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Heart Rate Variability based Classification of Normal and Hypertension Cases by Linear-nonlinear Method

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ABSTRACT

The aim of this study is to analyse and compare the heart rate variability (HRV) of normal and hypertension cases using time domain, frequency domain, and nonlinear methods. For short term HRV analysis, a five-minute electrocardiogram (ECG) of 57 normal and 56 hypertension subjects were recorded with prior verification of their clinical status by a cardiologist. Most time domain features of hypertension cases have clearly reduced values over normal subjects, frequency domain features, like power in different spectral bands, also have the distinguishable decreased values, whereas sympathovagal balance has clear edge over hypertension cases than normal cases. Nonlinear parameters of Poincare plot, approximate entropy and sample entropy, have higher values in normal cases when compared with hypertension cases. Support vector machine-based binary system classifies these two classes with 100 per cent accuracy and 100 per cent sensitivity when all time domain, frequency domain, and nonlinear features were used. It may work as a better predictor for in patients with hypertension.

Keywords: Heart rate variability, RR tachogram, hypertension, time domain, frequency domain, nonlinear, support vector machine classifier

1. INTRODUCTION

Hypertension is the condition in which the arteries are consistently in elevated blood pressure (BP), hence also called high BP, generally exceeding 140/90 millimeter of mercury (mm Hg). Since it does not show any symptoms for many years or even decades, high BP is a silent killer as it damages critical organs of the human body. Recent studies in the literature[1-2] indicate that hypertension is one of the major causes of mortality in old-age people[3] and workload stressed middle-aged group[4-5]. Heredity[6], stress, exercise[7], alcohol intake[8], smoking[9], are the major causes of hypertension. Heart rate variability is the subsequent R peak to R peak (RR) interval variation of the electrocardiogram (ECG) for a particular duration which maintains sympathovagal balance by correlating sympathetic and parasympathetic activities. HRV analysis is being considered as a popular diagnostic tool in cardiology to assess the activities of autonomic nervous system, and has been used for many years for its simplicity, accuracy, and non-invasive application. However, normal range of HRV in a healthy population has still not been identified though it is widely discussed and specifically mentioned in the standard literatures[10], since there are lots of influencing factors which affect the normal RR interval significantly, like age, gender, race, region, diet, habits, etc. Earlier research reported comparison of HRV analysis of normal subjects considering different age groups[11] and gender, as well as comparison of HRV analysis of normal subjects wrt subjects suffering from any particular diseases[12-13] by time domain and frequency domain methods[1-13].

In the present study, comparative analysis of HRV for normal and hypertension subjects using features derived from both linear and nonlinear methods has been carried out. Linear method includes time domain and frequency domain. Nonlinear method includes Poincare plot, approximate entropy, and sample entropy algorithms. A sensitivity analysis was carried out for feature selection to determine the most discriminatory features between normal and hypertension groups. It was observed that combined features such as variance of RR interval (Variance), standard deviation of normal-to-normal RR intervals (SDNN), Root mean square of successive difference of RR intervals (RMSSD), Percentage of number of adjacent RR intervals having more than 50ms (pNN50) of time domain, power in very low frequency (P-VLF) in ms^2, power in low frequency (P-LF) in ms^2, power in high frequency (P-HF) in ms^2, power in total frequency range (P-Total) in ms^2, LF/HF of frequency domain by fast Fourier transform (FFT) analysis, standard deviations SD1, SD2 of Poincare plot, coefficient of approximate entropy (ApEn) and coefficient of sample entropy (SampEn) of nonlinear features provide maximum class separability, these selected features are used for design of binary support vector machine (SVM) classifier[14].

