Chapter 1

1.1 Introduction

According to statistical findings of World Health Organization (WHO), the following observations are made-

1. Globally, cardiac diseases are major cause of death.
2. An estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths.
3. Developing countries with low and middle income group populations are disproportionately affected. Over 80% of deaths due to cardio vascular diseases (CVD) take place in low and middle income countries and occurs in almost equal distribution in men and women.
4. Most cardiovascular diseases can be prevented by addressing risk factors such as tobacco use, unhealthy diet & obesity, physical inactivity, high blood pressure, diabetes and raised lipids.
5. Raised lipid levels and high blood pressure account for 16.5% of total deaths. This includes 51% of deaths due to strokes and 45% of deaths due to coronary heart diseases. [1]

The effects of unhealthy diet and physical inactivity may cause high blood pressure, glucose level and or lipids in blood, overweight and obesity. [1]

Cessation of tobacco use, reduction of salt in the diet, consuming fruits and vegetables, regular physical activity and avoiding use of alcohol have been shown to reduce the risk of cardiovascular diseases. Cardiovascular diseases can also be prevented by treating hypertension, diabetes and raised blood lipids. [1]

Cardiac deaths are due to heart attacks and strokes. Heart attacks and strokes are acute events and are mainly caused by blockage preventing blood flow to the heart or brain. The most common reason for this is a build-up of fatty deposits on the inner walls of the blood vessels that supply the heart or brain. Strokes can also be caused by bleeding from a blood vessel in the brain or from blood clots. [25] and [39]

If awareness campaigns are embarked by the governmental organisations, prevention of the diseases can be possible. Awareness can also be spread about lifestyle changes and unhealthy food habits that help to prevent onset and promotion of the disease. [2]
1.1.1 Diagnosis of the cardiac disease and cardiac care

There is a gradual deterioration in cardiac performance before a cardiac stroke or arrest occurs. The deterioration in cardiac performance is visible in only in HRV analysis at preclinical stage. HRV analysis is not in use in current clinical practise. Incorporating HRV analysis in the diagnostic routines of diabetic and hypertensive subjects would reduce the mortality and morbidity rate significantly. The attempt to establish correlation between the echocardiogram findings and HRV analysis is focused towards validating the HRV analysis as an early diagnostic tool that can be used to control the morbidity and mortality rate due to cardiac diseases. [3]

1.2 Comparison of different diagnostic modalities used in diagnosis of cardiac disease.

The different diagnostic modalities used for the detection of cardiac diseases are-

1) Electrocardiogram: Electrical impulse is required for effective contraction and relaxation of heart. This diagnostic modality gives information about the signal generation and conduction of the electrical impulse. This diagnostic method is safe non-invasive, cost effective and does not need any processing time. Conductive electrodes are connected all over the chest and signals generated from electrode are tested for one minute. ECG waveform details like voltage amplitude and time gap between the prominent features of ECG are used as diagnostic parameters. [4]

The intensive cardiac care unit in India uses Holter monitoring for 24 hrs. This data is statistically analysed for diagnosis. Study of ECG provides waveform specific information required for diagnosis. [4]

2) Blood tests (cardiac markers): This is a more specific diagnostic modality. Dye inserted in blood marks the route of the blood flow and thus the blood vessel cross section can be viewed as the blood flows. This modality gives specific information. Majority of dye are enzyme based but some are synthesised chemically. Activation time for the test varies from 2-24 hours. [4]

Hence, the test cannot be conducted at the time of cardiac episode. Dye induced can be carcinogenic and hence the test cannot be repeated for many times.

3) Cardiac stress test: this diagnostic modality helps to determine,
1) Whether there is adequate blood flow to the heart during increased levels of physical activity.

2) Whether the medications to control angina and ischemia is effective.

3) Whether any likelihood of having coronary heart disease and the need for further evaluation.

4) Whether the treatment to improve blood flow within the heart in case of coronary heart disease is effective.

5) Identify abnormal heart rhythms.

6) Develop a safe exercise program.

There are many different types of stress tests, including:

- **Treadmill stress test:** This test conducted to find out the performance of heart while performing exercise. The changes in the ECG during the exercise are studied. If subject is normal and has a normal ECG, but is complaining of fatigue, excessive sweating or is overweight or obese, stress test is used as evaluation tool. Subject walks on a treadmill while being monitored to evaluate the heart’s performance under physical stress and if he/she complains of chest pain or changes in the ECG acquired during the exercise suggest that heart is structurally defective or not getting enough blood.

- **Dobutamine or Adenosine Stress Test:** This test is used in people who are unable to exercise. A drug is given to make the heart respond as if the person were exercising. This way the doctor can still determine how the heart responds to stress, but no exercise is required.

- **Stress echocardiogram:** An echocardiogram is a graphic outline of the heart's movement. A stress echocardiogram can accurately visualize the motion of the heart's walls and pumping action when the heart is stressed, it may reveal structural, functional fault or lack of blood flow. The test reveals the information in condition of heart in stress that no other diagnostic modality can.

