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Immunohistochemical features of the collagen' formation in the uterus of fetuses with a gestational term of 21-28 weeks from mothers, whose pregnancy was complicated by preeclampsia of different stage of severity

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Abstract

In the following article we are going to provide the results of research on uterus' structure in case of fetuses with a gestational term of 21-28 weeks from mothers, whose pregnancy was complicated by PE of different severity stage (15 cases) comparing to one in case of fetuses from mothers with a physiological pregnancy (15 cases). All fetuses have died intranatally as a result of an acute disorder in uterine-placental and uterine-fetal circulation. The research methods: macroscopic, organometric, histological, immunohistochemical, morphometric and statictical. By applying an organometric method we have revealed a probable decrease of indexes of weight, length and thickness of the uterine' wall in case of fetuses from mothers with PE comparing to ones in case of fetuses from healthy mothers. The observative histological research had not revealed any significant changes in the strucutre of the organs' wall in case of fetuses from the study groups. Thus, all organs were represented by mucous, muscular and serous membranes with a clear boundary between them. The comparative morphometric research had revealed the following features of the uterus' wall structure in case of fetuses from mothers with PE. The indexes of thickness of all structural

components of the organ's wall were clearly decreased comparing to ones in case of fetuses from mothers with a physiological pregnancy. In the uterine endometrium of fetuses from mothers with PE of moderate stage of severity the features of proliferative (hormonal) activity are taking place, however, in the meanwhile, in case of organs of fetuses from mothers with PE of severe stage of severity we could notice a probable decrease of glands' number as well as a lack of a proliferative activity in them (hypoplastic changes). By applying immunohistochemical method with using MCAT to CD 95 we have disclosed a probable increase of an apoptotic index in organs of fetuses from mothers with a complicated pregnancy towards one in case of fetuses from healthy mothers. Among the specific features of the uterine myometrium strucutre in case of fetuses from mothers with PE we could name the following ones: decrease of the vascular component percentage as well as increase growth of the connective tissue. Moreover, the structure of the connective tissue is represented mostly by the collagen of the III type, while, in case of organs of fetuses from healthy mothers the collagen of the I type prevails. In walls of the vessels of arterial type in case of uterus of fetuses from mothers with PE we could notice an increased glow of the collagen of the III type as well as a probable decrease of glow in case of collagen of the IV type. However, in case of organs' vessels of fetuses from healthy mothers we could notice an increse of glow of the collagen of the IV type. There is a fact, which attracts an attention to it. Namely, all aforementioned changes in the uterine wall in case of fetuses from mothers with PE are minimally manifested, when the mild course of disease took place, and was maximally manifested in case of severe one. All changes in the uterus in case of fetuses from mothers with PE of different stage of severity, that were postulated above, could contribute to formation of glanduar hyperplasia, endometrial polyps, precancerous diseases as well as endometrial cancer in the subsequent ontogenesis, as well as it could lead to impaired pregnancy and infertility. All aforementioned changes in organs of fetuses from mothers, whose pregnancy was complicated by PE of different stage of severity, were connected with changes in the vascular bed of the mother-placenta-fetus system as well as with endocrine disorders, that take place in case of this pathology, in the organism of pregnant woman.

Key words: fetus; pregnancy; uterus; collagen; preeclampsia.

The revelance of topic. The preeclampsia of pregnant women is a key problem of the modern obstetrics and gynecology [1, 2]. Thus, the mortality of pregnancy women and their fetuses in case of PE increases and reaches up to 11-15% among general number of cases [2, 3], while the frequency of development of fetuses, who have features of underdevelopment of

the different stages, reaches up to 80-85% [4, 5]. All vascular and endocrine changes, that had been described in the mother-placenta-fetus system in case of this pathology, are leading to gross violation of implementation and formation of the fetal internal organs [6, 7]. First of all, it applies to female genitals of fetuses [7, 8]. It is commonly known, that the PE could be manifested in case of girls, who were born from mothers that had this disease during the pregnancy [9, 10]. The modern literature also provides cases of development of the germinal function disorder as well as, even, primary infertility of offsprings from such mothers [10, 11]. Girls, who were born from women with PE, are classified at a risk group towards development of complications of pregnancy and future childbirth [9, 11]. However, despite of the problem's urgency, the immunohistochemical features of the uterus development in case of fetuses from mothers with PE have not been still studied.