2. DATA

In the present study, an ECG of Lead –II was recorded using 16 channel BIOPAC™ MP 150 system in corporation with Acknowledge 4.0 software using 500 Hz sampling frequency and its ECG amplifier module 100C[15]. The module was kept in its normal mode with amplifier gain at 1000 and the channel

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to be used was calibrated prior to recording. An approximately six-to-seven minutes duration of data was recorded in supine-rest condition, noise-free and calm ambience, whereas only 300 s of clean data was used for short term HRV analysis as per standard guidelines[10], after manual inspection. A total of 120 male subjects were involved for ECG recording, out of which 61 were hypertension cases in the age group ranging from 35 years to 65 years, and 59 were the normal cases in the age group of 18 years to 65 years. In both the normal and hypertension cases, the overall range of age group was considered to utilise the average effect of the data to avoid a possible bias that can influence the analysis. ECGs of 61 hypertension patients were recorded in relaxed-supine condition at Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, after consulting a cardiologist about its symptoms. Similarly, an ECGs of 59 normal and healthy subjects were recorded after medically examined them and confirming that they have no cardiac disorders and are also not having any history as well. A well informed consent was taken from each subject or subject's caretaker prior to data recording and making the patients fully aware that recorded data will be used only for research purpose. A manual inspection was carried out on all data set before it was being used for analysis and distorted data was being excluded for the study, thus, 5 and 2 numbers of data were excluded from hypertension and normal cases, respectively.

3. METHODS

The generalised block diagram of different stages involved in HRV analysis using time domain, frequency domain and nonlinear methods beginning with ECG data recording is shown in Fig. 1. In both normal and hypertension cases, RR tachogram, which is a pictorial representation of successive RR interval with respect to progressive beat, was generated using the Acqknowledge 4.0 software of BIOPAC system.

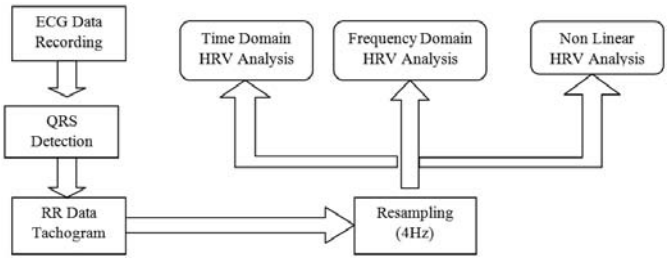

Figure 1. Generalised block schematic of linear and nonlinear HRV analyse.

This generated RR tachogram contains unevenly placed samples as RR interval is varying from one beat to another beat in both cases of normal and hypertension, hence, re-sampling was carried out with 4 Hz frequency to maintain the uniformity along the entire length tachogram data[16]. This re-sampled RR interval tachogram in text format was then ready to use as a data for the HRV analysis by time domain, frequency domain and nonlinear methods. The typical comparison of RR tachogram generated from normal subject and hypertension patient is shown in Fig. 2 which clearly discriminates the normal cases with hypertension.

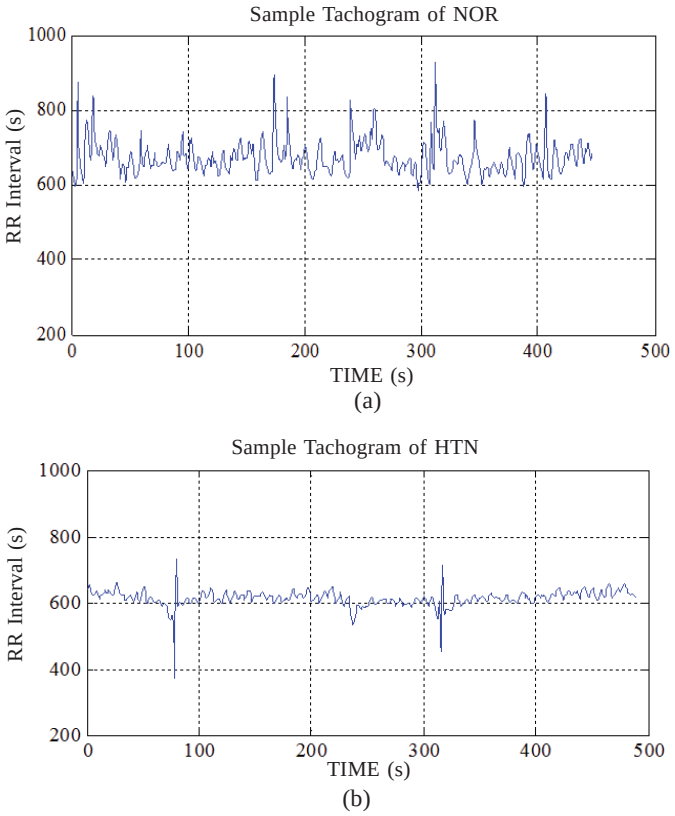

Figure 2. Comparison of RR tachograms of: (a) Normal case, and (b) Hypertension case.