- **Nuclear stress test:** This test helps to determine which parts of the heart are healthy and function normally and which are not. A small amount of radioactive substance is injected into the patient. Then the doctor uses a special camera to identify the rays emitted from the substance within the body; this produces clear pictures of the heart tissue on a monitor. These
pictures are done both at rest and after exercise. Using this technique, areas of the heart that have a decreased blood supply can be detected.

Preparation for these types of stress tests will vary from preparation for the exercise stress test. Though this is versatile modality, there is a risk associated with the test. It is always necessary to conduct the test in presence of expert medical and paramedical staff. The chemically induced stress tests cannot be performed repetitively due to the risk involved.

4) Coronary angiogram:

Coronary angiography is a special X-ray of the heart (coronary) arteries. A dye is injected down the coronary arteries through a catheter. The arteries and their smaller branches then show up clearly on an X-ray. Therefore, coronary angiography can show the exact site and severity of any narrowing of the coronary arteries. This helps the doctor to decide further treatment.

5) Echocardiogram:

This diagnostic modality is used to map the anatomy, working and blood dynamics of the heart by the mapping of ultrasonic frequency signals reflected from the heart. This is a safe noninvasive modality that gives quick results. It is costs less compared to other modalities except ECG. Intra operator diagnostic variation ranges from 5-10%. The images are very noisy and needs an expert to analyze them. [5]

To summarize, all the diagnostic modalities have their own merits and demerits. More or less all of them are used as per the demand of the situation. ECG and echocardiogram are preferred because they are safe, non-invasive and do not require preparation time or process.

Early detection of the disease can control the morbidity and mortality rate of the disease. Diabetic and hypertensive subjects are observed to have greater tendencies of atherosclerotic deposits in the blood vessel. This restricts the blood flow. If there is restricted blood flow in the coronary artery, the heart will not get required blood supply and slowly that part of the heart will be dead. This condition is called myocardial ischemia. The myocardial ischemia further develops into myocardial infarction. Myocardial infarction is an irreversible condition that leads to heart failure and death. If the left ventricular wall of the heart develops a dead tissue, the blood supply will be inadequate. This may give rise to further complications.
It is very essential to diagnose the onset of atherosclerotic deposits and the reduction in cardiac performance. The prevailing diagnostic modalities are unable to diagnose the deterioration of the heart at the onset of reduced blood supply.

The Heart Rate Variability (HRV) analysis technique has the strength of early diagnosis. HRV analysis needs minimum 128 samples of ECG signal in supine and sitting position. If the patient is terminally ill, sample of supine position is used for analysis. Cost involved is less and test can be conducted by paramedical staff.

1.2 Significance of the above mentioned doctoral studies.

In case of subjects with diabetes mellitus, the blood sugar levels are high due to inability of blood cells to assimilate sugar. After intake of insulin, or long gap in duration of intake of food, the blood sugar level is low. Since the natural balance of insulin release and glucose assimilation is lost, diabetic subjects will be events of hyperglycemia and hypoglycemia. Due to hypoglycemia, the cardiac system gets affected. Diabetic subjects with uncontrolled sugar fluctuations are more likely to develop myocardial ischemia. Prevalence of hyperglycemic condition has more atherosclerotic deposits in the blood vessels. [10] This obstructs the blood flow. Reduced blood supply to the heart walls results in reduction in thickness of heart wall. Prevailing condition is called myocardial ischemia. Myocardial ischemia is reversible. Myocardial ischemia further develops in to myocardial infarction, an irreversible dead tissue of the heart wall. [3] This disorder cannot be diagnosed since there are no clinical signs and symptoms. Diagnostic tools used in the current clinical practice cannot diagnose the disease at preclinical stage. Early diagnosis is possible by the Heart Rate Variability analysis. Heart rate Variability analysis use statistical tools to understand physiological, neural and hormonal performance of the subject by acquiring long duration ECG signal. [3]

It has been observed that in case of diabetic subjects, the changes are observed in HRV indices [3] as-

1) Increase in heart rate
2) Decrease in SDNN
3) Decrease in total power
4) Decrease in power in HF band
5) Decrease in sympatho-vagal balance
6) Decrease in orthostatic stress index
Since there are no clinical symptoms and the changes are not visible in short duration of ECG, HRV analysis has unique strength of preclinical diagnosis. Especially in case of diabetic patients, the changes in HRV are more prominent and increase with the duration of diabetes. Changes in HRV can correlate with diabetic condition that lead to reduced electrical power required for contraction of heart. Detection of changes in HRV indices are essential. HRV indices are acquired from ECG of 3-5 minutes in supine and sitting position. This diagnostic modality is most cost effective, safe and gives instantaneous results. [3]

Echocardiogram diagnoses functional abnormality and wall motion abnormalities. Structural and hemodynamic performance evaluation is possible by performing echocardiography. This diagnostic modality is safe, gives instantaneous results. The limitation of this modality is some diagnostic variation subject to the cardiologist’s expertise exists. The images are noisy and interpretation is tricky. Echocardiography is costlier than ECG and takes 20-30 minutes. Whenever any clinical symptom is visible, the cardiologist recommends echocardiography in the current diagnostic practice. Echocardiography diagnoses the current prevailing conditions but does not have any preclinical diagnostic capability. [4]

By the correlation established from HRV indices,

1) The echo cardiologist will know what to expect from the echocardiogram of the patient. So he/she can focus the examination in accordance. This will help in reducing his/her time and effort.