The aim of research is to disclose main features of the collagen formation in uterus of fetuses with a gestational term of 21-28 weeks, who were born by pregnant women with preeclampsia of different stage of severity.

As **the research material** we have chosen 15 organs of fetuses from mothers, whose pregnancy was complicated by the PE of different stage of severity (group of comparison) towards 15 uterus of fetuses from mothers with a physiological pregnancy (main group). In the group of comparison we have provided the following distribution of fetuses relatively to the stage of the mother's PE severity: 5 fetuses from mothers with a mild course of the disease; 5 fetuses from mothers with PE of moderate stage of severity as well as 5 fetuses from mothers with PE of severe stage of severity. All fetuses had died intranatally as a result of an acute disorder of utero-placental and utera-fetal circulation on the gestational term of 21-28 weeks. The stage of the PE severity was aknown according to the medical documentation' data. Namely: we have evaluated indexes of the arterial pressure' level, amount of proteine in urine as well as a presence edema. The mothers of fetuses from the main group were healthy according to the medical cards of pregnant women.

Research methods: macroscopic, organometric, histological, histochemical, morphometric, statistical.

After removal organs were examined, as well as main sizes of the fetal uterine were measured. From every organ there were 2-3 pieces cut so, that all layers of the organs could be on a section. The material was fixed in a neutral formalin buffer solution in the aim of reducing the effect on tissues. Afterwards it was performed on alcohols of increasing concentration. In 24-48 hours the material was filled with paraffin [12]. From the manufactured blocks there were 2-3 section made with a thickness of 3-5 μm, as well as it

was stained by the histological (by hematoxylin and eosin) as well as histochemical methods (the Brache method, the Folgen-Rossenbeck method, the Schiff reaction).

In the aim of staining by histochemical methods pieces of tissues were fixed in the Carnois fluid (6 parts of an absolute ethanol, 3 parts of the chloroform, 1 part of the glacial acetic acid), which was prepared directly before the ovaries' fixation. At the end, the specimens were transferred to an absolute alcohol and were filled with paraffin.

In order to determine relative volumes of the main stractural components of the fetuses' uterine the sections were studied by morphometric methods.

The data was processed statistically on the personal computer by using following statistical packages „Excell for Windows", „Statistica 7.0. for Windows", „SigmaStat 3.1. for Windows"1 [13].

The results and discussion. In all cases the location of organ was typical. Namely: the body and the bottom of the uterus were situated in a pelvis major, while the cervix was situated in a pelvis minor. The fallopian tubes were extending from the lateral ends, while the ovarian ligament was attached to the posterior surface.

During macroscopic observation we have revealed the following data: the organs are pear-shaped, surface is smooth, grayish-bluish. On the section the organ's tissue is red with a moderate blood supply. On this stage of gestation uterus is represented by the body and the cervix. We have to notice, that the cervix occupies up to 3/4 of the general organ's length. The ratio of organ's body length and cervix length of uterus of fetuses from healthy mothers was 1:2,7l while the same indexes in case of fetuses from mothers with a complicated pregnancy this ratio was 1:2,8.

The average organometric indexes of fetuses' organs from the study groups are presented in the Table1.

By analyzing data from the Table 1 we could lead to the conclusion, that the average indexes of weight, length and thickness of organs of fetuses from mothers with PE are clearly decreased relatively to ones in case of fetuses from healthy mothers. Moreover, there is a fact, which attracts our attention. Namely, that the indexes were minimally decreased in case of fetuses from mothers with a mild stage of the PE severity, and were maximally decreased in case of fetuses from mothers with a severe stage of the PE.

