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REVIEW

Fight against dengue in India: progresses and challenges

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Abstract At the end of the last century, India has faced resurgence of many infectious diseases, of which dengue is one of the most important in terms of morbidity and mortality. The National Vector Borne Disease Control Program data show that dengue is established in India and is becoming endemic to many areas (dengue cases have increased steadily from ~450 to ~50,000 from 2000 to 2012). Despite extensive efforts being made in developing the effective dengue control measures, the number of dengue cases, their severity, and geographical boundaries are expanding alarmingly and posing dengue as one of the deadly disease. Recently, the increasing burden of dengue in the country has attracted the scientific as well as Indian Government's administrative attention; however, a lot remain to be achieved for managing the disease under threshold level. Like other vector-borne diseases, better management of the dengue needs balanced approach involving various aspects like disease prevention, cure/treatment, and the vector control, simultaneously. We have briefly discussed here the situation of dengue in India and have tried to highlight the worrying facets of dengue control and its implementation in Indian perspective. The review on various aspects of dengue control has revealed an urgent need for permanent surveillance programs, coupled with improvised disease diagnostics, effective anti-dengue treatment measures, and controlling the disease transmission by following an effective implementation of vector control programs.

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Introduction

Until very recently, dengue has been classified under the neglected tropical diseases. However, recent studies on spread and occurrence of dengue epidemics from many parts of the world have forced federal governments to declare it as a disease of prime importance at par with malaria (Guha-Sapir and Schimmer 2005; http://www.news-medical.net/health/Dengue-Fever.aspx). Dengue has been reported in over 100 countries, and it is estimated that 2.5 billion people (40 % of the world population) live in areas where dengue is endemic (Guzmán and Kouri 2002; Rasgon 2011). According to World Health Organization (WHO) reports, about 50 to 100 million cases of dengue including 24,000 deaths are reported annually all over the world depending on the disease favoring climatic conditions (Guzmán and Kouri 2002). Dengue is caused by an RNA virus (DV) belonging to family Flaviviridae. There are four serotypes of DV, viz., DV1, DV2, DV3, and DV4 (Erum et al. 2010), all of which are transmitted by day-biting mosquitoes, and the principal vector responsible for transmission of dengue worldwide is *Aedes aegypti*, while *Aedes albopictus* acts as a secondary vector (Gratz 2004). Dengue infections affect all age groups and produce differential symptoms ranging from asymptomatic, or mild viral infection, to a severe and occasionally fatal disease (Ranjit et al. 2009). Dengue fever (DF) is a self-limiting disease and causes febrile illness; however, there are two severe clinical manifestations of dengue known as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) (Aggarwal et al. 1998). Occurrence of dengue due to one serotype generally provides lifelong immunity, while very low or negligible immunity to the other serotypes (Bhattacharjee and Bhattacharjee 2011). Importantly, individuals infected with one or more serotypes remain vulnerable to infections by the other dengue serotypes (Teixeira et al. 2002), and complicated dengue arises when two different serotypes attack at the same time.

The risk of severe dengue infections is increasing day by day in both the developing and developed countries (Monath 1994). The highest number of dengue infections are contributed by Thailand (~17–43 % of the total number of dengue cases reported), followed by India, Brazil, and Indonesia (Jansen et al. 2008). In India, dengue has become one of the important infectious diseases causing epidemics almost every year since 1990s. The continuous occurrence of dengue outbreaks and the increasing severity of the disease have raised the need for in-depth understanding of vector biology and control, dengue pathology, epidemiology, and immunopathology to develop and deploy effective dengue control measures. Researchers in India are actively involved in various aspects like development of anti-dengue vaccines, drugs, and customization of vector control measures to get rid of this deadly disease; however, integration of different dengue control measures could be a better option. For an integrated approach in dengue control, we need a simultaneous progress in each aspect of dengue research, right from human–vector–virus biology, pathogenesis, immunology, epidemiology, population biology, drug and vaccine development, diagnostics, etc. The present paper highlights different aspects of dengue control specifically addressing the present challenges in Indian perspective. We have also emphasized on the worrying facets of dengue control in India that needs immediate attention as successful disease control should aim at vulnerable points for managing the disease effectively. Only the latest papers showing remarkable progress in important areas of dengue research have been reviewed here.

