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Original article

Investigation of the high frequency band of heart rate variability: identification of preeclamptic pregnancy from normal pregnancy in Oman

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Background: The spectral analysis of heart rate variability (HRV) shows a decrease in the power of the high frequency (HF) component in preeclamptic pregnancy compared with normal pregnancy; such a decrease is associated with an increase in the low frequency (LF/HF) ratio of the HRV. The physiological interpretation is that preclamptic pregnancy and normal pregnancy is associated with a facilitation of sympathetic regulation and an attenuation of parasympathetic influence of HR compared with nonpregnancy.

Objective: We used a spectral analysis of HRV to identify preeclamptic pregnancy in Oman.

Methods: Fast Fourier transform (FFT) spectral analysis was used to show whether patients with preeclamptic pregnancy have a reduction in the power of the HF band of HRV compared with subjects with normal pregnancy. The soft-decision wavelet-based technique is then implemented to scan the HF band to find which part of it is associated with preeclampsia. Data was obtained from eight preeclamptic pregnant subjects and nine normal pregnant controls of the same pregnancy duration.

Results: The classical FFT approach to the LF/HF power ratio of HRV is a possible classification factor. The identification accuracy obtained was 76.47%, while the sensitivity (identification of patients) and the specificity (identification of normal subjects) were found to be 75% and 77.77%, respectively. The soft-decision wavelet-based technique with five decomposition stages of Coif5 wavelets, finds that B10 and B11 (out of 32 bands) covering the frequency range of (0.1406–0.1563) Hz, and (0.1563–0.1719) Hz, respectively, are the most dominant parts of the HF band affected by preeclampsia. The identification accuracy, sensitivity, and specificity using this range are found to be 94.11%, 100%, and 88.88%, respectively.

Conclusion: Soft-decision wavelet decomposition is shown to be a successful tool for identification of preeclampsia.

***Keywords*:** HRV, FFT, LF/HF, preeclampsia, soft-decision wavelet-decomposition

Preeclampsia affects 10% of all pregnancies worldwide and causes substantial maternal and fetal morbidity and mortality. In Muscat, the capital of Oman, a recent study showed a preeclampsia prevalence of 7.5% of all pregnancies and it was found to be slightly higher in primigravida than in multiparous pregnancies [1].

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A leading cause of maternal and neonatal death worldwide, preeclampsia is a syndrome that arises in pregnancy and is diagnosed by increased systemic arterial pressure and proteinuria [2]. The pathophysiological mechanisms underlying this disorder are not completely understood. Impairment of the autonomic nervous system functions may be the cause of preeclampsia [3] although there is still a debate regarding whether preeclampsia is associated with disturbances in the sympathetic and parasympathetic functions of the autonomic nervous system [4].

Autonomic function can be assessed invasively by microneuroangiography and noninvasively using several laboratory techniques: the deep breathing test, Valsalva maneuver, orthostatic tolerance, ice immersion and handgrip dynamometry [5].

Autonomic activity has been evaluated using spectral analysis of heart rate variability (HRV). The information obtained from such an analysis includes [6]:

- The very low-frequency (VLF) power-spectral density (PSD) components, between 0.0033 Hz and 0.04 Hz, which are possibly related to long-term regularity mechanisms (e.g., the rennin-angiotensin system, the thermoregularity peripheral blood flow adjustment).
- The low-frequency (LF) components, between 0.04 Hz and 0.15 Hz, linked to sympathetic modulation, but also including some parasympathetic influence.
- The high-frequency components, from 0.15 Hz to 0.4 Hz, which reflect parasympathetic (vagal) activity.

The frequency-domain analysis of HRV has shown a decrease in the power of the high frequency (HF) component in preeclamptic pregnancy compared with normal pregnancy; such a decrease is associated with an increase in the LF/HF ratio of the HRV [2]. The physiological interpretation for that was normal pregnancy is associated with a facilitation of sympathetic regulation and an attenuation of parasympathetic influence of heart rate compared with non-pregnancy. Such alterations are influenced more in preeclamptic pregnancy compared to normal pregnancy [2].

