THE NEW ARMENIAN MEDICAL JOURNAL
Vol.8 (2014), No 1, p.68-72

# A NOVEL TROPHOTROPIC MECHANISM OF FETAL WELLBEING

LAKHNO I. V.

Kharkiv Medical Academy of Postgraduate Education, Kharkiv, Ukraine

*Received 10/12/2013; accepted in final form 1/12/2014*

***ABSTRACT***

*The spectral characteristics of maternal and fetal heart rate variability and umbilical vein hemodynamics were investigated in 63 pregnant women with preeclampsia that was associated with the suppression of the vagal tone. Sympatovagal value above 2.0 was a marker of pregnancy complication. It was determined that fetal compromise in preeclamptic patients was accompanied with decreased total spectrum power and fractal components of heart rate variability and the relative predominance of central sympathetic control. The resulting state influenced negatively on fetal myocardial metabolic response and was characterized with T/QRS ratio above 1.5. The autonomic nervous regulation reduction of the fetus demonstrated the loss of independence from the maternal hemodynamics that had synchronized the maternal and fetal heart rate by increased vagal tone power. The fetal distress development marked an increased regulatory role of maternal origin slow-wave processes and depletion of the proper myogenic umbilical cord arrangements which reinforced the penetrating of umbilical vein pulsative waves.*

**Keywords:** *preeclampsia, fetus, heart rate variability, umbilical vein.*

## INTRODUCTION

Uteroplacental and fetal hemodynamycs deterioration is one of the main events in the scenario of the preeclampsia early onset and fetal growth retardation [*Boito S. et al., 2004; Ghosh G.et al., 2009; Baschat A., 2011*]. Doppler ultrasonographic investigation in routine practice have contributed enormously to the fetal condition assessment. Umbilical vein plays a role of peripheral fetal heart [*Baschat A., 2011*]. The research of umbilical vein oscillations spectral characteristics may determine the origin of controlling signals [*Huidobro-Toro J. et al., 2001; Resch B. et al., 2003; Meng F. et. al., 2007*].

Over the recent years the spectral characteristics of maternal and fetal heart rate variability (HRV) were determined [*Brown C. et al., 2008; Karvounis E. et al., 2010; Aziz W. et al., 2012*]. Maternal hemodynamical oscillations (variability) present a convenient instrument to support fetal nutritional condition on optimal level. The investigation of the fetal autonomic tone and T/QRS ratio may optimize the diagnosis of fetal distress [*Brown C. et al., 2008; Rzepka R. et al., 2010*]. However, the regulation determines not only heart activity. Additional research of the spectral portraits of hemodynamical processes in the fetoplacental system could provide more information of fetal intrauterine condition in physiological pregnancy and preeclampsia.

The investigation was aimed to survey spectral characteristics of umbilical vein hemodynamics in case of normal gestation and in preeclampsia.

## MATERIAL AND METHODS

The study protocol was approved by the Bioethics Committee of the Kharkiv Medical Academy of Postgraduate Education. Observed pregnant ladies were informed about the methods of the study, its aim, indications and eventual complications before inclusion in the study. All patients gave written informed consent to participate in the investigation.

The study of Doppler spectrograms of the umbilical vein blood flow was performed in 85 patients at 37-41 weeks of gestation. All pregnant women were divided into several clinical groups. Group I involved 22 women with physiological course of pregnancy and normal fetal condition. In Group II there were 33 pregnant women with mild and moderate preeclampsia. Thirty patients with severe pre-

***ADDRESS FOR CORRESPONDENCE:***
Kharkiv Medical Academy of Postgraduate Education
58 Korchagintsev Street, 61176, Kharkiv, Ukraine
Tel: (380955) 347 208
E-mail: igorlakhno@rambler.ru

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eclampsia made Group III.

Doppler ultrasonography was performed on the ultrasound system "Voluson 730" ("GE Healthcare", USA). The obtained Doppler spectrogram of the venous umbilical blood flow was subjected to further processing (Figure 1).

The curves of maximum blood flow velocity were isolated and their spectral components determined. The spectra were calculated by sampling step $\Delta t$=0.01 seconds for a sample of 256 points. The resulting spectrum was obtained by averaging over all samples of this contingent.

