

An Estimate of Fetal Autonomic State by Time Spectral and Nonlinear Analysis of Fetal Heart Rate Variability

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Abstract: In this study we present a noninvasive method that enables the investigations of the fetal heart rate (FHR) fluctuations. The system is designed to measure the fetal heart rate variability for the evaluation of autonomic nervous system (ANS) and to investigate its development as a function of the gestational age and body mass index (BMI). Our Medical Engineering group has designed & developed a real time new method to assess instantaneous fetal heart rate variation (beat to beat) during gestation period with automated analysis of FHR variability using Doppler ultrasound method. We studied 64 maternal abdominal Doppler ultrasound signals. From these, we identify 41 ceases of pregnancies that we divided into three groups according to gestational age: Group A, 26-29 \pm 1 wk (7th month pregnancy); Group B, 30-33 \pm 1wk (8th month pregnancy); and Group C, 34 onwards \pm 1 wk (9th month pregnancy), whose body mass index (BMI) ranging from 20 to 37. 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 defined a coefficient of variance (CVRR) as an index of parasympathetic activity, and a low frequency/high frequency (LF/HF) ratio as a sympathetic activity. The R-R interval variability which shows the variation between consecutive heart beats, change over time was eventually adopted to calculate for time-domain, frequency domain and non linear analysis. In the frequency domain analysis power spectral density (PSD) of the RR series is calculated by analyzing powers and peak frequencies of different frequency bands. The value of CVRR in the normal pregnancy group displayed a clearly increasing trend with gestational age ($y = 0.383x + 13.16$; $R^2 = 0.009$) (one-way ANOVA: $P = 0.75655$). The value of CVRR in the normal pregnancy group displayed a clearly decreasing trend with BMI. In contrast, the LF/HF ratio in the normal pregnancy group displayed a slight increasing trend over the gestational period. The value of LF/HF ratio in normal pregnancy group displayed clearly decreasing trend with body mass index (BMI) $y = - 0.013x + 0.965$; $R^2 = 0.040$ (one-way

ANOVA: $P = 0.081282$). Analysis based on the time domain, frequency domain and non linear analysis of heart rate variability enable an evaluation of autonomic nervous system (ANS) activity. It is also observed that the parasympathetic nervous activity increased with gestational age in the normal pregnancy group and heart rate variability was found to be diminished in case of fetus from obese mother which is indicative of problems in the ANS activity. The dispersion of both short (SD1) & Long term (SD2) is smaller in normal weight mother fetus. The different fHRV parameters evaluated show a particular range for identification of autonomic maturation in the developing fetus.

Keywords: Autonomic nervous system; Doppler ultrasound; heart rate variability; multiple regressions.

I. Introduction

Heart rate is a variable signal and provides a balance between the sympathetic and parasympathetic nervous systems. The heart rate variation may contain indicators of present disease, or warnings about impending or future cardiac vascular diseases. These indicators may be present at all times or may occur at random during certain intervals in the time scale. It is difficult and time consuming to pinpoint these abnormalities in a huge cardiac data. Heart rate variability (HRV) constitutes a tool for assessing the activities of the autonomic nervous system (ANS). In this work, we have proposed a computer based analytical system to find the heart rate and analyzed it to obtain HRV Power-spectrum for investigation of the ANS during fetal gestational development. We have designated indices based on the HRV power-spectra power values (= areas under the power-spectrum plot between spectral peaks) and frequency shift of the peaks from their normal frequency values. We have shown the efficacy and sensitivity of these

indices to differentiate between normal and abnormal growth. Thus we have demonstrated how effectively these HRV power-spectral indices can enable advance diagnosis of fetus autonomic nervous system [1] - [3].

We have demonstrated how effectively Spectral analysis of the HR fluctuations provides quantitative amplitude and estimate of the cardiac ANS activity. Finally, we have composed an Integrated Index made up of these power-spectral indices, to facilitate distinguishing and diagnosing fetal autonomic neuropathy in terms of just one index or number [4].

Fetal heart starts pulsating at around 250 beats per minutes (BPM) at the 12th week 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. 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 fetal heart rate (FHR) are responsible for fetal well-being. Congenital heart defects 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] - [6].

Heart Rate Variability (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. 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. HRV measurements analyze how these RR intervals, which show the variation between consecutive heartbeats, change over time [3].

Analyses based on the time and frequency domains of heart rate variability using Doppler ultrasound method enable an evaluation of fetal ANS diagnostic indices. These diagnostic indices derived from fetal heart rate data can be utilized to predict the fetal future life growth and can be utilized for preventive measures. Our design system not only measures heart rate variation but also heart rate power spectrum which can be utilized for determining diagnostics indices helpful for the medical community.

Manoj S. Sankhe et al. proposes a hypothesis that a LF/HF ratio [Parametric autoregressive (AR) and 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. The result of the methods is comparable. Age, CVRR %, HR Std, and RMSSD are significant predictors (or significantly related to) of LF/HF ratio as an index of fetal sympathetic activity in both the methods. CVRR % is positively related to LF/HF ratio as an index of fetal sympathetic activity in both the methods [7].

Faezeh Marzbanrad et al. propose a new noninvasive method for automated estimation of fetal cardiac intervals from Doppler Ultrasound (DUS) signal. This method is based on a novel combination of empirical mode decomposition (EMD) and hybrid support vector machines—hidden Markov models (SVM/HMM). EMD was used for feature extraction by decomposing the DUS signal into different components (IMFs), one of which is linked to the cardiac valve motions, i.e. opening (o) and closing (c) of the Aortic (A) and Mitral (M) valves. The noninvasive fetal electrocardiogram (fECG) was used as a reference for the segmentation of the IMF into cardiac cycles. The hybrid SVM/HMM was then applied to identify the cardiac events, based on the amplitude and timing of the IMF peaks as well as the sequence of the events. The estimated timings were verified using pulsed Doppler images. DUS signal is nonlinear, nonstationary, and noisy and it is variable on a beat to beat basis. Therefore, using a combination of EMD as a data-driven method for decomposing nonlinear and nonstationary signal and hybrid SVM/HMM for automated identification of the events improves the estimation of cardiac intervals [8].

Paulo C. Cortez et al. proposes a FHRV analysis based on the evaluation of time domain parameters (statistic measures); frequency domain parameters; and the short and long term variability obtained from the Poincare plot. A normal distribution is presumed for each parameter and a normality criterion is proposed. Specific and overall classifications are proposed to help improve the fetal conditions interpretation, expanding the conventional FHR analysis [9].

A method of estimation of a fetus condition includes abdominal ECG registration, correlation processing of the received data, fetal R-R intervals allocation, estimation of distribution parameters and diagnostic index calculation, describing activity of sympathetic nervous system of fetus. This technique is used in real-time mode and serves as an approach to the problem of fetal stress diagnostics by means of maternal abdominal ECG processing [10].

An analysis based on heart rate variability in normal subjects of various age groups using the various time domains, frequency domain and nonlinear parameters show that, with aging the heart rate variability decreases [11].

Janusz Jezewski et al. compared Doppler ultrasound and direct electrocardiography acquisition techniques for quantification of fetal heart rate variability, and showed that evaluation of the acquisition technique influence on fetal well-being assessment cannot be accomplished basing on direct measurements of heartbeats only. The more relevant is the estimation of accuracy of the variability indices, since analysis of their changes can significantly increase predictability of fetal distress [12].

An estimation of fetal autonomic state by time-frequency analysis of fetal heart rate variability confirmed that there is a neural organization during the last trimester of the pregnancy, and the sympathovagal balance is reduced with the gestational age [13].

Time-domain and frequency domains analysis of heart rate variability using fetal magnecardiography enable an evaluation of fetal autonomic nervous system (ANS) activity. The result show that sympathetic nervous activity increased with gestational age in the normal pregnancy group [14].

A Heart rate variability non-invasive monitoring of autonomic nervous system function special measurements, based on time and frequency domain analysis was introduced [15]. The results show that, heart rate variability gives many parameters that are related to the functioning of two branches of autonomous nervous system: sympathetic and parasympathetic system.

The HRV indexes are obtained by analyzing the intervals between consecutive R waves, which can be captured by instruments such as electrocardiographer, digital-to-analog converter and the cardio-frequency meter, from external sensors placed at specific points of the body. The results show that, changes in the HRV patterns provide a sensible and advanced indicator of health involvements [16].

A group of experiments performed to investigate whether anxiety during pregnancy can be linked with the autonomic nervous system via different heart rate variability parameters, confirmed that the ANS modulation is slightly influenced by the anxiety level, but not as strongly as hypothesized before [17].

A novel technique for fetal heart rate estimation from Doppler ultrasound signal on a beat-to-beat basis offers a high accuracy of the heart interval measurement enabling reliable quantitative assessment of the FHR variability, at the same time reducing the number of invalid cardiac cycle measurement [18].

The cardiovascular indices in pregnant women are significantly altered in comparison to non-pregnant women, thus highlighting the importance of cardiovascular monitoring during pregnancy [19].

Obesity is emerging as an important global health problem. There is good evidence that women with a high body mass index ($BMI \geq 30$) before or during pregnancy are at greater risk for complications in pregnancy including birth defects such as heart defects, neural tube defects, and other abnormalities, difficulty seeing all of the baby's organs, difficulty monitoring the baby's heart rate tracing with the fetal heart monitor, gestational diabetes, delivery by emergency caesarian section, heavy bleeding after delivery, and increased risk of stillbirth . The continued rise in obesity and related diseases is of global concern. In 2010, 1 in 4 U.S. women of reproductive age (aged 18-44 years) were obese. Confidential Enquiries into Maternal and Child Health (CEMACH) *Perinatal Mortality 2006* report reveals that 'of the women who had a stillbirth and a recorded BMI, 26% were obese ($BMI >30$) [20].

