RT)-PCR in patients with DHF from August 2010 to December 2010 showed the predominance of the DENV-1 serotype, which accounted for more than 95% of DF/DHF cases in the Western Province of Sri Lanka;[15] this is similar to the observations made by the Epidemiology Unit of Sri Lanka during that period. Therefore, it appears that the serotype shift may have contributed in some way to the larger DF/DHF outbreaks in the last 2–3 years in the country.

All DENV-2 isolates from Sri Lanka are closely related and belong to the Indian subcontinent/Malaysia genotype. Moreover, there is no evidence of any recent introduction of a DENV-2 strain from outside the island, because the DENV-2 strains from Sri Lanka are more closely related to one another than to any other DENV-2 strain.[13]

DENV-3 strains from Sri Lanka isolated in the 1980s and 1990s belong to the Indian subcontinent genotype (III).[16,17] Genotype III of the DENV-3 strains from Sri Lanka are divided into two distinct clades linked to mild (IIIA) and severe (IIIB) disease epidemics in the island.[16] Moreover, the DENV-3 strains from Sri Lanka isolated in 2003 and 2004 form a new distinct clade that is closely related but different from the DENV-3 clade IIIB viruses that were isolated in the 1990s. This new 2003/2004 clade includes an isolate from 1993, which strongly suggests that the clade is derived from strains that have been circulating on the island for some time.[13]

Unlike group A viruses, the Sri Lankan group B viruses may be associated with severe disease, as the group B viruses are inherently more virulent. Alternatively, the ability of pre-existing antibodies against DENV to neutralize group A viruses but enhance group B viruses may account for the severe disease in group B DENV-3 infections but mild disease in group A DENV-3 re-infections. DENV-2 and DENV-3 are the common serotypes reported in many parts of Sri Lanka. Individuals with previous primary DENV-2 infections have been shown to neutralize the DENV-3 group A viruses better than the DENV-3 group B viruses, and this might be contributing to the severe disease in group B DENV-3 infections.[18]

In Sri Lanka, regular epidemics of DF/DHF have been observed only since 1989. DENV-3 is responsible for many of the infections that progress to DHF.[19,20] DENV-3 isolates obtained before and after the emergence of DHF are very closely related and belong to subtype III, indicating that the emergence of DHF in the island was not due to the introduction of a new subtype of DENV-3 from outside. During DENV surveillance studies in 1997, only DENV-3 was isolated from hospitalized DF cases, whereas DENV- 1, DENV-2, and DENV-3 were isolated from patients visiting outpatient clinics.[21] These observations suggest that DENV-3 is responsible for severe DF in Sri Lanka. However, further studies are required to establish the relative contribution of DENV-3 to severe DF/DHF in Sri Lanka.

The DENV-4 strain isolated in Sri Lanka in 1978 and in 2003/2004 was the Southeast Asian genotype, which indicates that this genotype is established and has been circulating in the island for decades. Two DENV-4 isolates from 1992 belong to the Indonesian genotype, which might represent a transient introduction to the island.[13]

In 2003, DENV-1 and DENV-4 showed a genotype switch, which is not observed in the phylogeny of DENV-2 and DENV-3. Instead, new clades of DENV-3 genotype III viruses have replaced older clades, and DENV-2 has also shown a similar trend. The emergence of new clades of DENV-3 in 1989 and 2000 coincided with abrupt increases in the numbers of reported DF cases, implicating this serotype in severe epidemics (Table 1).[16]

3. Changes in the epidemiology of DF/DHF and DENV infection in the vectors

Globally DF was initially an ‘urban’ disease, in that the epidemics mainly occurred in densely populated urban settings.

Table 1
Changes in the outbreak DENV types over time in Sri Lanka

Year	DENV serotype responsible for major DF/DHF outbreaks in Sri Lanka	Ref.
1965	DENV-1, DENV-2	5, 11
1968	DENV-1, DENV-2	5, 11
1978	DENV-4	13
1980	DENV (IIIA)	16, 17
1990	DENV (IIIA)	13, 16, 17
1992	DENV-4	13
1993	DENV (IIIB)	21
1997	DENV (IIIB)	21
2003	DENV (IIIB), DENV-4	13
2004	DENV-1, DENV (IIIB), DENV-4	13
2006	DENV-1	13
2009	DENV-1	14
2010	DENV-1	15

DENV, dengue virus; DF, dengue fever; DHF, dengue hemorrhagic fever.

