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Dengue and chikungunya co-infection: An emerging threat to Bangladesh

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Abstract

Dengue and chikungunya are considered as the two most emergent mosquito-borne viral diseases worldwide. Spatio-temporal features, common vectors and clinical appearances made the viruses progressively inclined to bring about co-infection. Being an Asian as well as a tropical country, Bangladesh is more prone to experience outbreaks of dengue and chikungunya or in worst case scenario, the co-infection. Therefore, the present study comprehensively assessed the underlying cause, clinical presentation and therapeutic intervention of the co-infection. Likewise, the study delineated the present dengue and chikungunya co-infection scenario of Bangladesh to limit the potential risk and burden of such co-infection in public health care setting.

Keywords: Dengue, chikungunya, vector, co-infection, symptom, climate, Bangladesh

Introduction

Dengue infection has expanded significantly with in the most recent 20 years, getting to be one of the most exceedingly awful mosquito-borne human pathogens with which tropical nations need to bargain ^[1]. The disease is now endemic in more than 100 countries comprising the WHO regions of Africa, the Americas, the Eastern Mediterranean, South-East Asia and the Western Pacific. The America, South-East Asia and Western Pacific regions are the most seriously affected ^[2]. On the other hand, Chikungunya has been documented in more than 60 nations in Asia, Africa, Europe and the Americas. Dissemination of chikungunya in mankind is caused by 02 types of mosquitos, *Aedes aegypti* and *Aedes albopictus* which are also responsible for transmitting dengue. These mosquitoes can be discovered gnawing all through light hours; however there might be pinnacles of action in the early morning and late evening ^[3]. Nevertheless, Dengue virus (DENV) and Chikungunya virus (CHIKV) are both single stranded RNA virus, both of them are quite different than each other ^[4].

DENV has been reported to exist as four serotypes, DENV- 1, DENV-2 DENV-3 and DENV-4; however, CHIKV is categorized into genotypes based on sequence differences and their origin. CHIKV genotypes are recognized as Asian, western African and east-central-south African ^[5]. Dengue ought to be suspected when 02 of these symptoms: serious cerebral pain, torment behind the eyes, muscle and joint pains, nausea, vomiting, swollen glands or rash, accompany a high fever (40°C/104°F) ^[6]. However, chikungunya is portrayed by a sudden beginning of fever usually accompanied by joint pain. Other regular signs and symptoms incorporate muscle torment, headache, nausea, fatigue and rash². Undifferentiated inflammable joint pain is an eminent clinical sign of dengue and chikungunya co-infection⁶. These co-contaminations can likewise result in diarrhea, deep bleeding, hepatomegaly and generally increased disease intensity ^[7].

At present, numerous tropical countries have perceived surprising rise and spread in instances of dengue and chikungunya ^[8]. Hence, dengue is endemic and chikungunya is a rising disease in Bangladesh. Since both the viruses are conveyed by similar vectors, concurrent or consecutive attacks by chikungunya and dengue viruses are certainly feasible ^[9].

Although, considerably more understanding should be achieved regarding co-infection due to dengue and chikungunya viruses, there is lack of sufficient information on how co-infection occurs or affects disease severity and outcome. Therefore, the purpose of the present review is to reveal insight on dengue and chikungunya co-infection especially in Bangladesh through exploration and analysis of published literature.

Methodology

The review work was done by searching, assembling and screening of plentiful literatures to identify all relevant and notable information pertaining to the dengue and chikungunya co-infection. Different biomedical databases such as PubMed, PubMed central, Scopus, Web

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of Science were searched for relevant publications and the reference list of those publications were checked as well. Additionally, information was also gathered from a few sites like World Health Organization, Medscape, Google Scholar and journals published by well-known publishers, for instance, Nature, Springer, Elsevier, and different journals that contained articles about dengue and chikungunya infection.

Catchphrases utilized for broad searching incorporate Dengue chikungunya co-infection, Chikungunya infection, Chikungunya in Asia, Chikungunya in Bangladesh, late episodes of Chikungunya in Bangladesh, Dengue infection, Dengue in world, Dengue in Bangladesh, Ongoing flare-ups of Dengue in Bangladesh and so forth.