In 2009, Riffat Jaleel showed a strong association of high pre-pregnancy BMI with a family history of diabetes and hypertension. It should be regarded as a high risk state because of its association with adverse obstetric outcome [21]. Monica Healthcare's clinical specialist Karnie Bhogal and

research fellow Indu Asanka Jayawardane , in 2009, highlighted some of the problems with Doppler ultrasound (cardiotocogram (CTG)) in monitoring obese mothers, and how by using the technology of abdominal fetal electrocardiogram (ECG) monitoring, the quality of care in relation to fetal heart rate (FHR) monitoring to this cohort can be improved. A study of 120 pregnancies, ranging from a body mass index (BMI) of 18 to 44, showed that obesity did not affect the success rate of the FHR data.

In this study we have designed and developed a new method to assess fetal heart rate variation during gestation period with automated analysis of FHR variability using Doppler ultrasound method for obese mother and non-obese mother. The Doppler ultrasound fetal heart rate acquisition technique overcome these obstacles successfully and provides reliable and accurate results from the middle until the last week of the pregnancy. This designed system detects all fetal heart beats reducing the number of invalid cardiac cycle measurements. Limitation of measuring system parameters for each pregnancy subject coupled with obesity in direct electrocardiography is overcome by Doppler ultrasound method. The success of data obtained showed that obesity did not affect the ability to obtain a successful recording. The study data suggests that a higher BMI does not interfere with the ability of the monitor to successfully detect the FHR with Doppler ultrasound method. Hence monitoring the fetus of an obese mother is no more difficult than a non-obese mother [2].

II. METHOD

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. Subjects enrolled in the present study were pregnancies ($n = 41$) at 26–39 weeks of gestation, whose body mass index (BMI) ranges from 19.2 to 36.6, who visits the hospital either as outpatients or inpatients.

We have special permission from BMC with approved patient protocol to get 200 female subjects for measurement of Doppler ultrasound fetal signal. Informed written consent was obtained from all subjects after being briefed about the clinical study, which was approved by the Ethics Committee of the Brihan Mumbai Municipal Corporation (BMC) Hospital. Doppler ultrasound signal is recorded from the abdominal transducer placed on mother's abdomen. The recording time was 5 minutes, although some fragments in which either Doppler ultrasound transducer lost the heart signal, was marked as signal loss and removed. The LF/HF ratio in a supine resting posture has been suggested for the evaluation of ANS activities. The methods of ultrasonography and cardiotocography, which are incapable of measuring CVRR, LF/HF ratio, and various fetal heart-rate variability analyses, can be improved upon with Doppler ultrasound, thereby enabling these indices to be determined. In the present study, we evaluated the significance of heart rate variability as an actual autonomic nervous system development of normal and abnormal fetuses at 26–39 weeks of gestation using Doppler ultrasound method.

Analysis of Doppler envelope is difficult due to a complex structure of the signal comprising components originating

from particular events of the cardiac cycle. Additionally, the shape of envelope changes from beat to beat. Amplitude-based detection methods are less accurate because they may detect events that do not correspond to each other in consecutive cardiac cycles. This consequently leads to incorrect interval determination.

R-R interval indicates instantaneous heart rate which is $(1/T * 60)$ beats per minute. This can be derived from electrocardiogram (ECG) by measuring the time between two consecutive QRS complexes. Same results are expected by measuring the time between the two consecutive movements of the same part of the fetal heart. So by focusing the Doppler ultrasound signal on the fixed part of the fetal heart, the waveforms generated are proportional to the velocity of the movements of that part which can be used for detection of the same event in the consecutive cardiac cycle. So detected waveform can be correlated to QRS complexes of the consecutive cardiac cycles. This can be validated by measuring time between two QRS complexes and at the same time measuring time between two detected events from Doppler ultrasound transducer. Timing diagram of direct electrocardiography and Doppler ultrasound method for HRV signal detection is shown in Figure 1. If practically $T_1 = T_2$ for the duration of the test procedure then it can be assumed that the HRV signal produced either by direct electrocardiography or Doppler ultrasound can be similar. Hence analysis will be similar.

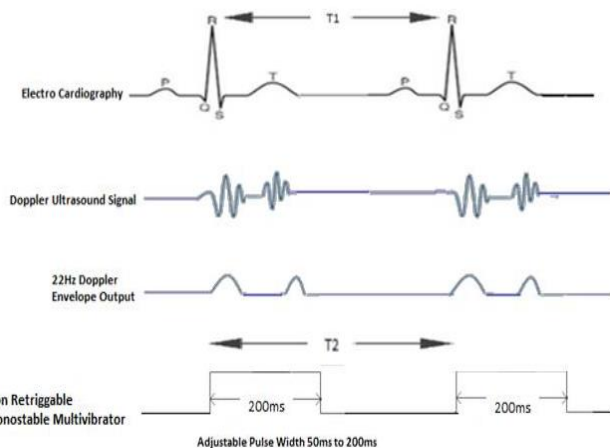


Figure 1. Timing diagram of direct electrocardiography and Doppler ultrasound method for HRV signal detection.

Fetal heart rate signals are recorded using Dipel make Doppler ultrasound (DFM-051) machine. Figure 2 shows a real time abdominal Doppler ultrasound recording setup in hospital and abdominal fetal ECG and Doppler electrodes placed on mother abdomen. The monitor is equipped with ultrasound transducer which continuously emits (with repetition frequency of 3 kHz) 2 MHz ultrasound wave of a very low power 1.5 mw/cm^2 . The wave reflected from moving parts of fetal heart (walls or valves) returns to the transducer, which has receiving elements. Frequency shifts between emitted and reflected waves is caused by the Doppler effect and provides information on the speed of moving object on which the ultrasound beam is focused.



Figure 2. Real time abdominal Doppler ultrasound recording setup in hospital.

Doppler ultrasound transducer is held on patient abdomen in the direction such that ultrasound waves emitted will pass the fetal heart movement. The reflected waves from a moving fetal heart rate are received by receiving element in the transducer. This signal is fed to the RF amplifier (2 MHz) and FM demodulator to detect the movement of the fetal heart.

Demodulated detected waveform has definite events relating to contraction and relaxations of fetal heart. Each event is a combination of different frequency components relating to motion of fetal heart and angle of incidence of the ultrasound wave on it. This signal is then passed through envelope filter (Band Pass Filter 22 Hz) with centre frequency of 22 Hz which results in generating two simple peaks per cardiac events. This signal is then passed through a variable threshold detector where threshold is kept at half the peak value of incoming signal.

Two separately detected pulses then pass through a non retriggerable monostable multivibrator for avoiding double triggering of a single cardiac event. The adjustable pulse width for this monostable multivibrator is 50 ms to 200 ms giving fetal heart rate range up to 300 BPM. This output is given to National instruments ELVIS II+ board to a personal computer USB port for HRV analysis. At the same time, Doppler signal related to heart movements and contained in the audio frequency range (from 0.2 to 1 kHz) is fed to the speaker, which helps in correct positioning of transducer on maternal abdomen. The maternal and per abdomen ECG is also monitored during the process for separate filtering and evaluation studies [5].

Measurement station has been based on a laptop PC with the ELVIS II+ (National Instruments) data acquisition board. This ELVIS II+ board has eight differential, sixteen single ended analog inputs and 16 bits resolution analog-to-digital (A/D) converter which can operate with the maximum sampling rate of 1.25 MS/s. Battery power supply and patient's electrical barrier ensures full standard safety for a patient, and minimizes power line interferences. All procedures for acquisition and processing of the signals have been developed in LABVIEW Version 10.0 (32 bit) environment (National Instruments). Figure 3 shows

Conceptual diagram of the real time hardware for Doppler ultrasound signal analysis.

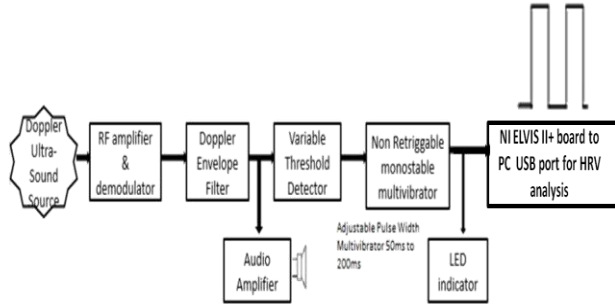


Figure 3. Conceptual diagram of the real time hardware for Doppler ultrasound signal analysis.

The R–R interval variability which shows the variation between consecutive heart beats, change over time which was eventually adopted to calculate for time-domain, frequency domain and non linear analysis. Based on frequency analysis, the ranges of the LF and HF domains were defined as 0.04–0.15 and 0.15–0.4 Hz, respectively. Figure 4 gives the result of Doppler ultrasound monitoring which demonstrates the convenience and simplicity of performing HRV analysis by using Lab VIEW. As Doppler ultrasound signal is more spread out in time, making its timing more difficult to measure, and it begins before the ECG complex. We have converted this Doppler ultrasound fetal signal into output pulse for quantification of heart rate variability [6].