The aim of this paper is to confirm this statement and to test this noninvasive technique on data collected in Oman. Moreover, there is a need to investigate which part of the HF region may have more influence related to preeclampsia. For this, a more sophisticated spectral analysis other than FFT is needed. The main objective is to develop a noninvasive method based on HRV with the great advantages over invasive microneuroangiography as it has minimum risk to the mother and the fetus.

The soft-decision power spectral estimation technique based on sub-band decomposition and wavelet-decomposition was implemented successfully in many applications such as identification of patients with obstructive sleep apnea and congestive heart failure and identification of parkinsonian tremor from essential tremor using accelerometer and surface EMG signals [7-12].

Materials and methods

Subjects

The HRV of nine normal pregnancy subjects and eight preeclamptic subjects were obtained from the antenatal clinic of Nizwa hospital in Nizwa, Sultanate of Oman and followed up to 6 to 8 weeks postpartum. Ethics committee approval for this study was obtained from our institutional committee. Preeclampsia is diagnosed according to the criteria of the international society for study of hypertension in pregnancy [13]. Arterial BP values > 140/90 mmHg, after the 20^{th} week of gestation confirmed by two consecutive readings at least 6 hours apart with protein-urea. Only hypertensive pregnant women between 23 to 36 weeks of gestation are included. Subjects were selected to ensure that they have no history of hypertension, cardio-vascular or renal diseases before pregnancy. Subjects with cardiovascular disorders, arrhythmias and diabetes, and those on treatment, which affect HRV, e.g. hypnotics (drugs which depress autonomic functions) or autonomic blockers are also excluded.

Data analysis method

In this work, the fast Fourier transform method was used first to find the power spectral density of the HRV data under test from both groups. The spectrum is then divided into three different bands (VLF (0.0033–0.4Hz), LF (0.4–0.15Hz), and HF (0.15–0.4Hz)) [6]. The power ratios (VLF/LF, VLF/HF, LF/HF) are then plotted. A threshold was found to separate data of patient and normal subjects. The threshold was found using the well-known receiving operating characteristic (ROC) technique [14]. ROC is a technique in which the threshold between two subjects can be selected automatically and the corresponding values of sensitivity, specificity, and accuracy are found accordingly.

Wavelet-decomposition

The block-diagram of the wavelet decomposition is shown in Fig. 1. The procedure starts by filtering the input RRI (R-R-Interval) signal $x(n)$ of length-N by low-pass (LPF) and high-pass (HPF) filters and then down-sampling by a factor of 2, to produce both the "approximation" $a(n)$ and the "details" $d(n)$. Assuming Haar-wavelets (as the simplest wavelet filters), $a(n)$ and $d(n)$ are obtained by:

$$a(n) = \frac{1}{\sqrt{2}}[x(2n) + x(2n+1)], \qquad (1)$$
$$d(n) = \frac{1}{\sqrt{2}}[x(2n) - x(2n+1)]$$

Depending on a priori information about the energy concentration of the signal, one band is to be considered and processed while the other band can be neglected resulting in reduced complexity and processing time. As an example, for a low-pass signal, the upper branch can be followed, while the lower branch can be ignored. The decomposed bands could also be decomposed further and further into high frequency and low frequency sub-bands using the same filters. The process of selecting one decomposition path out of the full decomposition is called a hard decision algorithm [7-8]. The band selection is established by an energy comparison between the low- and high-frequency subsequences *a(n)* and *d(n)* after the down sampling [8]:

$$B = \sum_{n=0}^{\frac{N}{2}-1} \left[a^2(n) - d^2(n) \right] \qquad (2)$$

According to the sign of *B*, the decision is taken: if *B* is positive, the low-frequency band is considered, and if *B* is negative, the high-frequency band is considered. Because we are not interested in the value of *B*, but only in its sign, the complexity of the algorithm can be further reduced if Eq. (2) is simplified and approximated as:

$$\mathrm{sgn}(B) = \mathrm{sgn}\left\{ \sum_{n=0}^{\frac{N}{2}-1} [\,|a(n)| - |d(n)|\,] \right\}. \qquad (3)$$

Energy comparison and band selection are repeated at each decomposition stage, resulting in following single decomposition path and neglecting the other to narrow down the estimate of the dominant frequency range of the original sequence. Given its simplicity, the method of hard-decision may not be very reliable in practice because at each stage the approximations to the estimated quantities result in a high estimation error. A particularly useful modification of the hard-decision algorithm is to perform full decomposition in each stage a specified number of times and assign a "probability measure", based on the value of B, which reflects the energy in each decomposed band. This process is called the soft-decision algorithm [8]. It emerged to be useful in estimating an approximate PSD of the RRI signal [9-12].

