CHAPTER 2
LITERATURE REVIEW

2.1 Introduction

This chapter provides a bird’s view about the research work done in the past two decades about the correlation of HRV and ANS and its clinical importance as early predictor of CVS diseases. The HRV has the unique character of extracting the condition of Autonomous Nervous System noninvasively.

2.2 Review of Earlier Work

Quite, a large number of papers appeared connecting to HRV and cardiovascular diseases [2], show the importance of HRV in monitoring the health of the cardiac system. The concept of HRV (i.e., difference in variation of time intervals between subsequent heart beat) is not new. It is of much interest in recent years in this field because of low cost microcontrollers with exceptional computational power, which have given rise to the advancement in the research field of HRV.

Boer RW et al [29] showed that HR, plasma adrenaline concentration, systolic BP, power spectrum of HR and diastolic BP values increased considerably when a person changes his posture from sitting to standing posture.

Viktor et al [30] studied the changes in HR spectrogram in supine and standing posture. Also, they studied the changes in breathing because of the change in positions. At present different dynamic ways of measuring HRV have been developed to understand the nonlinear fluctuations in HR, which could have been difficult to access this nonlinearity otherwise. Various techniques have been put forward for consideration.

Wolf A[11]. Studied the Lyapunov exponents 1/f slope, Detrended Fluctuation Analysis (DFA) and approximate entropy (ApEn). By obtaining HRV parameters, the change of HR in accordance with the mean HR can show the control of cardio-respiratory system. HRV is a worthy tool to carry out the systematic investigation on the activity of sympathetic and parasympathetic systems function of Autonomous Nervous System. Other significant applications of analyzing the parameters of HRV are in the situations of post infarction and in subjects with diabetes. HRV gives the activity level of sympathetic and parasympathetic nervous system which denotes the autonomous balance which can
be used to predict Sudden Cardiac Death (SCD) in individuals. The significant advantage of HRV is its ease to extract with appropriate reproducibility and also it is noninvasive.

Kovatchev et al [31], studied neonatal and systemic inflammatory response syndrome (SIRS) and neonatal sepsis and extracted the HR parameters and analyzed its characteristics and brought out a new technique called Sample Asymmetry Analysis (SAA). The normal infant is compared with that of the sepsis and the former was found with increased value of SAA where as the latter was found with decreased SAA values.

Crzyrz et al [32] have intensively studied on symbolizing RR intervals with binary symbols. It was found out that it can be the key for better information on heart beat sequenciality.

Verlinde et al [33], studied on the HRV of aerobic athletes and compared the former obtained parameters with that of the normal individual HRV parameters in all range of available frequencies and found that there was significant increase in the power spectrum values of aerobic subjects when compared with that of normal subjects. The spectrum was analyzed by using Fourier Transform. As HRV is quasi-periodic, wavelet analysis provide the appropriate technique to analyze the swinging component of HRV. In addition to the traditional methods, frequency resolutions can also be obtained. In repercussion time-dependent analysis of the spectrum of HRV, using wavelets was helpful in obtaining the patterns of heart rate control. Along with this, careful study over entire record showed that there were significant diminished values of HRV with vagal saturation subjects. By applying wavelet transform to HRV signals, it was possible to obtain time domain representation for various frequencies of HRV i.e., Very Low Frequency, low Frequency and High Frequency by using algorithm like multi-resolution orthogonal algorithm. Results show that analysis using wavelet gives significant data for the procurement of dynamic variations and patterns in HRV in myocardial ischemia. Both time domain and frequency domain parameters obtained using wavelet transform which was extracted during night period which in turn yields the nocturnal heart analysis, provides an efficient tool for diagnosing obstructive sleep apnea [22]. It provides significant information on risked population of middle aged people suffering from sleep related disorder in breathing.
In recent years Schumacher et al [34] studied the utility of analyzing linear and nonlinear parameters of HR signals. The changes in the functionality of ANS, in condition like myocardial infarction (MI), renal failure, diabetes, sleep disorders in relation to HRV was studied and discussed. The interrelation of ANS and cardiovascular functions can be extracted by using power spectrum of beat-to-beat HRV.

Mager et al [35] developed a technique of clustering individuals. For this they developed Kohonen’s self organizing map (SOM) where Continuous Wavelet Transform (CWT) variables were used as the input to the SOM and with same signatures of wavelet transform was clustered.