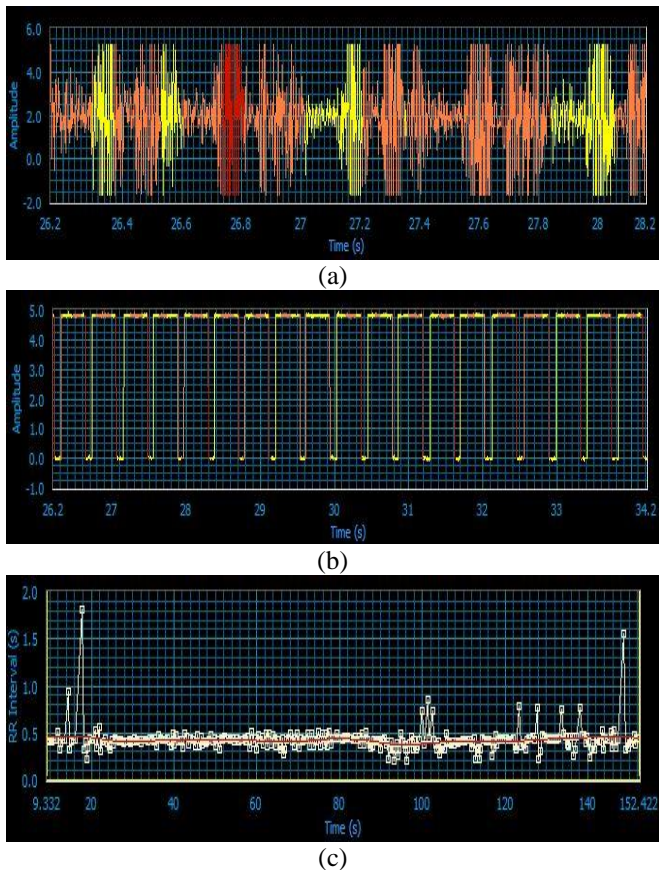


Figure 4. Result of Doppler ultrasound monitoring; (a) Recorded Doppler ultrasound signal (b) Converted Doppler

ultrasound fetal signal into output pulse for quantification of heart rate variability (c) HRV of fetal.

HRV analysis methods can be divided into time-domain, frequency-domain, and nonlinear methods. Denotations and definitions for HRV parameters in this work and in the developed software follow the guidelines given in [22]-[24]. The system is designed 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.

III. INDEXES OF HEART RATE VARIABILITY

A. Time Domain Measures of HRV

The RR interval time series is an irregularly time-sampled signal. This is not an issue in time domain, but in the frequency-domain it has to be taken into account. If the spectrum estimate is calculated from this irregularly time-sampled signal, implicitly assuming it to be evenly sampled, additional harmonic components are generated in the spectrum. Therefore, the RR interval signal is usually interpolated before the spectral analysis to recover an evenly sampled signal from the irregularly sampled event series. In the frequency-domain analysis power spectral density (PSD) of the RR series is calculated. Figure 5 (a) shows HRV of fetus for non obese mother having BMI 22.9 and (b) shows HRV of fetus for obese class 2 mother having BMI 36.6. It is observed that after processing raw signal it is found that the heart rate variability in panel (b) is much smaller than in panel (a).

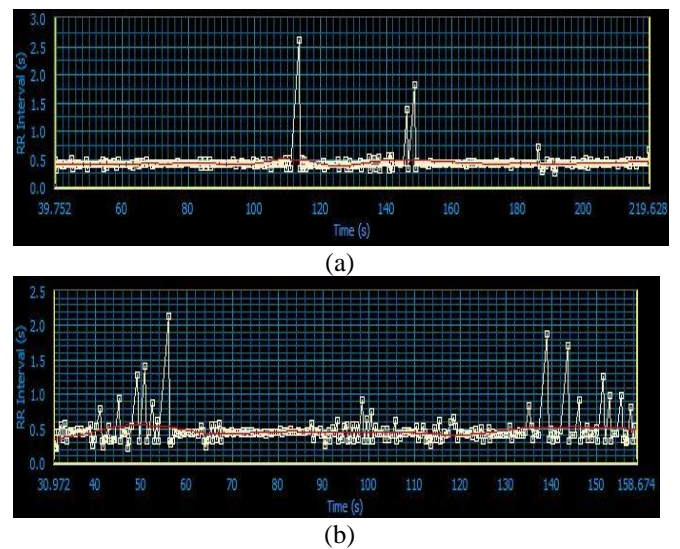
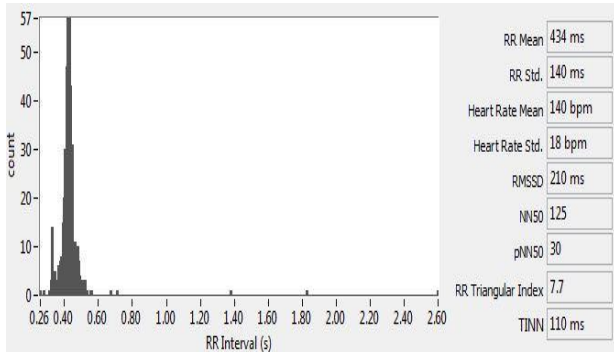


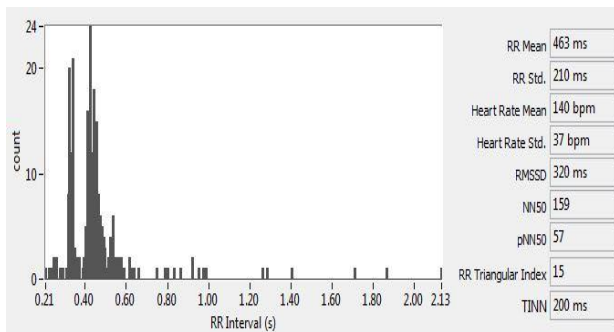
Figure.5 HRV of fetus for non obese mother having BMI 22.9 and (b) HRV of fetus for obese class 2 mother having BMI 36.6. After processing raw signal it is found that the heart rate variability in panel (b) is much smaller than in panel (a).

An RR interval is the time that elapses between two successive R waves. Heart Rate Variability (HRV) measurements analyze how these RR intervals, which show the variation between consecutive heartbeats, change over time. It is also observed that standard deviation of RR intervals & heart rate standard deviation are much higher in obese mother fetus (Figure 6). Changes in the HRV patterns provide a sensible

and advanced indicator of health impairments. Higher HRV is a signal of good adaptation and characterizes a healthy fetus with efficient autonomic mechanisms, while lower HRV is frequently an indicator of abnormal and insufficient adaptation of the ANS, provoking poor fetus physiological malfunction requiring further investigation in order to find a specific diagnosis.



(a)



(b)

Figure.6 Statistics of fetus for non obese mother having BMI 22.9 and (b) Statistics of fetus for obese class 2 mother having BMI 36.6. It is observed that standard deviation of RR intervals & heart rate standard deviation are much higher in obese mother fetus.

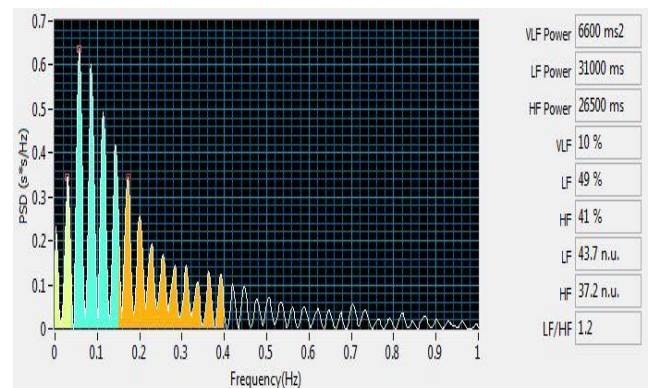
B. Frequency Domain Measures of HRV

Methods for calculating the PSD estimate may be divided into nonparametric [e.g. fast Fourier transform (FFT) based] and parametric [e.g. based on autoregressive (AR) models] methods [22]-[24]. The PSD is analyzed by calculating powers and peak frequencies for different frequency bands. The commonly used frequency bands are very low frequency (VLF, 0-0.04 Hz), low frequency (LF, 0.04- 0.15 Hz), and high frequency (HF, 0.15-0.4 Hz). The most common frequency-domain parameters include the powers of VLF, LF, and HF bands in absolute and relative values, the normalized power of LF and HF bands, and the LF to HF ratio. Also the peak frequencies are determined for each frequency band. For the FFT based spectrum powers are calculated by integrating the spectrum over the frequency bands. The parametric spectrum, on the other hand, can be divided into components and the band powers are obtained as powers of these components. This property of parametric spectrum estimation has made it popular in HRV analysis. Figure 7 (a) shows Spectral analysis of frequencies [Nonparametric Fast Fourier Transform (FFT) method] of fetus for non obese mother having BMI 22.9 and (b) Spectral analysis of frequencies [Nonparametric Fast Fourier Transform (FFT) method] of fetus for obese class2 mother having BMI 36.6. The LF/HF ratio is

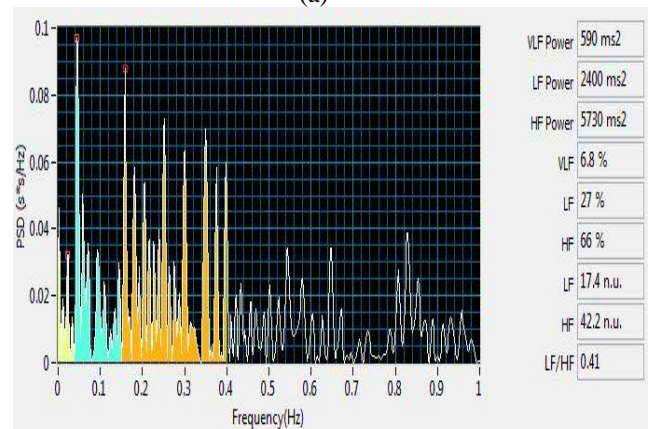
fetus for obese class2 mother having BMI 36.6. The LF/HF ratio is smaller in obese mother fetus.