Overview of the Co-infection

Global scenario

Globally the concurrent transmission of Dengue and Chikungunya was found in 98 countries^[10]. Among them; the co-infection by both the viruses was reported in 13 countries. Initially in 1962, four positive cases of such co-infection were observed in Thailand. Another prior reported case of dengue and chikungunya co-infection was found in India (1964)^[11-12]. Gradually more cases were reported from Angola, Gabon, Madagascar, Malaysia, Myanmar, Nigeria, Saint Martin, Singapore, Sri Lanka, Tanzania and Yemen. Such co-infections have also been evidenced from Bangladesh^[13-14].

Common Vectors

Aedes albopictus and *Aedes aegypti* mosquitoes are known as the vectors, transmitting both dengue and chikungunya viruses. Generally single or consecutive bites of one simultaneously co-infected or two separately sequentially infected mosquitoes respectively, assumed to be the reason of dengue and chikungunya co-infection^[4]. Multiple factors like climatic parameters, socio-demographic vulnerabilities and environmental influences act as critical components in the circulation and endurance of mosquito vectors, as well as influence the incidence of co-infection^[15]. Temperature variance, monsoon reliant mosquito breeding patterns, mosquito habitats, unplanned urbanization, population density and migration of population for livelihood have aided the expansion of the vectors worldwide and spread the infection in a concomitant manner^[16].

A study revealed the ability of the mosquito vectors to replicate both the virus simultaneously and deliver them concomitantly in a single bite. Moreover, a primarily infected mosquito vector of dengue virus could also be prone to secondary infection by chikungunya virus as well^[4]. In 2010, an artificial infection experiment also showed that the same *Ae. Albopictus* mosquito could concurrently be infected with dengue and chikungunya viruses^[17]. Another study on competitive suppression occurred in co-infected vector sample was carried out to investigate the infection pattern in factual manner. The data demonstrated that the viruses can potentially co-infect if the viral concentration is high enough despite of the infection order^[18]. Other studies also indicated co-transmission of dengue and chikungunya infection via mosquito sequentially infected by the two viruses^[19-20].

Some studies also focused on the genomic mutation of viruses as the technique of their spreading through new vectors in more regional settings and different countries^[21]. However, there is scanty technical expertise and inadequate resources about the vectors responsible for co-infection in endemic areas. This hinders the investigation for assessing the role of

vectors in co-infection and also greatly impact the prediction and control of viral outbreaks^[4, 7].

Common clinical presentation

Dengue & chikungunya both are self-limiting infections^[22]. However severe dengue infection can lead to Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). On the other hand, a severe chikungunya infection can cause polyarthralgia which could last even up to 1 to 3 years. Such state of chikungunya can lead to critical loss of productivity and majority of the patients reported low to very low overall quality of life^[23]. Moreover, neurological and optical manifestations are also found in severe chikungunya infection^[6, 24-29].

Several studies showed patients with these dual infections are predisposed to greater risk of mortality with severe clinical dispositions involving central nervous system and hemorrhage. These studies also urge for specialized treatments and better patient management^[30-31].

Although, some common clinical symptoms of both infections, such as febrility, are present in co-infected patients, unlikely some non-parallel symptoms e.g. undifferentiated inflammatory arthritis could also be found⁶. The co-infections can also result in diarrhea, deep bleeding, hepatomegaly and overall increase in disease severity^[7].

However another study claimed that dengue and chikungunya co-infected patients do not possess any distinct clinical disposition compared to their mono-infections^[32].

Co-infection situation in Bangladesh

Dengue has been recognized as endemic disease in Bangladesh with high occurrence in monsoon over the past two decades. Though it was found initially in 1964, but turned in to a large epidemic form in 2000, 2016, and 2018^[33-34]. Studies revealed the existence of all the four serotypes of the dengue virus (DENV- 1, DENV-2 DENV-3 and DENV-4) in Bangladesh at present^[35]. As mosquito borne viruses continue to arise, we predict that the occurrence of co-infection may erupt as well^[36]. Furthermore, in 2008 the first chikungunya outbreak was reported in Bangladesh. Other outbreaks of Chikungunya was acknowledged in 2011 and 2017^[23, 37-38].

