JOURNAL OF PURE AND APPLIED MICROBIOLOGY, Sept. 2015. Vol. **9**(3), p. 1943-1950

Influence of Genital Infection on Fetoplacental Complex

Akylbek Tussupkaliyev, Assembay Salamat, Nurlan Zhubanyshev, Dinara Bokenbay and Nurbek Isbussinov

West Kazakhstan Marat Ospanov State Medical University,
Republic of Kazakhstan. Aktobe city, 030000, Maresieva str., 68.

(Received: 17 March 2015; accepted: 23 April 2015)

To evaluate morphological status of placentas with genital infection. The material of the study included 50 placentas from women with genital tract infection (the study group). The control group consisted of 20 placentas from pregnant women without genital tract infection with uncomplicated pregnancy and labor. Based on the results of our study, we can conclude that infection penetrates into the amniotic cavity leading to chronic fetal hypoxia. Spasm and swelling of placental villi, leukocyte infiltration, fibrinoid necrosis, cleavage of the endoplasmic reticulum, basement membrane thickening, disturbed gas exchange between mother and fetus develop on the background of growth of bacterial population in the amniotic fluid caused by toxemia, hyperthermia and local action of pathogen enzymes. These structural placental changes lead to tissue hypoxia of the metabolic origin. Intrauterine infection of fetus can develop only in case of violations of permeability of placental barrier mechanisms for microorganisms. Permeability of protective physiological membranes disrupts because of degenerative changes and involvement of the placenta in the inflammatory process.

Key words: Genital infection, Pregnancy, Placenta, Intrauterine infection, Parturient women.

Study of the normal microflora of female genital tract is a complicated and time-consuming process. However, it is the important practical section of clinical biology because on the one hand autoflora interaction with pathogens plays an important protective role in purulent inflammatory diseases of the genital organs (Ankirskaya, Gurtovoy and Elizarova, 1989; Mammadaliyeva and Isenova, 1999). On the other hand, the species and quantity composition of mucous membranes of the microorganisms is controlled both by endocrine and immune systems depending on their condition. Modern infection diseases in obstetric and gynecologic patients are caused by autoflora with the predominance of mixed (anaerobic and anaerobic/aerobic) suppuration (Barashnev, Antonov and Kudashov, 1994), and not monomicrobic (aerobic or anaerobic) one.

Progressive growth of infectious pathology of fetus and newborn is one of the most important problems of modern perinatology (Lavrova, Samsygina and Mikhailova, 1997).

The increasing frequency of genital inflammation leads to an increase in intrauterine infection of fetus. Its frequency varies from 6% to 30% (Raisova, 1995, Mukasheva, 1995) and causes an increased perinatal morbidity and mortality. Specific weight of intrauterine infection in the structure of perinatal mortality ranges from 28% to 65% (Tussupkaliev, 2004). The proportion of intrauterine infection in the structure of early neonatal morbidity ranges from 5.3% to 27.4% (Koroleva and Kolobov, 2007), while the rate of stillbirth is equal to 16.8-40% (Tussupkaliev, 2004).

Under the term “genital tract infections” we mean a wide range of inflammatory processes of the upper and lower genital tract including

* To whom all correspondence should be addressed.
E-mail: tusupkaliev-akyl@mail.ru

sexually transmitted diseases. Causative agents of genital tract infections are the following pathogens: gram-positive and gram-negative cocci, gonococci, trichomonas, chlamydia, gardnerella, cytomegalovirus, opportunistic pathogens, Candida species, etc. (Tussupkaliev, 2001).

This is the genital tract infection that is one of the causes of miscarriage, antenatal and postnatal death of fetus and newborn, preterm rupture of membranes followed by consequent complications of labor (Nisevich and Talalaev, 2008).

An upward path is considered to be the main route of the fetal infection from mother's urogenital tract (Kravtsova and Bragina, 2003). Under certain conditions the infection can penetrate into the amniotic cavity through intact amniotic membranes causing inflammation (chorioamnionitis) and fetal intrauterine infection (Sushko, Novikova and Tupkova, 1998).