Figure 8 (a) Spectral analysis of frequencies [based on autoregressive (AR) models] of fetus for non obese mother having BMI 22.9 and (b) Spectral analysis of frequencies [based on autoregressive (AR) models] of fetus for obese class 2 mother having BMI 36.6. The LF/HF ratio is smaller in obese mother fetus.

High-frequency component ranging from 0.15 to 0.4 Hz, which corresponds to the respiratory modulation and is an indicator of the performance of the vagus nerve on the heart. Low frequency component ranging between 0.04 and 0.15 Hz, which is due to the joint action of the vagal and sympathetic components on the heart, with a predominance of the sympathetic ones. Components of very low frequency and ultra-low frequency indexes less used whose physiological explanation is not well established and seems to be related to the renin- angiotensin-aldosterone system, thermoregulation and the peripheral vasomotor tone. The total power and high frequency components are smaller in normal fetus. We defined a low frequency/high frequency (LF/HF) ratio as a sympathetic activity is smaller in obese mother fetus. The LF/HF ratio reflects the absolute and relative changes between the sympathetic and parasympathetic components of the ANS, by characterizing the sympathetic vagal balance on heart.



(a)



(b)

Figure.7 shows Spectral analysis of frequencies [Nonparametric Fast Fourier Transform (FFT) method] of fetus for non obese mother having BMI 22.9 and (b) Spectral analysis of frequencies [Nonparametric Fast Fourier Transform (FFT) method] of fetus for obese class2 mother having BMI 36.6. The LF/HF ratio is

smaller in obese mother fetus.

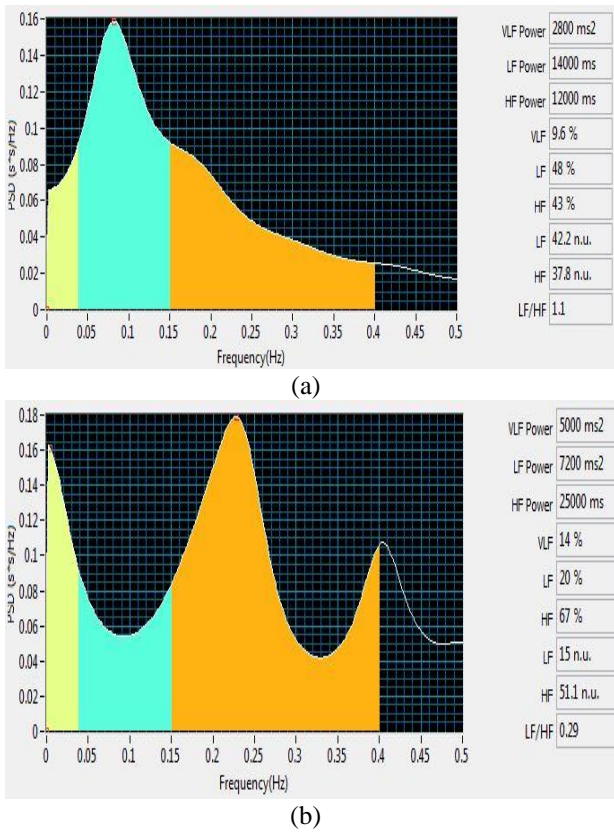


Figure.8 Spectral analysis of frequencies [based on autoregressive (AR) models] of fetus for non obese mother having BMI 22.9 and (b) Spectral analysis of frequencies [based on autoregressive (AR) models] of fetus for obese class 2 mother having BMI 36.6. The LF/HF ratio is smaller in obese mother fetus.

C. Nonlinear Measures of HRV

It is realistic to presume that HRV also contains nonlinear properties because of the complex regulation mechanisms controlling it. The interpretation and understanding of many nonlinear methods is, however, still insufficient. One simple and easy to comprehend nonlinear method is the so called Poincare plot. It is a graphical presentation of the correlation between consecutive RR intervals. The geometry of the Poincare plot is essential. A common way to describe this geometry is to fit an ellipse to the graph. The ellipse is fitted on to the so called line-of-identity at 45° to the normal axis. The standard deviation of the point's perpendicular to the line-of-identity denoted by SD1 describes short-term variability which is mainly caused by respiratory sinus arrhythmia (RSA). The standard deviation along the line-of-identity denoted by SD2 describes long-term variability. The analysis of Poincare plot can be performed in a qualitative manner (visual), by assessing the figure formed by its attractor, which is useful for showing the degree of complexity of RR intervals or quantitative, by adjusting the ellipse of the figure formed by the attractor, from which three indexes can be obtained: SD1, SD2 and SD1/SD2 ratio. SD1 represents the dispersion of points perpendicular to the line of identity and it seems to be an index of instantaneous recording of beat-to-beat variability; the SD2 represents the dispersion of points along the line of identity and represents the HRV in long-term records; the relationship of both (SD1/SD2) shows

the ratio between the short- and long-term variations of the RR intervals [20]-[22]. Figure 9 shows Poincare chart of fetus for non obese mother having BMI 22.9 and (b) Poincare chart of fetus for obese class 2 mother having BMI 36.6. The dispersion of both short (SD1) & Long term (SD2) is smaller in normal weight mother fetus.

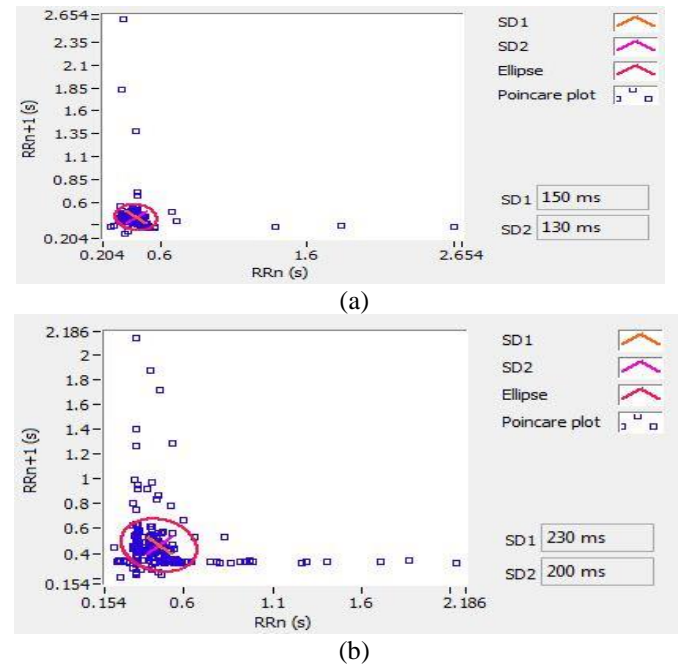


Figure.9 shows Poincare chart of fetus for non obese mother having BMI 22.9 and (b) Poincare chart of fetus for obese class 2 mother having BMI 36.6. The dispersion of both short (SD1) & Long term (SD2) is smaller in normal weight mother fetus.

IV. STATISTICAL ANALYSIS

The system is designed 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. We have taken the coefficient of variance (CVRR) of a patient's normal RR intervals as an index of parasympathetic activity which is defined as a ratio of standard deviation of normal RR intervals value to mean of such intervals and a low frequency/high frequency (LF/HF) ratio as a sympathetic activity index. The relationships among CVRR, LF/HF, and the gestational age in each group were analyzed by linear regression, while the inter-group changes in CVRR, LF/HF over the gestational period in each group were verified by one-way ANOVA. The pregnancy group was divided into three groups for classifying one-way ANOVA analysis of CVRR and LF/HF as follows: Group A, $26-29 \pm 1$ wk (7th month pregnancy); Group B, $30-33 \pm 1$ wk (8th month pregnancy); and Group C, 34 onwards ± 1 wk (9th month pregnancy).

The relationships among CVRR, LF/HF, and Body Mass Index (BMI) in each group were analyzed by linear regression, while inter-group changes in CVRR, LF/HF over body mass index (BMI) in each group were verified by one-way ANOVA. The pregnancy group was divided into three groups for classifying one-way ANOVA analysis of CVRR and LF/HF as

follows: Group A, BMI ≤ 25); Group B, 25 ≤ BMI ≤ 30; and Group C, BMI ≥ 30. Values are presented in figures are mean ± SD and 95% confidence interval. Statistical difference between groups tested to p < 0.05. Data were analyzed using Microsoft excel 2007 data analysis tool. Table 1 summarizes different time domain and frequency domain measures (mean ± SD) of HRV for three individual gestation groups and three individual BMI groups. In the box plots the central line represents the mean of all values in the particular gestation period and BMI groups for the respective indices defined earlier. The line above central line represents ‘mean + SD’ value and line below central line represents ‘mean – SD’ value.