Recent trends of dengue infections in India

The epidemiology of dengue in India is very interesting and ever changing (Fig. 1). The dengue remained silent for over two centuries after its first appearance in 1780 (Chaturvedi and Nagar 2008), and reappeared in 1963–64 in East-Coast India (Carey et al. 1966; Chatterjee et al. 1965; Chaturvedi and Nagar 2008; Sarkar et al. 1964). Thereafter, the infections spread Northwards and reached Delhi in 1967 (Balaya et al. 1969), Kanpur in 1968 (Chaturvedi et al. 1970a; Chaturvedi et al. 1970b), Vellore in 1968 (Myers et al. 1970), Maharashtra (Mehendale et al. 1991), Mangalore (Padbidri et al. 1995), and subsequently covered almost whole India (Gupta et al. 2012; Rao 1987) (Fig. 1). More interestingly, after reemergence, the disease remained almost benign and self-limiting for about two decades. For the first time, the severe form of dengue, i.e., DHF, was reported in 1996 from Delhi (Gupta et al. 2006). Thereafter, Delhi has experienced seven outbreaks consecutively until 2003 (Broor et al. 1997; Dar et al. 1999; Gupta et al. 2005) and then in 2006 and in 2010 (Garg et al. 2011; Raheel et al. 2011). Considering whole India, a large number of outbreaks have been reported from different states/parts of the country so far (http://idsp.nic.in/) (Chaturvedi and Nagar

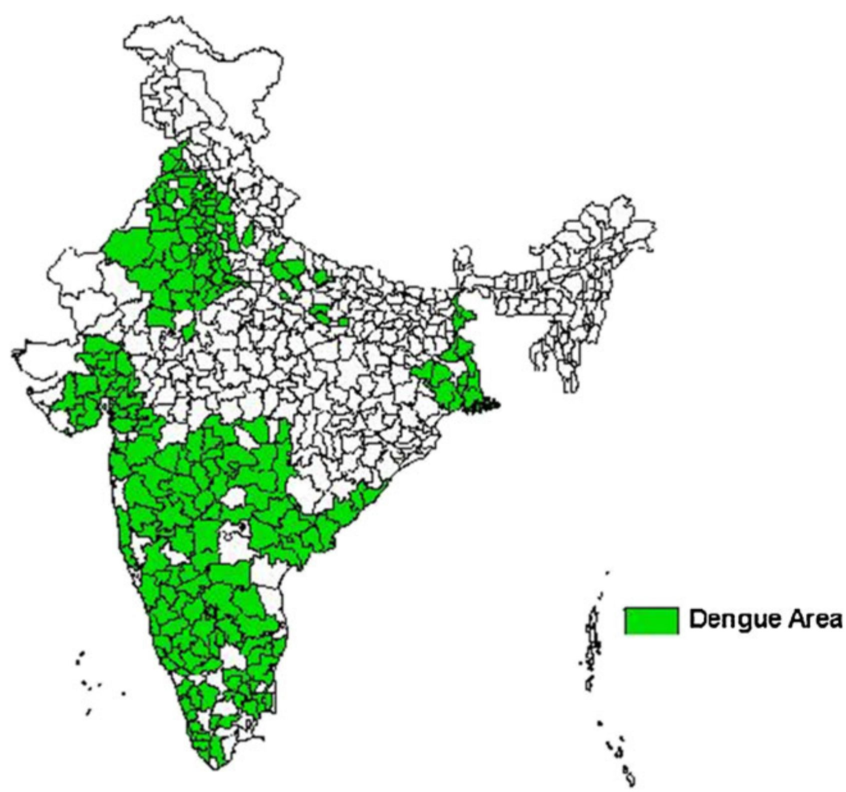

Fig. 1 Recent mapping of reports of dengue cases from different geographical areas in India. Source: http://nvbdcp.gov.in

2008) and the total number of dengue cases has shown rising trend in the country over the years (Fig. 2) (www.nvbdcp.gov.in). Recently, a number of dengue infection reports are emanating on daily basis from Delhi, Kolkata, Chennai and many other parts of the country this year, too (http://ibnlive.in.com/news/kolkata-faces-dengue-outbreak-govt-apathetic/288029-3-231.html; http://articles.timesofindia.indiatimes.com/2012-09-17/bangalore/33901609_1_fever-cases-dengue-fever-dengue-shock-syndrome; http://articles.timesofindia.indiatimes.com/2012-09-11/science/33762564_1_candidate-vaccine-vaccine-trials-dengue-vaccine; http://articles.timesofindia.indiatimes.com/2012-10-22/delhi/34652668_1_fresh-cases-shahdara-maximum-cases). The reasons for the frequent dengue outbreaks in different parts of the country are not well known; however, it is believed that the changing epidemiology of different serotypes (DV1–DV4) and their virulent genotypes might be responsible for this sudden shift (Halasa et al. 2011; Monath 1994; Rao 1987). A detailed report on the appearance and epidemiology of different serotypes of dengue virus in India has been published elsewhere (Chaturvedi and Nagar 2008; Gupta et al. 2012; Rao 1987).

