A novel dengue fever (DF) and dengue haemorrhagic fever (DHF) analysis using artificial neural network (ANN)

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Introduction

Artificial neural network (ANN) is a powerful nonlinear statistical paradigm for recognition of complex patterns with the ability to maintain accuracy even when some input data are missing. ANN is able to perform certain specific task that mimics the acts of human brain, with its neurons and synaptic connections [1—3]. In ANN, the output performance for particular input variables of the network is optimised by adjusting the weights during the training process. The back propagation-training algorithm is commonly used for ANN in medical databases and has been shown by many researchers to be a powerful tool for prediction, prognosis and diagnosis in medical applications [4—9]. The outcome of these research findings showed promising result and enable a more effective resource planning and patient management. However, the use of ANN as a prognostic tool in dengue fever (DF) and dengue haemorrhagic fever (DHF) diseases has not been reported in the literature. Hence, this paper will be the first attempt to apply ANN for prognostic purpose in DF and DHF.

DF is an acute febrile viral disease frequently presenting with sign and symptoms that include headache, myalgia, macular rash, loss of appetite, nausea, vomiting, abdominal pain, metallic taste of food, change in psychological state and moderate thrombocytopenia [10]. A significant number of DF patients will progress to dengue haemorrhagic fever (DHF). DHF is the complication of DF around the day of defervescence of fever. The mechanism of progression from DF to DHF is related to immune mediated injury to the endothelium of the capillary, leading to plasma leakage from the capillary system, resulting in haemoconcentration, ascites, and pleural effusion and shock. It has been well documented that these serious complications usually set in following the day of defervescence of fever [11—13]. Since the early clinical features of DHF are indistinguishable from DF [11,14—16], the major pathophysiological changes that determine the severity of disease in DHF and also differentiates it from DF is plasma leakage resulting in increasing haematocrit (20% absolute rise from the baseline) leading to haemoconcentration, and a serous effusion that may lead to hypotension [11,17,18]. Defervescence is defined as the day when a patient has no fever or the disappearance of a fever. Fever is defined as the state when the body temperature rises above 37.5 ◦C [19]. Furthermore, patients who progress to shock will suddenly deteriorate at the time of, or shortly following defervescence of fever. These patients are in danger of dying if appropriate treatment is not promptly administered. Septic shock syndrome with vasodilatation, abnormal haemostasis and plasma leakage are the three pathophysiologic hallmarks of DHF [11,14,15]. These characteristic features typically occur at the onset of defervescence of fever [11,14—16]. Thus, the final diagnosis of severity of any dengue infection is unfortunately a retrospective one, after the progression of the illness has come to its end. Although most patients recover without sequel but a small minority may die from dengue shock syndrome (DSS). As a result, the mainstay of treatment remains as early diagnosis, close monitoring and aggressive fluid replacement therapy when indicated. The majority of patients were probably admitted for close monitoring and aggressive treatment merely due to anticipation of DSS. Decision making on when to admit or discharge patient has been a great challenge for the managing physician because there are very few clinical studies that address these issues. If the potentially ill patients can be identified confidently in time, a lot of unnecessary admission can be avoided. This will definitely has major impact on health care cost saving in view of the huge incident of dengue fever in this region. Thus, it is very crucial to know the day of defervescence of fever. If this information is made known beforehand to the clinician, early and proper clinical management and treatment can be planned to avoid mortality. This paper describes the development of a prognostic system to predict the day of defervescence of fever in DF and DHF patients using Matlab's neural network toolbox [20]. The data have been collected from a total of 252 hospitalised patients (4 DF and 248 DHF patients).

Dengue fever (DF) and dengue hemorrhagic fever (DHF)

The dengue viruses are members of the Flavivirus family. They consist of four serotypes and are transmitted by *Aedes aegypti* and *Aedes albopictus* mosquitoes. It is the commonest arthropod-borne viral infection in man [21]. It is estimated that as many as 100 million dengue virus infections occur annually in the tropics, with over 10,000 deaths from DHF [22]. Besides a rapid global increase in incidence, there has been an increase in severe cases as well [12,23]. Malaysia had its largest outbreak in the year 1996; a total of 14,255 dengue cases were notified of which 533 were DHF with 32 deaths [24,25].

Adult DF is typically a flu-like illness characterized by fever, headache, eye pain, myalgia, arthralgia, and rash, which last from 5 to 7 days. DHF has been graded according to the WHO specifications into four grades of severity, where grades III and IV are considered to be DSS. Grade I is defined as patients having a fever accompanied by nonspecific constitutional symptoms, the only haemorrhagic manifestation is a positive tourniquet test that result in petechial rash. Grade II is defined as patients having a spontaneous bleeding from any site of their body skin. Grade III (DSS) is where a patient has circulatory failure manifested by rapid and weak pulse, narrowing of pulse pressure (20mmHg or less) or hypotension, with the presence of cold clammy skin and restlessness. Grade IV (DSS) is defined as patients having profound shock with undetectable blood and pulse [11].

The characteristics of DF and DHF described above provide features that are amenable for a nonlinear modeling especially using ANN.

Artificial neural networks (ANNs)

Artificial neural networks (ANNs) have been widely applied to non-linear modeling problems, and they are highly suitable for modeling complex databases of medical information. The work carried out in this paper employed a multilayer feed-forward neural network (MFNN) trained via steepest descent back propagation algorithm [3,4,8,26—39]. At each iteration of this algorithm the sum-squared-error (SSE) of the network prediction is used as the cost function. Many literatures refer to the SSE as the error goal [27—30,32—34]. The hyperbolic tangent function was used for the ANN activation [27]. Since the training algorithm may produce over fittings, pruning technique was employed.

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