The observative microscopic research on specimens, that had been stained by histological methods have revealed, that the uterus' wall in all cases was represented by endometrium, myometrium and perimetrium.

Table 1

The organometric indexes of organs of fetuses from the study groups with a gestational term of 21-28 weeks, (kg, m), M±m

Group	Parameter		
	Weight of uterus, kg	Length of uterus, m	Thickness of the uterus' wall, m
Main group	$3,24\pm0,11x10^{-3}$	$3,80\pm0,13x10^{-2}$	$7,25\pm0,18x10^{-3}$
Group of comparison/PE of the mild stage of severity	$2,95\pm0,10x10^{-3}$*	$3,53\pm0,12x10^{-2}$*	$6,74\pm0,24x10^{-3}$*
Group of comparison/ PE of the moderate stage of severity	$2,41\pm0,08x10^{-3}$*	$3,28\pm0,11x10^{-2}$*	$6,58\pm0,23x10^{-3}$*
Group of comparison/ PE of the severe stage of severity	$2,24\pm0,07x10^{-3}$*	$3,11\pm0,11x10^{-2}$*	$6,41\pm0,22x10^{-3}$*
KW ANOVA by Ranks test: H (2, N= 15)	0,9121463 p =0,7171	0,673560 p =0,6216	0,7551546 p =0,6855

Moreover, the boundary between layers is clearly distinguished in case of fetuses from the main group as well as in organs of fetuses from mothers with PE of the mild and moderate stages of severity. In the uterus of fetuses from mothers with PE of the severe stage of severity the boundary between layers was unclearly distinguished, while in couple of cases was absolutely impossible for distinguish. The indexes of thickness of main structural components of the uterus' wall of fetuses from the study groups are presented in the Table 2.

The data from the Table 2 is revealing a fact, that the muscular layer is prevailing in all observations. It means, that the thickness of the muscular component reaches higher indexes comparing to ones in case of mucous and serous membranes. There is a fact, which attracts our attention. Namely, there is a clear decrease of indexes of the thickness of main strucutral elements of the uterus' wall in case of fetuses from mothers with PE relatively to ones in case of fetuses from mothers, whose course of pregnancy was physiological one. Moreover, the maximal decrease of indexes could be noticed in case of fetises from mothers with the PE of the severe stage, while the minimal one could be noticed in case of the mother's PE of the mild severity.

Table 2

The indexes of thickness of main layers of the uterus wall of fetuses from the study groups on the gestational term of 21-28 weeks, (m)

Group	Thickness		
	endometrium	myometrium	perimetrium
Main group	2,57±0,09x10⁻³	3,14±0,11x10⁻³	1,54±0,04x10⁻³
Group of comparison/PE of the mild stage of severity	2,42±0,09x10⁻³*	3,02±0,10x10⁻³*	1,30±0,05x10⁻³*
Group of comparison/PE of the moderate stage of severity	2,38±0,08x10⁻³*	2,94±0,09x10⁻³*	1,26±0,04x10⁻³*
Group of comparison/PE of the severe stage of severity	2,33±0,18x10⁻³*	2,86±0,18x10⁻³*	1,22±0,04x10⁻³*
KW ANOVA by Ranks test: H (2, N= 15)	1,069527 p =0,5858	5,840708 p =0,0539	3,617061 p =0,1639

The structure of the musous membrane of organs was represented by superficial and deep layers, that correspond with basal and functional ones in case of an adult woman. Endometrium was covered with prismatic epithelium. The glandular component in organs of fetuses varies depending on the study group. Thus, in uterus of fetuses from mothers with s physiological pregnancy there are numerous tubular glands with proliferative activity in the superficial layer. In the deep layer there are single glands without manifestations of the proliferative activity, which are extending to 1/3 of the whole endometrium' thickness.