Estimation of power-spectral density

The following procedure is used to estimate the PSD of the decomposed sub-bands [8]:

1. The wavelet-decompositions are computed with all branches up to a certain stage *m* to obtain 2^m sub-bands.
2. All estimator results up to stage *m* are stored, and a "probability measure" is assigned to each path (i. e., frequency band) to bear the primary information.
3. If *J(L)* is the assigned probability of the input signal being primarily low-pass, the number *J(H)* = 1-*J(L)* is the probability that the signal is primarily high-pass. One simple way to make the probability assignments is to use the ratio of the number of positive comparisons between |*a(n)*| and |*d(n)*| in Eq.(3) to the total number of comparisons for a given stage.
4. At the following stage, the resulting estimate can be interpreted as the conditional probability of the new input sequence containing primarily low (high) frequency components, given that the previous branch was of predominantly low (high)-pass character. Using this reasoning and laws of probability, the assignments for the probability measure of the resulting sub-bands should be made equal to the product of the previous branch probability and the conditional probability estimated at a given stage. **Figure 2** shows this step of probability assignment for 8 sub-bands.
5. The probabilities $P(B_i)$ derived from the estimator outputs, where *i* is the index of the band, may be interpreted themselves as a coarse measurement of the PSD [8]. The higher the probability value of any band, the higher is its power-spectral content. For *m* decomposition stages, each band covers $0.5/2^m$ Hz of the RRI-spectrum between 0 and 0.5 Hz.

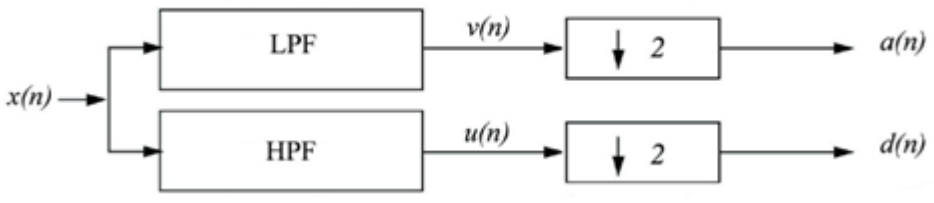

Figure 1. Single wavelet decomposition stage

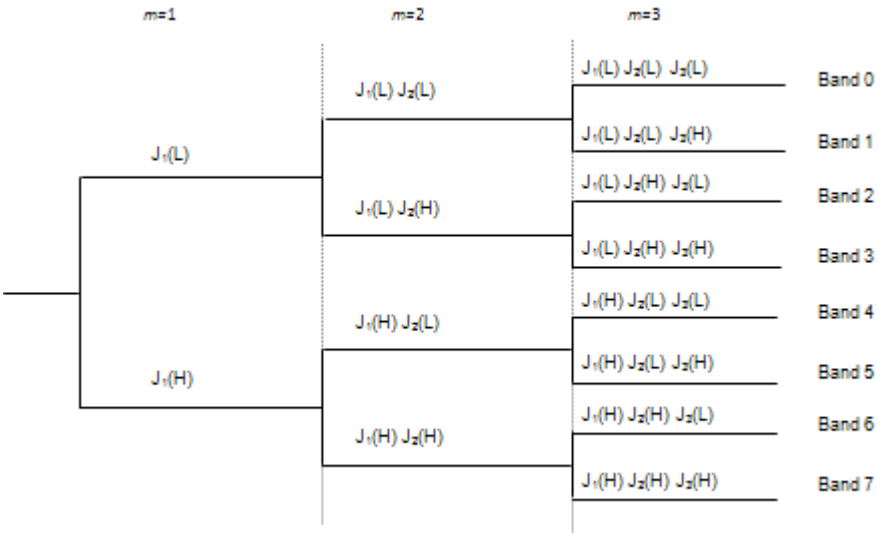

Figure 2. PSD estimation by probability measures

Classification performance

In this study, only a binary classification is considered, e.g. classification between two different cases termed "positive case" (preeclamptic pregnancy: patient) and "negative case" (normal pregnancy: normal). The performance of a classifier is evaluated by three main metrics: specificity, sensitivity, and accuracy, as follows [15]:

