Chapter 1

Introduction

1.1 Importance of Fetal Heart Rate Variability Measurements System

Acceptability of Heart Rate Variability (HRV) in human adult is documented and well accepted. It gives the diagnostics information of the nervous system development regulating heart, respiration and body temperature. The research team is working on designing the protocol to acquire the HRV signal of fetus and further processing it to derive diagnostic indices to monitor growth of fetus. The instrumentation system is designed for acquiring signal from fetal heart and compares the normal and abnormal cases in consultation with the medical experts [1, 2].

Fetal heart starts pulsating at around 250 beats per minutes (BPM) at 12th weeks of gestation period. It decreases down to around 120 to 160 BPM at 36 weeks (9th month). The average heart rate & heart rate variation are related to development of the fetal nervous system and development of different body organs. We have designed and developed system for fetal heart rate variation measuring system and the fetal heart rate data to define the diagnostic indices. These diagnostic indices can be utilized to predict the fetal outcome / progress as predictor for parental outcome. It may be in position to predict early fetal demise and hence the need for early intervention for fetal salvage [3, 4].

The most common method for fetal monitoring is recording of fetal heart rate and analysis of fetal heart rate variability (fHRV). The fHRV analysis has a physiological significance as the changes in FHR are responsible for fetal well-being. The importance of this subject was felt as every year about one out of 125 babies are born with some form of congenital heart defects. The medical reports show 12.8 percent of babies are born prematurely due to their nervous system defects such as congenital heart defects. This problem can be detected during gestation period if we measure the heart rate of the fetus during its growth. The defect may be so slight that the baby appears healthy for many years after birth, or so severe that its life is in immediate danger. Congenital heart defects originate in early stages of pregnancy when the heart is forming and they can affect any of the parts or functions of the heart [1]-[4].
Fetal heart rate variability is an important area of investigation as it provides early information about fetal distress and identifies those at risk for sudden infant death syndrome adverse perinatal outcome. Monitoring of a fetal condition by means of tracking the parameters of heart rate is considered to be one of the promising ways of modern antenatal diagnostics. The suggested technique is based on definition of fetal heart rate variability (fHRV) and calculating indices, which have high diagnostic value.

HRV was first used clinically in 1965 when Hon and Lee noted that fetal distress was accompanied by changes in beat-to-beat variation of the fetal heart rate, even before there was detectable change in heart rate. In 1996, a special task force formed between the US and European Physiological associations to outline current fields on HRV and set specific standards on using HRV in medical science and future practice. Since then a steady stream of new information and values continues to come out of HRV research. HRV refers to the beat-to-beat alterations in heart rate stress, certain cardiac diseases, and other pathologic states affect on HRV. Here we talk about HRV, we actually mean variability of RR intervals. Heart Rate Variability (HRV) measurements analyze how these RR intervals, which show the variation between consecutive heartbeats, change over time.

1.2 Preliminary Study

Through the ongoing Safe Passage study at Brihan Mumbai Municipal Corporation (BMC) Hospital, Mumbai. The proposed system is tested using real time Doppler ultrasound fetal data acquisition system & real time direct fetal electrocardiogram (FECG) machine [1]. Dipel make Doppler ultrasound (DFM-051) machine is used to measure maternal abdominal Doppler ultrasound raw signal [2]. Doppler envelope filter, variable threshold detector, non retriggerable monostable multivibrator having adjustable pulse width and special signal processing algorithm in LABVIEW is applied to obtain fetal heart beats and measure RR-intervals of fetus. We have taken coefficient of variance (CVRR) of a patient’s normal RR intervals as an index of parasympathetic activity which is defined as ratio standard deviation of normal RR intervals value to mean of such intervals. The index of sympathetic department of vegetative nervous system regulation activity is calculated from the FHRV estimation using power spectrum analysis of low-to-high frequency ratio with nonparametric [Fast Fourier Transform (FFT) based] &
parametric [Based on Autoregressive (AR) models] methods and then is chosen to be the resulting diagnostic index.