Several studies reported the seasonal and climatic relationship with the dengue and chikungunya outbreaks in Bangladesh. Most of the dengue cases were reported in monsoon and post-monsoon season (July-October). However, since the last few years dengue cases were also reported in the pre-monsoon season at a significantly higher rate. This could be due to sporadic precipitation, and prolongation of the monsoon season throughout the year^[34]. Additionally, the outbreaks of chikungunya notably presented the same seasonal and environmental features like dengue and a serology-based study reported acute clinical cases of chikungunya concurrently positive for dengue as well, during the chikungunya outbreak^[23, 39]. Outcomes of the subsequent survey on chikungunya in 2017 revealed that, the concentration of vectors is much higher in the monsoon and post-monsoon periods and climate variation promote the mutation process among the viruses in the environment. This probably leads to the emergence of chikungunya virus at the same time of the dengue outbreaks^[23, 34, 39].

Case reports of co-infection in Bangladesh

Recently, a number of dengue and chikungunya co-infected patients, have been reported in Bangladesh. One case study from chikungunya outbreak in 2017, reported a 75 year old

diabetic and hypertensive patient who was subjected to high grade continued fever, severe bodyache, drowsiness, dehydration, tachycardia. She was diagnosed as Anti-chikungunya IgM, anti-dengue IgM and IgG positive. Although the radiological findings was indicative to osteoarthritis, the other investigations like low haemoglobin and platelet count and rise in erythrocyte sedimentation rate were suggestive of co-infection. The patient was treated with paracetamol, antiemetics and intravenous normal saline [40].

The first case report of a primigravida with 36th week of pregnancy, diagnosed with dengue viral infection within an acute phase of chikungunya. The mother had a first onset of febrile condition and persistent joint pain, ten days before she was admitted to hospital. After that, she was found to be highly febrile again (5 hr continuous fever), flushed, tachycardiac, anaemic and lymphopaenic with high erythrocyte sedimentation rate and the sign of fetal distress was also observed which indicated the occurrence of emergency caesarean section. The neonate had congenital pneumonia, but no evidence of vertical infection was found [41].

Another case study presented, a 50 year old lady diagnosed with dual viral infection. The patient was found to be positive for both dengue nonstructural protein 1 (NS1) and immunoglobulin M (IgM) for chikungunya. She experienced a three day long high grade continued fever and generalized body ache along with leucopenia, lower normal platelet counts and a little raised erythrocyte sedimentation rate. Therefore, the patient was hemodynamically stable but suffered for feet pain for about two weeks after the end of fever. In the course of therapy, she got paracetamol and oral prednisolone tapered off over few weeks [42].

One more study reported two cases of the co-infection, firstly a young adult presented with 3 days high grade fever, headache, generalized body ache and tachycardia was diagnosed as a case of dengue-chikungunya co-infection. The patient was found with normal blood pressure, haemoglobin, total and differential white blood cell and platelet count. But gradually he developed generalized maculopapular rash and pruritus, more importantly suffered from persistent low back pain for about three months. The patient was treated with paracetamol, fexofenadine and also put on sulphasalazine. The other patient, a 45 year old male was presented in hospital with 3 days high grade fever, generalized aches and pain along with two episodes of vomiting. The patient had earlier history of febrile illness with maculopapular rash and pruritus which responded to paracetamol and fexofenadine respectively. However, the physical examination revealed low blood pressure, dehydration and tachycardia in the patient. Paracetamol, antiemetics and intravenous normal saline was applied in the treatment. Both the aforementioned patients were subjected to early onset of 5 day long febrile illness with generalized body and joint ache about 15 days before consulting to hospital [43].