$$Specificit\ y\ (\%) = \frac{TN}{TN + FP}.100\%\ , \qquad (4)$$

$$Sensitivit\ y\ (\%) = \frac{TP}{TP + FN}.100\%\ , \qquad (5)$$

$$Accuracy\ \ (\%) = \frac{TP + TN}{TP + FP + TN + FN}.100\%\ , \qquad (6)$$

where the entities in the above equations are: (TN (true negatives), TP (true positives), FN (false negatives), FP (false positives)), and T is the total number of data under test.

Specificity indicates the ability of a classifier to detect negative cases, i.e. the normal cases. Sensitivity represents the ability of a classifier to detect the positive cases, i.e. the patient cases. Accuracy, which is the ability to identify both subjects correctly, represents the overall performance of a classifier. It indicates the percentage of correctly classified positive and negative cases among the total number of cases.

Results

FFT Results

The LF/HF ratio of the power spectrum of all subjects is found by applying FFT. A threshold is selected using ROC to discriminate between patients and normal subjects. **Figure 3a** shows the ROC results and **Figure 3b** shows the LF/HF ratios of the data separated by the threshold found in **Figure 3a**.

SD-WDEC Results

The SD-WDEC has been applied to scan better the HF region of the RRI spectrum in an attempt to identify which part of this region has more effect on preeclampsia, or in other words, to see which part can be used to discriminate more efficiently between preeclamptic pregnancy and normal pregnancy. An 8-band, 16-band, and 32-band SD-WDEC have been implemented and effects of all bands on discrimination between the two subjects have been studied and the best bands for discrimination have been indicated. **Figure 4a** shows the results (power) of B3 out of 8 bands (SD-WDEC, with three stages), while **Figure 4b** shows the results (power) of B4 out of 8 bands. The results (power) of the subjects of B5 and B6 (out of 16 bands, obtained using SD-WDEC with 4 stages), respectively can been seen in **Figure 5a and b**. The results (power) of B10 and B11 obtained from SD-WDEC of 5 stages are shown in **Figure 6a and b**, respectively. **Figure 7a** shows the ROC results of the summation of the powers of B10 and B11 out of

32 bands, while **Figure 7b** shows the classification results using this identification factor.

The Identification results of all versions of the SD-WDEC used in this section with that of the FFT used in Section 3.1 are listed in **Table 1**.

Table 1. Identification Results between preeclamptic pregnancy and normal pregnancy

Method	Frequency	Sensitivity	Specificity	Accuracy
FFT	0.04–0.15 Hz	75%	77.78%	76.47%
SD-WDEC, B3 of 8	0.125–0.1875 Hz	75%	88.88%	82.35%
SD-WDEC, B4 of 8	0.1875–0.25 Hz	75%	88.88%	82.35%
SD-WDEC, B5 of 16	0.125–0.1563 Hz	87.5%	77.78%	82.35%
SD-WDEC, B6 of 16	0.1563–0.1875 Hz	87.5%	77.78%	82.35%
SD-WDEC, B10 of 32	0.1406–0.1563 Hz	100%	88.88%	94.18%
SD-WDEC, B11 of 32	0.1563–0.1719 Hz	87.5%	88.88%	88.24%
SD-WDEC, B10+B11	0.1406–0.1719 Hz	100%	88.88%	94.18%