We have proposed a new technique which provides the true beat-to-beat values of fetal heart rate (FHR) signal with Doppler ultrasound monitoring. We studied 64 maternal abdominal Doppler ultrasound signals. From these, we identify 41 subjects of pregnancies whose body mass index (BMI) ranging from 20 to 37. This identified group is further classified into three groups according to gestational age: Group A, 26-29 ± 1 wk (7th month pregnancy); Group B, 30-33 ±1wk (8th month pregnancy); and Group C, 34 onwards ± 1 wk (9th month pregnancy). Doppler ultrasound signal was recorded using Doppler ultrasound fetal monitor in local hospital. The method consists in three steps: Doppler envelope filter, variable threshold detector and non retriggerable monostable multivibrator having adjustable pulse width for heartbeats detection.

We got the special permission from BMC with approved patient protocol to get 200 female subjects for measurement of FECG. Written informed consent was obtained from all subjects after being briefed about the clinical study, which was approved by the Ethics Committee (Ethics approval number: N0. HO/ 14017 RNCH Date: 07. 12. 2011) of the Brihan Mumbai Municipal Corporation (BMC) Hospital. Each of recordings consists of two simultaneously acquired signals: Doppler ultrasound signal from the abdominal transducer and the direct fetal electrocardiogram from the electrode placed on mother’s abdomin. The recording time was 5 minutes, although some fragments in which either fetal electrode was disconnected or the ultrasound transducer lost the heart signal, were marked as signal loss and removed.

1.3 Study Aims

The primary goal of this work is to design and develop non invasive reasonably accurate and cost effective real time Doppler ultrasound fetal data acquisition technique for fetal heart rate variation measurement and the fetal heart rate data to define the diagnostic indices. These diagnostic indices can be utilized to predict the fetal feature life growth and can be utilized for preventive measure. This designed and developed system not only measure heart rate variation but also heart rate power spectrum which can be utilized for determining diagnostics indices as a guidance for the medical community.
The present study has four objectives:

- We present method of an abdominal fetal electrocardiogram (ECG) registration and Doppler ultrasound signal registration for estimation of a fetus condition and investigation of FHR fluctuations.
- Correlation processing of the received data, fetal R-R intervals allocation, estimation of distribution parameters and diagnostic index calculation, describing activity of sympathetic and parasympathetic nervous system of fetus.
- To design the system to measure the fetal heart rate variability for the evaluation of autonomic nervous system (ANS) indices. The system is used to differentiate the autonomic nervous system diagnostic indices of normal and abnormal fetus using Doppler ultrasound method.
- To clarify the significance of heart rate variability parameters in the fetus for the pregnancy subject coupled with obesity for advance diagnosis and to test the hypothesis that maternal body mass index (BMI) determines fetal cardiac sympathetic activity.

1.4 Salient Contributions

- We have designed non invasive and cost effective real time direct electrocardiography and Doppler ultrasound fetal data acquisition technique, correlation processing of the received data, fetal R-R intervals allocations, estimation of distribution parameters and diagnostic index calculation, describing activity of sympathetic and parasympathetic nervous systems of fetus. We studied 64 maternal abdominal signals. From these, we identify 41 subjects of pregnancies whose body mass index (BMI) ranging from 20 to 37.
- The system is design to measure the fetal heart rate variability for the evaluation of autonomic nervous system (ANS) indices in the normal and abnormal fetus. This study defines new diagnostic indices. These indices are derived from heart rate variability power spectrum. We defined a coefficient of variance (CV_{RR}) as an index of parasympathetic activity, and defined a low frequency/high frequency (LF/HF) ratio as an index of sympathetic activity. The values of these indices show statistical significance in comparing autonomic nervous system development in normal and
abnormal fetus.

- HRV parameters are less random as gestation age increases for normal fetus. This is evaluated by using various time domains, frequency domain and nonlinear parameters for various gestation age groups. The different linear and nonlinear parameters are evaluated show a particular range for identification autonomic maturation in the normal developed fetus.