Not only the number of cases and severity of disease has increased, India has also witnessed a major shift in the geographical range of the disease. Earlier, dengue was considered a disease of urban and peri-urban areas, the dengue infections are also being reported from the rural areas (Arunachalam et al. 2004; Kumar et al. 2001; Mahadev et al. 1993; Mehendale et al. 1991; Singh et al. 2000; Tewari et al. 2004). An entomological survey in many villages revealed that *A. aegypti* is present in rural areas of Andhra Pradesh, Karnataka, Maharashtra, and Gujarat states. In addition to this, mapping of the vector-borne diseases shows that disease burden has significantly skewed towards dense forested areas that are inhabited by the socio-economically backward rural communities (www.nvbdcp.org). Thus, both rural and urban areas have become potential sites for dengue outbreaks in India. The spread of infections to rural areas might be due to migration of the vectors through rural water supply and appearance and circulation of all the four serotypes of DV all over the country (Chaturvedi and Shrivastava 2004; Dar et al. 2006; Dash et al. 2004, 2005, 2006, 2011). Nonetheless, the vector and pathogen populations are majorly influenced by unprecedented population expansion and unexpected swelling of unplanned urbanization, sub-standard housing, deteriorating basic sanitary conditions, inadequate water supply, and waste management systems. Increasing industrialization and urbanization are providing large populations of susceptible hosts and creating the breeding sites for mosquito vectors; thus, all these factors need to be considered while developing an effective dengue control measures in India.

Dengue control measures and their implementation: an Indian perspective

Dengue is spreading all over the world and has become the important infectious disease of almost every country located in the tropics. For dengue prevention and control, a global strategy has been developed and circulated worldwide (Guzman et al. 2010; WHO 2009), and several new, improved, or validated tools and strategies for dengue control and prevention have been developed so far (Guzman et al. 2010). Moreover, various institutions and national governments in collaboration with WHO are making efforts to improve diagnostics and clinical treatments and to achieve a successful anti-dengue vaccine in near future. However, the frequent reoccurrence of dengue outbreaks, e.g., in India with increasing number and severity (discussed above), indicates that despite of exhaustive efforts worldwide, dengue treatment as well as detection is still elusive. Thus, effective

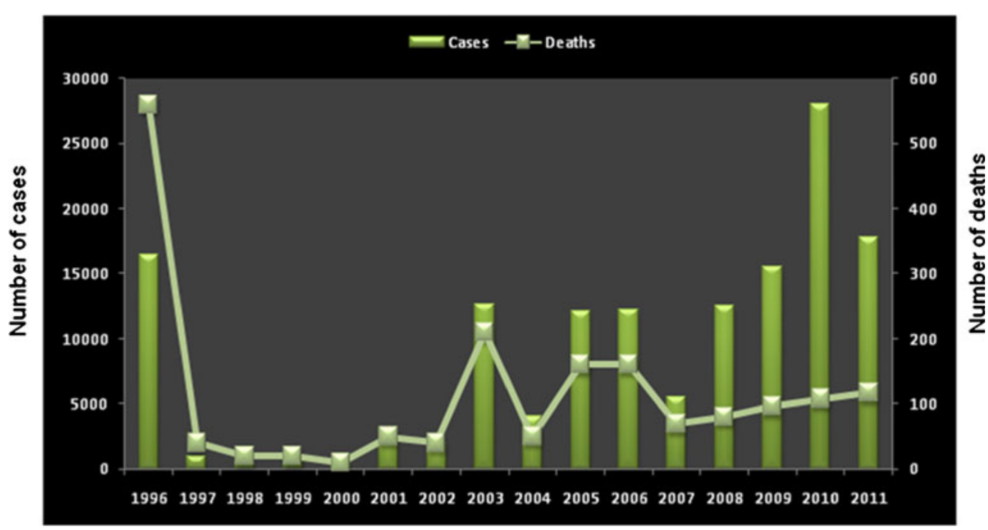

Fig. 2 Number of dengue/dengue hemorrhagic fever cases and deaths in India (changing with time from 1996–2011). Source: http://nvbdcp.gov.in

disease management in the country needs development as well as planned deployment of new improvised tools for dengue prevention and control.

