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Computer-aided diagnosis of diabetic subjects by heart rate variability signals using discrete wavelet transform method

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ABSTRACT

Diabetes Mellitus (DM), a chronic lifelong condition, is characterized by increased blood sugar levels. As there is no cure for DM, the major focus lies on controlling the disease. Therefore, DM diagnosis and treatment is of great importance. The most common complications of DM include retinopathy, neuropathy, nephropathy and cardiomyopathy. Diabetes causes cardiovascular autonomic neuropathy that affects the Heart Rate Variability (HRV). Hence, in the absence of other causes, the HRV analysis can be used to diagnose diabetes. The present work aims at developing an automated system for classification of normal and diabetes classes by using the heart rate (HR) information extracted from the Electrocardiogram (ECG) signals. The spectral analysis of HRV recognizes patients with autonomic diabetic neuropathy, and gives an earlier diagnosis of impairment of the Autonomic Nervous System (ANS). Significant correlations with the impaired ANS are observed of the HRV spectral indices obtained by using the Discrete Wavelet Transform (DWT) method. Herein, in order to diagnose and detect DM automatically, we have performed DWT decomposition up to 5 levels, and extracted the energy, sample entropy, approximation entropy, kurtosis and skewness features at various detailed coefficient levels of the DWT. We have extracted relative wavelet energy and entropy features up to the 5th level of DWT coefficients extracted from HR signals. These features are ranked by using various ranking methods, namely, Bhattacharyya space algorithm, *t*-test, Wilcoxon test, Receiver Operating Curve (ROC) and entropy.

The ranked features are then fed into different classifiers, that include Decision Tree (DT), *K*-Nearest Neighbor (KNN), Naïve Bayes (NBC) and Support Vector Machine (SVM). Our results have shown maximum diagnostic differentiation performance by using a minimum number of features. With our system, we have obtained an average accuracy of 92.02%, sensitivity of 92.59% and specificity of 91.46%, by using DT classifier with ten-fold cross validation.

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1. Introduction

According to the International Diabetes Federation (IDF), it is estimated that in 2013 a total of 381 million people were diagnosed with diabetes across the globe, out of which 23 million people are from Southeast Asian countries [26]. Due to lack of finance or access to healthcare, most of the populations around the world are unaware that they may be suffering from diabetes [26]. Statistics shows that around 1.9 million people are diagnosed with diabetes in USA every year and 79 million have pre-diabetic conditions [7]. By 2030, the number of diabetes subjects is estimated to get almost double (2.8% in 2000 and 4.4% in 2030), as its incidence is increasing rapidly every year Sarah et al. [47]. Diabetes and its complications have shown a notable impact on individuals, families, and health systems and countries' economy. The USA alone spends around $245 billion annually on the diagnosed diabetes patients. It is predicted that by 2050, 1 in 3 Americans adults may have diabetes if the current tendency is continued [7,10].

Diabetes mellitus (DM) is a condition that is defined by hyperglycemia state (blood glucose level), which in turn leads to microvascular, and macrovascular damage [60]. Even though, finding a cure for this DM condition is difficult, emphasis is laid on early diagnosis of DM. In this regard, it is well known that a

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person with diabetes exhibits autonomic neuropathy (AN), damage to the nervous system or cardiovascular autonomic neuropathy (CAN), a well-known complication of DM that affects the central and peripheral vascular systems and causes abnormalities in the heart rate signal [1]. Thus, diabetes can also be diagnosed by studying the heart rate variability.

Concerning heart rate variability, the heart rate (HR), a non-stationary/nonlinear signal, is obtained by calculating the time elapsed between two ventricular contractions or the time between two consecutive R-waves (R–R interval) on the ECG signals [27]. The HR Variability (HRV) is one of the reliable methods for qualifying physiological dysfunction in terms of the condition of sympathetic and parasympathetic nervous system [6,25]. The analysis of HRV enables us to evaluate overall cardiac health in terms of the heart rate regulation, based on the status of the autonomic nervous system responsible for regulating cardiac activity [37].

Spectral analysis of the short-term HRV enables quantitative evaluation of the neurologic oscillations, and delivers values for neural regulation of heart rate [9,51,34]. The spectral analysis of HRV (spectral parameters like the power spectrum of HRV signal) recognizes patients with autonomic diabetic neuropathy, and gives an earlier diagnosis of impairment of the autonomic nervous system (ANS) [15,21]. Significant correlations are observed between impaired ANS and the HRV indices obtained by spectral analyses using nonparametric and parametric methods namely, fast Fourier Transform (FFT) and autoregressive (AR) method respectively [12]. Time–frequency domain analysis of HRV makes it easier to quantify the ANS activity in DM subjects [48]. Even though the autonomic functions are better assessed by using frequency domain features, the accuracy of spectral power is limited by the low level of the signal to noise ratio [6].