Intrauterine infection is often hidden behind such diagnoses as intrauterine hypoxia, asphyxia, intracranial injury (Evsyukova, Patrusheva and Savicheva, 1995; Strunina, 1993; Fomicheva, Zarubina and Minaev, 1997). Many infectious and inflammatory diseases during pregnancy have common signs: infection of fetus and newborn may be caused by an acute infection of the mother and activation of chronic, persistent infection during the pregnancy; a large part of diseases of pregnant women, resulting in intrauterine infection, occur in latent or subclinical form; activation of persistent infection is possible in case of any violation of homeostasis in the body of a pregnant woman (Lavrova, Samsygina and Mikhailov, 1997).

Given non-specific clinical manifestations of intrauterine infections during pregnancy, their diagnosis is difficult in most cases. It may be possible by combination of clinical, laboratory and instrumental methods. Main pathogenetic mechanisms of fetal condition violation except infectious factors are the following: metabolic changes, immune system disorders, dysfunction of fetoplacental complex (Anastasieva, 1997).

According to a number of papers, fetoplacental insufficiency develops in 24-33.8% of women (Fomicheva, Zarubina and Minaev, 1997; Vedeneev, 1997) in the group of pregnant women being at high risk of intrauterine infection. Infectious and inflammatory diseases of pregnant women adversely affect all parts of fetoplacental complex. Infection of the ovum is often accompanied or followed by abortion or fetal growth retardation (Anastasiev, 1997, Serov, Manukhin and Kuzmin, 1997; Fuks & Griban, 1991). Objective of the study: to evaluate morphological status of placentas affected with genital infection.

METHODS

The material of the study consisted of 50 placentas from women with genital infection (study group). The control group consisted of 20 placentas of pregnant women without genital infection, having uncomplicated pregnancy and labor.

Macrophotometric, histological and histochemical, and microphotometric methods were used in the study. The study of placenta was conducted according to the methodical recommendations "Postmortem examination of the placenta" (Almaty, 1994) authored by A.M. Belinskaya *et al*. and carried out in the pathomorphological laboratory of the Research Centre for Maternal and Child Health Ministry of the Republic of Kazakhstan.

Macrophotometric study included determination of placental mass, area, length and place of the umbilical cord attachment. We described the appearance of maternal and fetal surface of the placenta, determined its shape, the presence of additional lobes, limbus and seals on the placental surface. We paid a particular attention to the structure of the lobes, the presence of blood clots, infarctions, hemorrhages, and calcifications on the maternal surface. We also described the state of fetal membranes - their color, clarity, and impregnation by meconium.

Following the visual examination, we excised 6-8 pieces from each placenta which were fixed in 10% neutral formalin and Carnoy's solution, processed through alcohols of increased strength, and embedded in paraffin. 5 µm sections were stained with hematoxylin and eosin by the method of Van Gison, Mallory. Argyrophilic fibers were stained by Foot method, and fibrin was stained by Shueninov. Neutral glycosaminoglycans were detected by periodic acid Schiff reaction by Shabadash with processing of sections by salivary

amylase. Acidic glycosaminoglycans were detected by staining sections in 0.5% toluidine blue solution specially selected in phosphate buffer at different pH (2.3 and 4.7).

In order to determine the area of afunctional zones, terminal villi and immature forms of chorionic villi, we performed stereomorphometric study of the volumetric ratios of structural components of the placenta via the ocular grid for cytological studies by the method of Avtandilov G.G. (1973).

RESULTS

Results of macromorphometric studies indicate that the mass of the placenta in women with genital infection (651.05 + 18.2) g was significantly higher ($p < 0.05$) than in the control placentas (556.5±10.3) g, it had less area (274.26±7.1) cm vs (315.24±8.6) cm ($p < 0.05$).