The best procedure to deal with the burden of an infectious disease is to focus on three important steps, i.e.; (1) prevention, (2) cure/treatment, and (3) control and/or eradication. Integrated approach involving all the three aspects could be the best option for managing the dengue burden under threshold level. Prevention needs appropriate surveillance and accurate case reporting system using better diagnosis facilities, infrastructure, organized network of the health centers present all over India, trained staff, and detailed and authentic record management. "Prevention is better than cure," but proper cure using effective chemotherapeutics and potent treatment measures should be available if disease is not preventable. Since there are no vaccines and drugs for dengue, the treatment so far available is "life supportive" and is very expensive and thus out of reach for the poor communities. In this case, controlling the emergence, migration, and transmission of the dengue virus by reducing the vector population remains the ultimate step in curbing the dengue infections. In this paper, we have addressed some important issues related with these three steps that need attention for the effective dengue control in India.

1. Prevention of dengue

    (a) Surveillance and reporting system for dengue cases

    The dengue surveillance in India is of sentinel type (Beatty et al. 2010) and is dependent on the records of the government hospitals spread all over the nation. There are 170 sentinel surveillance hospitals established in the endemic states of the country (http://indiacurrentaffairs.org/spread-of-dengue-in-india/); further, these hospitals are linked with 13 apex referral laboratories (Chakravarti et al. 2012) having advanced diagnostic facilities. Officially, disease surveillance is the responsibility of state government (Chakravarti et al. 2012); however, National Vector Borne Disease Control Program (NVBDCP) reviews the dengue situation in India in different states and at different time intervals and maintains the data systematically (www.nvbdcp.gov.in). Periodic reviews and field visits are made by the concerned health officials to review the dengue situation and record the data. Government of India reviews these data and provides technical assistance, funding, and commodities to the endemic states and Union Territories accordingly. Moreover, Government of India has started two health surveillance programs, i.e., the National Surveillance Program for Communicable Diseases and the Integrated Disease Surveillance Program (http://idsp.nic.in/). The detailed account on the disease surveillance system in India that starts from villages and goes up to the whole nation covering various zone/regional–district–divisional levels have been reviewed elsewhere (Prasad et al. 2010). Despite exhaustive efforts, the reoccurrence of dengue outbreaks in different parts of India shows the weaknesses of the control program and/or its implementation. Moreover, dengue case reporting in India is not legally required (Beatty et al. 2010) and the number of dengue cases could be misleading as reported in the case of malaria (Dhingra et al. 2010). These discrepancies in the case reports (Garg et al. 2008) might be due to (1) the misdiagnosis of the infection cases (Chaturvedi and Nagar 2008), (2) the occurrence of silent or asymptomatic dengue infections (Guha-Sapir and Schimmer 2005), (3) people not being well aware of dengue symptoms and thus failing to avail the best possible health attention (Kabilan et al. 2004), (4) major deaths in rural India taking place at home without any medical care, usually confirmed dengue cases who avail the medical facility are only reported, (5) unregulated private healthcare setup failing to accurately report cases (Garg et al. 2008), and (6) poor medical and diagnosis facilities (Chaturvedi and Nagar 2008) which also contribute in the underreporting of dengue infections in India. In addition to these factors, surveillance of the vector-borne diseases is majorly restricted to endemic regions and includes only the families which are covered by medical centers (Sivagnaname et al. 2012). Although the data from such small areas (endemic states) and small populations (which get health facilities) are the major contributions to epidemiology of dengue in India (www.nvbdcp.gov.in), the true burden of the disease in the country is hardly revealed. Thus, it is necessary to develop best surveillance system in each individual state and, if possible, should go down to the level of districts or blocks covering each and every corner of the nation. A recent opinion article published in an Indian journal (Sivagnaname et al. 2012) has raised some issues attracting the attention to develop a permanent surveillance system in India. However, these issues have been addressed by many authors and they have provided important suggestions for the development of best surveillance system for dengue (Beatty et al. 2010; Bhattacharjee and Bhattacharjee 2011; Prasad et al. 2010; Sivagnaname et al. 2012) that could effectively contribute in dengue control. Moreover, WHO has identified this problem and has already started DengueNet an internet based central data management system (http://www.who.int/csr/disease/dengue/denguenet/en/index.html; WHO 2002, 2004) to improve dengue surveillance program. Initially, it was implemented in the USA; however, the efforts for using DengueNet in India have been started since 2003 (Alert 2004). Major attention of this project is on strengthening laboratory networking, training, disease and vector surveillance, quality assurance, and information sharing and reporting (http://www.whoindia.org/EN/Section3/Section218_842.htm).

