Non-invasive diagnosis of risk in dengue patients using bioelectrical impedance analysis and artificial neural network

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Introduction

Dengue disease is one of the current major public health affairs and is endemic in the Americas, southern Europe, North Africa, the eastern Mediterranean, Asia, Australia, various islands in the Indian Ocean, the south and the central pacific and the Caribbean [12, 29, 41]. Approximately, 2.5 billion people facing risk and it are predicted that this number will increase as transmission spreads to neighboring geographic regions [11, 13]. The World Health Organization (WHO) estimated of 100 million cases of dengue fever (DF) occurs annually [11]. In Malaysia, DF was reported as early as 1901 and the first report of the DF with hemorrhagic symptoms was made in 1962 [30, 34, 36]. In 1973, the first major outbreak of dengue hemorrhagic fever (DHF) (45 cases) was reported [39]. Since that time, the increase of dengue cases in Malaysia has been very significant, e.g., 19,544 cases with 50 deaths reported in 1997, and then increased to 27,373 dengue cases with 58 deaths in 1998 [1, 9, 34]. Recently, from 2004 to 2008, the number of dengue cases reported in Malaysia has increased from 33,895 (102 deaths) to 49,335 (112 deaths) [28].

Dengue virus is considered as arthropod-borne virus due its transmission cycle between Aedes mosquitoes and humans [41]. Dengue virus consists of four serotypes (DEN1, DEN2, DEN3, and DEN4) which are causing the DF, DHF, and dengue shock syndrome (DSS). Typically, DF begins with a sudden temperature increase accompanied

by headache, myalgia, macular rash, loss of appetite nausea, vomiting, abdominal pain, metallic taste of food, change in psychological state, and moderate thrombocytopenia [2, 20, 22, 41]. If early clinical management or appropriate fluid therapy was not provided, DF will progress to DHF. The progress of DHF begins when the fever subsided or known as defervescence of the fever. DHF is an infection associated with an increase in microvascular permeability, a decrease in plasma volume, and in severe forms hypotension and shock. If the appropriate therapy still not provided, circulatory failure will occur and lead to the DSS. DSS is fatal stage manifested by rapid and weak pulse and narrow pulse pressure [41]. Therefore, delay in the fluid therapy management will lead to progress of the dengue disease to the maximum stage (DSS) and may cause fatality to the dengue patient.

Accurate diagnosis in time and monitoring of severity of any dengue infection is needed in order to identify the severity of the disease and providing the appropriate treatment. In order to treat and control the dengue disease, many strategies have been developed and promoted. Two conventional techniques have been used to diagnose and to monitor the risk in DHF patients. The first technique is observing the onset and progression of plasma leakage by measuring the total increase in hematocrit (HCT) or the hemoglobin (Hb) concentration [15, 19, 20, 41]. The advantages of this method not only diagnose the DF but it can distinguish the DHF [14, 32, 41]. The second technique is to monitor the dengue patients' platelet (PLT) counts and liver function [28]. Even though those techniques can give accurate diagnoses, they are time consuming, invasive, and may harm the patients [20, 21]. The reasons behind this as follow: those techniques require frequent blood taking which may cause further injury to the subcutaneous tissue and potentially hazardous to the DHF patients. Moreover, monitoring of the patients can be done by admitting and hospitalizing the patients. However, admitting and hospitalizing

the patient cannot be arbitrarily or based on uncertain identification due to the huge number of the dengue patients in the country [20].

Recently, several studies were conducted to achieve accurate diagnosis without facing the above-mentioned drawbacks. Ibrahim et al. [20] applied bioelectrical impedance analysis (BIA) technique to monitor and classify the daily risk in DHF patients. Significant outcome was attained by using this technique and proved that the capability of the BIA to classify the daily risk of DHF patients. Another study [21] has reveals the non-invasive system for predicting the day of defervescence of fever in dengue patients using artificial neural network (ANN). Clinical symptoms and signs are used as inputs to the ANN. Accordingly, 90% prediction accuracy was achieved for predicting the day of defervescence of fever in dengue patients. Recently, Faisal et al. [6] employed self organized map clustering technique instead of the conventional statistical method to identify the risk criteria for classifying risk in the dengue patients.

This paper focuses on the diagnosis of risk classification in the dengue patients utilizing the BIA and a multilayer feed-forward neural network (MFNN) techniques.

Methodology

The procedures for designing the dengue risk diagnose system shows in Fig. 1.

Clinical data

Database comprises of 223 healthy subjects (158 females and 65 males) and 207 (90 females and 115 males) serologically [5, 27] confirmed dengue patients during their hospitalization were prospectively studied. The dengue database was divided into blood investigation and BIA

data. The blood investigation consists of 27 parameters such as PLT, HCT, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and Hb [18, 20]. The blood investigation and the BIA data were taken for 5 days with reference to the day the fever subsided. Fever day ?0 is defined as the day the fever subsided, i.e., when the body temperature fell below 37.5_C. Fever days after fever day ?0 are fever days ?1 and onwards [18, 20]. The blood measurement was taken from fever day ?0 until the fever day ?4 (fourth day after fever subsided). The BIA database comprises of patient information and 17 BIA parameters including the resistance, reactance, body capacitance (BC), fat mass, intracellular water, etc.

BIA

BIA is an in vivo technique involved the application of a small average constant current of less than 1 mA at a single frequency of 50 kHz through the human body, and measuring the body's bioelectrical tissue conductivity (BETC) parameters, namely, R, phase angle (a), BC, and capacitive reactance (X_c) via four surface electrodes [35]. Previous studies [19, 20, 22] shown that single frequency technique is able to give good results in dengue patients. Two electrodes were placed on the patient's right hand, one at the base of the knuckles and another slightly above the wrist joint. Another two electrodes were placed on the right foot; one nears the base of the toes and the other slightly above the ankle joint. A constant current was applied to the base of the knuckles and base of the toes, and the voltage signal was picked up by the other two sensor electrodes (slightly above the ankle and wrist joint). The voltage drop will determine the resistance and reactance (X_c) of the whole body. This data can then be converted to estimate the extracellular water (ECW), intracellular water, fat free mass (FFM), and fat mass through regression equations.

Risk quantification

In this study, the severities of dengue risk criteria were determined based on the following blood investigations [18, 20, 41]:

i. PLT count is less than or equal to 30,000 cells per mm^3 [4, 18]

ii. HCT increase by more than or equal to 20% [41]

iii. AST and ALT levels rose by fivefold the normal upper limit for AST and ALT [18, 26].

The risk quantification was performed on daily basis where blood investigations of the patients were evaluated for each day. Based on the blood investigation, the patients were then divided into two groups [18, 20]:

i. Group 2 (Lower risk group) accounted for the DHF patient who did not experienced any of the defined risk criteria, or experienced only 1 of the 3 risk criteria.

ii. Group 3 (Higher risk group) accounted for DHF patient who experienced 2 or more risk criteria.

The dengue patients were then classified according to their groups and subsequently, their corresponding BIA data were obtained and quantified. The healthy subjects were automatically grouped as the control group (Group 1) with no past medical history and no blood investigations evaluated.

Pre-processing of ANN

Database preparation involves parameter selection, data massaging, and data grouping.

Parameter selection

In the parameter selection phase from the BIA database only three parameters were selected to be the input of the MFNN. The input parameters are: day of fever, gender, and reactance values. The selection of these parameters was based on multi-logistic analysis [18]. The quantified risk was assigned as the network target.

Full text is available at :

http://www.ncbi.nlm.nih.gov/pubmed/20683676

http://link.springer.com/article/10.1007/s11517-010-0669-z