



Short Review

Evolving herbal formulations in management of dengue fever



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ABSTRACT

Dengue is endemic in more than 100 countries and it is estimated that annually above 390 million infections occur globally. During the period between 1996–2015, a massive increase of more than 500 per cent has been recorded in number of dengue cases reported in India. Till date, there are no specific globally accepted treatments for dengue fever in any system of medicine. Dengue does not cause very high mortality if properly handled and is currently being managed by clinicians through various adjuvant and alternative therapeutic options. Various plant based preparations have been used in different parts of India for combating dengue and are simultaneously also being scientifically validated by researchers. However, number of such scientific validation studies on phytomedicines are very less in India. Out of twenty-two plants reported against dengue, only four have been studied scientifically. *Azadirachta indica*, *Carica papaya*, *Hippophae rhamnoides* and *Cissampelos pareira* extracts were found effective and demonstrated improvement in clinical symptoms and direct inhibitory effect on dengue virus. *C. papaya* clinical trial showed increase in platelet count and faster recovery. These plants may be explored further as probable candidates for drug discovery against dengue. There is a need to search more such herbal formulations, which are being practiced at local level, document properly and validate them scientifically to confirm efficacy, mechanistic action and safety, before use. The herbal formulations being used by communities are the low hanging fruits which may provide alternative or adjuvant therapy if proper validation, value addition and product development steps are followed. This paper aims to review the recent status of dengue cases, deaths and evolving curative herbal solutions adapted and reported from India to combat the disease.

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1. Introduction

The incidence of dengue, a viral infection, has rapidly risen in humans through extensive transmission by the bites of infected female *Aedes aegypti* mosquitoes. Dengue Haemorrhagic Fever (DHF) or severe dengue was initially documented during the dengue epidemics in Thailand and Philippines in 1950s; it is now becoming the leading cause of sickness and mortality in several Asian and Latin American countries, including India. Four different types of closely linked virus serotypes responsible for dengue are DENV-1, DENV-2, DENV-3 and DENV-4. These viruses are predominantly transmitted when infected female mosquito *A. aegypti* bites healthy individuals. Once infected, humans act as carriers and provide favorable environment for multiplication of the virus,

which subsequently gets transferred to uninfected vectors during bites [1]. Patients suffer with eminently high fever along with some associated symptoms such as moderate to severe headache, pain in joints and behind eyes, vomiting, rashes and inflamed glands. If not handled well, dengue becomes complicated and patient suffers due to respiratory distress, fluid accumulation, severe bleeding, organ damage etc. which becomes fatal in critical cases [1].

Presently, dengue is endemic in more than 100 countries across the globe including India; prior to 1970, only nine countries were reported to have epidemics of severe dengue [1]. Bhatt et al. (2013) analyzed under-reporting of the actual number of dengue cases and estimated that annually about 390 million infections occur throughout the globe [2]. In India, dengue virus was first isolated in the year 1944 in Kolkata from the serum samples of infected US soldiers [3]. In 1996, the first major epidemics of Dengue Haemorrhagic Fever (DHF) and/or Dengue Shock Syndrome (DSS) occurred near Delhi and Lucknow in Uttar Pradesh and thereafter the virus started spreading across India [4–6].

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Currently, the Indian population is infected by dengue viruses and sizable numbers of mortalities are recorded every year. India has a rich biodiversity and tradition of using plant-based medicines for preventive and curative healthcare. Traditionally large numbers of plants are reported for their use against contagious diseases, including infection caused by viruses. During recent years, there are many online and offline published contents which demonstrate and portray use of plants and their formulations for their therapeutic effects against dengue. This paper aims to review the recent status of dengue cases, deaths and evolving curative herbal solutions adapted and reported from India to combat the disease. Data on utilization of various herbal and traditional medications popular among clinicians, patients and common public for contending dengue are also compiled.