The glandular component in organs of fetuses from mothers with PE is changing as follows. Namely: in case of endometrium of fetuses from mothers with PE of the mild stage of severity there are a few glands without manifestations of the proliferative activity; in case of fetuses from mothers with PE of the moderate stage of severity there was a big amount of gland in the condition of the proliferative activity noticed; in case of the research towards fetuses from mothers with PE of the severe stage of severity there is a decreased number of glands noticed, while the proliferative activity is revealed only in single specimens.

By applying immunohistochemical methods with a use of MCAT to CD 95 we have revealed a number of an apoptotically altered cells in the endometrium of uterus of fetuses from the study groups. The average data on an apoptotic index is presented in the Table 3.

Table 3

The indexes of an apoptotic index in the endometrium of fetuses from the study groups, (%)

Group	The apoptotic index
Main group	14,72±0,52
Group of comparison/PE of the mild stage of severity	17,64±0,62*
Group of comparison/PE of the moderate stage of severity	19,27±0,67*
Group of comparison/ PE of the severe stage of severity	23,16±0,81*

Note. $p \leq 0,05$

By analyzing data from the Table 3 we could come up with the following solution. Namely, the indexes of an apoptotic index in the endometrium are clearly increased in case of uterus of fetuses from mothers with PE relatively to this data in case of organs of fetuses from healthy mothers. Moreover, we could observe also a direct relation between this index and the stage of the PE severity: the index reaches its maximum in case of fetuses from mothers with PE of the severe stage; while reaches its minimum in case of organs of fetuses from mothers with a mild stage of the PE.

The myometrium in all observations was represented by outer and inner layers. In the outer layer there are subserous and vascular zones. To the point, the subserous zone obtains 5-10% of the myometrium thickness in all cases, while the vascular one obtains 40-50% in walls of fetuses from mothers with a physiological pregnancy; 30-40% - in case of organs of fetuses from mothers with a complicated pregnancy. By applying the immunohistochemical method with a use of MCAT to main types of collagens we have postulated, that the collagens of the I and the III types are prevailing in the structure. The average indexes of the collagens glow in uterus of fetuses from the study groups are presented in the Table 4.

The data from the Table 4 is disclosing the fact, that there is prevalance of the collagen of the III type in a strucutre of uterus' myometrium in case of fetuses from the study groups. In organs of fetuses from mothers with a complicated pregnancy we could notice a clearly increased glow of both of the collagen of the I type, as well as one of the III type. Moreover, the intensity of glow varies according to the mother's PE's stage of severity. Namely, the maximal indexes are reached in case of fetal uterus of fetuses from mothers with PE of the

severe stage of severity, while the minimal ones are reached in case of mothers with PE of the mild stage of severity.

Table 4

The indexes of the glow' intensity of the collagens in the structure of the connective tissue of myometrium in the uterus of fetuses from the study groups on a gestational term of 21-28 weeks (conv.un.opt.dens.)

Group	The intensity of glow	
	collagen of the I type	collagen of the III type
Main group	0,177±0,006	0,215±0,008
PE of the mild stage	0,196±0,007	0,307±0,002
PE of the moderate stage	0,215±0,008	0,318±0,011
PE of the evere stage	0,217±0,008	0,327±0,012
KW ANOVA by Ranks test: H (2, N= 15)	12,465738 p = 0,0236	10,789624 p = 0,0485

The staining by picrofuxin by van Gieson in organs of fetuses from mothers with PE has revealed a fact of the connective tissue' growth around muscular fibers in the form of big red cells.

