



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF  
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.1304353>Available online at: <http://www.iajps.com>

Research Article

**INNOVATIVE APPROACHES TO DIABETES MELLITUS  
STUDY DURING PREGNANCY****Tatyana V. Pavlova<sup>1\*</sup>, Natalia B. Pilkevich<sup>1</sup>, Lyudmila O. Zemlianskaia<sup>2</sup>, Eugene V., Zhernakov<sup>1</sup>, Anton N. Kaplin<sup>3</sup>**<sup>1</sup>Belgorod State University 308015, Belgorod, Pobeda str., 85, Russia<sup>2</sup>City hospital №2, gynecological department, Gubkina str., 46, 308036, Belgorod, Russian Federation<sup>3</sup>Kursk State Medical University, 305041, Kursk, Karla Marksa str., 3, RussiaE-mail: [pavlova@bsu.edu.ru](mailto:pavlova@bsu.edu.ru)**Abstract:**

**Purpose:** To study the features of the fetoplacental complex during pregnancy using innovative research methods (Atomic force microscopy (AFM), scanning and transmission electron microscopy). **Methods:** During the study of placenta morphological properties AFM was performed in the probe laboratory of Ntegra-Aura (Russia). The studies were performed in contact modes of intermittent or constant profiles using commercial Si or SiN cantilevers (NSG01, NT-MDT, Russian Federation) under the conditions of low atmospheric vacuum. AFM images were processed and implemented using the NOVA software (NT-MDT, Russian Federation) and ImageAnalysis (NT-MDT, Russian Federation). **Results:** During the study of placental insufficiency, it is necessary to take into account the total changes obtained at all clinical methods of the study. According to the morphological methods of the study, the frequency of placental insufficiency among pregnant women with the 1st type of diabetes was 75%, and in the case of complication with preeclampsia it made 100%. At the 1st type of diabetes, the changes in placenta are characterized by an unstable balance between adaptive ones, aimed at the exchange improvement between a mother and a fetus, due to the improvement of placental blood circulation, which is especially characteristic of the 1st type of diabetes complicated by preeclampsia and maladaptive, characterized by alteration at all structural levels. Identified new pathomorphological changes in placenta allow to perform a differentiated approach to the prevention and the therapy of placental insufficiency among pregnant women with the 1st type of diabetes. **Conclusions:** Thus, we showed that the incidence of placental insufficiency among pregnant women with the 1st type of diabetes was 75%. The presence of preeclampsia caused the increase of this complication frequency to 100%. The revealed leading mechanisms of placenta lesion will allow to outline the pathogenetically substantiated schemes of placental insufficiency therapy among these patients. The possibility of scanning electron and AFM Atomic force microscopy (AFM) in diagnostic, screening studies and as an express method makes it attractive for pathologists, cytologists and obstetrician-gynecologists.

**Key words:** atomic force microscopy, scanning electron microscopy, diabetes, placenta**Corresponding author:**

**Tatyana V. Pavlova,**  
Belgorod State University 308015,  
Belgorod, Pobeda str., 85,  
Russia

QR code



Please cite this article in press Tatyana V. Pavlova et al., *Innovative Approaches to Diabetes Mellitus Study during Pregnancy*, *Indo Am. J. P. Sci*, 2018; 05(06).

## INTRODUCTION:

The issues of diabetes mellitus (DM) remain one of the central problems of combat with non-communicable diseases. Every fifth Russian is in a state of prediabetes. This is 30 million people, which is 20% of our country population [1-3]. The combination of diabetes and pregnancy is of particular importance in the whole world. There is a clear trend towards the number increase concerning the pregnant women with diabetes mellitus [1-3]. With the 1st type of diabetes, the fetoplacental complex exists in the conditions of microcirculation disorder, cellular metabolism and chronic hypoxia. The volume and the severity of its function violations depend on the duration of the disease, the severity of its course, the degree of metabolic process compensation, the presence of obstetric complications, primarily - pre-eclampsia and other characteristics [2, 4-6]. An integrated approach to the study of this problem using modern research methods makes it possible to develop new approaches to study the pathogenesis and the morphogenesis of a complicated pregnancy, and to outline the ways to prevent and treat pathologies of a mother, a fetus and a newborn. A positive trend in the fight against diabetes becomes more dynamic. A major role in the fight against this disease belongs to the fundamental science [4, 5, 7-10].