2. Status of dengue infections and deaths in India

Reported infected cases and mortality due to dengue in Indian states were thoroughly evaluated for last 20 years using licensed version of www.indiastat.com. The data in Fig. 1(A&B) illustrate dengue cases and related deaths during 1996–2015 and also depict its status in different states and union territories of India. An increase of more than 500 per cent has been observed in the number of dengue cases during the period between 1996 (16,517 cases) to 2015 (99,849 cases). Data indicate that in India dengue viruses are getting all the required support systems for their rapid transmission and multiplication, i.e. favorable climatic conditions, abundantly available vectors, and human population for infection. In spite of increasing number of cases, a gradual decrease of about 40 per cent in mortality has been recorded from the year 1996 (545 deaths) to 2015 (220 deaths). Improvements in the Indian health-care systems, easy accessibility to medical practitioners, awareness

among stakeholders, early reporting and precise diagnosis, and availability of timely and better treatment options for patients may be some of the reasons for reduced mortality due to dengue infections. However, still there is a need to develop a drug which can target the dengue virus and also immunize individuals against primary as well as secondary infections. In 2015, Delhi (15,867) had the highest number of reported cases of dengue, followed by Punjab (14,128), Haryana (9921) and West Bengal (8516). Maximum number of deaths due to dengue was recorded in Delhi (60) followed by Kerala (25), Maharashtra (23) and Punjab (18) (Fig. 1A&B). There is no positive correlation between the number of cases reported and deaths occurred in various states of India. This may be due to various levels of preventive and curative therapies and also depends upon the immune responses of the patients during the treatment phase. Negligence by the patients and other stakeholders may be the key cause of increased death after infection.

3. Evolving herbal treatment options for dengue

Till date, there are no specific globally accepted treatments for dengue fever in any system of medicine. Dengue does not cause very high mortality and is currently being managed by clinicians through various adjuvant and alternative therapeutic options; however the patient suffers a lot during the treatment. Due to non-availability of specific drugs similar to other infectious diseases, patients often panic once detected with dengue. Preparations and formulations based on plants have also been tried and used by traditional healers and simultaneously being scientifically validated and documented by modern researchers. In this article we have reviewed various plants and their preparations which have been reported for dengue and are summarized in Table 1. Google, Google Scholar and Pubmed were searched using the following key

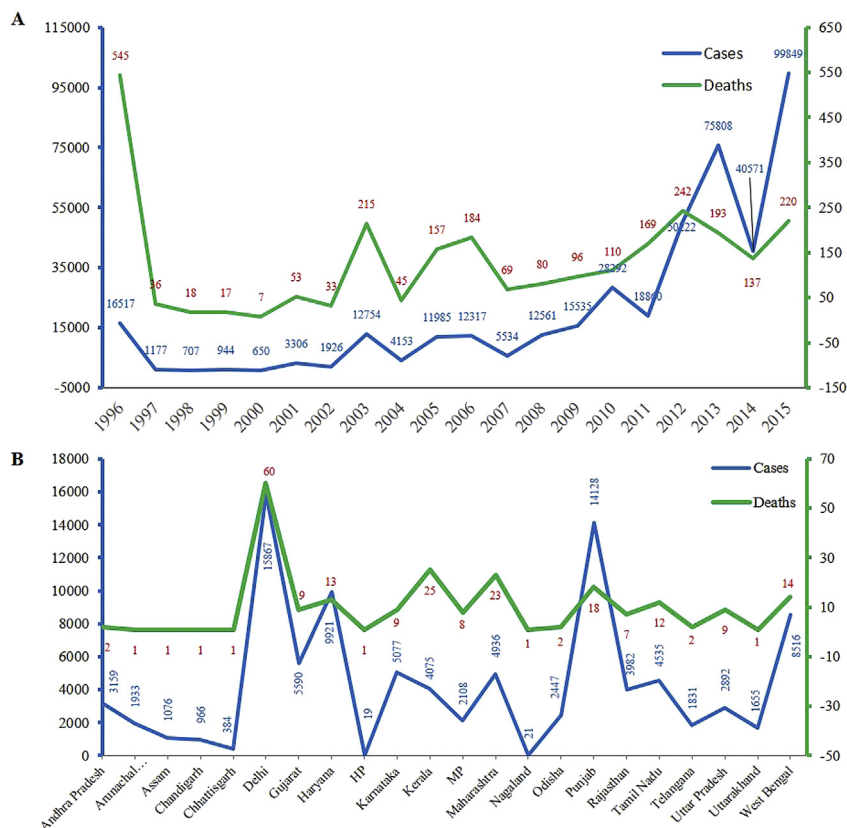


Fig. 1. A – Status of cases reported and deaths in India during 1996–2015. B – State wise infection and deaths due to dengue in India.

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