The vascular component of organs of fetuses from the study groups is represented by arteries and veins, in which by applying immunohistochemical method we have revealed a glow of the collagen of the IV type, indexes of which are reaching the following levels: in organs of fetuses from the main group - 0,134±0,005 conv.un.opt.dens., in case of fetuses from mothers with PE of the mild stage of severity - 0,127±0,004 conv.un.opt.dens., in case of fetuses from mothers with PE of moderate stage of severity - 0,110±0,004 conv.un.opt.dens., in case of fetuses from mothers with PE of severe stage of severity - 0,083±0,003 conv.un.opt.dens. By analyzing these data, we could come up with the following conclusion: the intensity of glow of the collagen of the IV type in organs of fetuses from mothers with a complicated pregnancy is clearly decreased relatively to one in case of fetuses from healthy mothers.

The perimetrium in all cases is represented by loose fibrous connective tissue, which is sometimes fused with mesothelium.

Thus, in this article we have presented histochemical features of the collagen formation in the uterus wall in case of fetuses with a gestational term of 21-28 weeks. We

have compared the uterus wall structure in case of fetuses from mothers with physiological pregnancy from one side, as well as in case of fetuses from mothers, whose pregnancy was complicated by PE of different stage of severity from the other one. It was postulated, that in case of organs' wall of fetuses from mothers with PE oppositely to organs of fetuses from healthy mothers the organometric indexes likewise indexes of thickness of main structural components were clearly decreased. In the endometrium of uterus of fetuses from mothers with a complicated pregnancy we could notice an increased apoptotic index. All changes, that were mentioned above, are determined mainly by vascular disorders in the mother-placenta-fetus system, that take place in case of this pathology [14, 15]. In the endometrium of fetuses from mothers with a complicated pregnancy we could notice also changes of amount and activity of the glandular component, which could be explained by endocrine disorders both as in the placental tract, as well as in the organism of pregnant woman [16, 17]. All changes, that have been postulated above could consequently lead to formation of the precancerous pathology and, even to the endometrial cancer [18, 19, 20].

In the myometrium of fetuses from mothers with a complicated pregnancy we could notice a decrease of the volume of the vascular component as well as a massive growth of the connective tissue, which was confirmed by the application of the immunohistochemical method. The disorder of maturing of the collagens as well as their intensified growth are determined by vascular and metabolic disorders in placenta in case of this pathology [21, 22, 23]. The level of clarity of aforementioned changes varies relatively to the stage of the mother's disease severity, which could be explained by the presence of more severe manifestations of the disease in case of PE of the moderate and severe stage of severity [24, 25].

Conclusions

1. The indexes of weight, length and thickness of the uterus wall in case of fetuses from mothers with PE are clearly decreased relatively to ones in case of fetuses from healthy mothers.

2. Under the prism of structure the uterus wall is formed correctly in all cases. In the uterus wall we could identify mucous, muscular and serous membranes. However, we could also notice, that the average indexes of thickness of the main strucutral components of the organ's wall in case of uterus of fetuses from mothers with PE are clearly decreased relatively to ones in case of fetuses from mothers with a physiological pregnancy.

3. The endometrium of uterus of fetuses from the study groups has a typical structure and is represented by two layers. However, speaking about mucous membrane of the

fetuses' organs in the group of comparison we could notice changes of amount and proliferative activity of the glands, that are differing relatively to the stage of the mother's disease's severity. The features of the clear proliferative activity are taking place in case of fetuses from mothers with a moderate stage of the PE severity; while in case of fetuses from mothers with PE of the severe stage of the severity we could notice a decrease in amount as well as a lack of the glands' proliferative activity. It means, that the structure of endometrium in case of fetuses from mothers with PE of the mild stage of the severity is close to one in case of fetuses from the group of comparison. In the meanwhile, in case of fetuses from mothers with PE of the moderate stage of the severity in endometrium we could notice features of the hormonal activity, that are characteristical for hyperplastic type of the organ's strucutre. In case of fetuses from mothers with PE of the severe stage of the severity though we could signify hypoplastic changes.