Parameters	Gestation Weeks (n=41)			‘P’ Value	Body Mass Index (n=41)			‘P’ Value
	26-29 ± 1 wk (n=9)	30-33 ± 1 wk (n=11)	34-wks onwards (n=21)		BMI≤25 (n=22)	25≤BMI≤30 (n=12)	BMI≥30 (n=7)	
CV _{HR}	27.1711 ±12.685	23.0306 ±14.9967	26.7747 ±15.2489	0.75655	28.2275 ±14.449	20.3812 ±14.8985	27.7952 ±12.7304	0.30028
SDNN	116.968 ±38.7064	97.3963 ±71.6385	116.751 ±69.799	0.73591	123.800 ±67.7118	85.2125 ±68.3640	119.3742 ±36.95	0.26641
RMSSD	174.294 ±90.9640	146.807 ±111.681	173.98 ±109.79	0.76987	184.564 ±106.840	125.480 ±105.154	181.5886 ±89.15923	0.27259
Pnn50	37.8355 ±12.5670	33.7572 ±16.831	34.482 ±13.0768	0.78779	33.3354 ±14.0201	35.6325 ±14.6775	39.2871 ±12.38015	0.61168
RRTI	0.182 ±3.63431	9.54 ±4.2410	9.32190 ±3.9827	0.863452	9.7959 ±4.444119	8.795 ±3.544805	10.18 ±2.68969	0.7080
TINN	132.63 ±50.968	133.69 ±70.087	133.22 ±59.9353	0.582418	129.340 ±72.0707	110.297 ±47.9676	124.6557 ±37.88783	0.68824
LF/HF (Nonparametric FFT Based)	0.64444 ±0.223506	0.634545 ±0.373667	0.607143 ±0.261154	0.936911	0.71363 ±0.32190	0.51333 ±0.18107	0.524 ±0.2032	0.081282
LF/HF (Parametric AR Based)	0.645556 ±0.236385	0.48 ±0.145465	0.584286 ±0.21743	0.19367	0.623182 ±0.19836	0.5225 ±0.228637	0.48286 ±0.18491	0.19903

Values are presented as mean ± SD and 95% confidence interval. Statistical difference between groups tested to p < 0.05

Table 1. Summarizes different time domain and frequency domain measures (mean ± SD) of HRV for three individual gestation groups and three individual BMI groups.

V. RESULTS

A. Coefficient of Variance (CVRR) as an Index of Parasympathetic Activity

As a result of the carried out research, 41 subjects of pregnancies whose body mass index (BMI) ranging from 20 to 37 were studied. The value of CVRR in the normal pregnancy group displayed a clearly increasing trend with gestational age (y = 0.383x + 13.16; R² = 0.009) (Figure10). Inter-group changes in CVRR in normal pregnancy showed no significant difference to the gestation period (one-way ANOVA: P = 0.75655) (Figure11).

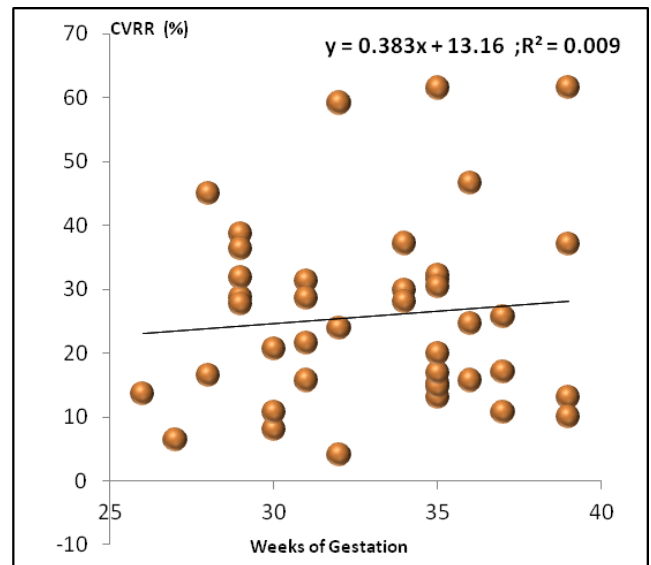
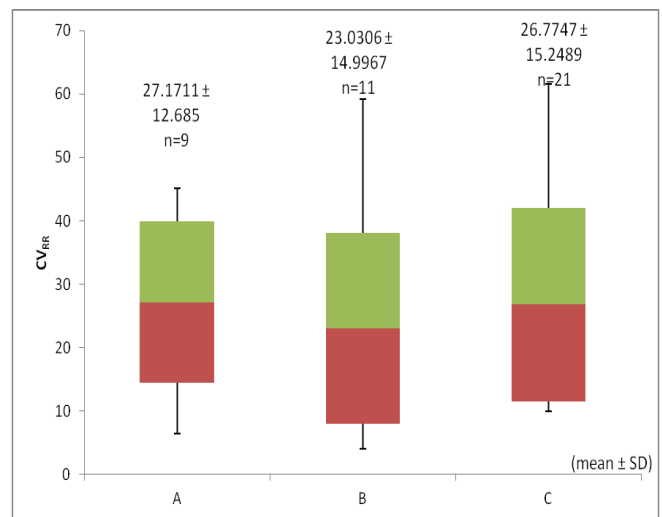


Figure. 10 Correlation between the coefficient of variance (CVRR) and gestational age in normal pregnancy.



One-way ANOVA: P = 0.75655

Figure. 11 Inter-group changes in the coefficient of variance (CVRR) during normal pregnancy. 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).

The value of CVRR in the normal pregnancy group displayed a clearly decreasing trend with BMI (y = - 0.2509x + 32.368; R² = 0.0056) (Figure12). Inter-group changes in CVRR in normal pregnancy showed no significant deference to the BMI (one-way ANOVA: P = 0.30028) (Figure13)

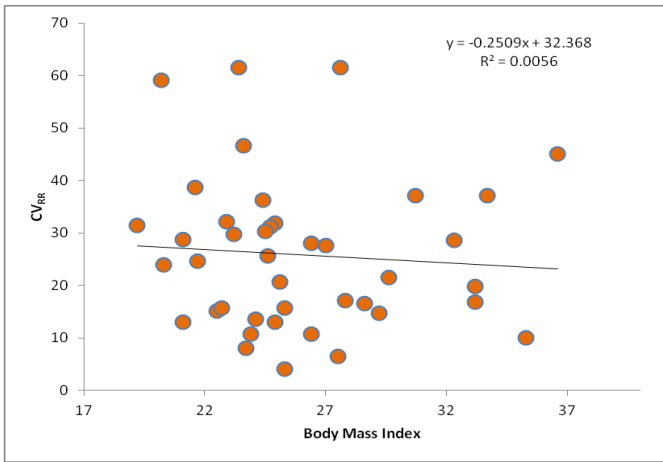


Figure. 12 Correlation between the coefficient of variance (CVRR) and body mass index (BMI) in normal pregnancy.

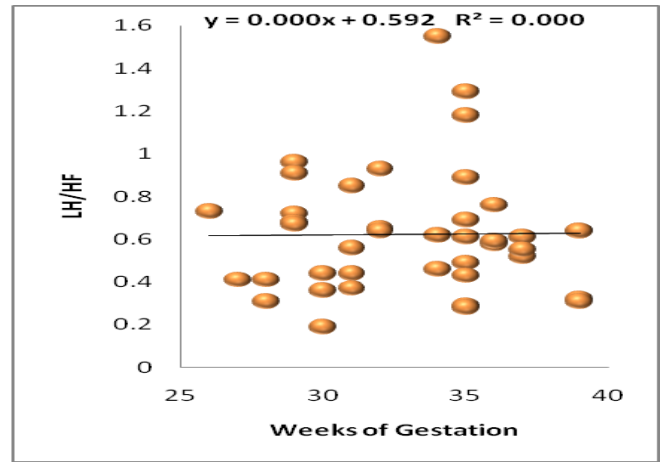
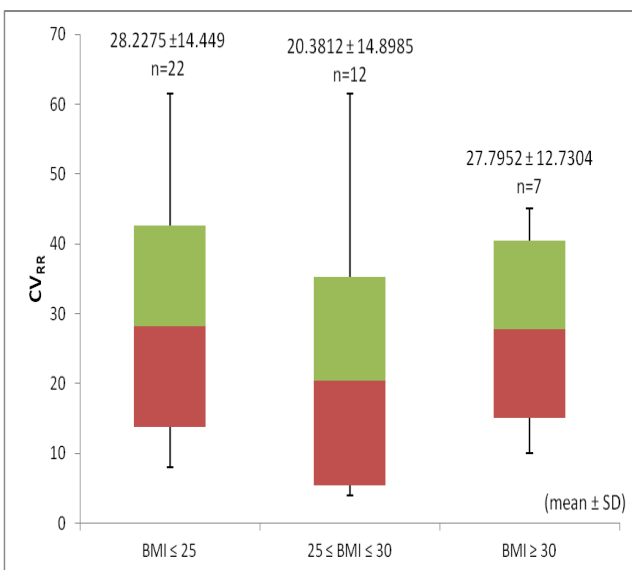


Figure. 14 Correlation between the low frequency/high frequency (LH/HF) ratio and gestational age in normal pregnancy with Nonparametric [Fast Fourier Transform (FFT) Based] method.

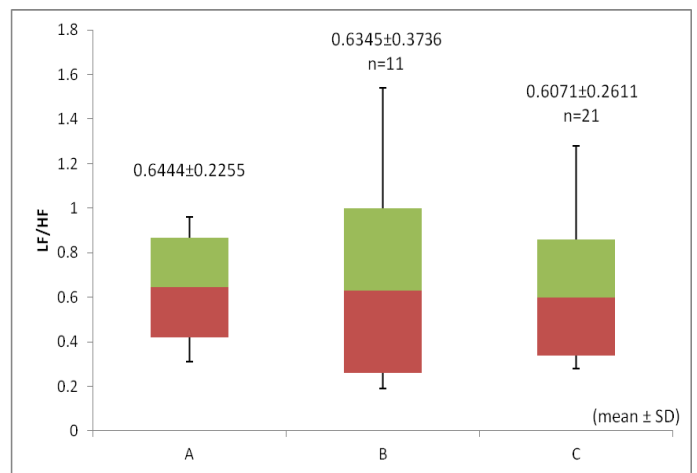


One-way ANOVA: P = 0.300282453

Figure. 13 Inter-group changes in the coefficient of variance (CVRR) during normal pregnancy. Group A, BMI ≤ 25; Group B, 25 ≤ BMI ≤ 30; and Group C, BMI ≥ 30.