Fetal and maternal HRV and fetal electrocardiogram (ECG) parameters were obtained with the application of the first fetal noninvasive computer electrocardiographic system in Ukraine "Cardiolab Baby Card" (ScRC KhAI-Medika, Ukraine)". The quality of the Ukrainian ECG recordings were tested by experts [*Silva I. et al., 2013*]. The registration was carried out from maternal abdominal wall during periods of fetal activity for 10 minutes long.

The results were processed by parametric statistical methods (mean – M, error – m) with the application of statistics software package Excel adapted for biomedical research.

## Results

The obtained data demonstrated that maternal HRV in preeclampsia was characterized with predominance of sympathetic baroreflexes. The mean sympathovagal index value was 2.4±0.8. The suppression of vagal regulation and the lack of hemodynamic adaptation to gestational hypervolemic condition were determined. The decreased total power of HRV in Group III was associated with an increased stress index. The mean total power in severe preeclampsia was 1164.6±212.8 $ms^2$ and stress index made 1468.5±123.26 conventional units (*c.u.*) ($p$<0.05).

The study on fetal HRV indices in observed patients (*see* Table) allowed establishing significant differences between groups. In pregnant women with preeclampsia the level of autonomous nervous regulation of the fetus was suppressed with decrease of ECG main spectral components: very low (VLF), low (LF) and high frequency (HF).

The values of stress index and amplitude mode (number of cardiointervals) were higher in preeclampsia groups. In the majority of Group III cases a significant predominance of sympathetic regulation over the parasympathetic was shown. The presence of tachycardia was a manifestation of hemodynamics centralization. In case of bradycardia

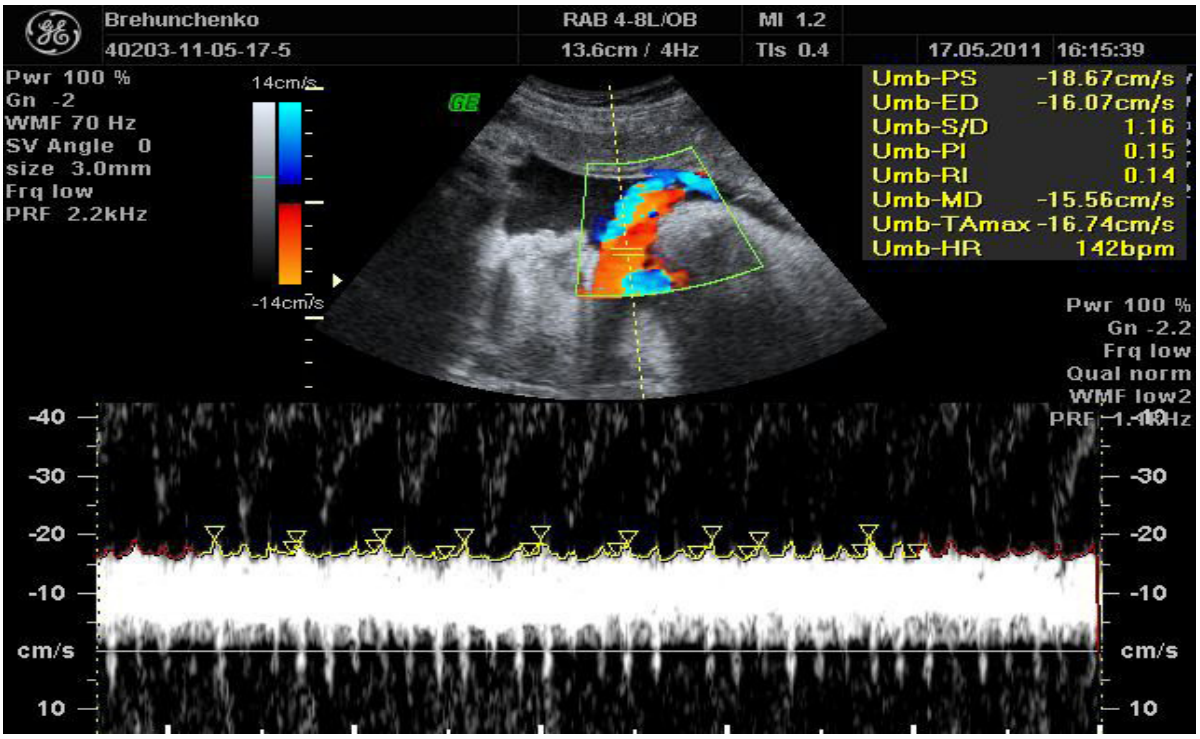


**Figure 1**. *Doppler venous umbilical hemodynamics in normal pregnancy (the peaks of fluctuations are indicated by arrows).*

