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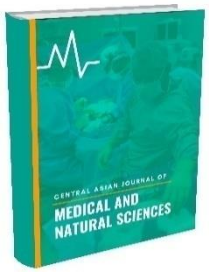

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Etiological Factors of Premature Leaking of Amniotic Fluid

1. **A. X. Karimov**
2. **G. A. Sharipova**

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[1] Doctor of medical science, professor of obstetrics and gynecology in family medicine department in Tashkent medical academy

[2] PhD researcher of obstetrics and gynecology in family medicine department in Tashkent medical academy

Abstract: In this paper is presented a literature review on the etiology and risk factors of prenatal rupture of membranes. The article discusses risk factors for prenatal rupture of amniotic fluid during full-term (38-40 weeks) and preterm (32-34 weeks) pregnancy. To predict premature leaking of amniotic fluid and take measures to prevent it, it is necessary to take into account the risk factors for this pathology.

Key words: genital infection, pregnancy, prenatal rupture of membranes.

Actuality

Premature rupture of membranes (PRM) represents one of the most important problems in obstetric practice. It is relevance is associated with an increase in maternal morbidity, perinatal and neonatal morbidity and mortality. The anhydrous interval is the time between the rupture of amniotic fluid and the birth of the fetus. There is also a latent period - the time between the rupture of water and the onset of regular labor. Childbirth complicated by PRM during full-term pregnancy, according to various sources, ranges from 8.2% to 15.3% and does not have a tendency to decrease. In prematurity, the incidence of PRM was noted from 12% to 22.5%. It should also be noted that PRM tends to re-develop in subsequent births with a frequency of up to 20-32%. This pathology contributes to an increase in complications during childbirth on the part of the mother and fetus, which leads to an increase in the frequency of surgical delivery, obstetric injuries, postpartum diseases and perinatal morbidity and mortality. Premature births together with PRM plays magnificence role in the structure of perinatal morbidity and mortality, and which is one of the most common causes of the onset of labor. The incidence and severity of neonatal complications depend on the gestational age at which PRM occurs (1,2,7).

Premature rupture of membranes (PRM) is the spontaneous rupture of the membranes before regular contractions of uterus begin. A number of authors call this condition “premature rupture of membranes,” which corresponds to the European term “premature rupture of membranes.” According to a number of authors, births complicated by prenatal leaiking of amniotic fluid during full-term pregnancy range from 9.2% to 21.8%, with premature birth (before 37 weeks of gestation) – from 10

to 37% and do not have a tendency to decrease. It should also be noted that PRM tends to recur in subsequent births with an incidence of up to 20-35% (7). According to some authors, PRM during premature birth is observed in cases of multiple pregnancy and polyhydramnios (2). Despite the accumulated knowledge about the causes of PRM, the question of the etiology and risk group of this pregnancy complication still remains open (3,4). It is known that amniotic fluid is a biologically active medium surrounding the fetus. Throughout pregnancy, amniotic fluid performs a wide variety of functions, ensuring the normal functioning of the mother-placenta-fetus system. An intact amnion with a sufficient amount of amniotic fluid is necessary not only for the development of the fetus (lungs, movements), but also protects the fetus from ascending infection. Of course, this may be a consequence of mechanical stress on the membrane. For example, during childbirth, during multiple pregnancy or polyhydramnios. And a possible reason may be a decrease in amnion resistance. Currently, there are different concepts regarding the etiology and risk factors for the development of premature rupture of membranes, according to which the most often initiating mechanisms for the development of this pathology are intrauterine infection of the fetus, neuroendocrine pathology, autoimmune processes in the mother-placenta-fetus system, various forms of extragenital pathology of the mother and etc. However, as is known, one of the patterns in the development of pathological conditions and diseases of various origins is a dynamic change in cause-effect relationships, when, following the triggers for the development of pathology, standard pathological processes and reactions are included, ensuring the implementation of efferent links in the development of pathology (5,6, 8). Studying the mechanism of rupture of membranes at the tissue and cellular level made it possible to identify an altered zone in the area of rupture of membranes, which was morphologically characterized by thickening of the connective tissue component, thinning of the cytotrophoblast layer and decidua, as well as destruction of the connection between the amnion and chorion. At the cellular level, enzymes (phospholipases, elastases, matrix metalloproteinases and/or other proteases) and biologically active substances (eicosanoids, especially prostaglandin E2 class, cytokines) were found in the area of membrane rupture. These changes are similar to the physiological ones that occur when the membranes rupture during timely labor, however, the stimuli that provoke rupture of the membranes during premature and full-term pregnancy are most likely different. In addition, the cause of prepartum rupture of membranes should be considered to be the influence of vascular endothelial factor, while local inflammation occurs secondary to PRM (4). The causes of PRM can be bacterial vaginosis, multiple pregnancy, polyhydramnios, premature contraction of the myometrium, bleeding in the first trimester of pregnancy, nicotine addiction, preterm birth (PB) or a history of PRM. The discharge of amniotic fluid occurs due to a decrease in the resistance of the amnion to pressure. The American College of Obstetricians and Gynecologists (ACOG) (4) points out the following risk factors leading to this gestational complication: previous pregnancies that ended prematurely with DRPO; inflammatory diseases of the maternal genital organs and intra-amniotic infection; isthmic-cervical insufficiency; instrumental medical intervention; bad habits and diseases of the mother; abnormalities of the uterus and multiple pregnancies; some maternal diseases; injuries. Risk factors for premature leaking of amniotic fluid at full term birth are:

a) features of the obstetric and gynecological history: anomaly of the uterus, two or more induced abortions in the anamnesis, two or more spontaneous abortions in the anamnesis;

b) complications of pregnancy: multiple pregnancy, threat of miscarriage at different stages, anemia of pregnant women, breech presentation of the fetus, placental insufficiency, acute respiratory viral infections at different stages of pregnancy, preeclampsia;

c) concomitant extragenital diseases: inflammatory diseases of the urinary system, diabetes mellitus of various types (9,10).