However, in both Sri Lanka and India this pattern appears to have changed with the disease now spreading to rural areas as well.[22]

Epidemiologically, during the 19th century DF was considered as a sporadic disease, causing epidemics at long intervals. However, dramatic changes in the epidemic pattern have occurred and DF/DHF currently is ranked as the most important mosquito-borne viral disease in the world.[23] DF is now one of the leading causes of hospitalization and death among children in the tropical regions of the world.[24] The rapid increase in DENV activity in India and Sri Lanka (Figure 1) from 1999 to 2003 suggests its potential to cause even more severe epidemics in the future.[23]

Although vector densities are generally much higher in urban areas when compared to rural settings, vector densities in the latter are now seen to be increasing.[25,26] Therefore, the potential 'threat' of major DF/DHF outbreaks in rural areas is imminent in the tropical dengue endemic regions of the world. In Sri Lanka, although the highest incidence of DF/DHF is seen in the Western Province (44.9% in 2007), there has been a dramatic increase in the incidence in all other provinces.[25] In the recent past, the incidence of DF/DHF has been more marked in the North Central Province (11.8% in 2007 vs. 4.8% in 2004), Wayamba Province (15.9% in 2007 vs. 10.2% in 2004), and Sabaragamuwa Province (12.2% in 2007 vs. 6% in 2004 (Epidemiology Unit, Ministry of Health, Sri Lanka). Therefore, there is a potential threat of severe DF/DHF epidemics occurring throughout the country in the future.[25]

The mosquito *A. aegypti* has been thought to be the main vector responsible for virtually all DF/DHF epidemics. *A. albopictus* has been considered as a vector in which the DENV is maintained but does not contribute to the transmission rate in epidemics. Aedes mosquitoes are primarily container breeders and they thrive in both clean and organically rich water in both natural and artificial containers.[27]

An entomological study showed the presence and abundance of *A. albopictus* in many of the locations in all of the districts surveyed. Furthermore, in that study, 100% of the DENV-positive pools were made of *A. albopictus*, highlighting the importance of *A. albopictus* in the transmission of DENV. The ability of *A. albopictus* to be infected with low virus loads and the degree to which it permits replication within the mosquito itself could have an impact on the maintenance and the transmission of DENV in the long run.[27]

Co-circulation of two or more DENV serotypes in a single pool or in different pools of mosquitoes within the same district is suggestive of hyper-endemic transmission of DENV in the districts of Colombo, Gampaha, and Kurunegala.[12] Thus there is evidence of the capability of *A. albopictus* as a vector in transmitting DENV in the absence or low abundance of *A. aegypti*. *A. albopictus* is underrated in the transmission of DENV, especially during the peak transmission periods of DF/DHF in Sri Lanka.[12] DF/DHF cases have been encountered in areas where there is no *A. aegypti* breeding, but *A. albopictus* breeding is prevalent.[28] In Kandy, a city in the Central Province of Sri Lanka, four species of Aedes larvae were collected from water storage tanks, with the majority being *A. albopictus* (41.05%) and *A. aegypti* (13.43%); the remaining tanks contained larvae of *Aedes macdougalli* (39.55%) and *Aedes vittatus* (5.97%).[29] The greater susceptibility of *A. albopictus* to DENV infection is said to have led to greater DENV adaptation, thus Sri Lanka as a whole may be at serious risk of multiple DF/DHF outbreaks in the future with the evolution of DENV strains.[12]

A. aegypti and *A. albopictus* are widely adapted to urban and suburban environments in Sri Lanka.[30] Recent studies have shown that *A. aegypti* and *A. albopictus* lay eggs in brackish water, and their larvae and pupae survive to emerge as adults in brackish water collections. Brackish water habitats have been identified with *Aedes* larvae in the peri-urban areas of Sri Lanka. The brackish water larval sites identified are located in popular beaches and in coastal areas 1 km from densely populated residential areas; this finding is consistent with the potential role of Aedes adapted to brackish water in DENV transmission.[31]