3.1 Linear Methods

In time domain, the parameters like number of RR intervals (RR_{no}), maximum value of RR intervals (RR_{max}), minimum value of RR intervals (RR_{min}), mean value of RR interval (RR_{mean}), median value of RR intervals (RR_{median}), mean value of Heart Rate (HR_{mean}), SDNN, variance value of the RR intervals, coefficient of variance value of RR intervals (CV%), standard deviation of successive difference RR intervals (SDSD), RMSSD and pNN50 were calculated. For both normal and hypertension cases, sensitivity analysis was carried out where the parameters having similar range were excluded for classification, thus, included parameters were Variance, SDNN, RMSSD and pNN50.

Similarly in frequency domain, the power using power spectral density (PSD) in all frequency ranges in ms^2, i.e., *P*-VLF (0 to 0.04 Hz), *P*-LF (0.04 to 0.15 Hz), *P*-HF (0.15 to 0.4Hz) and *P*-Total (0 – 0.4 Hz), normalised powers P_n-VLF, P_n-LF, P_n-HF, P_n-Total in the same said frequency ranges and LF/HF ratio, which signifies the sympathovagal balance, were calculated[7]. Two methods were used to compute the features from frequency domain, namely

- Non-parametric: FFT analysis with 256 samples, Welch periodogram and Hann windowing, by 50% overlapping, which provides the smoother PSD curve within different frequency bands
- Parametric: auto regressive (AR) modelling method where final prediction error (FPE) technique was used to determine the order of the model and Yule-Walker method was used to estimate the variance predictor. The prediction errors were calculated for various model orders, and the

best with least error was selected for all data.

$$FPE[p] = \sigma_p^2 \left[\frac{N+(p+1)}{N-(p-1)} \right] \quad (1)$$

here, σ_p^2 is the variance of the predictor, p is an order of the model and N is the number of samples[5-6]. A sensitivity analysis was carried out on all the features computed by both parametric and nonparametric methods and excluded features for classification were P_n-VLF, P_n-LF, P_n-HF and P_n-Total and also all the parameters of AR modelling to avoid possible redundancy, hence, included features were P-VLF in ms^2, P-LF in ms^2, P-HF in ms^2, P-Total in ms^2 and LF/HF. A typical comparison of PSD by FFT for both normal and hypertension cases is shown in Fig. 3 which provides the information about the variation of power in different frequency ranges.

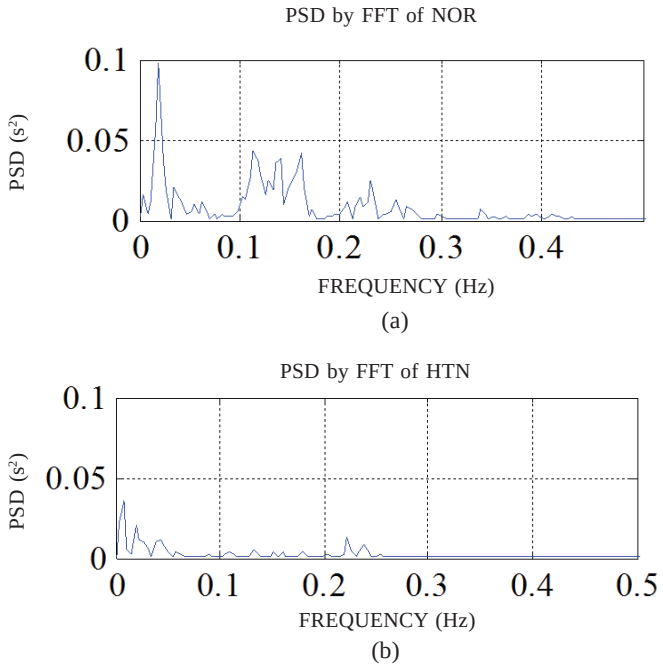

Figure 3. Comparison of PSD by FFT of : (a) Normal case, and (b) Hypertension case.