In this regard, the purpose of the study was to study the features of the fetoplacental complex during pregnancy using innovative research methods (atomic force, scanning and transmission electron microscopy).

## MATERIALS AND METHODS:

Within the framework of the work performed, they conducted the study, the examination, the treatment and delivery on the basis of the BOCH Perinatal Center in Belgorod. 35 pregnant women were observed, 25 of them were with the diabetes of the 1st type, 5 women underwent pre-eclampsia and 10 women made the control group.

### 2.1. The study of pathomorphological changes in placenta

The placenta was studied macroscopically. Immediately after a childbirth, the pieces for light, electron (transmission and scanning) and atomic force microscopy were cut from the placenta and recorded in media. The pieces were poured into the mixture of eponaraldite for transmission microscopy. Then, half-thin and ultra-thin sections were prepared on LKB-Y microtome. Ultrathin sections were for viewing and photographing in "JEM" electron microscopes. For scanning electron microscopy, the samples were used without a treatment or were fixed in a standard glutaraldehyde fixator and then viewed in FE1 Quanta 200 3D raster microscope. Besides, the tissues were ana-

lyzed using AFM Atomic force microscopy (AFM). The samples were viewed and photographed after a brief fixation in formalin solution. All this makes possible the use of Atomic force microscopy (AFM) as an express method. Besides, paraffin blocks can be used to study the samples, especially if there is a need to study the sections obtained from them in a light microscope to select the necessary areas. Atomic-force microscopy (AFM) was performed by us in the probe laboratory Ntegra-Aura (Russia). The studies were performed in the contact modes of intermittent or constant profiles using commercial Si or SiN cantilevers (NSG01, NT-MDT, Russian Federation) under the conditions of low atmospheric vacuum. AFM images were processed and implemented using NOVA software (NT-MDT, Russian Federation) and ImageAnalysis (NT-MDT, Russian Federation).

## RESULTS AND DISCUSSION:

### 3.1. The study of placenta morphological characteristics

The results of placenta morphological characteristic study showed that their weight among the women with the 1st type of diabetes was  $490 \pm 30.0$  g, and among those complicated by pre-eclampsia -  $510 \pm 20.0$  g. The non-functional zones were  $8.5\% \pm 0.9\%$  and  $8.9\% \pm 1.0\%$ , respectively. Hemolyzed erythrocytes, thrombi and fibrin filaments were found in the maternal surface in the vessel lumen. The violation of blood circulation also prevailed during a complicated pregnancy.

In the case of the 1st type of diabetes, long-term adaptation processes were observed aimed at metabolic process improvement between maternal and fetal blood flow in the form of increased placental vascularization, as well as an increased metabolism (the number of syncytial nodules, an increase of pinocytosis, the number of vesicles in the syncytiotrophoblast of capillary endotheliocytes, the area of plasmolemma, the increase of diffused chromatin and the expansion of the endoplasmic reticulum). The transition of homeostasis to a new structural level in connection with the difficulties of metabolism is accompanied by such urgent measures as the desquamation of the syncytiotrophoblast with the exposure of the basal membranes of capillaries for a direct exchange between the maternal and the fertile bloodstream.

It should be noted that in the process of placental insufficiency development the following changes take place: the increase of sclerotized and fibrinoid

altered hairs, the destruction of syncytiotrophoblast microbodies and endothelium, the development of sclerosis and fibrinoid necrosis of the stroma. Non-functional areas appear. A hair tree is shortened. Stem and intermediate hairs predominate. The area, occupied by the accumulation of fibrin and erythrocytes, increases in the intervillous space (Figures 1, 2).

