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Review

Impediments of reporting dengue cases in India

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ABSTRACT

Dengue has emerged as one of the most important mosquito-borne, fatal flaviviral disease, apparently expanding as a global health problem. An estimated 3.6 billion people are at risk for dengue, with 50 million infections per year occurring across 100 countries globally. The annual number of dengue fever cases in India is many times higher than it is officially reported. This under reporting would play a major role in the government's decision-making. Underestimating of the disease in India encumbers its people from taking preventive measures, discourages efforts to ensnare the sources of the disease and deliberates efforts for vaccine research. In this article, we highlight the probable impediments of under reporting leading to its impact on national and global public health and also offer key remedies to effectively address the issues across the clinics to the community level.

Contents

Introduction

Dengue is a self-limited, flu-like systemic arboviral disease transmitted between humans by *Aedes* mosquitoes. An estimated 3.6 billion people are at risk for dengue [1], with 50 million infections per year occurring across 100 countries globally [2]. Global increase in urbanisation has facilitated endemicity of dengue, especially in Asia and parts of South America [3]. India experiences cyclic epidemics of dengue over the years and the infection imposes for the leading cause of hospitalisation and death among children in the country [4]. Concurrent infection in some patients with multiple serotypes of dengue resulted from co-circulation of several serotypes of the virus in India [5]. Unplanned urban development, poor water storage, sub-standard sanitary conditions, increasing international travels and rising role in global economy could account for growing public health problem of dengue in India. A recent review has reported that India alone contributes to 34% (about 33 million infections) of the total global threat of dengue leading to hyper-endemicity, prevailing mostly in urban areas [6]. Notably, India reported an annual average of 20,474 dengue cases and 132 deaths by the disease in 2006–2012 [7]. Indian Health Ministry reported more than 138 Indian people killed by the dengue virus during the first 10 months of 2013, with more than 55,000 cases recorded across the country. According to the National Vector Borne Disease Control Programme [NVBDCP] data, the worst affected areas in India in 2015 were Delhi, Punjab, Haryana, Gujrat, Karnataka and Kerala with a range of about 4000–15,000 cases and 9–60 deaths [7]. However, the wide spread problem of under reporting of dengue cases from India has come into focus very

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recently and the real burden of dengue in the country is heavily ignored [5,8]. Interestingly, a recent study reports that an average of six million people a year in India had a symptomatic illness between 2006 and 2012 with dengue [5]. Shepard et al. retrospectively collected data from 10 medical colleges across five regions of the country. The study reports annual average of 5,778,406 clinically diagnosed dengue cases during 2006–12; which is about 282 times greater than what is reported by the Indian Ministry of Health [5]. The NVBDCP data shows increase of case reporting in 2015 compared to the previous year in several states; viz. Arunachal Pradesh, Haryana, Punjab, Uttar Pradesh etc. [7].

Fallacies in WHO case definition?

Dengue patients present with myriad of symptom profile; the commonest being non-specific fever, similar to other viral infections. Quite a significant number of people in India get infected with dengue virus every year, especially during epidemics posing a serious threat to the health system with regard to their preparedness in controlling this menace. Therefore, it is imperative to define and categorise dengue symptoms for early diagnosis and helping clinicians to recognise a case for reporting. The WHO case definition is the important tool for public health surveillance studies for early intervention and hence can significantly reduce morbidity and mortality. However, some researchers have reported of fallacies in the WHO case definition [9,10]. In India, this definition holds great significance as health resources are very limited especially in remote areas and clinicians rely deeply on clinical diagnosis aided by some basic laboratory tests. Notably, the WHO definition is not straight forward and relies on tests that reflected the situation in south east Asia in the 1960s [9]. With the advent of time, the application of this case definition required performance of different and repeated clinical tests (haematocrit, platelets, radiographs, serum albumin or protein, microscopic analysis of urine). This poses critical challenges for highly populated countries like India, with limited resources of trained health professionals, referral laboratories, accessibility to radiological support, and facilities to detect DHF by haematocrit and plasma leakage signs. Therefore, it was suggested that when the WHO case detection criteria are strictly followed, many severe cases, including those that involve shock and fatality, may be overlooked [11]. However, this may impact numbers for DHF, but not of DF. This is also evident from studies that 18% of severe dengue did not fulfil all four criteria considered necessary for the diagnosis of DHF by WHO, whereas over-inflation of the DHF figures was found when WHO provisional classification scheme was used [12]. The newer version of WHO case definition will permit for more sensitive management of the severe disease and allowing comparison of data across all regions [13,14]. Clinicians in the Pan American Health Organization (PAHO), Caribbean Epidemiology Center (CAREC) and World Health Organization (WHO) have also developed alternative classifications to guide proper clinical management [15]. Considering the limited laboratory facilities catering to the vast population and geographical extent in India, the WHO/PAHO/CAREC modified classification (discussed in the next section) [15] can be effectively implemented in India to aid correct identification of cases, effective surveillance and disease management.