2) The extent of changes in HRV can assess the cardiac health. Standard diagnostic methodology can be established.

3) This will also eliminate the variation in the diagnosis between echo cardiologists.

1.4 Scope of the problem.

The data samples are collected for control group, diabetic group and diabetic and hypertensive group. To ensure the different degrees of deterioration with prevailing diabetic and hypertensive disease, diabetic and hypertensive subjects with myocardial ischemia and infarction. All the samples are collected ensuring the variation of age, sex, economic class. Granularity is ensured from the selection of patients as they register for examination in the hospital. ECG and echocardiogram of the selected sample is acquired. HRV analysis indices and
echocardiogram findings are compared to assess correlation between the two diagnostic modalities.

The HRV analysis gives an important indication of status of cardiac performance. The FFT/AR analysis separates the low frequency (0.04-0.15 Hz) and high frequency (0.15-0.4 Hz) bands. The ratio of normalized power in these bands spectrum has a higher value ratio (usually around 1.0) in case of normal subjects. In case of diabetic subjects, power in HF band is higher. This reduces the ratio value. It has been observed that with ratio progressively goes on reducing as the number of years for prevalence of diabetes increases. So this in an early indication before the symptoms of reduced cardiac performance occurs. [3]

The increase in parasympathetic (HF) power results in reduction in heart wall motion. [24] This change can be observed from the echocardiogram. This also reduces the left ventricular ejection fraction. Reduced value of left ventricular ejection fraction indicates the reduced cardiac performance.

1.4.1 step by step procedure defining the scope of the research.

Data Specification criterion

1) The data specification.
2) Identification of data category
3) Inclusion and exclusion criterion specification.
4) Specify the category and stratification type.
5) Statistical test to establish result.

II Understanding of ECG and echocardiogram for –

1) The interpretation of the functioning of the heart
2) Cardiac health analysis from the ECG and echocardiogram.
3) Significant indices that are evaluated through echocardiogram.

III HRV analysis

1) To acquire the supine and sitting ECG of 5 minutes duration with LABVIEW interface for different groups of patients.
2) To obtain the RR interval file for the same.
3) To get the linear and nonlinear HRV parameters from the analysis tool.
IV Establishing correlation

1) To establish correlation between the ECG and Echo cardiogram findings.

2) To analyze the indices of both the diagnostic modalities and statistically.

3) To establish mathematical analogy for the pathophysiological changes due to prevalence of diabetes and changes observed in the study of diabetic cohort compared to that of the normal cohort.

1.5 Details of the data specification.

Study caveats:

1. All subjects are located at the Fortis- S L Raheja Hospital at Mahim, Mumbai.

2. Prior Coronary Angiographic evidence of ischemia is not mandatory.

3. All subjects including controls are above age 25 years.

4. Standard 2 lead ECG is used for the study.

6. Echograms are performed on ‘Philips iE 33’ Echocardiograph.

7. Anticipated Cohort registry and complete ion of cohort inclusions will be between the period of Dec 2012 to July 2012.

8. Diabetic patients need not be on clinical glycemic control status at the time of study.

1.6 Study Considerations inclusion and exclusion criterion

1. The study will entail a Control Group and two Study Cohorts of minimum 15 each. Control Group will constitute non diabetic subjects with no evidence of myocardial ischemia or infarction.

2. Inclusion and Exclusion criteria are established for the Groups.
3. Cohort candidates are sequentially and concurrently registered on occurrence at the Echocardiography Lab at the Hospital.

5. Cohort candidates are allocated to the various groups on occurrence, in compatibility with the inclusion/exclusion criteria.

6. Candidate data sets are recorded in text, softcopy, compact disc and hard copy and preserved under security with the Hospital Echocardiography Lab.

7. Study Datasets will be accessed only by the Principal Researcher, Cardiology Associate of the study and the identified Echocardiography Lab technician.

1.6.1 Inclusion Criteria:

Control Group: All non diabetic, normotensive, non Ischemic patients over age 25 years, both sexes included.

Male to female ratio not specified and is determined by the registration of cases during the period of data collection.

Study Group I: Known Diabetes for at least 5 years duration with known clinical history of Ischemic or infarcted Heart Disease. Both the sexes are included.

Study Group II: Known Diabetes for at least 5 years duration without known clinical history of Ischemic or infarcted Heart Disease. Both the sexes are included.

1.6.2 Exclusion Criteria:

Patients whose are less than 25 years age.

Patients suffering from type-1 diabetes.

Patients with less than 5yrs. of diabetes history in study group I and II.

Patients with known history of electrolyte imbalance related ECG abnormalities.

Patients with known history of Digitalis induced ECG abnormalities.
### 1.6.3 Typical Data sheet

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<th>PID</th>
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<td>Hypertensive/ Diabetic</td>
<td>AGE</td>
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Figure-1.1- Data sheet