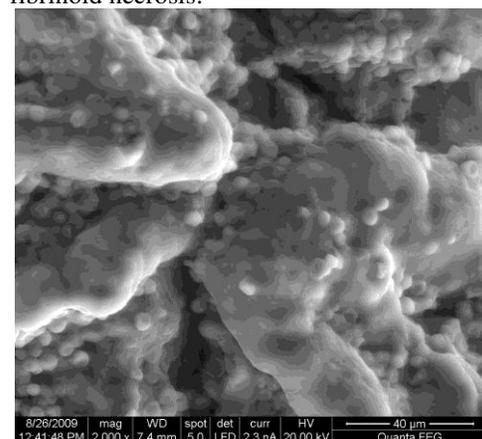
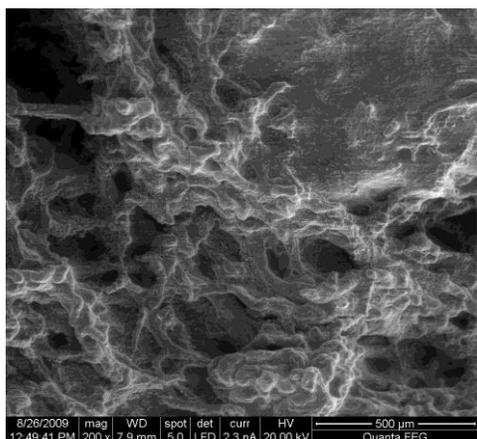


Figure 1. Fragment of the placenta of a woman with type 1 diabetes.

There is a site with a heart attack and a functional zones. In the villiferous tree, the intermediate villi predominate. In the intervillous space of the terminal department, the content of erythrocytes is increased.

SAM. Fig. B (X2000) fragment of Fig. A (200).

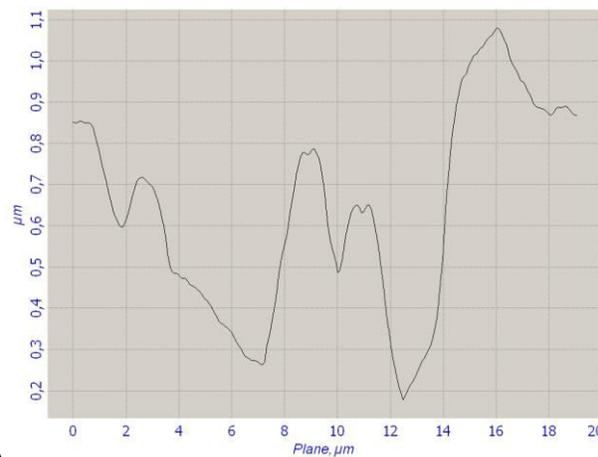
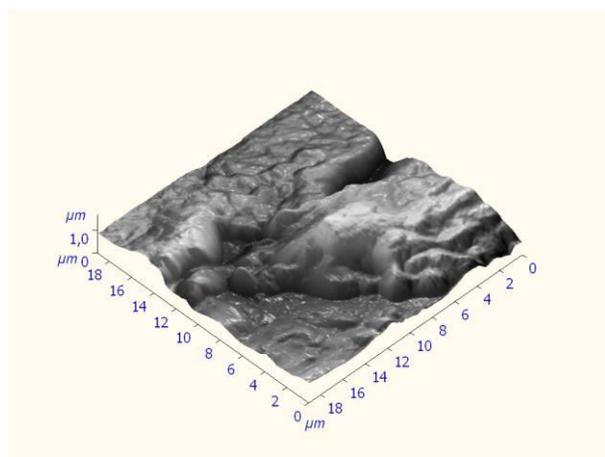


Figure 2. Fragment of the placenta of a woman with type 1 diabetes.

There is a site with a heart attack and a functional zones. Stem and intermediate villi predominate with a small difference in their volume.

Atomic force microscopy. Fig. A three-dimensional image. Fig. B graphic representation

The changes in the placenta during the 1st type of diabetes complicated by preeclampsia have the same direction as in the previous group, but the relationship between placenta adaptive and maladaptive changes becomes extremely unstable. Besides, there are the changes that were less often with diabetes:

edema, pronounced full-blood, the number of under-developed hairs increase.