The eastern coastal district of Batticaloa, which was devastated by the 2004 Asian tsunami, lies in the dry zone of Sri Lanka and is one of the districts badly affected by DF/DHF in recent years. A seasonal shift in the density of the two *Aedes* species has been observed in Batticaloa. *A. aegypti* tends to predominate during the pre-monsoon season and *A. albopictus* during the monsoon season. Since the monsoon rains fall in Batticaloa district from October to December, the density of Aedes increases during this period and a positive association between rainfall and Aedes density has been observed.[32] The high density of Aedes mosquitoes recorded in June 2008 has been attributed to the unexpected rain experienced in that month.[32]

The continuous application of vector control methods solely in freshwater pre-imaginal development habitats in the urban environment may select for genetic changes in the DENV favoring the development of *A. aegypti* and *A. albopictus* in artificial collections of brackish water in coastal urban areas, which in turn may lead to vector adaptation to natural brackish water habitats in the future. Such changes could have serious consequences for the health of millions of people in many parts of the world, through a higher incidence of DF/DHF, chikungunya, and urban yellow fever, as these are transmitted through Aedes mosquitoes.[33,34]

The shift in various aspects of epidemiology of DF/DHF, as observed in Sri Lanka, has been seen in other dengue endemic countries in the world as well. Cyclical epidemics of DF/DHF have been reported from several Asian countries, such as India, the Philippines, and Thailand, with increasing numbers of cases from the 1950s through the 1970s. Increases in disease transmission and the frequency of epidemics have also been the result of circulation of multiple serotypes in Asia.[35] Of the 2.5 billion people around the world living in dengue endemic countries with a risk of contracting DF/DHF, nearly half live in 10 countries of the Southeast Asia region. Nearly 75% of the current global disease burden due to DF/DHF is reported in the Southeast Asia region together with Western Pacific region. Until 2003, only eight countries in the region had reported DF/DHF cases. By 2009, all member states except the Democratic Peoples' Republic of Korea had reported DF/DHF outbreaks. Korea is the only country in the Southeast Asia region that has no reports of indigenous transmission of DENV. Timor-Leste reported an outbreak in 2004 for the first time. Bhutan also reported its first DF/DHF outbreak in 2004.[35] Nepal reported its first indigenous case of DF in November 2004.[35,36]

In Indonesia, the number of reported DF/DHF cases started to rise from 2004, reaching a plateau between 2007 and 2009, and is

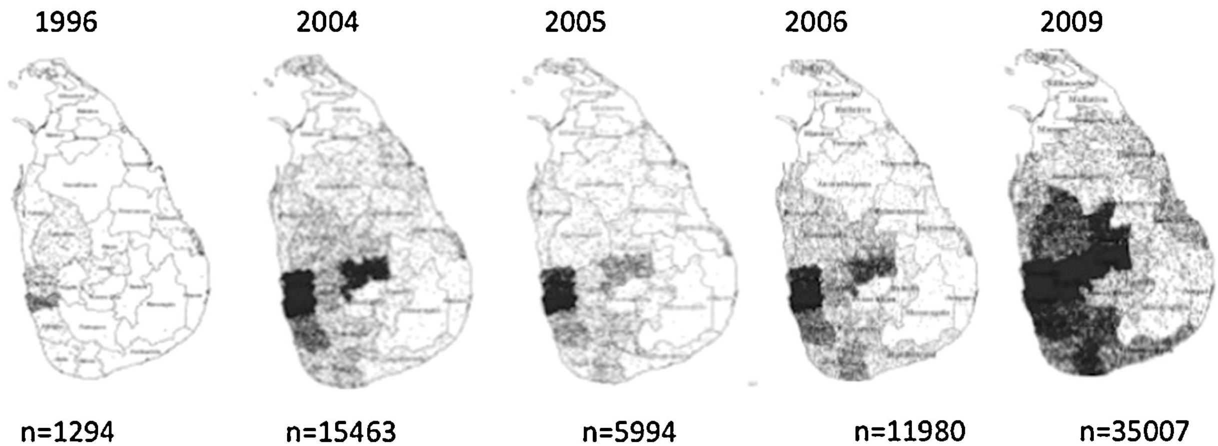

Figure 1. Temporal and spatial distribution of DF/DHF in Sri Lanka: cases reported to the Epidemiology Unit, Sri Lanka (accessed August 17, 2013).

following an endemic pattern. In other countries such as Bangladesh, Myanmar, and the Maldives, DF/DHF follows an endemic pattern. Moreover, there has been an increase in the proportion of severe DF cases, particularly in Thailand, Indonesia, and Myanmar.[35,36] In India and Thailand, the prominent strain of DENV has been DENV-1, which is linked to high morbidity and low mortality.