3.2 Nonlinear Methods

Algorithms used here to calculate the features were Poincare plot, approximate entropy, and sample entropy. Poincare plot is the graphical representation of present and next RR interval[21], if x and y are the present and the next state RR interval series, respectively, then from Eqn. (2), the features SD1 and SD2 can be calculated which represent the standard deviation short term and long term variability, respectively of data point perpendicular to the axis of line-of-identity, i.e., SD1 and SD2 are the standard deviations of x_1 and x_2 respectively. A typical comparison of Poincare plot of normal subject and hypertension patient is shown in Fig. 4.

$$\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} \cos\cos\frac{\pi}{4} & -\sin\frac{\pi}{4} \\ \sin\frac{\pi}{4} & \cos\frac{\pi}{4} \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix} \quad (2)$$

Approximate entropy is a measure of complexity or

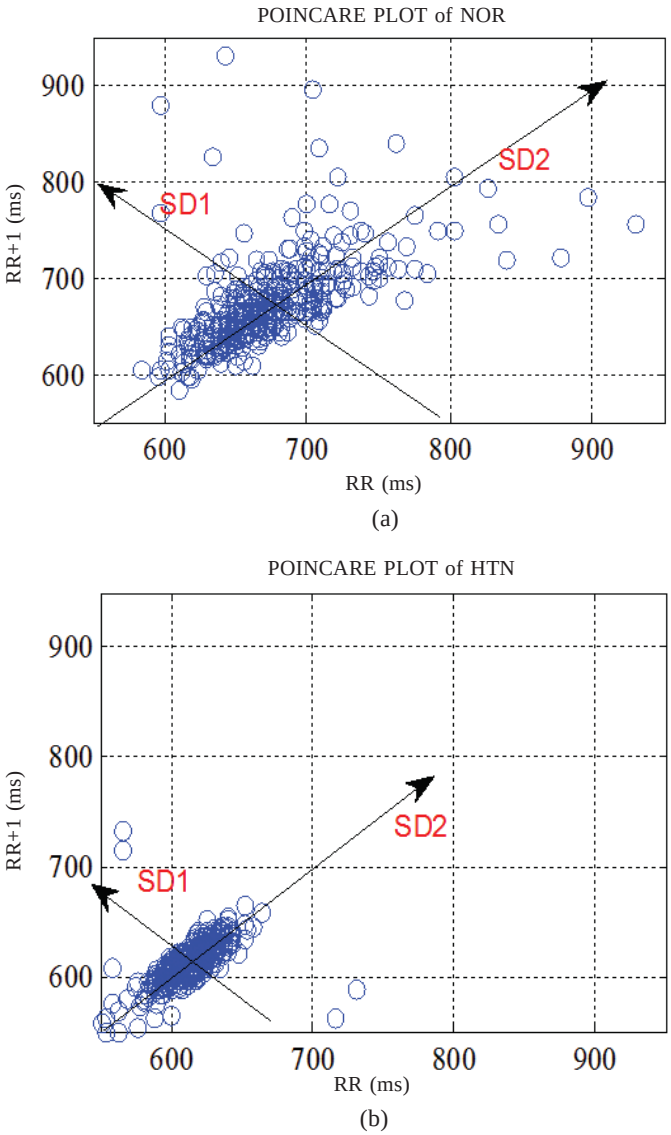

Figure 4. Comparison of Poincare plot of: (a) Normal case, and (b) Hypertension case.