- We tested the hypothesis that maternal body mass index (BMI) determines fetal cardiac sympathetic activity. Heart rate variability (HRV) parameters of fetal are measured for obese & non-obese mother prior to delivery. In consultation with gynecologists and child specialist it has been verified that the new born babies have more neurological problems following deliveries from obese mothers compared with deliveries from non-obese mothers. The results obtained from regression clearly indicates that orthostatic index which is ratio of LF/HF ratio as a sympathetic activity is found to be declined with increase in BMI or in other words neurological development index declined.

- We have tested the hypothesis that a LF/HF ratio [Nonparametric Fast Fourier Transform (FFT) Based] as an index of fetal sympathetic activity is a function of ten variables, age, gestation week, body mass index, CVRR %, HR Mean, HR Std, RMSSD, NN50, pNN 50 and non linear index SD1/SD2 ratio, a multiple regression analysis was performed. We can see that age, CVRR %, HR mean, HR Std, and RMSSD are significant predictors (or significantly related to) of LF/HF ratio [Nonparametric Fast Fourier Transform (FFT) Based] as an index of fetal sympathetic activity. Gestation week, Body mass index, pNN50 and SD1/SD2 index is not a significant predictor of LF/HF ratio [Nonparametric Fast Fourier Transform (FFT) Based] as an index of fetal sympathetic activity.

- We have tested the hypothesis that a LF/HF ratio [Parametric(AR) Based] as an index of fetal sympathetic activity is a function of ten variables, age, gestation week, body mass index, CVRR %, HR Mean, HR Std, RMSSD, NN50, pNN 50 and non linear index SD1/SD2 ratio, a multiple regression analysis was performed. We can see that age, CVRR %, HR Std, and RMSSD are significant predictors (or significantly related to) of LF/HF ratio [Parametric (AR) Based] as an index of fetal sympathetic activity. Gestation week,
Body mass index, HR Mean, NN50, pNN50 and SD1/SD2 index is not a significant predictor of LF/HF ratio [Parametric (AR) Based] as an index of fetal sympathetic activity.

1.5 Organization of Thesis

The thesis is organized as follows:

- **Chapter 1** gives importance of fetal heart rate variability measurements system, study aims, salient contributions and organization of the thesis.
- **Chapter 2** explains the mechanism of autonomic nervous system, problems faced in fetal heart rate variability measurement system and its clinical complications. The extensive literature survey brings out different fetal heart rate measurement methods and equipment set up used and their limitations in clinical applications, different transforms used and their limitations for measurement of fetal heart rate variability.
- **Chapter 3** describes the method of an abdominal fetal electrocardiogram (ECG) registration and Doppler ultrasound signal registration, correlation processing of the received data, fetal R-R intervals allocation, estimation of distribution parameters and diagnostic index calculation, inclusion and exclusion criteria for initial enrolment, describing activity of sympathetic and parasympathetic nervous system of fetus.
- **Chapter 4** describes indexes of heart rate variability analysis in normal fetus. These heart rate variability measurements have important information to assess fetal development during gestation period. HRV measurements serve as an approach to the fetal autonomic nervous system diagnostics.
- **Chapter 5** proposes the system to measure the fetal heart rate variability for the evaluation of autonomic nervous system (ANS) indices. The parasympathetic nervous activity increased with gestational age in the normal pregnancy group.
- **Chapter 6** describes about correlations of fetal cardiac sympathetic activity with maternal body mass index. Low frequency/high frequency (LF/HF) ratio as an index of sympathetic activity in normal pregnancy group displayed clearly decreasing trend with body mass index.
- **Chapter 7** describes nonlinear measures of HRV. Analysis of fHRV based on the
methods of non-linear dynamics might elicit valuable information for the physiological interpretation of HRV and for the assessment of the risk of sudden death.

- **Chapter 8** covers overall results and discussion of real time ECG and Doppler ultrasound data acquisition measurement system, different diagnostics indices, particular range for identification autonomic maturation in the normal developed fetus, correlations of fetal cardiac sympathetic activity (LF/HF) with maternal body mass index and non linear index for normal and abnormal fetus.
- **Chapter 9** gives the overall conclusions of the work along with suggestions for future work.