In the early 1960s, DF/DHF cases were confirmed in Sri Lanka by antibody detection, either by IgM detection in a single serum sample or by demonstrating an increase in the antibody levels in paired sera. Cases occurred in epidemic proportions for the first time in Sri Lanka during 1965–1966 with sporadic cases of DHF. Initially, the disease was mainly spread in the western coastal belt, but it was later found in other suburbs as well. In 1965, there was a DF outbreak throughout the country with 51 cases and 15 deaths. After that, epidemics occurred in many parts of the country fairly regularly, in 1966, 1967, 1968, 1972, 1973, and 1976, and the number of cases reached a peak in 1988/1989.[5,6]

In 2002, DF/DHF was ranked as the third most common notifiable disease in Sri Lanka (first and second were malaria and tuberculosis).[37,38] In recent years, deaths due to DF/DHF have been greater than those due to malaria, and DF/DHF is becoming the number one killer mosquito-borne infection in Sri Lanka.[37] Currently malaria is in the elimination phase in the country. There are specific anti-malarial drugs for the malaria parasite and the malaria parasites are more stable genetically than RNA bound DENV; DENV are more prone to genetic changes, producing many strains within a type. Anopheles mosquitoes are night biters, so barrier protection becomes effective. Collectively, these factors might have contributed to the effectiveness of malaria control programs in the country. On the other hand, DF and DHF have become established due to several factors: (1) there is no specific antiviral drug for DENV and there is no effective vaccine as yet, despite many ongoing studies and trials; (2) DENV are genetically unstable RNA bound viruses and are more prone to genetic changes; (3) populations are becoming exposed to new DENV strains; (4) DENV vectors are day biters so barrier protection for preventing exposure becomes ineffective. These factors together might have contributed to the establishment of DENV in the country, causing regular outbreaks of severe DF/DHF.

At present, DF and DHF are prevalent in many urban and semi-urban areas of Sri Lanka with seasonal and periodic epidemics occurring regularly in the island.[27] In recent decades a higher incidence of DF/DHF has occurred in the districts of Colombo, Gampaha, Kalutara, Kurunegala, Kegalle, Ratnapura, and Kandy.[39] From 2000 to 2008, the reported number of suspected and serologically positive DF/DHF cases varied from 4749 to 15 643, involving 25–88 deaths, with a major epidemic in 2004.[29] Since the 30-year ethnic conflict in the country came to an end in 2009, DF/DHF has become endemic in northern and eastern Sri Lanka, with a high incidence in the capital cities of the northern and eastern provinces of the island, Jaffna and Batticaloa, respectively.[40] This spread of DF/DHF to the north and the east might be due to the open movement of people in both directions from the south to the north and east, and vice versa; this open movement of people for trade and other purposes was absent or very limited during the conflict era, prior to 2009.

Another important aspect of the epidemiology of DF/DHF in Sri Lanka is the shift in the affected age group from children to adults; also, in many age groups, males have predominantly been affected. According to a regional study done by the World Health Organization (WHO) in Sri Lanka based on reported cases from 1996 to 2005, there were consistently and significantly larger proportions of males with DF/DHF in those aged 15 years. This male preponderance was reported in every province of the country. Among those aged 1–4 and 5–14 years, there were significantly fewer male cases than expected, although there was some annual variation.[41] The highest incidence occurred in the 5–9 years age-group.[5] Before 2000, one large peak of DF/DHF cases was observed in children and a few cases were observed in adults. After 2000, two reported DF/DHF peaks were observed in children and young adults. Moreover, the mean age of reported DF/DHF cases was shown to have increased from 15 years in 1996 to 25 years in 2006.[13]

Provincial DF/DHF epidemiology in Sri Lanka underwent a marked change between 1996 and 2005. The proportion of reported DF/DHF cases from the Western Province, in which the country's largest city, Colombo, is situated, decreased from 84% in 1999 to 37% in 2003. The age distribution of reported cases shifted from children aged less than 15 years making up more than 60% of cases in 1996–1999 to less than 40% of cases in 2001–2005.[41]

