MEDWIN PUBLISHERS
Committed to create value for Researchers

Virology & Immunology Journal

Some Issues and Challenges Faced in Dengue

Chandramathi S and Sekaran SD*

Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Malaysia

Editorial

Volume 1 Issue 2

Received Date: September 01, 2017

Published Date: September 02, 2017

***Corresponding author:** Shamala Devi Sekaran, Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Malaysia, Tel: +6-012-2253292; Email: shamala@um.edu.my

Editorial

Dengue disease, a rapidly spreading arthropod-borne viral illness is a major public health problem as its clinical symptoms can vary from mild self-limiting dengue fever to severe dengue. In addition treatment is limited to rehydration therapy as there are no antivirals. Dengue viruses (DENV 1-4) belong to the complex family of closely knitted Flaviviridae and are transmitted primarily by *Aedesa egypti*. There are more than 125 dengue endemic countries with global incidences from 200 to 400 million cases per year. Incidences are still on the rise due to various intractable factors mainly climate change, unplanned urbanization, international travel, viral evolution and many areas still exist where dengue is under-reported due to either inadequate provision of diagnostic resources or clinical misdiagnosis as dengue signs can be similar to other acute tropical viral diseases. Recent advances in technology have helped individuals from various platforms such as science, medicine, pharmacy, and policy making bodies to bring the dengue incidences under control in some endemic areas.

Early diagnosis enables prompt disease management and it is noteworthy that adequate knowledge of the disease pathogenesis is certainly crucial where the type of diagnostic tests rely on the disease phases. Diagnostic tests include direct and indirect methods. During the early phase, virus and viral components are present at higher levels during the spread of infection which has just begun to trigger the adaptive immune system, whereas, during the late phase antibodies produced by the adaptive immunity will be more suitable at this period. The direct method which enables Serotyping is highly sensitive as compared to the serological tests that identify antibodies against all four DENV serotypes but may also be cross-reactive with other flaviviruses. Currently, the main issue faced with serological assays is the high cross-reactivity with other co-circulating flaviviruses especially in highly endemic areas. Many diagnostic settings have now incorporated the NS1 rapid test with serology though the issue now is whether there is any cross-reactivity with Zika NS1 as we do know that this region has a high homology of 53-55% with dengue. Despite recent advances a sensitive, affordable point of care test that multiplexes the different markers and differentiates co-circulating flaviviruses is still at large. Newer technologies such as micro fluidics, paper-based diagnostics, chip-based systems, micro- and nanofabrication technologies are being developed but however were not adequately and independently validated more so because of the lack of standardized protocols and also problems with the availability of standardized and well-characterized clinical specimens. Most of these utilize antigen specific monoclonal antibodies that can bind specific viral antigens with high affinities. Cell based methods have been developed to distinguish between the different DENV serotypes and between DENV and ZIKV viruses. Others are working towards the development of antigen capture ELISAs that use similar ZIKV- and DENV-specific anti-NS1 mAbs. However these need to be more user friendly which may then lower the sensitivity and increase the cost. The extensive cross-reactivity among co-circulating flaviviruses has confounded serological diagnosis of recent and past flaviviral infections. Highly specific antibody detection methods are required for surveillance, seroprevalence and vaccine studies and for these it will eventually be necessary to consider timing of sample collection as well as number of samples needed to make a “definitive” diagnosis. This is more important for surveillance than for treatment or management. Companies/researchers developing diagnostic assays will

need to consider this. The question then is do we need a perfect assay? No geographical setting will be identical and hence the test(s) to be used to enable patient management will not necessarily be the one for surveillance and public health authorities. However this may not be cost-effective in areas with large yearly outbreaks.

To date many investigations have been carried out to understand the pathogenesis and identify potential risk factors to severe dengue. The progression of mild dengue to severe dengue is postulated to be due to an over-exaggerated host immune response involving cells, antibodies and cytokine storms, leading to increased vascular permeability that results in a potentially fatal severe dengue. While most studies have found significant association of cytokines production, contradictory results have also been reported. Perhaps severe dengue may also be due to damage-associated molecular patterns generated during the inflammatory process. This may be another option to consider for diagnosis especially in identifying individuals who may be at risk of severe leakage and shock. Development of assays to identify these factors is crucial for successful management of this disease as the differential expression of immune related proteins will provide insights of the pathways of disease progression and thus enable novel treatment strategies and appropriate clinical management.

The complexity of diagnostic tests often results in misdiagnosis of dengue infection hence contributing to the increase of disease burden. Thus it is essential to include other measures in controlling the disease spread such as vector control and the introduction of vaccines.

Various vector control mechanisms have been used with varying efficacies and if used can result in reducing mosquito indices and thus incidences of dengue too. The key environmental control strategy is elimination of current and potential mosquito breeding areas and this remains fundamental in inhibiting vector proliferation and human-vector contact. Sustainability of these strategies is difficult as it involves human behavioural change. Concerns with toxicity to the environment, resistance development have led to newer biological methods such as the sterile insect technique, usage of certain fish species in water containment areas and insect bacterial species (*Wolbachia pipientis*), into the *Aedes* mosquito population. Although the success rate of such natural ways of inhibiting the transmission may seem to be impressive, the long-standing success rate involving large endemic areas can still be challenging. Vaccines to dengue have been ongoing for many years and has been a struggle. The insufficient evidence of what is the protective co-relates and its levels remain a challenge which has hindered vaccine development. However the usage of vaccines should be conducted in conjunction with vector control so as to reduce risks to severe dengue as overtime cross-reactive antibodies develop and these may enhance infection. By keeping the mosquito indices low the original memory is retained without too much cross-reactive responses occurring as a result of multiple natural exposures.

The need to create global awareness of dengue continues to rise and concrete efforts involving all disease aspects namely diagnostics, risk factors, vector control and vaccination will be instrumental in curbing the incidence and spread of this disease.