Moreover, in endometrium of fetuses from mothers with PE we have to underline an existance of the increased apoptotic index relatively to one in case of organs of fetuses from mothers with a physiological pregnancy.

4. In myometrium of the uterus of fetuses from the study groups we have revealed collagens of the I and III types. The intensity of glow of the collagens of the both types is clealry increased in case of uterus of fetuses from mothers with PE.

5. The main feature of the myometrium structure in case of fetuses from mothers with PE is a decrease of percentage of the vascular component in the strucure of layer as well as intensifying of the collagen formation in it.

6. In the walls of vessels of the fetuses' organs from mothers with PE we have revealed a decrease of intensity of glow of the collagen of the IV type relatively to organs of fetuses from mothers with a physiological pregnancy.

7. The maximal decrease of indexes, that had been evaluated in this article, takes place in case of organs of fetuses from mothers with a severe stage of the PE severity, while the minimal one takes place in case of the mild course of the disease.

8. All changes of the structural components of the uterus' wall of fetuses from mothers with PE of different stages of severity, that had been revealed, could consequently lead to formation of the glandular hyperplasia, endometrial polyps, precancerous diseases as well as endometrial cancer. Moreover, it could also lead to the disorder of the germinal function in the female organism.

9. The structural changes in uterus of fetuses from mothers with PE are determined, first of all, by changes in the vascular bed of the feto-placental complex as well as by endocrine disorders in the mother's organism, that take place in case of this pathology.

The perspectives of the future research. To disclose immunohistochemical features of the collagen formation in case of uterus of fetuses from mothers with PE of different stage of the severity with a gestational term of 29-36 weeks as well as 37-38 weeks.

References

1. Brewer J. Endothelin-1, oxidative stress, and endogenous angiotensin II: mechanisms of angiotensin II type I receptor autoantibody-enhanced renal and blood pressure response during pregnancy / J. Brewer, R. Liu, Y. Lu [et all] // Hypertension. – 2013. – № 62 (5). – P. 886-92.
2. Brown H. K. Biological determinants of spontaneous late preterm and early term birth: a retrospective cohort study / H. K. Brown, K. N. Speechley [et al.] // BJOG. – 2015. – № 122. – P. 491-9.
3. Cao B. Placental microbiome and its role in preterm birth / B. Cao, M. J. Stout [et al.] // Neoreviews. – 2014. – № 1. – P. 537-545.
4. Cheong J. N. Programming of maternal and offspring disease: impact of growth restriction, fetal sex and transmission across generations / J. N. Cheong, M. E. Wlodek, K. M. Moritz // Physiol. – 2016. – № 1. – P. 4727-40.
5. Chen D. B. Regulation of placental angiogenesis. / D. B. Chen, J. Zheng // Microcirculation. – 2014. – Vol. 21 (1). – P. 15-25.
6. Cignini P. Predictive value of pregnancy-associated plasma protein-A (PAPP-A) and free beta-hCG on fetal growth restriction: results of a prospective study / P. Cignini, L Maggio Savasta [et al.] // Arch. Gynecol. Obstet. – 2016. – № 293. – P. 1227-33.
7. Conley A. J. Review of the reproductive endocrinology of the pregnant and parturient mare / A. J. Conley // Theriogenology. – 2016. – № 1. – P. 355-65.
8. Contreras-Villarreal V. Reproductive performance of seasonally anovular mixed-bred dairy goats induced to ovulate with a combination of progesterone and eCG or estradiol / V. Contreras-Villarreal, C. A. Meza-Herrera [et al.] // Anim. Sci. J. – 2016. – № 87. – P. 750-5.
9. Dakouane-Giudicelli M. Inhibition of human placental endothelial cell proliferation and angiogenesis by netrin-4 / M. Dakouane-Giudicelli, S. Brouillet [et al.] // Placenta. – 2015. – № 36. – P. 1260-5.