B. LF/HF Ratio as an Index of Sympathetic Department of Vegetative Nervous System Regulation Activity

In contrast, the LF/HF ratio [Nonparametric Fast Fourier Transform (FFT) Based] in the normal pregnancy group showed slight increasing trend over the gestational period $y = 0.000x + 0.592$ $R^2 = 0.000$ (Figure14). Inter-group changes in LF/HF [Nonparametric Fast Fourier Transform (FFT) Based] in normal pregnancy showed no significant deference to the gestation period (one-way ANOVA: P = 0.936911) (Figure15).



One-way ANOVA: P = 0.936911135

Figure. 15 Inter-group changes in the low frequency/high frequency (LH/HF) ratio during normal pregnancy 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) with Nonparametric [Fast Fourier Transform (FFT) Based] method.

The LF/HF ratio [Parametric Autoregressive (AR) Based] in the normal pregnancy group slightly decreases trend over the gestational period $y = -0.0007x + 0.593$ $R^2 = 0.0002$ (Figure16). Inter-group changes in LF/HF [Parametric Autoregressive (AR) Based] in normal pregnancy showed no significant deference to the gestation period (one-way ANOVA: P = 0.19367) (Figure17).

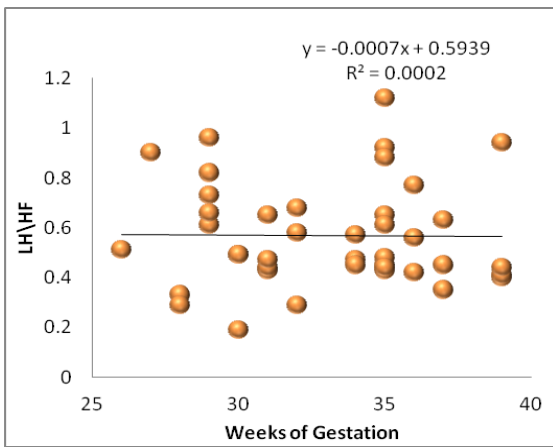


Figure. 16 Correlation between the low frequency/high frequency (LH/HF) ratio and gestational age in normal pregnancy with Parametric [Autoregressive (AR) Based] method.

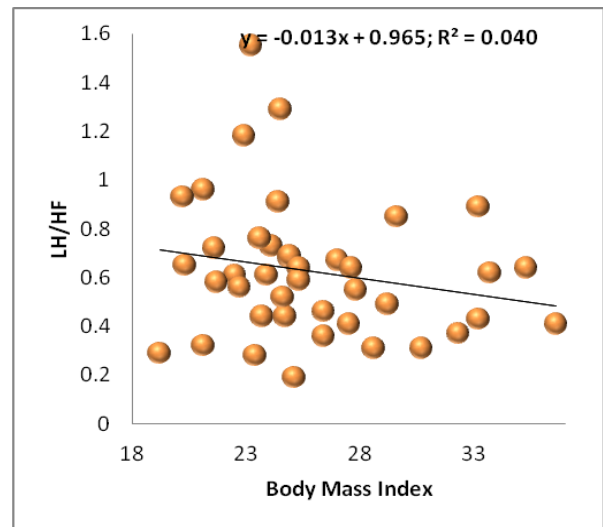
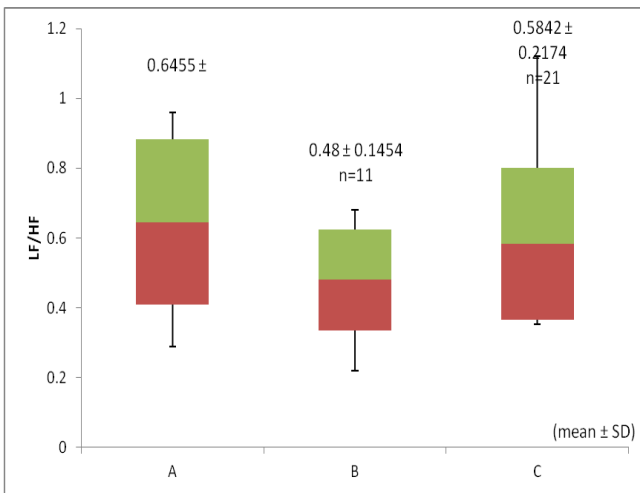
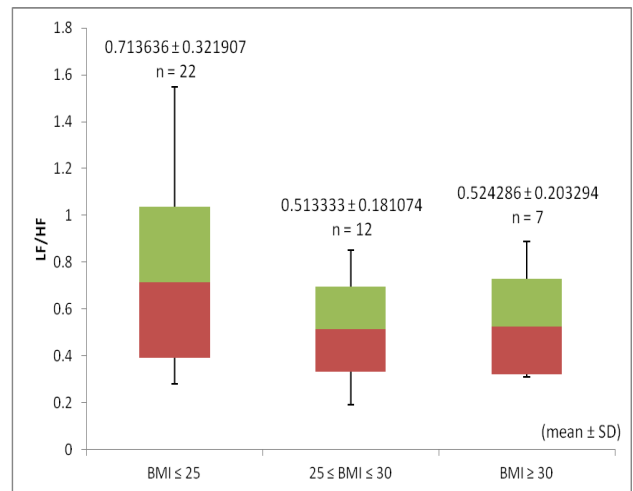


Figure. 18 Correlation between the low frequency/high frequency (LH/HF) ratio and body mass index in normal pregnancy with Nonparametric [Fast Fourier Transform (FFT) Based] method.



One-way ANOVA: P = 0.19367

Figure. 17 Inter-group changes in the low frequency/high frequency (LH/HF) ratio during normal pregnancy Group A, 26-29 ± 1 wk (7th month pregnancy); Group B, 30-33 ± 1 wk (8th month pregnancy); and Group C, 34 onwards ± 1 wk (9th month pregnancy). with (Parametric Autoregressive model).



One-way ANOVA: P = 0.081282

Figure. 19 Inter-group changes in the LF/HF ratio during normal pregnancy. Group A, BMI ≤ 25; Group B, 25 ≤ BMI ≤ 30; and Group C, BMI ≥ 30 with Nonparametric Fast Fourier Transform (FFT) Based method.

The value of LF/HF ratio [Nonparametric [Fast Fourier Transform (FFT) Based] in normal pregnancy group displayed clearly decreasing trend with body mass index (BMI) $y = - 0.013x + 0.965; R^2 = 0.040$ (Figure18). Inter-group changes in LF/HF in normal pregnancy showed no significant deference to the BMI (one-way ANOVA: P = 0.081282) (Figure19).

The value of LF/HF ratio [Parametric Autoregressive (AR) Based] in the normal pregnancy group displayed a clear decreasing trend with body mass index (BMI) $y = - 0.011x + 0.8555; R^2 = 0.051$ (Figure 20). Inter-group changes in LF/HF ratio in normal pregnancy showed no significant deference to the BMI (one-way ANOVA: P = 0.19903) (Figure 21).

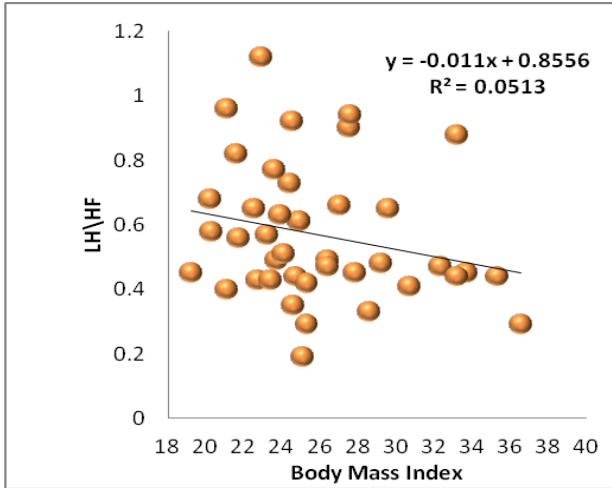
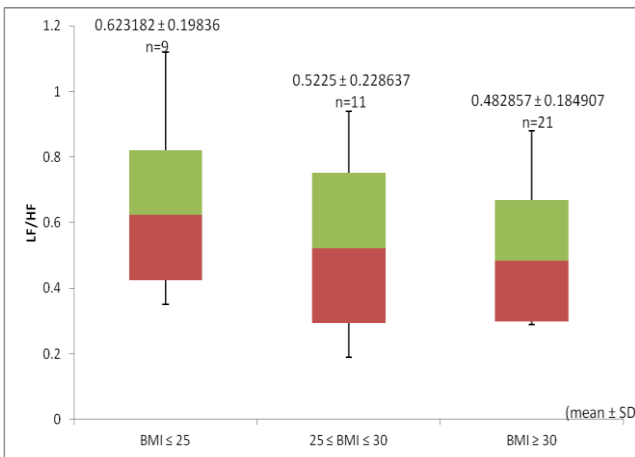


Figure. 20 Correlation between the low frequency/high frequency (LF/HF) ratio and body mass index in normal pregnancy with Parametric [Autoregressive (AR) Based] method.



One-way ANOVA: $P = 0.19903477$

Figure. 21 Inter-group changes in the LF/HF ratio during normal pregnancy. Group A, $BMI \leq 25$; Group B, $25 \leq BMI \leq 30$; and Group C, $BMI \geq 30$ with Parametric [Autoregressive (AR) Based] method.