During macroscopic study in 50% of cases of the study group the placenta had a modified form (triangular, bean-shaped, square) with tortuous, thin margins, and focal seals of yellow color on the fetal surface of placenta - 1x2 cm and 2x2.5 cm in size. 30% of placentas had a limbus or protuberance. Margin and intermediate attachment of the umbilical cord were predominate in 80% of cases. On the maternal surface of all placentas there were blood clots, petrifications, focal hemorrhages and infarction zones located around the periphery of the placenta. In all cases sulci and gyri on the maternal surface of placenta were poorly developed, lobes had small and medium size, there were large areas of tissue with the size of 6x5 and 8x5 cm divided into lobules. In 1/3 of cases fetal membranes are thickened, swollen with small focal hemorrhages, impregnated with meconium, have yellow-green, dull color. In 70% cases placentas were thin, translucent, shiny.

Microscopic examination of placentas in pregnant women with genital infection in preterm labor (in term of 30-34 weeks) (n = 22) revealed common disorders of uterus-placental circulation. It was manifested by a dramatic increase in the lumen of the decidua basalis vessels, uneven plethora, and thickening of blood vessels walls. Decidual cells were degenerated with extensive foci of necrosis and fibrinoid deposition.

Stroma with significant edema and focal hemorrhages. Fibrinoid (Nitabuch's) layer is thickened. It is adjacent to clots, vast fields of fibrinoid with necrotic immured chorionic villi and calcification foci. Diffuse and focal lymph leukocyte infiltrations were revealed in the decidua basalis in all cases. This indicates that there is considerable inflammation in the basal plate of the placenta (Figure 1).

Intervillous space is narrowed, contains common loci of bleeding, blood clots, fibrinoid fields and cobs, chorionic villi that are close to each other. Afunctional parenchyma composes 30-35% of the area of the placenta.

Small, single-row terminal villi constitute 28-30% of the area of the placenta. They are covered with cynthium, fibronized stroma. Capillaries are dilated and plethoric. Endothelium lining the walls of blood vessels is thickened, with large nuclei prominating in the vessel lumen. The basal membrane of syncytium and capillaries is thickened, sclerotic. Argyrophilic fibers are thickened. Small focal hemorrhages can be often

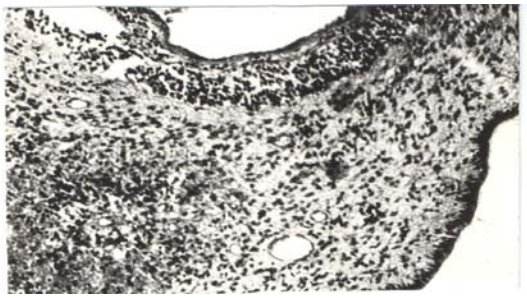

Fig. 1. Diffuse leukocyte infiltration of chorionic plate

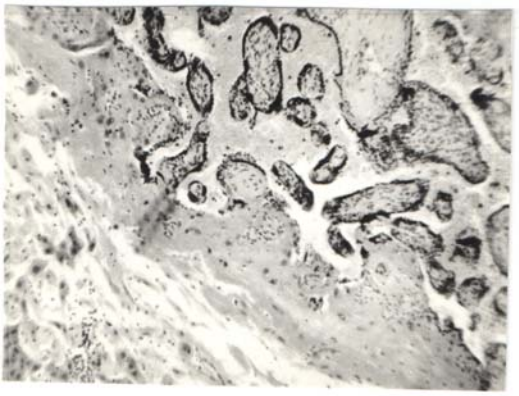

Fig. 2. Dystrophy of decidual cells with foci of extensive necrosis and vast fibrinoid fields.

seen in the stroma of villi. Syncytium and capillaries membranes are rare (1-2), with isolated, calcified syncytial nodes.

Intermediate mature and immature chorionic villi constitute 40-45% of the placental area. Villi are large, round and oval-shaped, do not contain capillaries, coated with two-row epithelium (syncytio- and cytotrophoblast) with loose edematous stroma, containing single Kashchenko-Gofbauer cells (immature intermediate villi).

Mature intermediate villi are large, shapeless. They have numerous branches containing small centrally located capillaries. Villi do not form syncytiocapillar membranes. They are covered with a single syncytium layer. Sometimes it proliferates forming syncytial nodes. The stroma of villi consists of fibrocytes and fibroblasts, often edematous.