10. Dessì A. The biomarkers of fetalgrowth in intrauterine growth retardation and large for gestational age cases: from adipocytokines to a metabolomic all-in-one tool / A. Dessì, C. Pravettoni, F. Cesare Marincola [et al.] // Expert. Rev. Proteomics. – 2015. – № 5. – P. 1-8.

11. Fatima U. Foetal autopsy-categories and causes of death / U. Fatima, R. Sherwani [et all] // Clin. Diagn. Res. – 2014. – № 8. – P. 105-8.

12. Gailly-Fabre E. Pregnancy-associated hormones and fetal-maternal relations / E. Gailly-Fabre, V. Kerlan, S. Christin-Maitre // Ann. Endocrinol (Paris). – 2015. – № 76. – P. 39-50.

13. George E. M. Endothelin as a final common pathway in the pathophysiology of preeclampsia: therapeutic implications / E. M. George, A. C. Palei, J. P. Granger // Curr. Opin. Nephrol. Hypertens. – 2012. – № 21 (2). – P. 157-62.

14. Grabar' V. V. Interconnection between assisted reproductive technologies, pregnancy complications and risk of birth defects / V. V. Grabar' // Georgian. Med. News. – 2014. – № 227. – P. 7-14.

15. Hahn S. Biomarker development for presymptomatic molecular diagnosis of preeclampsia: feasible, useful or even unnecessary? / S. Hahn, O. Lapaire, N. G. Than // Expert. Rev. Mol. Diagn. – 2015. – № 16. – P. 1-13.

16. Heyward C. Y. The decidua of preeclamptic-like BPH/5 mice exhibits an exaggerated inflammatory response during early pregnancy / C. Y. Heyward, J. L. Sones [et al.] // Reprod. Immunol. – 2017. – № 120. – P. 27-33.

17. Henriques A. C. Endothelial dysfunction after pregnancy-induced hypertension / A. C. Henriques, F. H. Carvalho [et al.] // Int. J. Gynaecol. Obstet. – 2014. – № 124. – P. 230-4.

18. Jauniaux E. The role of oxidative stress in placental-related diseases of pregnancy / C. Y. Heyward, J. L. Sones [et al.] // Gynecol. Obstet. Biol. Reprod. (Paris). – 2016. – № 45. – P. 775-785.

19. Kanawaku Y. An autopsy case of a pregnant woman with severe placental and fetal damage from domestic violence / Y. Kanawaku, S. Takahashi [et al.] // Am. J. Forensic. Med. Pathol. – 2015. – № 36. – P. 125-6.

20. Katzman P. J. Chronic inflammatory lesions of the placenta / P. J. Katzman // Semin. Perinatol. – 2015. – № 39. – P. 20-6.

21. Kwak-Kim J. Y. T helper 1 and 2 immune responses in relationship to pregnancy, nonpregnancy, recurrent spontaneous abortions and infertility of repeated

implantation failures / J. Y. Kwak-Kim, A. Gilman-Sachs, C. E. Kim / Chem. Immunol. Allergy. – 2015. – Vol. 88. – P. 64-79.

22. Lambert G. Preeclampsia: an update / G. Lambert, J. F. Brichant [et al.] // Acta Anaesthesiol. Belg. – 2014. – № 65. – P. 137-49.

23. Lambert G. Preeclampsia: an update / G. Lambert, J. F. Brichant [et al.] // Acta Anaesthesiol. Belg. – 2014. – № 65. – P. 137-49.

24. Ling L. Evaluation of plasma endothelial microparticles in pre-eclampsia / L. Ling, H. Huang [et al.] // Int. Med. Res. – 2014. – № 42. – P. 42-51.

25. Masoura S. Biomarkers of endothelial dysfunction in preeclampsia and neonatal morbidity: a case-control study / S. Masoura, I. Kalogiannidis [et al.] // Eur. J. Obstet. Gynecol. Reprod. Biol. – 2014. – № 175. – P. 119-23.