4. Role of climatic factors in the spread of DENV

Climate (temperature, rainfall, and humidity) change due to global warming can expand the geographical range of vector mosquitoes, extend the disease transmission season, shorten the gonotrophic cycle, and reduce the time taken for ingested viruses to develop to infective stages in mosquitoes, thereby increasing the propagation rates of arboviral diseases transmitted by *A. aegypti* and *A. albopictus*.[33,42–44]

There is a strong positive correlation between DF/DHF outbreaks and the rainfall pattern, which increases the number of breeding habitats of Aedes vectors. In semi-arid areas in India, *A.*

aegypti is an urban vector and populations typically fluctuate with rainfall and water storage habits.[45] In Southeast Asian countries where the annual rainfall is greater than 200 cm, *A. aegypti* populations are more stable and are established in urban, semi-urban, and rural areas. However, in countries like Indonesia, Myanmar, and Thailand, the mosquito densities are higher in semi-urban areas than in urban areas due to the traditional water storage practices.[46]

In contrast to the strong positive correlation between DF/DHF outbreaks and the rainfall pattern in many tropical countries, in some areas of the world DF/DHF outbreaks occur before the arrival of the rainy season or in relatively dry areas. Conversely, even in locations with a rainy season, such as Singapore, a positive correlation between rainfall and vector population density could not be found.[47] In certain regions of the tropics where there are two annual rainy seasons, a positive correlation has been observed in only one season.[48] The impact of rainfall on adult vector density is not the same for all vector species. *A. aegypti* prefers indoor habitats, and hence it is less affected by rainfall than *A. albopictus* and other vectors that have outdoor larval habitats.[1]

Two DF/DHF peaks occur annually in association with the monsoon rains, when the densities of two mosquito vectors (*A. aegypti* and *A. albopictus*) are high in Sri Lanka. Generally, the first peak occurs in June/July, coinciding with the south-western monsoon that commences in late April. The second peak, comparatively a smaller one, usually occurs at the end of the year and is associated with the north-eastern monsoon rains that prevail from October to December.[5]

Temperature is another important factor controlling the seasonality of DF/DHF outbreaks in sub-tropical or temperate regions. It influences vector distribution, the blood feeding activity of the vector, the extrinsic incubation period, and adult longevity. *A. aegypti* has been shown to transmit DENV when the temperature is above 20 °C but not less than 16 °C. A positive correlation has been shown between the temperature and the female vector abundance. In addition, high temperatures may increase the frequency of blood feeding due to a rapid reduction in energy reserves.[49] It is expected that global warming may further facilitate the expanded distribution of DENV mosquito vectors in temperate regions such as northern parts of North America and Europe.[50] This concern has become a far more serious matter with the expanding distribution of *A. albopictus*.[51]

Altitude also plays a vital role in limiting the distribution of *A. aegypti*. In India, *A. aegypti* breeding sites range from sea level to 1000 m above sea level. Lower elevations (less than 500 m) have moderate to heavy mosquito populations, while mountainous areas (over 500 m) have low populations.[52]

5. Prevention of DF/DHF

In the absence of a vaccine or specific antiviral treatment for DF and DHF, preventive measures aim to reduce the population density of the vectors, *A. aegypti* and *A. albopictus*. The control of DF/DHF in tropical countries is mainly achieved through surveillance of *A. aegypti* and *A. albopictus* larvae to eliminate the larval development habitats, with the use of insecticides and public education.[53–54]

A study conducted in the Kandy District of Sri Lanka showed that the mechanical and biological measures alone are not sufficient to prevent Aedes breeding. This finding suggests the need for an efficient supplementary chemical method for Aedes larval control in domestic water storage containers. Furthermore, the prevention of *A. aegypti* and *A. albopictus* breeding in water storage containers would greatly help to control DF/DHF. Therefore, DF/DHF control programs should pay more attention to the control of Aedes breeding in domestic water storage containers.[27]

Effective waste collection and the proper disposal of garbage by the local government bodies, commitment of individuals and communities in reducing the source, and law enforcement against the occupants of premises with Aedes mosquito breeding spots are necessary for the control of DF/DHF in the country.