During the study of placental metabolism main link ultrastructural features - terminal hairs, we noted a significant breakdown of transplacental exchange possibilities. So, the number of microhairs and the

destruction of the remaining ones were reduced in syncytiotrophoblast, and the destruction of remained ones prevailed and together with a significant decrease in pinocytosis it prevented the entry of substances from a mother's bloodstream. The layer of syncytiotrophoblast with a significant destruction of ultrastructures contributed to the disruption of synthesis in the placenta: protein (the necrosis of nuclei, the decrease of ribosome number and a rough endoplasmic reticulum), carbohydrate (the reduction of glycogen granules and smooth endoplasmic reticulum), the appearance of fatty degeneration with the accumulation of fatty vacuoles. Besides, the expansion of the basal membranes and the increase in the

area of fibrinoid necrosis led to an additional violation of transplacental exchange. And, finally, the transfer of substances violated into the flow of blood directly, which was caused by the disruption in the basal capillary membrane structure with the development of sclerosis and fibrinoid necrosis, the decrease in the area of endotheliocytes and the destruction of the nucleus and cytoplasmic organelles. Pinocytosis was expressed very little here, along with the invaginations of endotheliocyte plasmolemma. The variants of underdeveloped hairs are observed. The focal level of adaptation reactions is developed. The developing picture can be characterized as placental insufficiency in 100% of cases.

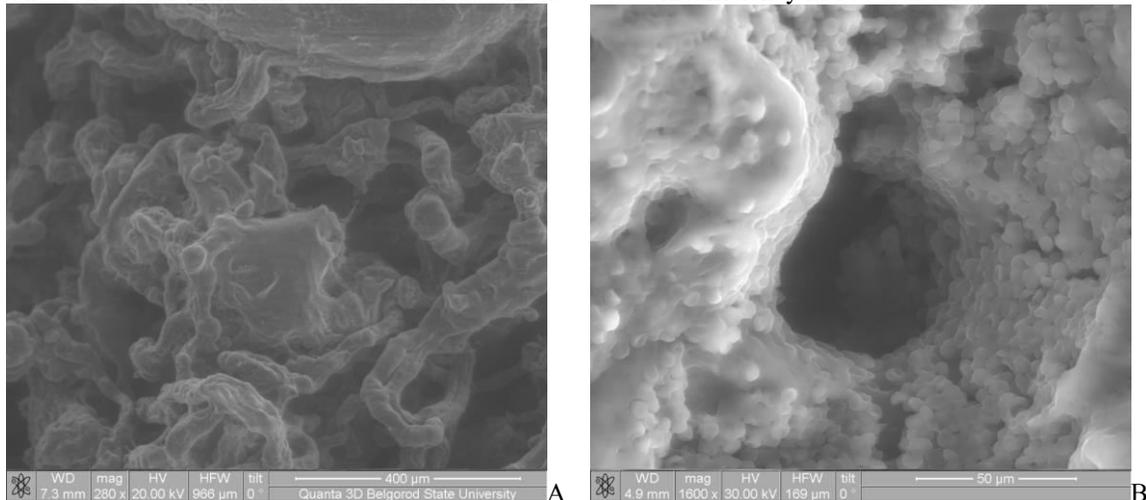


Figure 3. Fragment of the placenta of a woman with type 1 diabetes complicated by preeclampsia. There is a site with a white infarction, functional zones and thrombus in the intervillous space. In the villiferous tree, the intermediate villi predominate. Sharply decreases the number of terminal villi and syncytial nodules on their surface. Fertility of stem villi with sludge in the endothelial zone.

SAM. Fig. B (X1600) fragment of Fig. A (280).