irregularity of a signal[17], where more regular or predictable RR interval series, the lower will be the value of ApEn and vice versa. The steps involved to understand the approximate entropy are as follows: Consider the data sample sequence with N as length of the data and two fixed parameters must be presumed, which are m, the embedding dimension of the vector formed, and r, the similar tolerance and in the present work, the considered values of m and r were 2 and 0.2 of standard deviation, respectively. By considering the data sample sequence RR_{Total} =(RR_1, RR_2, ..., RR_N) can be represented as $RR(i)$, i = 0,1,.....,N. . From $RR(i)$, m dimension vectors $X(1)$ *to* $X(N-m+1)$can be formed as $X(i) = [x(i), x(i+1), ..., x(i+m-1)]$, where $i = 1$ *to* $N-m+1$ and $X(j) = [x(j), x(j+1), ..., x(j+m-1)]$, $j = 1$ *to* $N-m+1$. Define $d(X^m(i), X^m(j))$, the distance between vector $X^m(i)$ and vector $X^m(j)$ as the maximum absolute difference between their corresponding scalar elements, i.e.,

$$d(X^m(i), X^m(j)) = \max_{k=0\sim m-1}[|x(i+k), x(j+k)|] \quad (3)$$

Note: *d* would be greater than all other differences between the corresponding elements.

Hence, $N^m(i) = no.\ of\ d[X(i), X(j)] \le r$, then $C^m(i) = N^m(i)/(N-m+1)$.

Now, taking the natural logarithm of each $C^m{}_i(r)$, average it over *i*, denoted as

$$\Phi^m(r):\ \Phi^m(r) = \sum_{i=1}^{N-m+1} \ln C_i^m(r) \quad (4)$$

Increase the dimension from m *to* $m+1$, repeat steps and find $\Phi^{m+1}(r)$, then,

$$ApEn(m,r) = \lim_{N\to\infty}[\Phi^m(r) - \Phi^{m+1}(r)] \quad (5)$$

Hence, In general for finite length *N*, $ApEn$ is represented as

$$ApEn(m,r) = \Phi^m(r) - \Phi^{m+1}(r) \quad (6)$$

Sample entropy is another similar algorithm which measures the complexity in the time series data in which it avoids the self-similarity as compared to approximate entropy[18], hence, the value of coefficient of sample entropy is a little higher than the coefficient of approximate entropy. The values of *m* and *r* were considered same the as that of approximate entropy.

The extracted features after the sensitivity analysis were variance, SDNN, RMSSD, pNN50 of time domain, *P*-VLF, *P*-LF, *P*-HF, *P*-Total, LF/HF of frequency domain by FFT technique, SD1, SD2 by Poincare plot, ApEn and SampEn of nonlinear method, used for classification by SVM classifier separately for features derived from time domain, frequency domain, nonlinear algorithms, and combined features all together. In the present study, SVM classifier was implemented using LibSVM library[19]. Separation of training data with minimum expected risk was done by attempting to construct an optimum hyperplane in the higher dimensional feature space. Kernel functions were used for nonlinear mapping of the training data from input space to higher dimensional feature space. Initial normalisation was done between 0 and 1 with min-max normalisation procedure to avoid bias caused by unbalanced feature values. In this present study, to obtain good generalisation performance in correct choice of the regularisation parameter *C* and kernel parameter γ, an extensive search was carried out in the parameter space for the values of $C \in \{2^{-4},.., 2^{15}\}$ and $\gamma \in \{2^{-12},.., 2^{5}\}$ using 10-fold cross-validation on training data, as *C* attempts to maximise the margin while keeping low value for training error[20-25, 27-30]. Out of 57 normal cases, two data sets were prepared which consisted of 25 cases for training and testing each. In the same way, from 56 hypertension cases, two data sets were formed which consist of 25 cases for training and testing to maintain the uniformity between the training and testing data sets.