VI. MULTIPLE REGRESSIONS

The purpose of multiple regressions is to predict a single variable from one or more independent variables. Multiple regression is an extension of simple linear regression. It is used when we want to predict the value of a variable based on the value of two or more other variables. The variable we want to predict is called the dependent variable (or sometimes, the outcome, target or criterion variable). The variables we are using to predict the value of the dependent variable are called the independent variables (or sometimes, the predictor, explanatory or regressor variables) [25].

In single regression we have been concerned with predicting the value of a response on the basis of the value of a single input variable. However, in many situations the response is dependent on a multitude of input variables. Suppose that we are interested in predicting the response value Y on the basis of the values of the k input variables x_1, x_2, \dots, x_k . The multiple

linear regression model supposes that the response Y is related to the input values $x_i, i = 1, \dots, k$, through the relationship

$$Y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_k x_k + e \quad (1)$$

We have taken all time-domain, frequency domain and non linear parameters together to perform multiple regression analysis.

A. LF/HF Ratio [Parametric (AR) Based] as an index of Sympathetic Activity

We could use multiple regression to understand whether LF/HF ratio [Parametric(AR) Based] as an index of fetal sympathetic activity can be predicted based on age, gestation week, body mass index, CVRR, HR Mean, HR Std, RMSSD, NN50, pNN 50) and nonlinear (SD1/SD2 index) parameters.

Multiple regression was conducted to examine whether 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, non linear index SD1/SD2 ratio.

There are three general tables that must be interpreted in the write-up of the regression analysis. The summary output table is shown in table 2. The information that needs to be taken from this table is the R-square (0.4647). The R-square is the proportion of variation in the dependent variable (LF/HF ratio as an index of fetal sympathetic activity) [Parametric (AR) Based] as an index of fetal sympathetic activity that is explained by the ten independent variables. It is expressed as a percentage. So 46.47 percent of the variation in dependent variable LF/HF ratio as an index of fetal sympathetic activity can be explained by ten independent variables in the model.

SUMMARY OUTPUT

Regression Statistics

Multiple R	0.681738142
R Square	0.464766895
Adjusted R Square	0.28635586
Standard Error	0.176641621
Observation	41

Predictors: (Constants), Age, Gestation Week, Body Mass Index, CVRR, HR Mean, HR Std, RMSSD, NN50, pNN 50, Non linear Index SD1/SD2 ratio.

Table 2. Multiple regression summary output table

The ANOVA table (Table 3) shows whether the proportion of variance explained in the first table is significant or not significant. It also tells whether the overall effect of the ten independent variables on dependent variable (LF/HF ratio as an index of fetal sympathetic activity) is significant or not significant. The significant (or p-value) is 0.02075856 which is below the .05 level; hence, we conclude that the overall model is statistically significant, or that the variables have significant combined effect on the dependent variable $F(10, 30) = 2.60503, p < 0.1$

ANOVA					
	df	SS	MS	F	Significance F
Regression	10	0.812829689	0.081282969	2.605034461	0.020758756
Residual	30	0.936067872	0.031202262		
Total	40	1.748897561			

a. Predictors: (Constants), Age, Gestation Week, Body Mass Index, CVRR, HR Mean, HR Std, RMSSD, NN50, pNN 50, Non linear Index SD1/SD2 ratio.

b. Dependant Variable: LF/HF ratio [Nonparametric Fast Fourier Transform (FFT) Based] as an index of fetal sympathetic activity.

Table 3. Multiple Regression ANOVA table

Look at the sig. (*p*-values) first in table 4. We can see that age (*p*-value 0.02500), CVRR % (*p*-value 0.00722), HR Std (*p*-value 0.036755), and RMSSD ((*p*-value 0.023961) are significant predictors (or significantly related to) of LF/HF ratio [Parametric (AR) Based] as an index of fetal sympathetic activity.

The standardized beta tells us the strength and direction of the relationships (interpreted like correlation coefficients) CVRR (Beta = 0.082968, *p* < 0 .1) is positively related to LF/HF ratio [Parametric (AR) Based] as an index of fetal sympathetic activity. Gestation week (Beta = -0.003506, *p* > 0 .1), Body mass index (Beta = -0.00056, *p* > 0 .1), HR Mean (Beta = -0.00360, *p* > 0 .1), NN50 (Beta = -0.00015, *p* > 0 .1), pNN50 (Beta = -0.00279, *p* > 0 .1) and SD1/SD2 index (Beta = -0.228919, *p* > 0 .1) is not a significant predictor of LF/HF ratio [Parametric (AR) Based] as an index of fetal sympathetic activity.

	Coefficients	Standard Error	t Stat	P-Value	Lower 95%	Upper 95%	Lower 95.0%	Upper 95.0%
Intercept (LF/HF Parametric, AR Model)	2.018021029	0.902547723	2.235916	0.032947	0.17477268	3.8612694	0.17477268	3.86126938
X Variable 1 (Age)	-0.019553897	0.008287578	-2.3942	0.025008	-0.036479389	-0.0026284	-0.03647939	-0.0026284
X Variable 2 (Gestation Week +1 Week)	-0.003506203	0.008249585	-0.42902	0.673858	-0.020354103	0.0133417	-0.0203541	0.0133417
X Variable 3 (Body Mass Index)	0.000563387	0.007529613	0.074823	0.940852	-0.014814133	0.0159409	-0.01481413	0.01594091
X Variable 4 (CVRR (%)=RR Std/RR Mean)	0.082968899	0.028782946	2.882581	0.007225	0.024186485	0.1417513	0.02418649	0.14175131
X Variable 5 (HR Mean)	-0.003607079	0.004614993	-0.77572	0.443989	-0.013103631	0.0058895	-0.01310363	0.00588947
X Variable 6 (HR Std)	-0.023254621	0.01069807	-2.18598	0.036755	-0.044980459	-0.0058895	-0.04498046	-0.0058895
X Variable 7 (RMSSD)	-0.00940398	0.003801223	-2.37829	0.023961	-0.016803532	-0.0012773	-0.01680353	-0.0012773
X Variable 8 (NN50)	-0.0001494	0.000844972	-0.18361	0.856332	-0.00188775	0.0015779	-0.00188775	0.00157787
X Variable 9 (pNN50)	-0.002794079	0.006176262	-0.45239	0.654243	-0.015407689	0.0098195	-0.01540769	0.00981953
X Variable 10 (SD1/SD2 Index)	-0.228919728	0.408391575	-0.56026	0.579462	-1.063382396	0.6055429	-1.0633824	0.60554294

Dependent Variable: LF/HF ratio [Parametric (AR) Based] as an index of fetal sympathetic activity.

Table 4. Multiple Regression coefficients- The effect of individual independents variable on dependent variable.

B. LF/HF Ratio [Nonparametric Fast Fourier Transform (FFT) Based] as an Index of Sympathetic Activity

Multiple regression was conducted to examine whether 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.

There are three general tables that must be interpreted in the write-up of the regression analysis. The summary output table

is shown in table 5. The information that needs to be taken from this table is the R-square (0.361287). The R-square is the proportion of variation in the dependent variable (LF/HF ratio as an index of fetal sympathetic activity) that is explained by the ten independent variables. It is expressed as a percentage. So 36.12 percent of the variation in LF/HF ratio as an index of fetal sympathetic activity can be explained by ten independent variables in the model.

SUMMARY OUTPUT	
Regression Statistics	
Multiple R	0.6010716
R Square	0.361287
Adjusted R Square	0.1483127
Standard Error	0.2601175
Observations	41

Predictors: (Constants), Age, Gestation Week, Body Mass Index, CVRR, HR Mean, HR Std, RMSSD, NN50, pNN 50, Non linear Index SD1/SD2 ratio.

Table 5: Multiple regression summary output table.

The ANOVA table (Table 6) shows whether the proportion of variance explained in the first table is significant. It also tells whether the overall effect of the ten independent variables on dependent variable (LF/HF ratio as an index of fetal sympathetic activity) is significant or not significant. The *p*-value is 0.127661516 which is not below the 0.1 level; hence, we conclude that the overall model is statistically not significant, or that the variables do not have a significant combined effect on the dependent variable F (10, 30) = 1.69694, *p* > 0 .1

ANOVA					
	df	SS	MS	F	Significance F
Regression	10	1.148171878	0.1148172	1.696945332	0.127661516
Residue	20	2.029833	0.0676611		
Total	40	3.178004878			

Predictors: (Constants), Age, Gestation Week, Body Mass Index, CVRR, HR Mean, HR Std, RMSSD, NN50, pNN 50, Non linear Index SD1/SD2 ratio.

Dependant Variable: LF/HF ratio [Nonparametric Fast Fourier Transform (FFT) Based] as an index of fetal sympathetic activity.

Table 6: Multiple Regression ANOVA table

Look at the sig. (*p*-values) first in table 7. We can see that age (*p*-value 0.11350), CVRR % (*p*-value 0.00460), HR mean (*p*-value 0.007017), HR Std (*p*-value 0.08827) and RMSSD ((*p*-value 0.00782) 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 (Beta = -0.0033438, *p* > 0 .1), Body mass index (Beta = -0.00526, *p* > 0 .1), NN50 (Beta = -0.00063, *p* > 0 .1), pNN50 (Beta = 0.00474, *p* > 0 .1) and SD1/SD2 index (Beta = 0.08643, *p* > 0 .1) is not a significant predictor of LF/HF ratio [Nonparametric Fast Fourier Transform (FFT) Based] as an index of fetal sympathetic activity.

The standardized beta tells us the strength and direction of the relationships (interpreted like correlation coefficients). CVRR (Beta = 0.1297954, $p < 0.1$) is positively related to LF/HF ratio [Nonparametric Fast Fourier Transform (FFT) Based] as an index of fetal sympathetic activity [7].