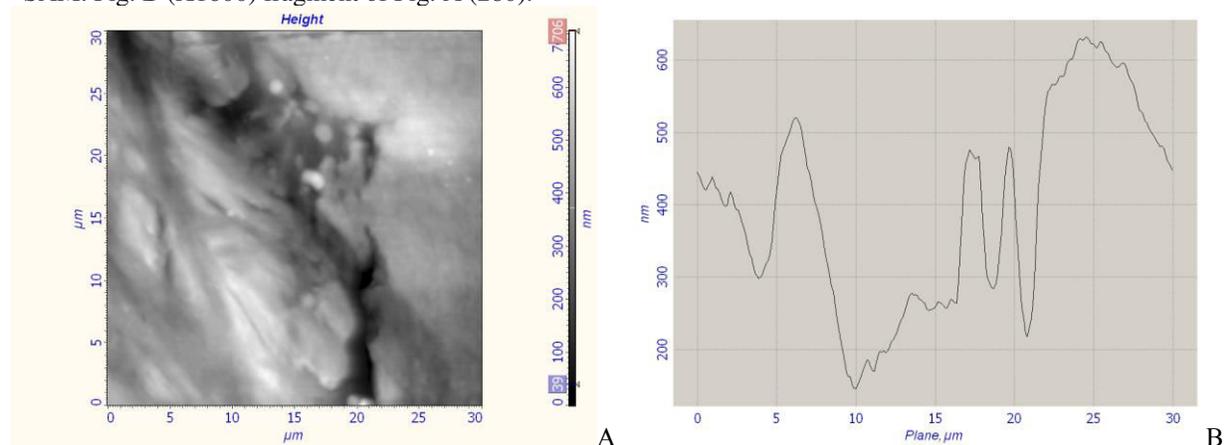


Figure 4. Fragment of the placenta of a woman with type 1 diabetes mellitus complicated by preeclampsia. There is a site with a sclerotized stem nap. In the vessel - a thrombosis. Atomic force microscopy. Fig. A three-dimensional image. Fig. B graphic image

All this makes a difficult condition of the fetus more difficult. The results of complex clinical, ultrasound and morphological studies and their comparison confirm the need for a comprehensive approach to the clinical morphology of the placenta.

#### SUMMARY:

Thus, we showed that the incidence of placental insufficiency among pregnant women with the 1st type of diabetes made 75%. The presence of pre-eclampsia caused the increase of this complication frequency to 100%. During the first type of diabetes, the changes in the placenta are characterized by an unstable balance between adaptive, aimed at the exchange improvement between a mother and a fetus, due to the improvement of the placental circulation, and disadaptation, having the character of alteration at all structural levels. The revealed leading mechanisms of placenta affection will allow to plan pathogenetically grounded schemes of placental insufficiency therapy among these patients.

The possibility of scanning electron microscopy (AFM) and Atomic force microscopy (AFM) in diagnostic, screening studies and as an express method makes it attractive for pathologists, cytologists and obstetrician-gynecologists.

#### REFERENCES:

1. Malyutina E.S., Petrukhin V.A., 2010. The influence of endocrinopathies (on the example of diabetes mellitus) on the development of uteroplacental relationships at various stages of pregnancy development. System analysis and management in biomedical systems, 9 (4): 830-833.
2. Evsyukova I.I., Kosheleva N.G. 2009. Diabetes mellitus: pregnant and newborn. M., 272 p.
3. Medved V.I., Bychkova I.A., 2009. Gestational diabetes: history and modernity. Rus. bulletin of Obstetrician-gynecologist, 3: 19-25.
4. Fedorova M.V., Krasnopolsky V.I., Petrukhin V.A., 2001. Diabetes mellitus, pregnancy and diabetic fetopathy. M.: 288.
5. Pavlova T.V., Kulikovskiy V.F., Pavlova L.A., 2016. Clinical and Experimental Morphology. M.: LLC "Medical Information Agency", 256 p.
6. Pavlova T., Petrukhin V., Malyutina E., Nesterov A., Pavlova L., Goncharov I., Kolesnikov D., 2012. Morphological features of the system mother-placenta-fetus during pregnancy on diabetes mellitus. *Virchows Archiv*, 461(Suppl 1):103.
7. Pavlova T., Malyutina E., Petrukhin V., Nesterov A., Bashuk I., Kolesnikov D., Goncharov,

I., 2015. Use of methods of scanning microscopy at pathology of placenta. *Virchows Archiv*, 67 (Suppl 1):1-144.

8. Pavlova T., Malyutina E., Petrukhin V., Nesterov A., Kolesnikov D., 2017. Morphogenesis of placenta at endocrinopathies (diabetes and thyroid pathology) in mother. *Virchows Archiv. The European Journal of Pathology. 29th European Congress of Pathology. Pathology for Patient Care 2 – 6 September 2017. RAI Amsterdam, The Netherlands. Virchows Archi.*, 471 (Suppl 1):328.
9. Baro, A.M., Reifenberger, R.G., 2012. Atomic force microscopy in liquid. *Biological Applications*: 1 edition: 189-190.
10. Cutchie, W.A., Cheung, N.W., Simmons, D., 2006. Comparison of international and New Zealand guidelines for the care of pregnant women with diabetes. *Diabetic Med.*, 460:26.