In the stem villi and in chorionic plate there is considerable sclerosis of the stroma with focal edema and hemorrhages. Lumen of blood vessels is dilated, plethoric. Blood clots can be often seen in the lumen. Syncytium covering the stem villi is desquamated on considerable extent and replaced with fibrinoid. Leukocyte infiltration of blood vessels walls and chorionic plate stroma was considerable in all the cases studied.

Fetal membranes are thickened, edematous. Amnion epithelium is thinned, desquamated on considerable extent. Its stroma is unfibered and swelled. This is also a manifestation of the inflammatory process.

Parietal decidua with discompensation of decidual cells, extensive necrosis and hemorrhages. In all cases there is diffuse inflammatory infiltration of leukocytes and lymphocytes in the membrane stroma. Signs of placentitis were revealed in 46.6% of all placentas studied, and in 40% of amnion samples.

Thus, the morphological study of placentas from 22 women with genital infection being in preterm labor in term of 30-36 weeks indicates severe disorders of uterus and placental circulation as well as severe degenerative changes in all structural components of the placenta due to inflammatory infiltration of decidua and chorionic plate membranes. This manifested as local and diffuse seropurulent basal deciduitis, chorioamnionitis and inflammation of membranes. In addition to these changes, there is a decrease in compensatory adaptive processes in the placenta: a decrease in the area of terminal villi, capillaries and syncytiocapillar membranes. There is also an increase in the area of immature forms of chorionic villi. Morphological changes detected in the placenta allow to think about decompensated form of chronic placental insufficiency in pregnant women with genital infection in 66.6% of cases. This leads to premature birth.

Microscopic study of placentas (28) of pregnant women with genital infections and urgent delivery in term of 39-40 weeks revealed similar changes in the placenta. These included circulatory disorders and degenerative changes to maternal and fetal parts of the placenta. The degree and extent of these changes depended on the severity and duration of obstetric and extragenital pathology in these women.

In 3 cases the morphological changes were focal and were moderately expressed. In these placentas we revealed mild thickening of the basal plate. Decidual cells were large and small without clear boundaries, had hyperchromatic nuclei and clear cytoplasm. Mostly they have been replaced by fibrinoid. Stroma was edematous. The lumen of blood vessels was filled with blood, blood vessels walls were thin. Intervillous space uneven: some dilated in some areas and narrowed in others. In subchorial and subbasal departments there were old and fresh bleeding, blood clots, excessive fibrinoid depositions, and small calcifications. In the other zones of intervillous space there were visible focal hemorrhages, fibrionoid cobs and small clots. Small terminal villi were dominated. They constitute 50-55% of the placental area, while immature forms of chorionic villi constitute 15-20% of the placental area. In the terminal villi we observed focal stromal edema, capillary angiomatosis, and thinning of syncytium.

The number of syncytiocapillar membranes was from 1 to 3 in each villus. In the stem villi and in the chorionic plate there was moderate hardening of the stroma. Lumen of blood vessels was moderately dilated and narrowed in some areas. It was filled with blood unevenly. Vessel walls are thickened and have severe perivascular sclerosis. Amnion that covers chorionic plate has single row, prismatic epithelium, with a light foamy cytoplasm and large hyperchromatic nuclei. In the fetal membranes there was moderate edema and

small focal hemorrhages.

In 4 placentas the described morphological changes were more considerable and were widespread. In the basal plate there was dystrophy of decidual cells with multiple necrosis and extensive fibrinoid deposits (Figure 2).

Sclerotic edematous stroma. Vascular lumen are narrowed, dramatically dilated and congested in some places. Visible focal hemorrhage around the vessels. Fibrinoid layer is thickened unevenly. Old and fresh foci of bleeding, blood clots, fibrinoid are adjacent to it. Intervillous space is narrowed due to the proximity of the villi, bleeding, blood clots, excessive fibrinoid deposition. Afunctional zones constitute 20-25% of the area of placenta. Terminal villi are small, closely spaced. Syncytium is thinned, with degenerative changes.