4. RESULTS

Results of both linear and nonlinear methods have been presented, where linear method has time domain and frequency domain techniques, and nonlinear method has Poincare plot, approximate entropy, and sample entropy algorithms. The comparison of all time domain features from normal subjects and hypertension patients is shown in Table 1. A sensitivity analysis was carried out over entire time and frequency domain parameters, and clinically significant features were considered for analysis and classification, which are shown in Tables 2. and 3, respectively. In nonlinear method, comparison of SD1, SD2 of Poincare plot, ApEn and SampEn for normal and hypertension subjects are shown in Table 4. SD1 and SD2 reflect short-term and long-term variability of the RR signals respectively. All features in this nonlinear method are having the higher values in normal persons compared to hypertension cases. SVM classifier provides the accuracy of 58%, 64% and 66% also hypertension sensitivity as 92%, 92% and 80% when classified separately with time domain, frequency domain, and nonlinear methods, respectively whereas when classified with combined features, it showed the 100% accuracy with 100% sensitivity for both normal and hypertension cases and is shown in Table 5.

Table 1. Comparison of all time domain features for normal and hypertension cases

Feature	Normal (Mean ± SD)	Hypertension (Mean ± SD)
RR_{no}	316.01 ± 4.44	311.50 ± 6.32
RR_{min}	709.25 ± 14.09	763.03 ± 17.20
RR_{max}	969.05 ± 14.47	945.28 ± 13.81
RR_{mean}	830.30 ± 10.03	857.33 ± 14.95
RR_{median}	831.07 ± 11.34	857.39 ± 15.63
HR_{mean}	73.93 ± 1.12	72.89 ± 15.07
Variance	1736.20 ±101.48	1117.75 ±119.14
SDNN	37.69 ± 1.78	30.19 ± 1.47
SDSD	31.83 ± 1.45	26.40 ± 1.43
RMSSD	31.83 ± 1.45	26.36 ± 1.43
CV%	4.82 ± 1.52	3.50 ± 1.57
pNN50	12.00 ± 1.83	8.99 ± 1.95

Table 2. Comparison of clinically significant time domain features for normal and hypertension cases

Feature	Normal (Mean ± SD)	Hypertension (Mean ± SD)
Variance	1736.20±101.4	1117.75±119.1
SDNN	37.69 ± 1.78	30.19 ± 1.47
RMSSD	31.83 ± 1.45	26.36 ± 1.43
pNN50	12.00 ± 1.83	1.99 1.95

Table 3. Comparison of clinically significant frequency domain features for normal and hypertension cases

Feature	Normal (Mean ± SD)	Hypertension (Mean ± SD)
P-VLF (ms^2)	269.36 ± 49.47	139.15 ± 10.24
P-LF (ms^2)	183.93 ± 12.3	70.13 ± 24.50
P-HF (ms^2)	108.37 ± 9.82	45.09 ± 5.12
P-Total (ms^2)	561.66 ± 51.93	254.38 ± 22.41
LF/HF	2.19 ± 0.42	2.54 ± 0.63

5. DISCUSSION

A brief summerisation of different HRV analysis methods and classification algorithms expressing the accuracy and sensitivity with different categories of subjects is depicted in

Table 4. Comparison of nonlinear methods for normal and hypertension cases

Method	Features	Normal Mean ± SD)	Hypertension (Mean ± SD)
Poincare plot	SD1	22.99 ± 2.56	18.67 ± 1.76
	SD2	51.87 ± 6.00	37.39 ± 3.43
Approximate entropy	ApEn	1.0885 ± 0.02	0.9902 ± 0.02
Sample entropy	SampEn	1.5541 ± 0.01	1.5152 ± 0.02

Table 5. The classification results obtained by SVM

Feature	Confusion matrix	C	γ	Accuracy (%)	Sensitivity (%)
Time domain	NOR HTN NOR 6 19 HTN 2 23	1.0	0.001	58	24 92
Frequency domain	NOR 9 16 HTN 2 23	1.0	0.001	64	36 92
Nonlinear	NOR 13 12 HTN 5 20	1000	0.001	66	53 80
All	NOR 25 0 HTN 0 25	10000	0.1	100	100 100

NOR- Normal, HTN- Hypertension, C- Regularisation parameter, γ- Kernel parameter.