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***Table.***

Fetal heart rate variability parameters in observed contingent

| Index | Group I | Group II | Group III |
|---|---|---|---|
| SDNN, *ms* | 46. 2±8.2 | 31.4±6.8* | 12.3±1.7*/** |
| RMSSD, *ms* | 22.4±3.4 | 14.2±2.6* | 8.1±0.8*/** |
| pNN5O, % | 8.6±1.0 | 5.6±0.9* | 2.1 ±0.2*/** |
| AMo, % | 38.2±7.4 | 49.8±6.2* | 62.5±6.6*/** |
| Stress Index, *c.u.* | 140.6±22.8 | 464.2±52.4* | 1450.2 ± 112.6*/** |
| Total Power, *ms²* | 1634.8±364.2 | 1048.4±98.4* | 384.8±61.2*/** |
| Very Low Frequency, *ms²* | 1346.2±282.8 | 670.2±84.6* | 194.2±23.8*/** |
| Low Frequency, *ms²* | 192.6±31.1 | 312.2±66.8* | 143.6±25.1*/** |
| High Frequency, *ms²* | 95.2±19.4 | 66.1±14.9* | 48.2±14.1*/** |

*Notes: * – the differences were statistically significant compared to Group I ($p<0.05$); ** – the differences were statistically significant compared to Group II ($p<0.05$). Abbreviations*: ***SDNN*** *– Standard deviation of normal to normal intervals;* ***RMSSD*** *– root mean square of successive heartbeat interval differences;* ***pNN50*** *– percent of difference between adjacent NN intervals differing in more than 50 ms;* ***AMo*** *– amplitude mode (number of cardiointervals).*

episodes the appearance of pronounced increase in HRV did not occur. It was reasonable to argue that in the pathogenesis of antenatal decelerations a significant role belonged to dominance of the central sympathetic regulation that formed the fetal myocardium hypoxic injury and the suppressed sinus node response. The latter was proved with mean T/QRS ratio in Group III: 0.16±0.04. That was the possible nature of antenatal decelerations in preeclampsia (Figure 2).

In Group III pregnant women with severe preeclampsia the maintenance of fetal hemodynamics