They constitute 45-50% of the total area of the villi. The stroma of terminal villi is sclerotic, with signs of focal edema. Each villus has 4-6 capillaries. They are located both in the center and at the periphery. The basal membrane of capillaries and syncytium is thickened, and sclerotic. There are 1-2 syncytiocapillar membranes and in some villi they are absent. The severity of morphological changes to placenta increases in pregnant women with genital infection and obstetric pathology.

Microscopic study of the placenta from 21 pregnant women with genital infection revealed considerable circulatory problems and alternative-dystrophic changes of maternal and fetal part of the placenta. In the basal plate the majority of decidual cells are destroyed. Preserved decidual cells are small and arranged in small groups among the vast fields of fibrinoid.

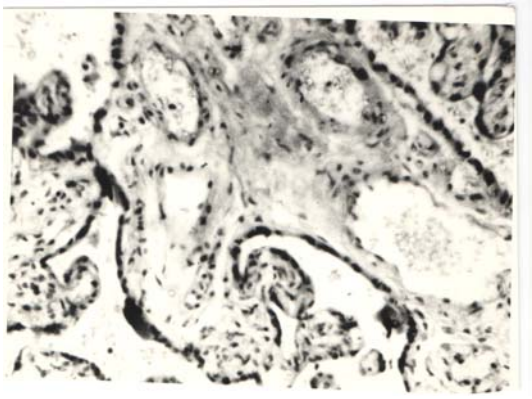

Fig. 3. Capillary walls are thickened, subepithelial and subendothelial membranes are thickened, stroma is sclerotic

Walls of vessel are thickened, sometimes loosened. Visible focal hemorrhages around the vessels (Figure 3).

Edematous stroma. Nitabuch's fibrinoid layer looks like a broad band with small and medium-sized petrifications. Intervillous space is unevenly narrowed with widespread hemorrhage and massive deposits of fibrinoid surrounding large areas of villi, blood clots, petrifications. Afunctional zones constitute 30-35% of the placental area.

Terminal villi are small with irregular full-blooded capillaries coated with a single layer of thinned syncytium with focal nuclear pyknosis. Capillary walls are thickened, with proliferating endothelium. Subepithelial and subendothelial membranes are thickened dramatically, sometimes homogenized. Stroma of terminal villi is sclerotic, sometimes there is visible focal hemorrhages. Terminal villi constitute 35-40% of the area. The number of mature and immature forms of intermediate villi is increased. Such villi constitute 30-35% of the total area.

Considerable stromal sclerosis, focal hemorrhages in the stem villi and chorionic plate. Walls of the blood vessels are thickened considerably due to hypertrophy of the muscle layer with narrowing and obliteration of the blood vessels lumen. Swollen endothelium proliferates in the lumen. Considerable muff-like sclerosis around vessels. There is plasmatic impregnation and fibrinoid necrosis in the vascular wall.

Amnion - epithelium is single-row, cylindrical, there are groups of necrotic cells. Underlying stroma is unfibired, edematous. Fetal membranes are thickened, edematous. Amnion epithelium has a single row, flattened, at the considerable distance it is desquamated or necrotic. In 21 cases we observed focal or diffuse leukocyte infiltration of fetal membranes. In 10 placentas there was leukocyte infiltration of chorionic plate - basal decidua plate and focal infiltration of intervillous space by segmented leukocytes. Silver impregnation revealed melting or considerable thickening, roughening of argyrophilic frame of villi, chorionic plate, subepithelial and subendothelial villi membranes.

Histochemical studies revealed glycogen

in the epithelium of the amnion and decidual cells at the basal plate in the form of individual grains. Periodic acid Schiff reaction positive and basophilic granulosity in the syncytiotrophoblast is weak. On staining with toluidine blue there was increased metachromatic reaction in the stroma of the villi surrounded by fibrinoid.