	Coefficients	Standard Error	t Stat	P-value	Lower 95%	Upper 95%	Lower 95.0%	Upper 95.0%
Intercept(LF/HF Non Parametric, FFT Based)	3.123009799	1.329066341	2.349777	0.025558872	0.408694227	5.837325371	0.408694227	5.837325371
X Variable 1(Age)	-0.019894117	0.012204054	-1.63012	0.113531786	-0.04481812	0.005029886	-0.044818121	0.005029886
X Variable 2(Gestation + 1 week)	-0.003943809	0.012148307	-0.27525	0.785008433	-0.02815355	0.021465994	-0.028153553	0.021465994
X Variable 3(Body Mass Index)	-0.005269068	0.011087895	-0.47521	0.638079713	-0.02791357	0.017375435	-0.027913571	0.017375435
X Variable 4(CVRR%) = RR Std/RR Mean)	0.129795375	0.042384008	3.062309	0.004605144	0.043234049	0.2163567	0.043234049	0.2163567
X Variable 5(HR Mean)	-0.012857362	0.006847449	-1.87769	0.070176766	-0.02684172	0.001126994	-0.026841718	0.001126994
X Variable 6(HR Std)	-0.027600578	0.015665323	-1.76189	0.08827659	-0.05959344	0.004392279	-0.059593435	0.004392279
X Variable 7(RMSSD)	-0.015956056	0.005597574	-2.85053	0.007820346	-0.02738783	-0.00452428	-0.027387826	-0.004524285
X Variable 8(NN50)	-0.000635451	0.001249435	-0.50859	0.614759117	-0.00318714	0.001916236	-0.003187139	0.001916236
X Variable 9(pNN50)	0.004749627	0.00909499	0.522225	0.605349078	-0.01382482	0.023324075	-0.01382482	0.023324075
X Variable 10(SD1,SD2 Index)	0.086490485	0.601685739	0.143647	0.886739653	-1.14237574	1.315236673	-1.142375743	1.315236673

Dependent Variable: LF/HF ratio [Nonparametric Fast Fourier Transform (FFT) Based] as an index of fetal sympathetic activity.

Table 7: Multiple Regression coefficients- The effect of individual independents variable on dependent variable

Conclusion

Analyses based on the time and frequency domains of heart rate variability using Doppler ultrasound method enable an evaluation of fetal ANS diagnostic indices. It is observed that the parasympathetic nervous activity increased with gestational age in the normal pregnancy group and declined with increase in body mass index in the normal pregnancy group. The results obtained from regression clearly indicate 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 is declined. It is observed that total power and high frequency components are smaller in a normal fetus. 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 different linear and nonlinear parameters evaluated show a particular range for identification of autonomic maturation in the normal developed fetus. It is also observed that the HRV parameters are less random as gestation age increases for normal fetus. It is also concluded that 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. The dispersion of both short (SD1) & Long term (SD2) is smaller in normal weight mother fetus. We can also 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.

References

[1] K .D. Desai, Manoj S. Sankhe, "A Real-Time Fetal ECG Feature Extraction Using Multiscale Discrete Wavelet Transform, "5th International Conference Biomedical

Engineering & Informatics, BMEI, Chongqing, china, pp 279–284, 2012 (Appeared in IEEE Explorer).

[2] K.D. Desai, Satish D. Jadhav, Manoj S. Sankhe, "A Comparison and Quantification of Fetal Heart Rate Variability using Doppler Ultrasound and Direct Electrocardiography Techniques," International Conference on advances in Technology, ICATE ,Mumbai, India. 2013(Appeared in IEEE Explorer).

[3] K. D. Desai, Manoj S. Sankhe. Heart Rate Variability Power Spectrum as Health Signature, Techno-path, Journal of Science & Technology Management, Vol 3 No 2 :pp 46-53, 2011.

[4] K.D.Desai, "A System for the detection of Diabetic Myocardial Infarction," Ph. D. Thesis V.J.T.I., Bombay,1996.

[5] Manoj S. Sankhe, K. D. Desai, Mohan A. Gadani, "Assessment of fetal autonomic nervous system activity by abdominal Doppler ultrasound recordings" Health Tech Innovations – 2015 Conference, organised by Society Applied Microwave Electronics Engineering & Research (SAMEER), IIT Bombay under the aegis of Department of Electronics and Information Technology , Government of India in technical collaboration with National Health Systems Resource Center (NHSRC) & Indian Council of Medical Research (ICMR), awarded as Best Concept note under the theme Technology Innovations in Diagnostic / Prognostic.

[6] K. D. Desai, Manoj S. Sankhe, "Correlations of Fetal Cardiac Sympathetic Activity with Maternal Body Mass Index", Indicon, 2013, IIT, Powai, Mumbai.

[7] Manoj S. Sankhe, K. D. Desai, "Fetal heart rate variability: multiple regression models using autoregressive analysis and fast Fourier transform", IBICA (2015), Kochi, India, Spriger proceedings: advance in intelligent systems and computing; eBook ISBN: 978-3-319-28031-8, Softcover ISBN: 978-319-28030-1, pp 447–462, 2015.

[8] Faezeh Marzbanrad, Yoshitaka Kimura, Kiyoe Funamoto, Rika Sugibayashi, Miyuki Endo, Takuya Ito, Marimuthu Palaniswami, Ahsan H. Khandoker, "Automated Estimation of Fetal Cardiac Timing Events From Doppler Ultrasound Signal Using Hybrid Models," IEEE Journal of Biomedical and Health Informatics, Vol. 18, No. 4, pp 1169-1177, July 2014.

[9] Paulo C. Cortez and João P. V. Madeiro, Fernando S. Schlindwein, "Classification System for Fetal Heart Rate Variability Measures Based on Cardiocographies ," Journal of Life Sciences and Technologies, pp 184-189, 2013.

[10] V.Kalakutskij, V.Konyukhov, E.Manelis, "Estimation of Fetal Heart Rate Using Abdominal ECG Recordings," IFMBE Proceedings, 2nd European Medical and Biological Engineering Conference, Vienna, 2002.

[11] Rajendra Acharya U, Kannathal N, Ong Wai Sing , Luk Yi Ping and Tjileng Chua, "Haert rate analysis in normal subjects of various age groups," Biomedical Engineering Online, 24, pp 1-8,2004.

[12] Janusz Jezewski, Janusz Wrobel, Krzysztof H oroba, " Comparison of Doppler Ultrasound and Direct Electrocardiography Acquisition Techniques for Quantification of Heart Rate Variability," IEEE Transactions on Biomedical Engineering. Vol.53,No.5.pp 855-863,2006.

[13] Maya David, Michael Hirsch,Jacob Karin, Eran Toledo, and Solange Akselrod, "An estimate of fetal autonomic state by time-frequency analysis of fetal heart rate variability," J Appl Physiol 102: 1057–1064, 2007.

[14] Akimune Fukushima, Kenji Nakai, Manabu Itoh, Hitoshi Horigome, Akira Suwabe, Kojorou Tohyama, Kouichiro Kobayashi, Masahito Yoshizawa, " Assessment of Fetal Autonomic Nervous System Activity by Fetal Magnetocardiograph,"Clinical Medicine: Cardiology, 2: pp 33–39, 2008.

- [15] Meldijana Omerbegovic, "Heart Rate Variability – Noninvasive Monitoring of Autonomic Nervous System Function," Professional Paper, pp 53-58, 2009.
- [16] Luiz Carlos Marques VANDERLEI, Carlos Marcelo PASTRE, Rosângela Akemi HOSHI, Tatiana Dias deCARVALHO, Moacir Fernandes de GODOY, "Basic notions of heart rate variability and its clinical applicability," Rev Bras Cir Cardiovasc, 24(2);pp.205-217, 2009.
- [17] Joachim Taelman, Steven Vandeput, Devy Widjaja, Marijke AKA Braeken, Ren'ee A Otte, Bea RH Van den Bergh, Sabine Van Huffel, "Stress during Pregnancy : Is the Autonomic Nervous System Influenced by Anxiety? ", Computing in Cardiology, 37;pp 725-728, 2010.
- [18] Janusz Jezewski, Dawid Roj, Janusz Wrobel and Krzysztof Horoba, "A Novel Technique for Fetal Heart Rate Estimation from Doppler Ultrasound Signal," Biomedical Engineering Online, 10:92 pp 1-17, 2011.
- [19] Sumana Panja, Kaushik Bhowmick, Nachal Annamalai and Shobha Gudi, "A study of cardiovascular autonomic function in normal pregnancy ," Al Ameen J Med Sci; 6(2) : pp170-175, 2013.
- [20] Dominique Acolet, Anna Springett, Shona Golightly, "Confidential Enquiries into Maternal and Child Health (CEMACH), Perinatal Mortality 2006," England, Wales and Northern Irelands, April 2008.
- [21] Riffat Jaleel, "Impact of Maternal Obesity on Pregnancy Outcome ," Journal of Surgery Pakistan (International), 14 (1) January - March 2009.
- [22] Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology, "Heart rate variability Standards of measurement, physiological interpretation, and clinical use," European Heart Journal 17, pp 354–381, 1996.
- [23] U. Rajendra Acharya, K. Paul Josep N. Kannathal Choo Min Lim, Jasjit S. Suri "Heart rate variability: a review," Med Bio Eng Comput 44:1031–1051, 2006.
- [24] Juha-Pekka Niskanen, Mika P. Tarvainen, Perttu O. Ranta-aho, and Pasi A. Karjalainen "Software for advanced HRV analysis," Computer Methods and Programs in Biomedicine, 2002.
- [25] Sheldon M. Ross, "Introductory Statistics," Academic Press, 2nd Edition, 2006.

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