Bracic et al[36] studied the human blood flow in relation to HRV in the time-frequency scale, utilized morlet wavelet as the mother wavelet for this purpose and the results proved that there was a better time resolution with high frequency variables and superiority in frequency resolution for low frequency contents. Oliver et al made a detailed study on different cardiovascular diseases associated with HRV using morlet as the mother wavelet. The power spectrum was analyzed in QRS complex of ECG signal to obtain the frequency variable in intraventricular conduction abnormalities (IVCA). The result obtained depicted that there was a significantly low value of frequency power with IVCA and with higher values of power, more numbers of peaks were found in high frequency range in IVCA with cardiac arithymias. HRV analysis was studied widely to measure the changes in the ANS tones when influenced by anesthetic drugs. Power spectrum measurements are widely used to access the HRV related to sympathetic and parasympathetic system.

The HRV is found to be affected by change in the tone of peripheral and central nervous system. In malfunctions, it is found that there was a change in the Heart rate which was created by the modified vagal tone and fluctuated sympathetic system. In acute brain damages and in depressions heart rate’s normal cyclic variations were considerably reduced. The results showed that HRV was comparatively a less predicting method, when considered with other modes of prediction algorithms like Glasgow Coma Scale. But HRV is a noninvasive and easy method of obtaining individual’s neurological conditions.
The subsequent condition of neurological function can be reflected by rate of obtaining the normal HRV, in series determinations. The important applications of HRV are in analyzing psychiatric malfunctions that arise when the sympathy vagal is not in balanced state. These can be detected by HRV and provide a useful tool in conditions like adrenergic and relative cholinergic variations and in mental ailments. There is some literature stating that HRV showed conflicting results in depressed subjects. At the same time many literature provide the proof that analyzes the HRV in depressed subjects with excellent results and can be used as a standard method of detecting depression [37].

Hayano J et al [38] worked on the analysis of HRV for addictions like smoking which degrades the normal functions of the human system. It can also be a unique and simple method of predicting the ill effects that could be due to addictions. Also, the individuals can monitor their HRV as it is a very simple method and cost effective, so that it can create the awareness on ill effects of addictions. The above review gives an insight of smoking effect on HRV and the change in the cardiovascular activities because of the smoking habits. It also gives the basic information on the different HRV parameters and their uses as diagnostics in various heart related ailments. Detailed study has been done to analyze the change in ANS by using HRV as the reference among both passive and active smokers. The overall results showed that there was a considerable change in the sympathetic tone which is increased in smoking individuals and the overall HRV has been reduced in smokers. The decreased HRV, because of the ill effects of smoking, is thoroughly analyzed and evaluated for its implications in clinical applications.

Acharya UR et al [39] worked on changes in HRV caused by the external and internal simulations and the response of the neural system was analyzed by extracting HRV. HRV is very much related to the health of the person, the reduced HRV indicates the person can be prone to stress and the mental conditions of the person is disturbed by decreased HRV. The HRV was found to increase significantly after the treatment for the mental ailments. They also studied HRV of alcoholics. It was found that there was decrease in the parasympathetic activity of the nervous system and sympathetic activity on the heart was found to increase in alcoholic subjects. The review studied the effect of alcohol on various individuals of different age groups. This demographical data showed
the change in the ANS activities because of alcohol consumption which was analyzed by extracting HRV parameters. Medline, PubMed and Scopus institutes searched the ill effects on alcohol and changes in the HRV caused because of smoking. These show the method that should be used for data collection which should be standardized by medical procedures.

The HRV considerably increased in subjects, who drink occasionally and with a limit, but HRV decreased in subjects who consume alcohol regularly and also who consume it with higher quantities. The HRV of subjects who withdraw alcohol after chronic alcoholism is less understood. The J curve of HRV was obtained in chronic alcoholic subjects. Hence HRV can be used as a bio marker for analyzing the ill effects of alcoholics and in creating awareness among the individuals.

Andr´e E. Aubertet et. Al [40] explained the dependability of HRV in sports especially athletes. They carried out the longitudinal and cross-sectional studies relating to athletes and their routine and explored the influence on HRV. The athlete’s sex, age and training methods, were considered and analyzed for influence of sports on HRV of the individual. Athletes with the desire of winning practice a lot and sometimes it was found to be harmful as extra effort which results in over-training. Athletes with over training can be easily predicted by simple HRV analysis, hence the athletes can see that they aren’t over trained and their level of training is optimal to their potential. The study of predictability in HRV among athletes and different methods for HRV in athletes are studied.