However, it is also noteworthy to mention that the WHO case definition helps in classification of the disease and its management strategies rather than directly impacting the reporting process. Majority of the dengue burden is due to DF; however, DHF only accounts for 5–20% of the total cases. Proper clinical judgement, extensive training and awareness of the disease among clinicians, along with prompt laboratory detection is more important in the reporting process rather than the WHO case definition which is mainly focussed for the management of the types. However, passive surveillance using case definitions would lack specificity due to similarity of dengue fever with several other fever [discussed below].

Problems in laboratory diagnosis

Diagnosis by the clinician is the most important aspect that accounts for case reporting in India. The problem compounds as the clinical symptoms of dengue disease vary case by case. According to the WHO/PAHO guidelines, one clinical manoeuvre (tourniquet test) and two laboratory studies (platelet counts and hematocrit) should be performed for the diagnosis of dengue haemorrhagic fever in general laboratory settings [15]. In endemic areas, physicians do not conclusively diagnose dengue based on specific laboratory criteria, but instead use the dengue classical triad of symptoms of fever, rash and headache, a positive tourniquet test and the dengue classical triad observed in the complete blood count [Thrombocytopenia (platelet = 65,000), atypical lymphocytosis (atypical lymphocyte = 8%) and haemoconcentration (Hct = 47%) [16]. However, the problems with tourniquet test had also contributed to the under reporting. A positive Tourniquet test (TT) reflects haemorrhagic tendency and capillary fragility. In several observational outbreak studies, the sensitivity of the TT in DHF varied from as low as 0% [17] to 57% [18]. Notably, studies of Phuong et al. and Lucas et al. reported variable results for positive TT between DHF (47% and 27% positive, respectively) and DF (39% and 26% positive, respectively) [12,19]. Moreover, percent positive TT was also noted in dengue-like febrile illnesses, e.g. 21% [18], 12% [19] and 5% [12]. Interestingly, previous reports suggest that no haemorrhagic tendencies have been observed in 32–46% of DHF cases in India [20,21]. Therefore, inclusion of positive TT could underestimate dengue occurrences in India. A modified TT with an elastic cuff was suggested [22], which can be easily adapted by the Indian clinicians for better reporting of DHF. Either TT positive or negative, the clinician should be well trained to suspect dengue and report bother DF and DHF. However, only depending on clinical diagnosis would not suffice the needs of holistic reporting. Viruses can evolve by gaining random mutations to subvert the host immune system and remain undetectable. Dengue virus is also not an exception; mostly when the infections are asymptomatic or apparent presenting as fevers of unknown origin.

Inclusion of increased haematocrit and decreasing platelet count in diagnostic criteria can also lead to misdiagnosis especially where laboratory diagnosis of dengue is difficult to conduct. The diagnosis of dengue haemorrhagic fever in the Indian population with the rise of haematocrit does not help much due to the high prevalence of anaemia [23]. Variable results for thrombocytopenia in DHF had been repeatedly reported; ranging from 8.6% in Indonesia [24], 48% in Sri Lanka [19], 54% in Bangladesh [25], 70% in India [26] and 78% in Cuba [27] outbreak studies. These great ranges of variability can result in false reporting of dengue cases due to non-specific haemorrhagic conditions. Of note, several studies suggest that dengue cases can also be misdiagnosed as other tropical diseases [28–31], as concurrent infection of dengue with other infections is possible. Studies from India also confirm this fact [32]. A study of 118 cases, who fulfilled the clinical WHO criteria for DF/DHF, were evaluated for serological evidence of dengue, hantavirus, chikungunya, Rickettsia typhi, Rickettsia tsutsugamushi, rubella virus, influenza A virus, and Leptospira. Results suggested that only 49% were serologically tested positive for dengue infection, while the rest were dengue-negative [28]. Therefore, differential diagnosis of dengue fever from other forms of fever in Influenza, acute viral exanthems (Measles, Rubella), Leptospirosis, several forms of purpura or viral haemorrhagic diseases,

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