(b) Identification of risk-prone areas and susceptible populations

Area-specific knowledge on type of dengue serotype, vector density, vector breeding, susceptibility of populations, and even secondary resources of dengue virus (sylvatic cycle) is the essential part of the surveillance system. In India, dengue risk prone areas are usually identified by regional entomological surveys (Dutta et al. 1998; Paramasivan et al. 2006; Singh et al. 2000, 2010; Victor et al. 2002) and serological surveys (Arunachalam et al. 2004; Kabilan et al. 2004; Kurukumbi et al. 2001; Padbidri et al. 2002). However, these surveys are considered to produce immature and limited information about the vector populations and their density (Sivagnaname et al. 2012) that could lead to wrong predictions about the dengue outbreaks and thus mislead the prevention strategies of dengue disease epidemics (Ooi and Gubler 2008). However, the field- and laboratory-based active dengue surveillance including identification of dengue virus in the humans as well as in the mosquitoes is essential for early indications of an epidemic in dengue-prone areas (Broor et al. 1997; Kabilan et al. 2004; Thenmozhi et al. 2000; Vajpayee et al. 2001). Further, the incidences of dengue infections are highly influenced by the population density of mosquito vectors and their vertebrate hosts, geographic location, surrounding environment, climatic conditions, summer temperatures and droughts, and the socio-cultural practices (Bohra and Andrianasolo 2001; Dhiman et al. 2010; Hubalek 2008; Raju and Sokhi 2008). Recent advances in remote sensing technology and Geographic Information System (GIS) have provided crucial information on dengue transmission. In India, a few such studies involving GIS modeling in dengue have been published so far (Bohra and Andrianasolo 2001; Madanayake et al. 2004; Raju and Sokhi 2008). These studies have correlated the dengue occurrence with the age group, socio-economic, cultural, climatic, demographic, and geographic factors. Such type of information could provide prior warning to take the appropriate disease preventive and control measures in time. In addition, the population-based serological surveys could provide the prior information on the communities or populations about their susceptibility status to dengue infections. In present genomic era, this scientific field has also made remarkable progress. Different genes and gene variants have been recently identified that show positive association with the dengue susceptibility (Khor et al. 2011; Loke et al. 2002; Sakuntabhai et al. 2005). Development and employment of such technologies in the fields could streamline the dengue prevention strategy and thus could result in better outcome.

(c) Rapid and accurate diagnosis of dengue infections

For effective control of disease outbreaks, a rapid and precise diagnosis of dengue is of paramount importance. In India, dengue is more commonly diagnosed by clinical symptoms and physical examination of the patients. Commonly, the patients showing clinical symptoms like high fever, itching and red spots on skin, joint and muscle pain, headache, vomiting, and loss of appetite are considered to be infected with dengue virus (Deen et al. 2006). Since the similar or overlapping clinical symptoms are also seen in the case of influenza, malaria, chikungunya, typhoid, and many other infectious diseases (Halstead 1997), the chances of misdiagnosis are very common. Thus, those suspected cases need to be confirmed by using improved diagnostic kits. In majority of the cases, MAC ELISA test kits (prepared by the National Institute of Virology, Pune) based on the detection of IgM (antibodies) are used in the referral laboratories. In addition, many other commercial antibody based diagnostic kits are also in application (Chakravarti et al. 2000, 2011). However, these antibody based kits are considered to have doubtful specificity and sensitivity (Gupta et al. 2012). Moreover, the antibodies used in these kits are produced several days after the appearance of clinical symptoms, and thus, to wait for their detection is a waste of valuable time of the patient. In this context, scientists have developed some alternative diagnostic tests based on molecular methods (Kumaria and Chakravarti 2005; Mishra et al. 2011). However, these tests could not be used in the fields as they require trained staff, well-established laboratory facilities, and specific equipments. In this context, recently, New Delhi-based J Mitra, in collaboration with the International Center for Genetic Engineering and Biotechnology (ICGEB), New Delhi, has developed an improved and cost-effective ELISA-based diagnostic test named as Dengue Day 1 test (http://biospectrumindia.ciol.com/content/BioSpecial/11202139.asp). In this test, detection of the virus is done by rapid solid-phase immunochromatographic technique on the first day of fever by using qualitative detection of dengue NS1 antigen and differential detection of IgM and IgG antibodies. The low-cost and rapid evaluation trials all over Indian laboratories have shown exciting results (http://biospectrumindia.ciol.com/content/BioSpecial/11202139.asp). However, still it is just a hope unless it works effectively in the field.