DISCUSSION

The conducted comprehensive morphological study of placentas from parturient women with genital infection indicates severe disorders of maternal and fetal circulation and a high degree of damage to the structural components of the placenta, reduced compensatory-adaptive reactions, reduced area of terminal villi, capillaries, syncytiocapillary membranes and increased immature forms of chorion and afunctsional zones.

These changes were observed in all cases and increased in co-infection of genital and obstetric pathology. At the same time there was leukocyte infiltration of basal and chorionic plate, intervillous space and fetal membranes, resulting in widespread and more severe pathological changes to the placenta. The revealed morphological changes underlie the development of chronic placental insufficiency in 74%. It may be present by subcompensated (90.6%) and decompensated (9.3%) forms. Focal diffusive placentitis was detected in 17.1%, seropurulent deciduitis in 37.4% cases, and amnionitis in 6.2% of cases of the full-term pregnancy.

During the morphological study of placentas from 20 women with uncomplicated pregnancy an average weight of the placenta was (556.5 ± 10.3), the area was (308.24 ± 8.66) cm. Placenta had round or oval form with smooth edges. The surface of fetal part of the placenta is gray-pink, shiny. Maternal surface is gray-red, has medium-sized lobules. Sulci are well-defined, there are small blood clots on the surface. Tissue is gray-red, friable, homogeneous. Fetal membranes are translucent, smooth, shiny. In 70% of cases the attachment of the umbilical cord is central, in 30% of cases it is off-center.

The microscopic examination revealed that the basal plate consists of a narrow layer of decidual cells of a round shape, with round hyperchromatic nuclei. Their cytoplasm is weakly basophilic, contains moderate amounts of glycogen. Degenerative changes to individual cells. Blood vessels are moderately dilated, lined with flattened trophoblast. Nitabuch's fibrinoid layer is presented as a narrow band with unevenly distributed preserved cytotrophoblast cells.

Intervillous space is unevenly dilated, free of blood. Depositions of red blood cells in some places of the subchorial zone. Also there are small focal hemorrhages. Terminal villi are small and constitute up to 60-70% of the plentha area. They are coated with one layer of syncytiotrophoblast. It produces separate thickening with nuclei clusters (syncytial nodes) and protuberances penetrated by stroma and capillaries (syncytial gemmas).

Stroma of terminal villi is friable, contains fibrocytes and fibroblasts. 1-3 capillary vessels are adjacent to syncytium, forming syncytiocapillar membranes. Some of them are dilated, filled with blood, and some - with free or collapsed space.

Villi are of large size, with fibrozed stroma. Lumens of many vessels are narrowed due to thickening of the wall, and sometimes dramatically dilated and plethoric. Epithelial cover lining large villi is replaced by fibrinoid in some places. Chorionic plate consists of connective tissue with numerous collagen fibers and uniform composition of cells - fibroblasts, histiocytes. Lumens of the blood vessels are dilated and filled with blood. The vessel wall has a well-defined muscle membrane lined with flattened endothelium. Langans' fibrinoid layer (not amnion one) is single-row, cylindrical, thickened, vacuolated. Its thickness is equal, sometimes contains small calcifications.

On staining of preparations by Van Gieson in the stroma of terminal villi there is a weak phukinofilia. It increases around the vessels. Fibrinoid structure of the stroma, basal membrane of amnion and chorionic villi with mild collagenization. This can be visualized by Foote method silvering. Metachromatic staining is absent in the stroma of terminal villi on staining with toluidine blue. There is just a weak diffuse staining in individual stem villi. Neutral glycosaminoglycan can be detected under chorionic as a wide plate revealed in periodic acid Schiff reaction. A small amount of them can be found in the intervillous space on the periphery of individual villi. Glycogen depositions in the form of fine grain were observed

in the epithelium of the amnion, chorionic plate, decidual cells, and in walls of fetal blood vessels.

Morphological structure of placenta in patients with uncomplicated pregnancy is characterized by a high degree of preservation and pronounced compensatory-adaptive reactions.

