EDITORIAL

Advanced Molecular Techniques and Diagnosis of Febrile Illness

The application of multiplex real time (Reverse Transcriptase - RT) polymerase chain reaction (PCR) in routine diagnosis of infectious diseases is unavoidable. In addition, the technique urgently might be an alternative tool in diagnosis of febrile illnesses caused by many different kinds of etiologies including bacteria, viruses and parasites. In Nepal, arboviral infections mainly dengue and chikungunya, scrub typhus, leptospirosis are considered as major emerging infections in the last two decades. In addition, these infections are the most predominant neglected tropical diseases in tropical and subtropical regions where more than 51% of the total population in Nepal are living. A few of these infections are responsible for chronic infection causing a high morbidity rate. A study reported up to 40% of acute chikungunya infections may lead to chronic infections. Similarly, the secondary infections can be more severe among f aviviruses such as Dengue and Zika due to antibody-dependent enhancement. Unlike the diagnosis of other neglected tropical diseases, the differential diagnosis of arboviral infections is quite diff cult as they all present similar clinical features, especially in Dengue Chikungunya and Zika viral infections. However, few studies showed a signif cant difference in clinical manifestations in specif c viral infections as well. Some clinical features are signif cantly associated with bacterial and viral infections. High grade fevers with longer mean duration of fever, severe musculoskeletal pain, central nervous system (CNS) related symptoms (such as altered mentation, confusion and loss of consciousness) and an elevated liver enzymes such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are highly associated with viral infections as compared to bacterial infections Finding such clinical manifestations may be helpful in the differential diagnosis of febrile illnesses as the point of care for future aspects. The other means of diagnosis commonly used in hospital settings of Nepal are serological methods including routinely used rapid diagnostic tests (RDTs) and Enzyme Linked Immunosorbent Assay (ELISA). However, these methods have few drawbacks including cross-reactivity, low sensitivity, and specif city making misdiagnosis of infections. Moreover, these methods are not applicable for early diagnosis of infections. An alternative to serological methods is molecular methods which are currently are not available for diagnostic purposes in most hospitals and health care centers. Although conventional PCR method has high sensitivity and specif city, it may take longer time and detect only a particular pathogen at a time. The molecular method mainly real time (RT) PCR has many advantages over other conventional methods because of which the applications of this technique for the diagnosis of infections or illnesses can't be avoided. The techniques are already introduced in diagnosis of respiratory viral pathogens to diagnose f u like syndromes in a very few hospital settings. However, many tertiary care hospitals in Nepal have not been facilitated to use this technique in routine diagnosis. In addition, febrile illnesses in tropical and subtropical regions are the most undiagnosed illnesses. As a consequence, a number of patients have been suffering from chronic bacterial and viral infections. Real-time (RT) PCR is the only ultimate tool in diagnosis of such illnesses. The method has not only higher sensitivity (> 95%) and specif city (100%) but also detects the possible pathogens as early as the f rst day of onset of illness. Because of good reproducibility, sensitivity and specif city, this method is considered as a gold standard method for the detection of RNA viruses in clinical specimens. In addition, the multiplex real-time (RT) PCR detects multiple pathogens in a single run making it more economic and less time consuming in the hospital settings of low and middle-income countries. It seems to be affordable to common people as well. While talking about the current situation of Nepal, several tertiary care hospitals have upgraded to real time PCR for diagnosis of COVID-19 during pandemic. Hence, the similar facility can be extended to detect of other pathogens in neglected tropical diseases and febrile illnesses in routine diagnosis.

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