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A Non-invasive System for Predicting Hemoglobin (Hb) in Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF)

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Abstract - Single frequency bioelectrical impedance analysis (BIA) is an inexpensive, quick and painless means of estimating body composition. In this paper, BIA parameters employed for predicting hemoglobin (Hb) in dengue patients. The BIA technique passes a low-amplitude electrical current, in the range of 500μA to 800μA, at a single frequency of 50 kHz. BIA data was sampled from 210 (comprises of 119 males and 91 females) serologically confirmed dengue fever (DF) and dengue hemorrhagic fever (DHF) patients, hospitalized at the Hospital Universiti Kebangsaan Malaysia (HUKM). After applying multiple regression analysis, it was found out that reactance, sex, weight and vomiting were found to be significant independent determinants of predicting Hb.

Keywords: modeling, bioelectrical impedance, dengue fever, dengue hemorrhagic, hemoglobin, multivariate analysis.

1. Introduction

Many infectious diseases such as dengue, malaria, typhoid and hepatitis produce characteristic variations in the composition of blood [1]. These variations can be a characteristic change in number, size or shape of certain blood cells. For example, in anemia, the red blood cell (RBC) count is reduced [1]. Other diseases may cause changes in the chemical composition of the blood serum and other body fluid, like the urine. In diabetes mellitus, for instance, the glucose concentration in the blood and in urine is characteristically elevated in size and shape, or a chemical analysis of the blood serum can, therefore, provide important information for the diagnosis of such diseases [1]. Similarly, other body fluids, smears, and small samples of live tissue, obtained by biopsy, are studied through the technique of bacteriology, serology and histology to obtain clues for the diagnosis of diseases. However, these techniques are invasive because for the bacteriology, serology and histology diagnosis, require the sample of human's smear from the throat, blood and tissue respectively. The latest commercial technique takes two hours to detect dengue fever by serological confirmation using samples of serum, plasma or heparinized whole blood [1]. This test is still invasive, expensive and can only be performed by trained medical personnel.

Dengue fever (DF) and dengue haemorrhagic fever (DHF), ranks highly among the newly emerging infectious diseases in public health significance and is considered to be the most important of the arthropod-borne viral diseases. Since the early 1970s, the World Health Organization (WHO) has been actively involved in developing and promoting strategies for treatment and control of dengue. In 1997, WHO published a second guide to the diagnosis, treatment and control of dengue haemorrhagic fever [1]. Dengue were reported throughout the year and started to increase from 1997 to 1998. In 1998, 27,373 dengue cases with 58 deaths were reported as compared to 19,544 cases with 50 deaths in 1997. This has shown an increase of 7,829 cases or 40.1% over the number of cases in 1997 [2]. Therefore, there is an urgent need to design a system that can give early detection.

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Currently, in Malaysia there is no computerized and non-invasive system available yet to give rapid diagnosis for dengue and dengue haemorrhagic fever. Early diagnoses of these diseases are very important for a better prognosis.

2. Patients and Methods

Two hundred ten adult patients aged 12 years old and above, suspected of DF and DHF admitted to the Universiti Kebangsaan Malaysia Hospital (HUKM), were monitored. The severity of the DHF is classified into grade I to IV, according to WHO recommendation [1]. Acute dengue infection was confirmed subsequently by the use of ELISA to detect elevated dengue specific IgM (primary infection) and IgG (secondary infection) [3]. Patient serum samples were tested for hemoglobin determination using an automated counter (Coulter STKS machine).

All patients were required to abstain from eating and drinking for 4h and from alcohol and physical exercise for 12h prior to the BIA measurements. The clinical data were recorded using the standardized questionnaire data collection form designed by Ibrahim et.al [4].

The patient's measurement was dated with referenced to day of fever settled when temperature dropped below 37.5°C [5]. Fever day 0 was the day of fever settled. Day after fever settled is designated as day 1. The patients were asked to lie supine on their bed and each measurement took approximately 3 minutes. Two electrodes were placed on the patient's right hand, one the base of the knuckles and another slightly above the wrist joint. Another two electrodes were placed on the right foot, one near the toes and the other slightly above the ankle joint. A constant current less than 1 mA and single frequency of 50 kHz was produced by a biodynamic Model 450 bioimpedance analyzer (Biodynamic Corporation, USA) and injected to the base of the knuckles and base of the toes and the signal was picked up by the other two sensor electrodes. Resistance, reactance, body capacitance and phase angle were measured by the BIA analyzer.

3. Statistical analysis

Statistics were calculated with SPSS version 11.5, using non-parametric test. Correlations between variables were analyzed using Spearman's rank correlation coefficient (ρ) and multiple linear regression analysis was used to determine the independent effect of parameters related with hemoglobin. Statistical significance was defined as $P < 0.05$ for all tests.

4. Results

210 patients (comprises of 119 males and 91 females) with mean age of 30.65 years were recruited. Correlations between variables were analyzed using Spearman's correlation coefficient. A matrix is displayed giving the correlation coefficient between the two variables such as gender and height (0.647), underneath is the significance values of the coefficient (0.000) and finally the sample size (210). The significance value for this correlation coefficient is less than 0.05, therefore, it can be concluded that there is a significant relationship between a gender and height.

Linear regression was used to identify the most significant variable among the bioelectrical impedance parameters. Resistance and reactance ($p>0.5$) were found to be significant.

Finally linear regression was used to identify all significant variables and adjusted R^2 to 43%. Hence the final model can be written as Equation 1.

$$Hb = 6.012 + 1.309a + 0.029b + 0.047X_c + 0.19c \quad (1)$$

where a is gender, b is weight, X_c is reactance and c is vomiting.

The actual and the calculated Hb can be seen in Table 1. This model shows an improvement in term of residual compared to [6].

Table 1: Casewise diagnostic for Hb modeling.

Case Number of Patients (210)	Hemoglobin	Predicted value	Residual
35 the lowest of Hb	6.7	11.303	-4.603
134 the highest of Hb	18.7	14.339	4.361
159 the second highest of Hb	18.6	15.727	2.873

Figure 1 showed the points on the normal probability plot sit on the diagonal line, suggesting that the normality assumption was not violated.

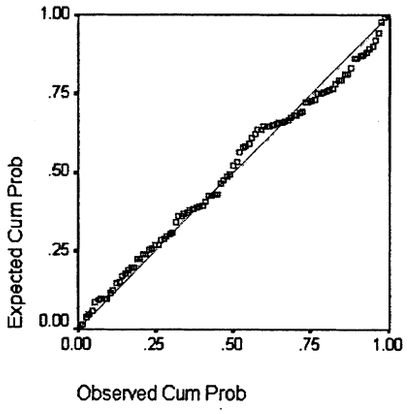

Figure 1: Normal P-P plot of regression standardized residuals.

5. Conclusion

In this study, the developed model based on four predictors, *i.e.* gender, reactance, weight and vomiting, for modeling Hb in dengue patients confirmed the previous finding [6].

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