Countries like Thailand, Malaysia, and Cambodia[55] have used Temephos to prevent Aedes breeding in domestic water storage jars and other water storage containers. The application of Temephos sand granules to domestic water storage containers in a field trial in Bangkok, at a dosage of l ppm, resulted in a more than 95% reduction in adult Aedes mosquito density.[56] In Kandy, the use of net covers for water storage cement tanks showed the potential to control Aedes larvae including *A. aegypti* and *A. albopictus*.[27] Moreover, plastic net covers provide good Aedes mosquito control in water storage cement tanks, and thus these measures need to be included in the health messages in order to encourage people to use such protective methods for the prevention of DENV breeding, thereby eliminating the risk of DF/DHF and chikungunya fever from the country.[27]

In Sri Lanka, District based DENV vector control programs consist mainly of source reduction and thermal fogging. Fogging is employed as a DENV vector control measure by the health authorities during disease transmission periods.[32] Malathion in liquid form was used until 2008 and was replaced by Pesguard® (a synthetic pyrethroid) in 2009.[32] Institutions such as hospitals, transport bus depots, factories, and schools are also cited as potential breeding areas for the DENV vectors. Discarded containers and water storage receptacles have been identified as important breeding sites for Aedes mosquitoes in the country. The control of DENV vectors is achieved largely through source reduction, health education, and vector adulticiding with thermal fogging in the country.

Another study done in Sri Lanka showed the possibility of using a different mosquito, *Toxorhynchites splendens*, as an additional measure for the control of *A. albopictus* breeding in man-made water collecting containers.[57] *T. splendens* has been used successfully in other countries like India to control Aedes. In an Indian coastal village, there was a significant reduction in the number of *A. aegypti* breeding in domestic water containers 6 months after the introduction of *T. splendens*.[58] Second instar *T. splendens* larvae have also been used successfully to suppress *A. aegypti* and *A. albopictus* breeding in domestic water containers in Malaysia.[59]

Considering the nature of breeding of DENV vectors in various districts, public awareness and continuous creative health education are essential to control the transmission of DENV. It is important that health authorities continue vector surveillance throughout the dry and wet seasons to avoid any future outbreaks in the country.[32]

6. Conclusions

Currently, DF/DHF cases are reported from all parts of Sri Lanka. Two peaks in absolute number and incidence of DF/DHF occur annually along with the monsoon rains, and the density of two mosquito vector species (*A. aegypti* and *A. albopictus*) is higher in these seasons. Generally, the first peak occurs in June/July, coinciding with the south-western monsoon, which commences in late April. The second smaller peak usually occurs at the end of the year and is associated with the north-eastern monsoon rains that prevail from October to December.

Both *A. aegypti* and *A. albopictus* are prevalent in the country and natural infections have been reported in both vectors. The studies conducted in Sri Lanka indicate that *A. albopictus* is more efficient in DENV transmission at present. Both *Aedes* species were found to be highly resistant to 4% DDT and completely susceptible to 5% malathion.

For the last 30 years all four DENV serotypes have been circulating in Sri Lanka. DENV-1 only accounted for 7% of infections. DENV-2 and DENV-3 were the predominant circulating serotypes until 2009 and were responsible for 86% of DENV infections. In the last decade, new genotypes of DENV-1 and new clades of DENV-3 (genotype III) have replaced the older ones, and these are the reasons for the recent DF/DHF epidemics.

A pattern in the DF/DHF outbreaks can be seen in the country, occurring with the monsoon showers. The recent extended rainy season with heavy rains and floods could be one of the reasons for DF/DHF becoming rampant and more unmanageable in the last 5 years in the island. The rains have been so torrential and heavy that the taking of timely precautions against the outbreak and spread of diseases has become extremely difficult. On the other hand, Sri Lanka cannot afford to make mistakes in predicting DF/DHF outbreaks as the consequences could be catastrophic. A collective approach to the control of DF/DHF, including environmental control in source reduction of the vectors, cumulative climatic forecast data, and mapping for outbreak prediction and case management at its best (as practiced now) may be useful in reducing the DF/DHF burden of this island nation. Although, establishing a collective control program and sustaining that program will be a difficult task, Sri Lanka should remain positive about sustaining the control program if lessons learned from its successful control of malaria are followed.

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