Comparison of the morphological picture of placentas of women with genital infection with the data of ultrasonic placento- and fetometry and microbiological studies in case of amniotic waters infection showed that there was more pronounced degree of circulation violation with swelling and spasm of the villi, fibrinoid necrosis, leukocyte infiltration in almost all cases of intraamniotic infection. Correlation coefficient of intraamniotic infection and fetoplacental insufficiency was 0.8 ($p < 0.05$), intraamniotic infection and afunctional zones - $r=0.64$ ($p < 0.05$), intraamniotic infection and the area of immature villi - $r=0.68$ ($p < 0.05$).

Thus, the infection of genital tract, after penetration in the internal genitals (in this case in the uterus), affects the placenta in 60.7% cases causing diffuse placentitis - 17.1%, seropurulent deciduitis - 37.4%. Morphological manifestations of inflammation of the placenta are the following: leukocyte-lymphocytic infiltration, reducing the area of terminal villi, capillaries, syncytiocapillary membranes and increased immature forms of chorion and afunctional zones.

Deep lesions of the placenta were manifested morphological by melting of chorionic plate, and villi membranes leading to the development of chronic fetoplacental insufficiency in 74% of cases. In 47.9% of cases of decompensated form of chronic fetoplacental insufficiency pregnancy ends with premature birth, while compensated forms of chronic fetoplacental insufficiency in women with genital infection usually end with a term labor.

Table 1. Microbial flora (predominant) of placenta in case of amnionitis and placentitis.

	Staphylococci	*Candida species*	*E. coli*
Placentitis	14%	14%	8%
Amnionitis	8%	4%	4%

Thus, we traced the association between placentitis and amnionitis rate on the background of positive bacterial cultures indicating that in 22% of cases there were staphylococci, in 18% of cases - Candida species and in 12% of cases - E.Coli (Table 1).

CONCLUSION

The analysis of our own results and literature data allowed us to conclude that the infection, having penetrated into the amniotic cavity, leads to chronic fetal hypoxia. Its mechanism is the following: growth of bacterial population in the amniotic fluid due to toxemia, hyperthermia and local action of pathogen enzymes. This leads to spasm and swelling of the villi of the placenta, their leukocyte infiltration, fibrinoid necrosis, cleavage of the endoplasmic reticulum, basement membrane thickening, and disturbed gas exchange between mother and fetus. These structural changes lead to placental tissue hypoxia of the metabolic origin. Intrauterine infection of fetus is possible only in case of violation of permeability of the placenta barrier mechanisms for microorganisms. Permeability of physiological placenta barrier mechanisms is violated in case of degenerative changes and involvement of the placenta in the inflammatory process (Ilizarov *et al.*, 2009).

Gas exchange between mother and fetus is disturbed in case of inflammation of the placenta. Chronic intrauterine hypoxia develops, which is usually accompanied by intrauterine growth retardation. There is disturbed circulation of maternal and child part of the placenta. The decrease in uterine vascular blood flow by 50% is proven experimentally and clinically. It leads to the deterioration of placental hemodynamics and the first signs of fetal hypoxia. Structural and functional changes in the placentas were revealed in case of bacterial, fungal and other infections of mother genitals. This explains why the fetus suffers from acute and then from chronic hypoxia on the background of the infectious agent persistence (Zinserling & Melnikova, 2002).

Severe changes to the nervous tissue of fetus develop when the partial pressure of oxygen

in the fetal blood decreases by 60-70% or more for 8-10 minutes (hypoxic encephalopathy). Intrauterine hypoxia causes necrosis and hemorrhages in the hypothalamic nuclei of the brain stem: maturation of lung surfactant is violated due to the affection of regulation centers responsible for the development of the respiratory system. This leads to respiratory-distress syndrome. Intranatal hypoxic-anemic encephalopathy often leads to severe neurological damages in postnatal period.