(d) Search for vaccine against dengue virus

The history of vaccine research for dengue is more than 60 years old, and there are number of candidate vaccines in the pipeline (Mustafa and Agrawal 2008; Swaminathan and Khanna 2003; Webster et al. 2009). After this long time research, live attenuated CYD TDV tetravalent vaccine by Sanofi Pasteur (Currie 2012; Guy et al. 2010, 2011; Sabchareon et al. 2012) has reached the advanced stage. Recently, large population trials for this vaccine in Thailand have reported that this vaccine is protective against DV1, DV3, and DV4; however, DV2 showed resistance to this vaccine (Halstead 2012; Sabchareon et al. 2012) and generally DV2 is considered as the most virulent and life threatening among the four serotypes. Thus, it has resulted into trivalent instead of tetravalent action and disappointedly failed to serve the fool-proof purpose (Seppa 2012). However, research on the other vaccine candidates is progressing simultaneously (Miller 2010; Schmitz et al. 2011; Shepard et al. 2004; Swaminathan and Khanna 2003; Webster et al. 2009; Wilder-Smith et al. 2010). In addition, scientists from ICGEB, New Delhi are currently engaged in developing a non-infectious dengue vaccine based on well established hepatitis B vaccine technology (http://www.oyetimes.com/news/17369-india-as-a-growing-vaccine-hub; http://biospectrumindia.ciol.com/content/BioSpecial/11202134.asp); however, it is still to go a long way to serve the expected purpose. In India, a number of promising antigens have been identified for vaccine research (Bharati and Vrati 2012; Gupta et al. 2012), and the Indian efforts in vaccine research have been discussed in a recent article by Bharati and Vrati (2012).

2. Advancements in anti-dengue treatment and chemotherapeutic drugs

Unlike malaria, which is being battled effectively with a combination of therapies to date, there is no specific medication or treatment available for dengue disease. Uncomplicated dengue infection resolves spontaneously; however, for patients with life threatening complications, only recommended treatment is "life supportive" (Guzmán and Kouri 2002). The cost of these treatments is so high that the low-income class communities which are usually prone to such infections could not avail such costly treatment/facilities. Those people once infected carry the virus with them until they die. Moreover, most of the time health centers neither have proper infrastructure nor better treatment facilities to help these poor communities. Keeping this in view, recently, National Institute of Virology (NIV), Pune has announced their collaboration with International Consortium on Anti-virals, Peterborough for developing anti-viral therapy against dengue in India. Simultaneously, Indian scientists are sincerely engaged in developing effective treatment measures for dengue (Chaudhary et al. 2006; Kharya et al. 2011). A number of dengue case management success stories based on better treatment options have been published as a case reports from India (Chaudhary et al. 2006; Kharya et al. 2011; Makroo et al. 2007; Nimmannitya 1995; Soni et al. 2001). Besides this, we have achieved success in finding anti-dengue molecules from plants (Kumar et al. 2012; Rout et al. 2012). ICGEB, New Delhi in collaboration with Department of Biotechnology (DBT) and Ranbaxy Research Laboratory conducted an experiment and tested total 200 samples for anti-dengue activity. The methanolic extract from *Cissampelos pareira*, the only plant extract patented so far, showed potency against all the four dengue serotypes with insignificant toxicity (Bhatnagar et al. 2009). However, the large-scale field evaluations of these trials are still awaited.