Nonlinear dynamic techniques are used in HRV signal analysis to circumvent the limitations of time and frequency domain analysis [4]. Nonlinear methods are needed for the analysis of nonlinear signals and systems [35]. The non-linear methods have been applied in HRV analysis [50,30] to predict diabetes [14,5,20] and cardiovascular disease (CVD) [23]. Nonlinear techniques can be coupled to frequency analysis techniques. Among all of these techniques, the DWT has the advantage of providing multiple resolutions. This method provides discrimination between two different signals with the same spectrum magnitude, thus distinguishing the subtle changes in the signals [17,2,56].

In normal and diabetic subjects, the HRV signal has been used to study and measure the activity and symptoms of the cardiac parasympathetic nervous system [41]. Their study reported that diabetic subjects' exhibit diminished cardiac parasympathetic activity before the appearance of autonomic neuropathy symptoms. Several studies conducted (Table 3) have reported that diabetic patients are characterized by reduced HRV, with less information about HRV across the spectrum of blood glucose levels. In 2000, Singh et al. [52] studied the correlation between hyperglycemia (increased blood glucose level) and reduced HRV. They reported reduced HRV variables in DM subjects and in subjects with impaired blood (plasma) glucose levels by using time domain features.

Awdah et al. [11] studied diabetic subjects with and without autonomic neuropathy by using the time domain analysis of HRV. Their results showed significant decrease in all the time domain measures for diabetic subjects with and without diabetic neuropathy compared to the control class. In 2005, Flynn et al. [22] used detrended fluctuation analysis (DFA) to study the HRV changes over a short time ECG recordings of 20 min. Their study reported reduced values of HRV for diabetic subjects. Chemla et al. [16] used autoregressive (AR) methods to study the HRV spectral components in diabetic patients. They found that diabetic subjects exhibit decreased spectral values, and that FFT method is more suitable for evaluation of short-term HRV spectral components in diabetic subjects.

Analysis in the time and frequency domain of RR interval has been carried out by Ahmad Seyd et al. [8], to quantify the autonomic nervous system (ANS) in DM patients. Significant differences in high frequency (HF) power, very low frequency (VLF) and low frequency (LF) power were noted between DM patients and normal classes in the frequency domain analysis of extracted data (NN interval – normal to normal interval). This study also observed significant difference in time domain analysis of root mean square of successive NN interval differences (RMSSD) and the standard deviation of NN interval (SDNN) between the DM and control groups.

Multiscale entropy (MSE) analysis method has also been used to diagnose the autonomic dysregulation in DM patients by Trunkvalterova et al. [58]. Their study performed the analysis of heart rate (HR) signal, systolic and diastolic blood pressure (SBP and DBP) signals in both normal and diabetic subjects, to evaluate the SampEn and linear measures. They reported that in young patients with DM, the changes in cardiovascular control were detected by the MSE analysis of SBP and DBP oscillations and HR signals. The relationship between HRV and duration of type 2 diabetes based on sex-differences was studied by Nolan et al. [38]. By this study result, an inverse relationship was reported between the Type 1 and Type 2 diabetes duration and HRV measures among male subjects only. The inverse association of HRV with increasing age of diabetes diagnosis, as well as increasing severity of coronary heart disease risk and obesity was observed in female subjects.

Then in 2012, Faust et al. [20] used time and frequency domain and nonlinear methods to study the HRV signals of both diabetic and normal subjects; they have proposed unique ranges for various features of the two classes. The HRV parameter in diabetic and non-diabetic patients with renal transplantation has been investigated in time and frequency domain by Kirvela et al. [31]; their result highlighted that in end-stage diabetic neuropathy patients the autonomic neuropathy is the main reason to cause severe impairment of HRV and partly by the co-existing heart disease.

Recently, a novel Diabetic Integrated Index (DII) has been developed by Acharya et al. [3], by using nonlinear parameters extracted from the HRV signal. This DII is a number which can distinguish and classify the two classes in terms of just one number. They also reported that the AdaBoost classifier yielded a high classification accuracy of 86% for the two classes (normal and diabetic). In this research group, Swapna et al. [54] used Higher Order Spectral features to classify diabetic patients from normal subjects; their method reported the highest accuracy, sensitivity and specificity of 90.5%, 85.7% and 95.2% respectively, by using Gaussian mixture model classifier. The magnitude plots of the HOS bispectrum obtained from HRV signals have been subjected to principal component analysis for feature reduction [28]. These principal components with SVM classifier reported an accuracy of 79.93%. However, Acharya et al. [5] reported 90% of accuracy, 92.5% of sensitivity and 88.7% of specificity with AdaBoost classifier coupled with four nonlinear features. Pachori et al. [42] (In press), proposed a new nonlinear method based on Empirical Mode Decomposition (EMD) to discriminate between normal and diabetic RR-interval signals. In their proposed method, EMD decomposes the RR-interval signal into IMFs from which five features (Fourier–Bessel series expansion, amplitude modulation bandwidth, frequency modulation bandwidths, analytic signal representation and second order difference Plot) are extracted. The study results show that the features extracted exhibits are statistically significant difference between normal and diabetic classes.

In our present work, in order to automatically diagnose and detect DM, we have performed DWT decomposition up to 5 levels and have extracted the energy, sample entropy, approximation

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