REFERENCES

1. Anastasieva, V.G. *Morphological and functional changes in the fetoplacental complex in case of placental insufficiency* (pp. 506). Novosoibirsk: Publisher "media sphere" 1997.
2. Akirskaya, A.S., Gurtovoy, B.L., & Elizarova, I.P. Intrauterine bacterial infection of the fetus and newborn. *Obstetrics and Gynecology,* 1989; **5**, 70-77.
3. Barashnev, Y.I., Antonov, A.G., & Kudashov, N.I. *Obstetrics and Gynecology,* 1994; *:* 26-31.
4. Vedeneeva, G.N. *Characteristics of cytomegalovirus infection in pregnant women and newborns* (Synopsis of thesis of Candidate of Medical Sciences, pp. 62). St. Peterburskogo State University named after Academician Pavlov, 1997; St. Petersburg.
5. Evsyukova, I.I., Patrusheva, E.N., & Savicheva, A.M. Actual problems of clinic, diagnosis and treatment of chlamydial infection in newborns. *Obstetrics and Gynecology,* 1995; **1***:* 18-21.
6. Ilizarova, N.A. *et al*. Pathological examination of the villi in patients with placental insufficiency of infectious origin. *Bulletin of the Siberian Branch of the Russian Academy of Medical Sciences,* 2009; **5**: 92-96.
7. Koroleva, L.I., & Kolobov, A.V. Morphological and functional characteristics of the placenta in case of intrauterine infection of term newborns by DNA viruses. *Journal of Obstetrics and gynecological disorders,* 2007; **3***:* 31-36.
8. Kravtsova, G.I., & Bragina, Z.N. *Pathology of the pregnancy. Pathology of the placenta: method. Recommendations* (pp. 27); 2003: Bragina. Minsk.
9. Lavrova, D.B., Samsygina, G.A., & Mikhailov, A.V. Etiology and indicators of high risk of intrauterine infection of fetus. *Pediatrics,* 1997; **3**: 94-99.
10. Mukasheva, G.K. The role of different intrauterine viral infections in the development of fetus and newborn pathology (Synopsis of thesis of Candidate of Medical Sciences. Moscow 1995.
11. Mammadaliyeva, N.M., & Isenova, S.Sh. Miscarriage of infectious genesis. Selected lectures on clinical obstetrics and gynecology (pp. 77-111). Almaty: Form Plus Almaty 1999.
12. Nisevich, L.L., & Talalaev, A.G. Intrauterine infection: mother-placenta-fetus. *Paediatric infection,* 2008; **2**: 9.
13. Raisova, A.T. Intrauterine infections. *Clinician,* 1995; **1**: 52-58.
14. Serov, V.N., Manukhin, I.B., & Kuzmin, V.N. Cytomegalovirus infection in pathology of pregnancy and fetus. *Obstetrics and Gynecology,* 1997; **6***:* 16-17.
15. Strunina, I.G. Infectious-inflammatory diseases of mother as a risk factor for the development of perinatal pathology (Synopsis of thesis of Candidate of Medical Sciences, pp. 24). Volgograd State Medical University, Moscow 1993.
16. Sushko, E.P., Novikova, V.I., & Tupkova, L.M. "*Neonatology*". Minsk: Higher school 1998.
17. Tussupkaliev, A.B. The value of intrauterine infection in obstetrics and perinatal pathology (Synopsis of thesis of Candidate of Medical Sciences, pp. 27). Aktobe State Medical Academy named after Marat Ospanov, 2001; Almaty.
18. Tussupkaliev, B.T., Gerasimenko, N.I., Tulegenova, G.A., & Shalekenova, S.E. Intrauterine infection in newborn infants (pp. 79). Aktobe: Typography Alma Print 2004.
19. Fomicheva, E.N., Zarubina, E.N., Minaev, V.I. *et al*. The role of ureaplasmal, mycoplasmal, and chlamydial infection in obstetric practice. *Obstetrics and Gynecology,* 1997; **2***:* 55-57.
20. Fuks, M.A., & Griban, A.N. Ultrasound diagnosis of pregnant women being at risk for fetal infection. *Obstetrics and Gynecology,* 1991; **8***:* 37-40.
21. Zinserling, V.A., & Melnikova, V.F. *Perinatal infections. Pathogenesis, morphological diagnosis, clinical and morphological comparisons: practical guide* (pp. 352). St. Petersburg: Elbi.