Barutcu I et.al.[41] studied the variation in the time interval of diastolic and systolic of cardiac function with HRV and concluded that there are two different types of variations, variability in diastolic time and variability in the systolic time. The differences among diastolic time, systolic time variability are obtained by using sample entropy and AR model methods. The peaks of the spectrum are obtained by analyzing the spectrum of Heart Rate with the AR model. The complex nature of HRV time series are calculated by using SampEn and ApEn. The diastolic time variations result in the fluctuations in RR and systolic time variation results in small variations in RR. They showed that diastolic time variations had better potential to obtain the variation of HRV but stability was kept higher by systolic time variation[14]. Its further scope includes the analysis of diastolic
time, systolic time variability, HRV and its clinical potential for estimating cardiac diseases.

Moody GB et al [42] studied various methods for nonlinear and linear generation of ECG. Mathematical model was proposed for generating artificial ECG using power spectrum, different waveforms and change in HRV. Four approaches were proposed: First approach was time series generation of HRV using Zeeman model. Second approach was based on standard deviation and mean. Third approach was the pulse frequency modulator integral and fourth approach was Gaussian combination approach for artificially creating ECG. Linear approaches are easier and simple to manipulate but nonlinear approaches are difficult to adjust as the complete signal is nonlinear. A generation of HRV artificially is considered to be optimal when it includes the Parasympathetic and sympathetic activities. Among the four approaches used, Zeeman model was found to be more efficient and can be used in pacemakers [15].

Jamsek J et al [43] proposed Joint Time Frequency (JTF) while conducting experiments on HRV in Pharmacology clinic. The study was carried out to analyze the response of drug dynamics with that of autonomous nervous system. Lab VIEW software was used to analyze the spectral data of JTF which is more recommended in non-stationary signals [27]. The study showed that compared to AR method and FFT, JTF approach gave the better information regarding the regulation of ANS. The scope included that the JTF spectrum which demanded the better data structure for standardizing the method.

The study on fuzzy logic in analyzing the HRV with linear and nonlinear methods of HRV analysis. Based on different arrhythmia, different weights were fixed. The analyses of RR in the ECG signal in both nonlinear and linear domain were carried out using a hybrid algorithm. The optimal score was calculated based on fixed weights for RR series. The RR series are considered to be normal when their scores are high [17].

Diabetic autonomous neuropathy is a major complication of diabetes and includes cardiac autonomous neuropathy (CAN), uremic leukemia and peripheral neuropathy which can lead to sudden cardiac death (SCD). The traditional Ewing battery of tests for autonomous function, which document the presence of neuropathy, is not sensitive to preclinical or asymptomatic cardiac autonomous neuropathy [1]. Heart Rate Variability
(HRV) analysis is able to detect variations in autonomous modulation of the heart rate prior to clinical symptoms of CAN are identifiable [2] and has been shown to be a useful assessment tool for diabetes associated cardiac dysfunction. Standards of measurement and interpretation of HRV have been recommended by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology and includes time and frequency domain as well as nonlinear measures.

Current HRV parameters used in HRV analysis are essentially static measures of a time signal. To obtain a better understanding of the relationship between autonomous control of the heart rate and diabetes a more dynamic measure of heart rate is required.

The Poincare Plot is a method proposed and utilized by Tulppo et al. (1996) for analysis of heart rate signals [3]. The Poincare Plot allows determining linear components of the inter-beat variability associated with short and long term correlations of the signal.

An extension of the Poincare Plot to determine and measure the temporal dynamics was proposed by Karmakar et al. (2011). The complex correlation method (CCM) relies on computing the beat-to-beat variation of the signal with increasing lag (beat intervals) rather than the global description of the Poincare plot, which provides indices based on n, and n + 1 beats. This study investigated whether the Poincare plot indices SD1, SD2 and CCM are able to differentiate between the beat-to-beat changes determined from the electrocardiogram (ECG) recordings of T2D and non-diabetic subjects [6]. The rationale of the study is that cardiac autonomous neuropathy and its effect on cardiac function may be better and more accurately described and quantified using a measure that reflects the systems’ dynamics over the recording interval [6].

The development of nonlinear techniques paved the way to enhance characterization of biological signals. Richman and Moorman [44] introduced sample entropy (SampEn), a family of statistics for measuring the regularity (or complexity) of time series, widely used with HRV. Either SampEn or approximate entropy, a related technique, proved effective in the context of paroxysmal atrial fibrillation (AF): i.e. discriminating terminating and non-terminating paroxysmal AF [5]. With respect to persistent AF.

Rother M et al. [45] investigated the effect of 4 rate control drugs on HR and arrhythmia related symptoms with permanent AF. They reported that all drugs reduced
the mean HR. An analytical expression for SampEn estimation based on autoregressive models (AR) has been recently proposed [24]. The purpose of this study was to investigate whether a rate control drug can also alter the SETH value. Given the fact that traditional spectral parameters [17] are based on AR models, they were analyzed as well (during AF, they only marginally reflect ANS activity so they are not commonly employed).