Factors from the obstetric and gynecological history and the chance of PRM were significantly increased by spontaneous miscarriages and non-developing pregnancies preceding this gestational process, prenatal rupture of amniotic fluid in a previous pregnancy, and anomalies of uterine development. In women with multiple pregnancies, premature rupture of membranes is more common - in 40.4%, while in the group with singleton pregnancies this complication occurred in 12.5% of cases (11,12). PRM is significantly more often preceded by a clinically significant threat of miscarriage in the 1st trimester of pregnancy. Placental insufficiency in the group with PRM, compared with the group with timely rupture of water, is significantly more common six times. Inflammatory diseases of the genital tract are associated with PRM. It has been established that the presence of a bacterial infection increases the chance of PRM by 3.0 times. Studies have revealed that with PRM, bacterial vaginosis was diagnosed in 55.8% of cases, nonspecific bacterial vaginitis in 44.2% of cases. According to the literature, trichomonas, herpes simplex virus, ureaplasma, and cytomegalovirus are detected in the vaginal microflora of pregnant women with PRM. And the main cause of PRM is an ascending vaginal infection.

Pathophysiologically, infection leads to increased production of cytokines and prostaglandins (E2 and F2) and, through a cascade, to the development of labor. T. Mohr names the main infectious agents in PRM: Group B Streptococci, E. coli, Fusobacteria, Peptostreptococci, Bacterioides, Ureaplasma urealyticum. Vaginal dysbiosis may predispose to the development of PRM. It can also be said with reasonable confidence that one of the options for preventing PRM is to normalize the microflora during pregnancy, especially in the third trimester (12,13,15). It is known that the main properties of nitric oxide are vasodilation and providing a disaggregating effect on platelets, as well as antioxidant and membrane protective effects. In this regard, the identified decrease in the level of nitric oxide metabolites in the blood of pregnant women with DPO is one of the risk factors for the development of vasoconstriction and thrombophilia. A pathogenetic relationship has been identified between the activation of lipid peroxidation processes, and the development of degenerative processes in the amniotic and chorionic membranes of the fetus in conditions of prolongation of pregnancy in patients with premature rupture of membranes (6, 7).

Many factors are involved in the etiology of antepartum rupture of membranes in preterm pregnancy. Among the risk factors for prenatal rupture of membranes during premature pregnancy, 3 groups are conventionally distinguished: maternal, uteroplacental and fetal (2, 7,12, 16, 17). Maternal factors include out-of-wedlock pregnancy, low socio-economic status, bad habits (tobacco, drugs), body mass index less than 20 kg/m², deficiency of copper and ascorbic acid in food, anemia, long-term treatment with steroids, premature birth, disruption of vascular collagen content. Great importance is attached to prenatal rupture of the membranes with a history of premature pregnancy. Recurrence risk reaches up to 30% compared to 3-4% in the group of women with physiological labor. Of the uteroplacental factors, the most common are:

- abnormalities in the uterus development (septum in the cavity),
- premature abruption of a normally located placenta (10-15%),
- shortened cervix in the second trimester to 2.5 cm (or less) due to progressive isthmic-cervical insufficiency or previous conization of the cervix,
- uterine distension due to polyhydramnios or multiple pregnancies, chorioamnionitis, repeated vaginal bimanual or transvaginal ultrasound examinations.

Fetal risk factors are also associated with multiple births. Iatrogenic causes of premature rupture of membranes during premature pregnancy are rare and occur mainly during invasive intrauterine interventions. The risk group for mechanical damage to the membranes during a diagnostic or therapeutic procedure includes pregnant women who undergo amniocentesis, chorionic villus biopsy,

suturing the cervix for isthmic-cervical insufficiency (17,19,20,21). PRM for gestational age 22-37 weeks is a consequence of multiple causes acting along different but often overlapping pathophysiological pathways, and it is not possible to identify a dominant etiological factor. According to studies by a number of authors, premature rupture of amniotic fluid during the 22-34th week of gestation is naturally accompanied by systemic activation of lipid peroxidation processes and excessive accumulation of lipid peroxidation intermediate products in the mother's blood and amniotic fluid - diene conjugates and malondialdehyde, an increase in the Oxystat indicator, reflecting the total increase peroxides.

In the pathogenesis of premature leaking of amniotic fluid, the following factors are of key importance: immunological: increased levels of pro-inflammatory cytokines IL-8 and TNF in blood serum and amniotic fluid; functional and morphological: increased expression of matrix metalloproteinase-1 and decreased expression of matrix metalloproteinase inhibitor-1 in the fetal membranes ([8, 19]. Thus, the prediction of PRM is made before pregnancy in the presence of the following risk factors for the development of premature birth: isthmic-cervical insufficiency, uterine development abnormalities, genital tract infection, hereditary genetic disorders, body mass index less than 19.0, low socio-economic status of women, smoking, history of premature birth, obstetric complications (hypertension, bleeding during pregnancy, infection, polyhydramnios), antiphospholipid syndrome. To predict premature leaking of amniotic fluid and carry out measures to prevent it, it is necessary to take into account the risk factors of this pathology:

- two or more miscarriages in history,
- multiple pregnancies, threat of miscarriage,
- acute respiratory viral infections at different stages of pregnancy,
- placental insufficiency,
- abnormal development of the uterus,
- threat of miscarriage at different periods,
- inflammatory diseases of the urinary system,
- diabetes mellitus of various types,
- preeclampsia,
- anemia of pregnant women,
- breech presentation of the fetus.

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