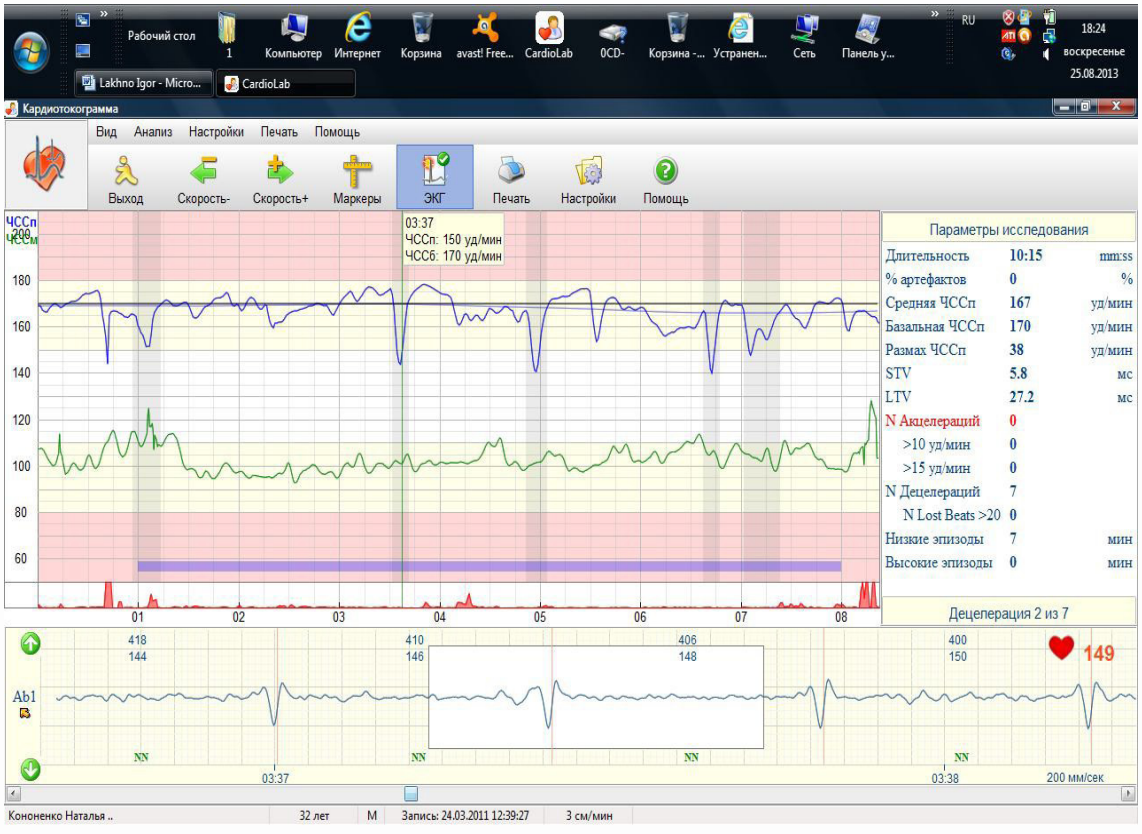


**Figure 2.** *The "window" in the "Cardiolab Baby Card" program (7 decelerations, basal rhythm: 170 per minute).*

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demanded too high "price" from the heart of fetus. The stress index in this group was above 1450.2±112.6 *c.u.* and amplitude mode (number of cardiointervals) – above 62.5±6.6%.

In patients of Group I the two mostly pronounced peaks with the frequency characteristics of 2 *Hz* and 7 *Hz* were recorded (Figure 3). Their amplitude was respectively: 0.16 ±0.01 *c.u.* and 0.15 ± 0.01 *c.u.* The first peak was associated with arterial blood flow component in the umbilical cord and matched the fetal heart rate, and the second one was determined by the contractile activity of the muscular layer of the umbilical cord vein.

In Group II there was a decrease in amplitude of the "venous myogenic" peak (0.08±0.01 c.*u.*), but a pronounced peak was recorded at a frequency of 0.5 *Hz:* 0.06 ± 0.01 *c.u.* (Figure 4).

The latter peak was determined by maternal heart rate and characterized the growing impact of regulatory maternal mechanisms on fetal hemodynamics. In Group III fetomaternal synchronization further increased ($p<0.05$). The amplitude of the peak at 0.5 *Hz* was 0.14±0.01 *c.u.* The peak in the region of 7 *Hz* was absent (Figure 5).

This pattern was characterized by the venous contractile activity exhaustion and was accompanied by pulsating type of blood flow. It was found that in case of fetal distress mother attempted to help the fetus by spreading hemodynamic oscillations through placental barrier with a frequency in the branch of vagal regulation (about 0.5 *Hz*).

### Discussion

The results of the investigation have given a possibility to suggest that in normal condition fetus supports its needs with its own regulatory mechanisms. The preeclampsia leads to the loss of independence. The gradual augmentation in the sympathetic influence on the regulation of fetal hemodynamics demonstrated the desire for compensation "at any price". In normal fetal condition T/QRS ratio was less than 0.1. The increase of the T/QRS (above 1.5) was shown to be associated with fetal myocardial ischemic lesions [*Karvounis E. et al., 2010; Rzepka R. et al., 2010*]. The depletion of self-regulation led to an increase of unusual for the fetus vagal regulation [*Aziz W. et al., 2012*].