3. Vector control and transmission of the disease

Since there is no vaccine and proper treatment for dengue infections, vector control is the primary option left to work on in order to reduce the burden of dengue like other vector borne diseases (Klasen and Habedank 2008). However, like pathogen diagnosis and treatment, hardships have also been seen in controlling the disease vectors. Nonetheless, there is no planned and separate national program exists for the control of dengue (Yadava and Narasimhan 1992). The major method of combating disease vectors is either by direct spraying on vector habitats or through the use of insecticide-treated bed nets as in the case of malaria (Raghavendra et al. 2011). In addition to this, dengue-controlling efforts are majorly aimed at reducing/destroying mosquito breeding sites. However, *Aedes* mosquitoes breed in tiny, transient pools of water, as found in discarded soda cans, tires, plant axils, air-cooler trays, flower pots, discarded receptacles, roof gutters, etc., and it is virtually impossible to remove all such breeding sites. Moreover, direct spraying on vector habitats is problematic as it effects the environment and the human health negatively. Use of insecticides has been further complicated by the development of insecticide resistance in *Aedes* mosquitoes that makes the dengue vector control more pathetic and a challenging task. Currently, more than 500 insect species have acquired some type of resistance to more than one class of insecticides (Horrigan et al. 2002; Tikar et al. 2009); however, temephos and fenthion as larvicides are still effective against Indian *A. aegypti* mosquitoes (Dash et al. 2001; Tikar et al. 2008). In addition, natural extracts from many plants have also shown potential for controlling *A. agypeti* mosquitoes in experimental studies (Govindarajan et al. 2011; Govindarajan and Sivakumar 2012; Gupta et al. 2012; Kumar et al. 2012; Mahesh et al. 2012; Maheswaran and Ignacimuthu 2012; Rajkumar and Jebanesan 2010). In order to prevent the development of resistance in mosquitoes against these presently working insecticides, effective monitoring and development of alternative vector control strategies are very essential. Recently, genetic vector control techniques have emerged as the potent alternatives for the existing vector control measures; however, the research on these aspects in India is at very nascent stage (Ravikumar et al. 2010; Sunish et al. 2011). Although sterile insect technique and incompatible insect techniques were tested in India in 1970s with long-term objectives of vector control, the proper implementation of the project failed due to the wrong projection of its goals as "bio-warfare" (Pates and Curtis 2005). After this incidence, the research in this direction remained almost silent in the country. However, considering the demands of the situation, the development of the genetic methods like *Wolbachia*-based dengue control, the release of insects carrying dominant lethal gene, etc. that are showing promising results in other endemic countries (Harris et al. 2011; Hoffmann et al. 2011; Lacroix et al. 2012; Walker et al. 2011) should be considered to be explored in Indian perspective.

4. Other important aspects of dengue control

(a) Involvement and active participation of general public

Development of effective disease control measures is very essential; however, their application could be a failure without the understanding and active involvement of general public in campaign against dengue control. This is because misconceptions and wrong beliefs are usually very common which hinder the proper treatment of the disease. People usually do not bother for the initial dengue symptoms like high fever, body ache, vomiting, and even live with them as long as they can tolerate. This can be illustrated by a case in which the parents of a 1.5-year-old child, who died in dengue outbreak of 1996 in Delhi, took initial dengue symptoms as childhood diseases and tried to treat her with home remedies and homeopathic medicines (personal experience). This kind of ignorance and self-medication aggravated the condition of the baby that resulted in untimely death. This shows the unawareness of the people about dengue causes, its symptoms, and consequences. The similar behavior of Indian community about dengue is also visible from the recent survey on knowledge, attitude, and practice conducted in Chennai after an outbreak in 2001 (Kumar et al. 2010). This survey revealed that the majority of the people in Chennai are unaware about the basics of dengue, its transmission, vector breeding sources, biting behavior of *Aedes* mosquitoes, and their preventive measures. Unawareness about the disease increases the number of hidden reservoirs for dengue virus and thus enhances easy spread of the disease. Generally, the dengue burden can be reduced significantly if people are made aware about the basics of dengue by organizing educational programs and informational campaigns (Singh et al. 2000). For this, mass media coverage should be adopted using all the types of electronic, print, and broadcast media including, newspaper, television, internet, general announcements, advertisements, radio, personal visits, etc. The effective role of media and mass communication could be well explained by the success of polio eradication from India (Dhole and Mishra 2012; Singh et al. 2001; Singh and Bharadwaj 2000). However, mass immunization against polio did the wonders; the role played by the mass media to create awareness about the importance of vaccine and hazards of polio and motivating the people for vaccination cannot be ignored. This strategy has been implemented for disseminating dengue awareness especially in urban areas of Delhi (Acharya et al. 2005; Gupta et al. 1998); the mass coverage is needed to create an impact. The mass coverage should be seen as one of the potential additive tools to the existing vector control measures to get rid of the mass breeding of the mosquitoes through environmental manipulation/removal of potential breeding sites by the active involvement of communities.