Laboratory Diagnosis

Due to the lack of distinguishing clinical highlights, laboratory diagnosis based on outbreak reports and endemic examples are the main route for satisfactory clinical management of co-infection situations [7]. Typically dengue infection with one sort of virus serotype, as a rule presents assurance against reinfection by the equivalent serotype; in any case, if an individual is contaminated by an alternate serotype, the possibility of creating DHF and DSS is higher, thus recognizing the genotypic status of the infection might be

significant for the disease management. Usually early dengue diagnosis by detection of dengue virus NS1 antigen and immunoglobulin M (IgM)/immunoglobulin G (IgG) antibodies is common diagnostic practice. However, Life threatening, extreme manifestations of dengue may happen even in the first week of clinical ailment when antibody (IgM) status is expected to be negative. Therefore, identify the type of dengue virus by Reverse-transcriptase polymerase chain reaction (RT-PCR) technology during this period might be beneficial in the early diagnosis and proper management of the illness [44]. Likewise, RT-PCR technology can also efficiently detect ribonucleic acids (RNAs) of chikungunya sufficiently early in disease course. But anti-chikungunya antibody (IgM) may be detected in later part of first week or at the beginning of second week [7].

Treatment and management

There is no specific antiviral drug treatment exist for dengue or chikungunya infection. Treatment is symptomatic and supportive. Common febrile illness of both dengue and chikungunya is treated with paracetamol and other supportive therapy. Exclusion of dengue is more important than establishing chikungunya virus infection during febrile periods, as patients may require nonsteroidal anti-inflammatory drugs (NSAIDs) such as naproxen for joint pain management in chikungunya, which is not advocated during dengue infection. Aspirin should also be avoided due to its effect on platelets. Published evidence does not support the use of corticosteroids, antibiotics or any other antiviral drugs in the management of these viral infections and indiscriminate use of these agents can be hazardous. Electrolyte imbalance, prerenal acute renal failure, bleeding manifestations should be watched carefully and managed accordingly [42, 45-46].

Like some other vector borne diseases, mosquito control is a significant intercession to anticipate dengue and chikungunya infections. World Health Organization (WHO) guidelines suggested that ecological intercessions, for example, crushing natural and human-made mosquito rearing locales in and around homes, which might be more financially savvy than chemical approaches to destroy larva and adult mosquitoes [42, 47]. Moreover, confining patients under mosquito nets during the viremic stage is an important intervention against disease transmission [39]. In this manner by taking appropriate public health measures the burden of dengue and chikungunya co-infections can be diminished [42]. However, ecological investigations, which more likely depict the spatial and temporal distribution of vector habitats, could target interventions in populations who are suffering from vector-borne maladies [37].

Concluding remarks

The transmission of vector borne infectious diseases has become an alarming issue around the world, particularly in tropical and subtropical regions because of their recurrent occurrences [48]. Among those diseases, some have turned out to be endemic in numerous areas initiating a large number of disease incidences each year.

The present study was focused to enlighten dengue and chikungunya co-infection scenario especially in Bangladesh. The study revealed lack of clarity in proper, differential and entire diagnosis between co-infections and mono-infections of both viruses, it happens because they often share early clinical symptoms and also for inadequate diagnostic facilities. This may lead to detrimental effects on the patients and increases the risk of inappropriate treatment. That is why several studies

[42, 46] emphasized on the differentiation of dengue from chikungunya during febrile periods of viral infections. In addition to this, the reported case studies indicated leucopenia and thrombocytopenia as common clinical manifestations in dengue whereas lymphocytopenia and raised erythrocyte sedimentation rate observed as identical for chikungunya infection [39, 40]. Likewise, negative NS1, nonexistent retro-orbital pain, neutropaenia and thrombocytopenia, and appearance of rash at onset of febrile illness, lymphopenia, high ESR and C-reactive protein (CRP) were considered as significant distinctive clinical highlights between the two infections [39, 49]. Besides, the first case of dengue and chikungunya co-infection during pregnancy reported the incidence of caesarean section because of fetal distress. Though previously unreported, this situation may become increasingly common [41].

Furthermore, the present study found shared ecological attributes, common vector distribution and co-endemicity as the most frequent causes of co-infections and acknowledged the sequential pattern (2016 and 2018) of Dengue flare-up in Bangladesh alongside an admist chikungunya erupt in 2017 [34, 50]. This current scenario has already set alerts in public health care set-up of Bangladesh. Hence, efforts to explore the detailed mechanism of dengue-chikungunya co-infection, to control the outbreaks and to raise public awareness are crucial. These may perhaps provide an opportunity for public health action to reduce burden of this co-infection.

Conflict of Interests

The author declares that there is no conflict of interests

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