The evaluation of the cardiovascular response to ECG stress test is a crucial step in the therapeutic rehabilitation of cardiac subjects providing important information on the estimation of functional capacity very useful for prognosis and for the proper rehabilitative training setting. The demonstration that exercise can promote cardio respiratory and metabolic adaptations in subjects with ischemic heart disease with and without impairment of systolic function has opened new therapeutic horizons. The cardiovascular response to stress is characterized not only by a strong adrenergic stimulation and an increase of mechanical and hemodynamic performance but also by an overall response governed by profound changes in the sympatho-vagal balance of the entire autonomous nervous system. Linear measures of heart rate variability (HRV) have been commonly used in the non-invasive evaluation of modulation of the autonomous control of the cardiovascular system, however, the use of these methods during exercise has been widely questioned due to the non-stationary nature of the signal. Some nonlinear measures of HRV, based on typical properties of chaotic systems and deterministic fractal, allowing description of cardiovascular oscillations of non stationary signals also over short term period let overcome these limitations. Very few papers addressed such issues and aim of the paper was to describe fractal behavior of HRV during the different stages of ECG Stress Test in cardiac subjects.

K. Ashoka Reddy et. al [46] studied method for reducing the motion artifacts in the ECG signal using cycle-by-cycle Fourier series analysis. According to Fourier, any signal with constant period can be divided into a group of sinusoids with its harmonics and fundamental frequency [7]. Fourier series works good when the signal is periodic, it cannot be applied for non stationary signal. Hence analyzing ECG using Fourier series is difficult as ECG is a quasi-periodic and non stationary. According to Fourier series first few significant coefficients are enough to store and retain the features of the given signal
with some accuracy. The results showed that, the resultant ECG signal constructed with the coefficients of Fourier series ECG signal was found to be artifact-free ECG signal.

Han-Wook Lee et al. [47] studied the application of Moving Average Filter (MAF) in reduction of motion artifacts in ECG. The MAF will be handy because of the quasi periodic nature of the ECG [8]. Moving average approach is generally a good module for reducing intermittent motion artifacts but the large amplitude motion artifact and the abruptly occurring motion artifact cannot be removed by moving average approach [9].

M. Raghuram et al. [48] studied different types of wavelets for reducing motion artifact. The various types of wavelets like coiflet, biorthogonal, Daubechies, reverse biorthogonal symlet types of wavelets are evaluated for reducing motion artifacts. The obtained results showed the values of SpO2 estimated ECG with reduced motion artifact in the ECG gave relatively similar values. Daubechies wavelet gave better results in reducing motion artifact while keeping the respiratory information intact [10].

K. Ashoka Reddy et al. [46] studied Singular Value Decomposition (SVD) for reducing artifacts in the ECG signal. Results obtained showed SVD was able to reduce the motion artifact in the signal and can clean the ECG signal to obtain artifact-less ECG signal. The values of the oxygen saturation were free from error even with the signals containing motion artifacts [11].

M. Raghu Ram et al. [48] studied efficient and simple filtering methods using adaptive filters to reduce motion artifact with the help of artificially generated noise signal. The advantage was that no extra hardware was used for generation of the noise. The filter feedback itself was used for generating the noise which was further used as reference signal for adaptive filtering. The LMS adaptive approach was used to reduce motion artifact by using motion artifact as the reference noise and by adjusting the filter’s coefficient adaptively[12].

K. Balasubramanian et al. [49] studied using applied tools for obtaining the P-wave of the ECG signal. They developed hardware for obtaining the P-wave of ECG and to measure the time interval of successive P-waves. The P-P interval was describe the pumping actions of heart and the physiological behavior of the cardiac system. The P-wave Locked Loop (PWLL) was used to extract P-wave as its amplitude is considerably
small. The results obtained showed that the experiments carried out by using RR series can also be carried out by using PP series of the ECG signal [18].

Allan Jovicet et al [50]. Studied the nonlinear character of HRV for four types of cardiac arrhythmias and the results obtained showed that more analysis standardizations are required for implementation of nonlinear parameters in clinical environments.

The detailed review done shows that the commonly used methods to analyze HRV are Linear and Non-linear methods. The review revealed that Matlab, Lab VIEW and Kubios Software are the most widely accepted softwares which can be used for the analysis.

We can also see that many researchers have shown the association of analysis of HRV for early identification of CVS changes for addiction and stressed individuals. Whereas there is no work established for young population and hence the study.