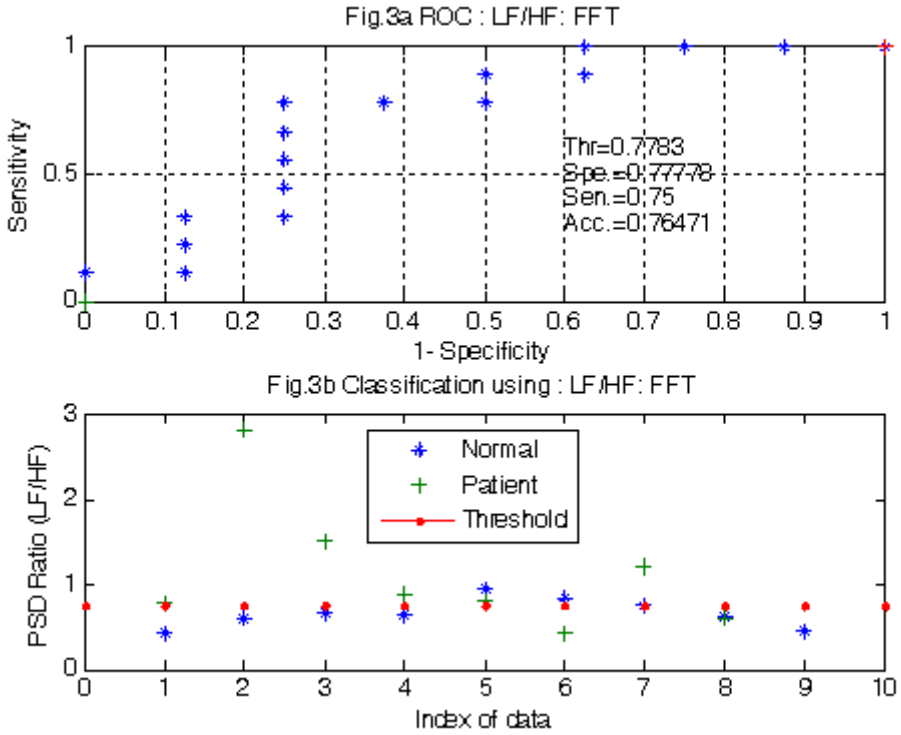

Figure 3. ROC and Classification using FFT with LF/HF

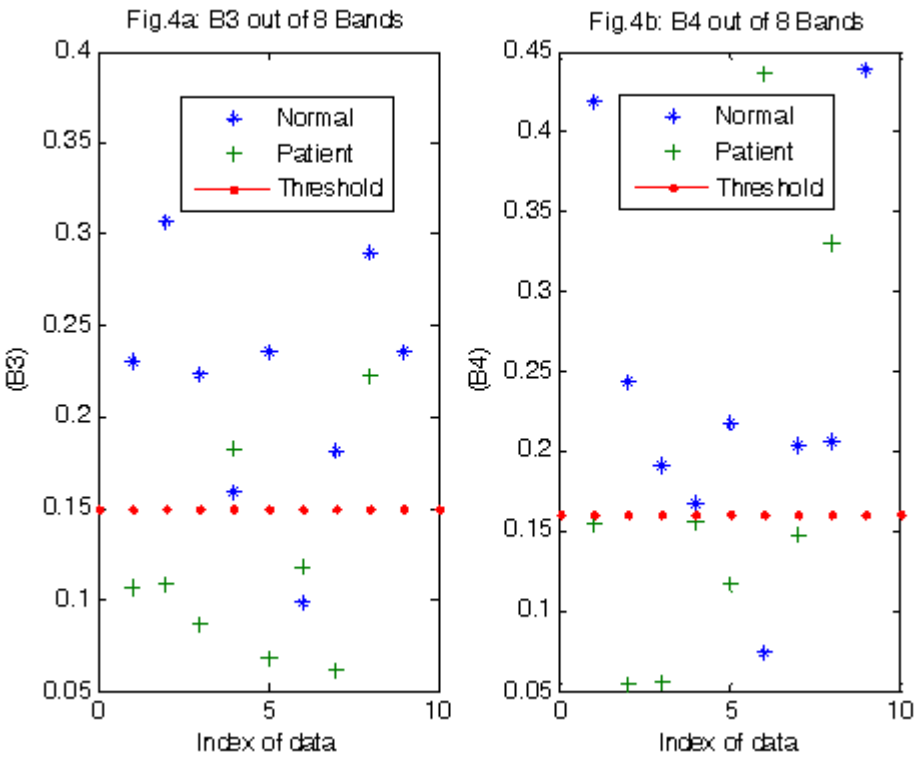

Figure 4. Classification using B3 and B4 out of 8 Bands

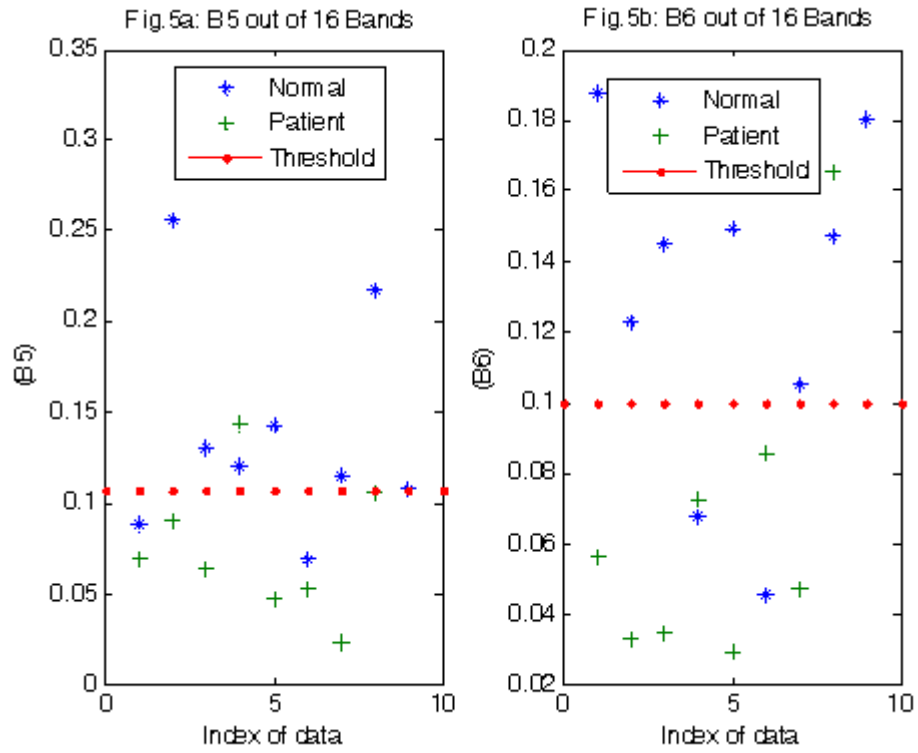

Figure 5. Classification using B5 and B6 out of 16 Bands

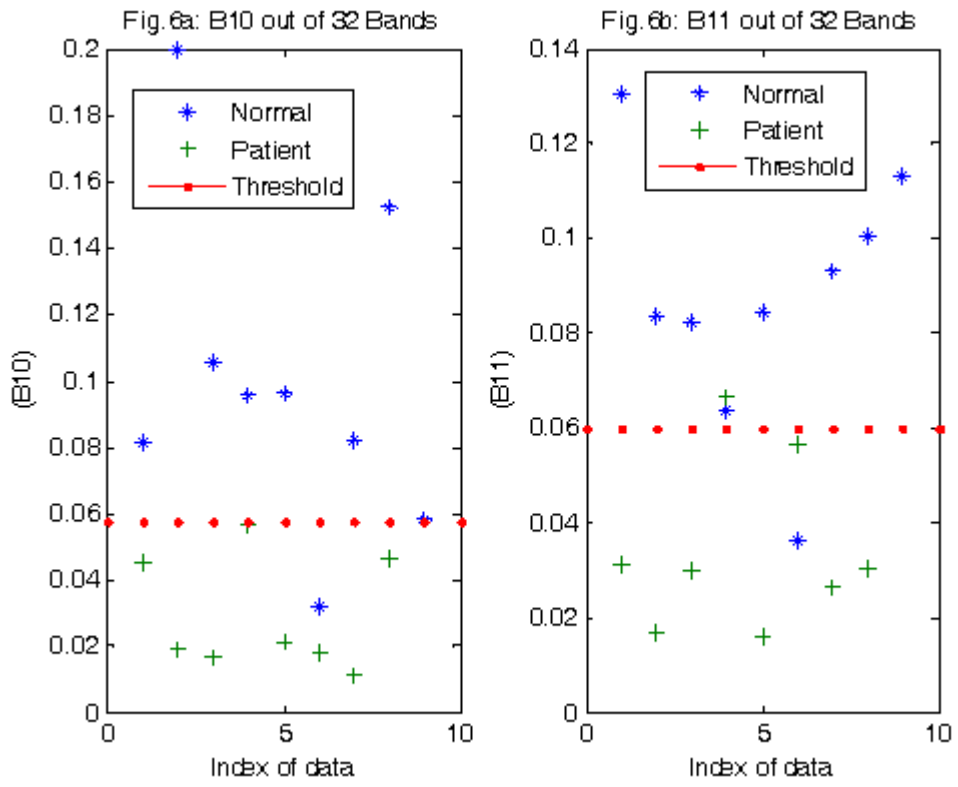

Figure 6. Classification using B10 and B11 out of 32 Bands

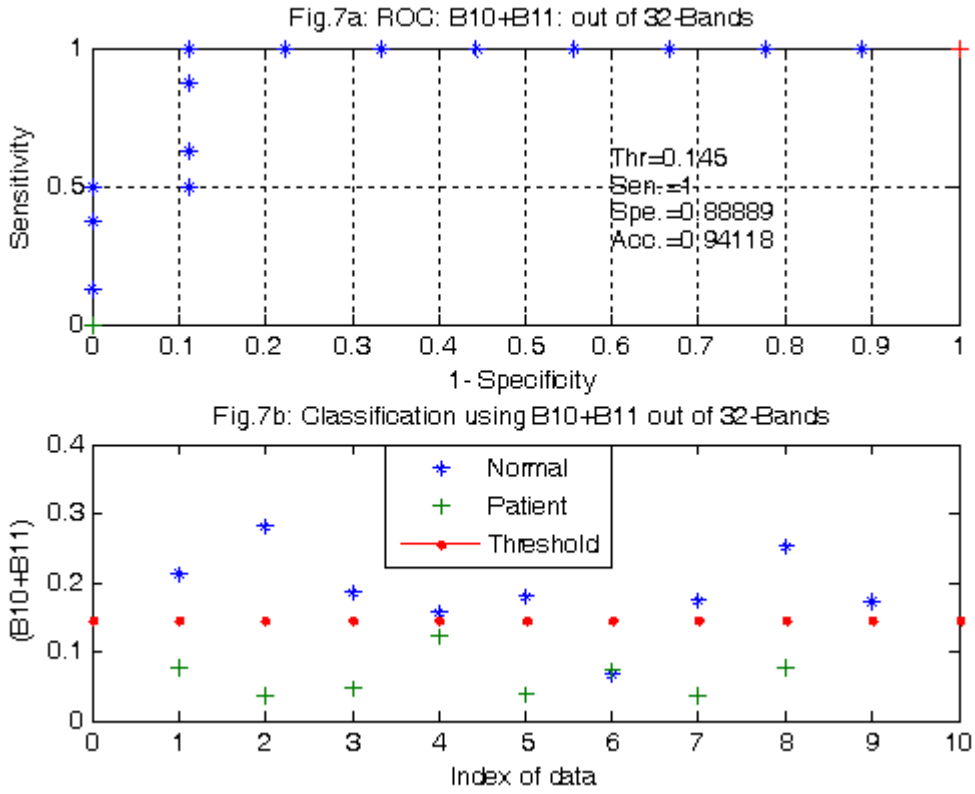

Figure 7. ROC and Classification using B10+B11 out of 32 Bands

Discussion

Results presented in this paper revealed that the HF power of the HRV spectrum decreases in preeclamptic pregnancy compared with normal pregnancy. For this reason, the LF/HF ratio increases with preeclamptic pregnancy compared with normal pregnancy. The LF/HF ratio succeeded to discriminate 13 out of 17 subjects in our study reaching an identification accuracy of 76.47%. Investigating the HF more deeply, the SD-WDEC algorithm has been used with Coif5 wavelets and with three different numbers of decomposition stages. Results show that with 5 levels of decomposition, the identification accuracy approaches 94.14%, by which the power of band 10, or the power of bands 10 and 11 are used as a discrimination factor. This very good accuracy was obtained from a region having a frequency range of 0.14 to 0.172 Hz. Hence, the power of this frequency region (0.14 to 0.172 Hz) was reduced with preeclamptic pregnancy compared with normal pregnancy. This important finding of this work, which is obtained by a high resolution spectrum analysis, cannot be obtained using classical FFT techniques. One limitation of this result is that it depends on a small number of data samples. Our future work is to test our finding on larger set of data.

The authors have no conflict of interest to report.

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