Interesting changes were observed for the completely independent umbilical venous blood flow. In

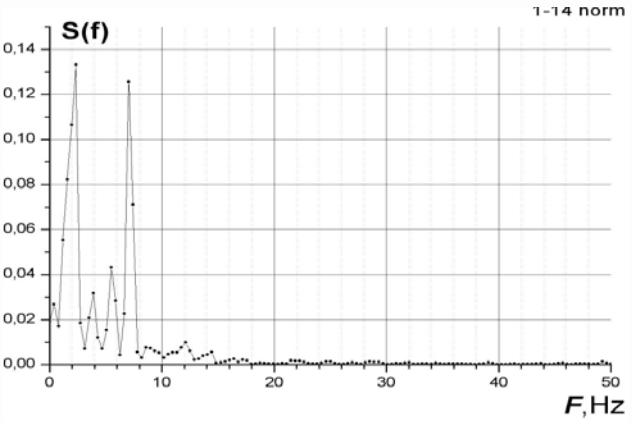


**Figure 3.** *Spectral portrait of blood flow in the umbilical vein in the patient with a normal fetal condition.*

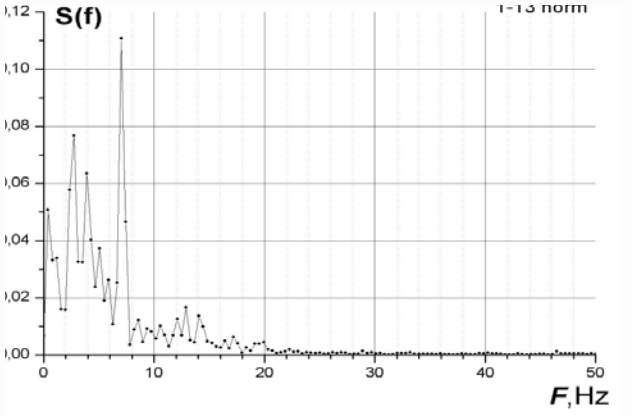


**Figure 4.** *Spectral portrait of blood flow in the umbilical vein in the patient with moderate preeclampsia.*

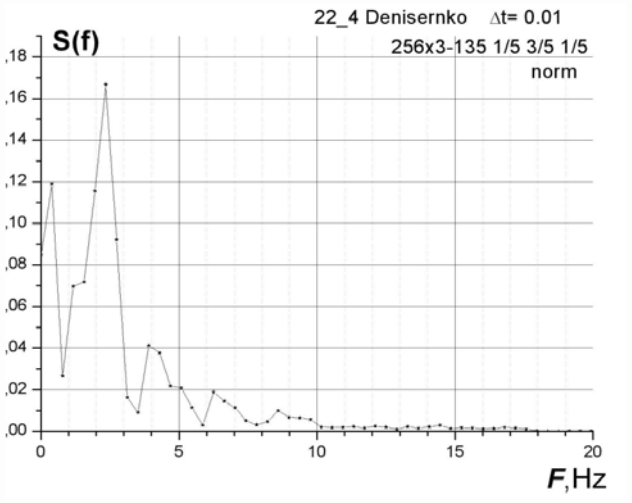


**Figure 5**. *Spectral portrait of umbilical venous hemodynamics in Group III patient with fetal distress.*



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preeclampsia the depletion of myogenic activity of the umbilical vein increased the role of slow-wave processes in the maintenance and ergo-, trophotropic reactions. Their origin was related to the maternal hemodynamic fluctuations (variability), which spread the influence on the fetus through the placental barrier [*Brown C. et al., 2008*]. The specified processes could play a compensatory role of adaptive fetal response. However, the nature of these changes is quite unstable and non-durable. In this case synchronization of the venous umbilical hemodynamics with the maternal heart rate was accompanied by pulsatile blood flow pattern and severe fetal suffering.

## CONCLUSION

The umbilical vein blood flow in case of physiological pregnancy was provided by proper myogenic contractile activity with a frequency of 7 *Hz* and also depended on the arterial component that was associated with the fetal heart rate.

In the pathogenesis of antenatal decelerations in preeclampsia a significant role belonged to the dominance of the central sympathetic regulation that formed the fetal myocardium hypoxic injury and the suppressed sinus node response.

At fetal distress in preeclampsia there was observed an increased regulatory role of maternal origin slow-wave processes and depletion of the proper myogenic umbilical cord arrangements, which had reinforced penetrating of the umbilical vein pulsative waves.

In future the applied approach might help to improve the diagnosis and treatment strategy for fetal distress.

***ACKNOWLEDGMENT***

*I would like to express my greatest appreciation to Professor V.I. Shulgin – the head of the "Cardiolab Baby Card" creators' team. I have greatly benefited from Professor E.A. Barannik and MD A.E. Tkachov in the ultrasonographic part of the investigation. I appreciate the feedback offered by my colleagues.*

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