Table 6. Summary of different classification algorithms with their reported results in terms of accuracy and sensitivity for HRV features

Authors	Methods	Accuracy (%)	Sensitivity (%)
Kim[31], *et al.*	MDA+ Linear and nonlinear	75	-
Tsipouras[26], *et al.*	NN+Linear	-	89.95
Ramirez-Villegas[24], *et al.*	NN+ Linear and nonlinear SVM+ Linear and nonlinear	86.67 87.12	73.33 90.91
Lee[32], *et al.*	SVM+ Linear and nonlinear	90	-
Babak[24], *et al.*	SVM+ Linear and nonlinear	99.16	95.77
Kampouraki[21], *et al.*	NN+ Linear and nonlinear SVM+ Linear and nonlinear	85 100	- -
Present work	SVM+ Linear and nonlinear	100	100

MDA-Multiple Discriminant Analysis, NN-Neural Network, SVM-Support Vector Machine.

Table 6. Kim[31], *et al*., reports 75 per cent accuracy by multiple descriminant analysis (MDA) classifier on linear and nonlinear HRV analyse. Tsipouras[26], *et al.* carried out by MITBIH database of 48 ECG data with time and time-frequency techniques of linear method and achieved the 89.95 per cent sensitivity by neural network (NN) classifier.

Ramirez-Villegas[24], *et al.* presented classification accuracy (86.67%, 87.12%) and sensitivity (73.33%, 90.91%) by NN and SVM, respectively using linear and nonlinear methods on healthy persons and cardiac risk patients of 45 each. Lee[32], *et al.* used HRV analysis by time domain and nonlinear features, while classifying tried for various techniques and it was found that SVM as better with 90 per cent accuracy. The Babak[23], *et al.* carried out HRV analysis by linear and nonlinear features on MITBIH arrhythmia data to get the classification accuracy 99.16 per cent and 95.77 per cent sensitivity with SVM classifier using generalised discriminant analysis technique for feature reduction. Kampouraki[21], *et al.* carried out the HRV analysis by time domain and nonlinear methods on two data sets, first data set comprises 20 young and 20 older persons and second data set with six cases in each healthy and coronary artery disease to carry out classification by NN and SVM to achieve a accuracy of 85 per cent and 100 per cent respectively.

In the present study, selected time domain features variance, SDSD, RMSSD and pNN50 have higher values in case of normal over hypertension subjects which manifests normal subjects are more active than hypertension patients. Similarly, in frequency domain method, the included features like power in each range of very low frequency, low frequency, high frequency, and also the power in entire range analysed and compared in both normal and hypertension cases where latter had lower values in above-said features and LF/HF is higher than normal which signifies the sympathovagal balance. In nonlinear methods, SD1 and SD2, both provide the elliptical structure of Poincare plot are having the higher values in normal cases and lower values in hypertension cases. The Coefficients of both approximate entropy and sample entropy are also having higher though values marginally in normal case as compared to hypertension, since the overall range is very less. Although most of the features were discriminative with certain overlapping range in normal and hypertension cases, SVM classifier was used to classify clearly between both cases of normal and hypertension.

SVM classification approach is one of the suitable techniques for binary classification. In the present study, SVM classifier classifies with less accuracy and sensitivity when classification was done by time domain, frequency domain features in linear method and nonlinear features individually but when all features combined, then it classifies with 100 per cent accuracy and 100 per cent sensitivity for both normal

and hypertension subjects as considered data sets to train and test were equal in number. It clearly indicates that combined features have the better effect than individual features derived from time domain, frequency domain, and nonlinear methods wrt to classification.

6. CONCLUSION

Time domain and frequency domain methods are still basic building blocks of heart rate variability analysis and these features can be utilised for classification to determine the normal healthy subjects and hypertensive patients. Nonlinear methods such as Poincare plot, approximate entropy, and sample entropy provide the additional information to distinguish clearly the normal healthy subjects with hypertensive patients. SVM-based classification technique is simple, yet most effective, specifically in binary classification which gives clear separability of hypertensive subjects with normal healthy subjects.

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