(b) Implementation of well-planned strategy to deal with dengue infections

Considering the large population size of India, burden of dengue (number of cases and number of deaths) is not very high; however, this does not mean it should be neglected until it emerged as the uncontrollable problem. Moreover, such pathogens/diseases should be curbed at initial stage so that they do not flourish and create high burden. However, the initial reaction towards any disease and its control could be well explained by the concept of "crisis mentality" which means the appropriate action against the disease is postponed until it turns into a large epidemic (Gubler and Clark 1995). In India, after the dengue outbreak in Delhi 1996, major emphasis was on developing only emergency control methods to manage the current situation (Addlakha 2001), while very low attention has been paid to control its reoccurrence and spread to other surrounding areas. This is because dengue is causing epidemics every year in Delhi (Gupta et al. 2006), and infections have even migrated to the other nearby areas (Chakravarti et al. 2012; Gill et al. 2008; Kaur et al. 1997; Nandi et al. 2008; Ukey et al. 2010). Thus, besides emergency control measures, the control strategy should also involve the necessary actions in time with prior warning. The emphasis should be on preventing breeding of mosquitoes and transmission of the virus, in order to efficiently control the disease (http://www.cseindia.org/programme/health/pdf/conf2006/adengue.pdf).

(c) Scientific research, infrastructure, funds, and facilities

Effective and successful control of any disease needs in-depth understanding on vulnerable points related to disease like basic biology of the pathogen, its epidemiology, genetics, population behavior, pathology, immunology, host biology, host–pathogen interactions, etc. Moreover, pathogens as microorganisms are usually very diverse and dynamic; thus, their population-specific analysis in Indian perspective is very necessary. Scientists in India have made considerable efforts in dengue control and its related fields (Abhyankar et al. 2006; Chaturvedi and Nagar 2008; Jaiswal et al. 2004; Khanam et al. 2007; Parida et al. 2001, 2005; Saxena et al. 2008); however, increasing severity and continuous epidemics of the disease needs extensive research covering various aspects related with dengue. Moreover, dengue is continuously involving new challenges that needs a lot of efforts in different directions, and for this, we need dedicated teams, extensive research, and excellent infrastructure in every corner of the country to provide quick and reliable diagnosis and appropriate treatment. At par with malaria research which is being studied at National Institute of Malaria Research, New Delhi and its ten field units established in the malaria endemic states (www.mrcindia.org), there is an urgent requirement to set up such dedicated research laboratories for dengue research in India. To our best knowledge, very limited number of research centers and the scientific groups are involved in dengue science in India (Table 1). The referral centers and sentinel hospitals established in different states are provided with the diagnostic laboratories and facilities. These

Table 1 List of major research centers involved in dengue research in India

Sl. no.	Institute name	Location	Major research area
1	National Institute of Virology (NIV)	Pune	Anti-viral and diagnostic kits
2	International Center for Genetic Engineering and Biotechnology (ICGEB)	New Delhi	Vaccine research and diagnosis
3	ICMR, Virus Unit, National Institute of Cholera & Enteric Diseases	Kolkata	Diagnosis
4	National Center for Disease Control (former NICD)	New Delhi	Epidemiology
5	All India Institute of Medical Sciences, Delhi	New Delhi	Diagnosis and epidemiology
6	Vector Control Research Center	Pondicherry	Vector control
7	Sanjay Gandhi Post-Graduate Institute of Medical Sciences	Lucknow	Clinical studies
8	Post- Graduate Institute of Medical Sciences	Chandigarh	Clinical and epidemiological studies
9	Defense Research Development and Establishment	Gwalior	Vector control
10	Institute of Preventive Medicine	Hyderabad	Epidemiology

laboratories usually conduct the clinical studies. Ensuring the diagnostic facility and availability of kits is the responsibility of the respective State Program Officers, NVBDCP. For free of cost dengue diagnosis, IgM MAC ELISA test kits are provided by NIV, Pune to these laboratories. Kits are supplied by NIV, Pune on receipt of requirement from the respective states based on the previous epidemiological situation of dengue (www.nvbdcp.gov.in). The funds for all these project are provided by Government of India (www.nvbdcp.gov.in).

Conclusions

Dengue is expanding its geographical boundaries from rarely few countries in 1970s to almost everywhere now, and this alarming shift in dengue epidemiology demands unanimous support and concerted efforts from multiple sectors/stakeholders for controlling the disease effectively. The present analysis of dengue and its control in India emphasizes on an urgent need to develop permanent surveillance program coupled with improvised disease diagnostics, effective anti-dengue treatment measures, and appropriate strategies to stop the disease transmission by tailing an effective implementation of the presently available vector control programs. More specifically, we need lots of efforts, dedicated teams, extensive research, excellent infrastructure, public participation, reliable diagnosis, and appropriate treatment with a goal to eliminate dengue from India.

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