УДК 616.24/.56-003.2-008.6/.8-056.7:575.224]-07: 618.2:618.4
https://doi.org/10.20538/1682-0363-2022-4-205-211

Clinical features of the course of cystic fibrosis during pregnancy and childbirth

Teteneva A.V.[1, 3], Chernyavskaya G.M.[1], Bespalova I.D.[1], Skorokhodova T.V.[1, 4], Koshchavtseva Yu.I.[1], Radionov D.I.[1], Kalyuzhina E.V.[1], Romanov D.S.[1], Radionova E.V.[1], Ustyuzhanina E.A.[2], Varfolomeeva I.A.[2], Stepanov I.A.[4], Karmanova A.V.[4], Golubyatnikova E.V.[4]

[1] *Siberian State Medical University*
2, Moscow Trakt, Tomsk, 634050, Russian Federation

[2] *Tomsk Regional Clinical Hospital*
96, I. Chernykh Str., Tomsk, 634063, Russian Federation

[3] *Medical and Sanitary Hospital No. 2*
3, Bela Kuna Str., Tomsk, 634040, Russian Federation

[4] *Regional Perinatal Center*
96/1, I. Chernykh Str., Tomsk, 634063, Russian Federation

ABSTRACT

Cystic fibrosis is one of the urgent medical and social problems of health care systems in most countries due to fairly high prevalence, development of multi-organ lesions, and poor outcomes.

Due to modern advances in the diagnosis and treatment of cystic fibrosis, not only has the average life expectancy of patients increased, but their quality of life has also improved, and it has become possible to maintain pregnancy and childbearing. Since cystic fibrosis can adversely affect the course of pregnancy, childbirth, and health of both mother and child, proper management of women with cystic fibrosis during pregnancy and childbirth is of particular relevance. The presented clinical case is an example of competent supervision at all stages of monitoring of a patient with cystic fibrosis during pregnancy and childbirth.

Keywords: cystic fibrosis, maintenance of pregnancy, childbearing, CF

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

Source of financing. The authors state that they received no funding for the study.

For citation: Teteneva A.V., Chernyavskaya G.M., Bespalova I.D., Skorokhodova T.V., Koshchavtseva Yu.I., Radionov D.I.1, Kalyuzhina E.V., Romanov D.S., Radionova E.V., Ustyuzhanina E.A., Varfolomeeva I.A., Stepanov I.A., Karmanova A.V., Golubyatnikova E.V. Clinical features of the course of cystic fibrosis during pregnancy and childbirth. *Bulletin of Siberian Medicine.* 2022;21(4):205–211. https://doi.org/10.20538/1682-0363-2022-4-205-211.

✉ *Bespalova Inna D.,* innadave@mail2000.ru

Клинические особенности течения муковисцидоза на фоне беременности и родов

Тетенева А.В.[1, 3], Чернявская Г.М.[1], Беспалова И.Д.[1], Скороходова Т.В.[1, 4], Кощавцева Ю.И.[1], Радионов Д.И.[1], Калюжина Е.В.[1], Романов Д.С.[1], Радионова Е.В.[1], Устюжанина Е.А.[2], Степанов И.А.[4], Карманова А.В.[4], Голубятникова Е.В.[4]

[1] *Сибирский государственный медицинский университет (СибГМУ)*
Россия, 634050, г. Томск, Московский тракт, 2

[2] *Томская областная клиническая больница (ТОКБ)*
Россия, 634063, г. Томск, ул. Ивана Черных, 96

[3] *Медико-санитарная часть (МСЧ) № 2*
Россия, 634040, г. Томск, ул. Бела Куна, 3

[4] *Областной перинатальный центр (ОПЦ) им. И.Д. Евтушенко*
Россия, 634063, г. Томск, ул. Ивана Черных, 96/1

РЕЗЮМЕ

Муковисцидоз (МВ) представляет собой одну из актуальных медико-социальных проблем систем здравоохранения большинства стран в связи с достаточно высоким уровнем распространенности, развитием полиорганных поражений и неблагоприятными исходами.

Благодаря современным достижениям диагностики и лечения муковисцидоза в настоящее время не только увеличилась средняя продолжительность жизни пациентов, но и улучшилось её качество, появилась возможность сохранения беременности и деторождения. В связи с тем, что МВ может неблагоприятно влиять на течение беременности, родов, состояние здоровья как матери, так и ребенка, вопросы правильного ведения больных во время беременности и родов у женщин, страдающих МВ, приобретают особую актуальность. Примером грамотной курации на всех этапах наблюдения за пациенткой в период беременности и родов на фоне МВ является представленный клинический случай.

Ключевые слова: муковисцидоз, сохранение беременности, деторождение, МВ.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Для цитирования: Тетенева А.В., Чернявская Г.М., Беспалова И.Д., Скороходова Т.В., Кощавцева Ю.И., Радионов Д.И., Калюжина Е.В., Романов Д.С., Радионова Е.В., Устюжанина Е.А., Степанов И.А., Карманова А.В., Голубятникова Е.В. Клинические особенности течения муковисцидоза на фоне беременности и родов. *Бюллетень сибирской медицины.* 2022;21(4):205–211. https://doi.org/10.20538/1682-0363-2022-4-205-211.

INTRODUCTION

Cystic fibrosis (CF) is one of the urgent medical and social problems of health care systems in most countries due to fairly high prevalence, development of multi-organ lesions, and poor outcomes [1–3]. CF is a genetic disease caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene and is characterized by damage to exocrine glands in a number of vital organs: respiratory tract, gastrointestinal tract, liver, pancreas, salivary and sweat glands, reproductive organs [2–6]. At the same time, pathology of the respiratory tract is the most common cause of complications and mortality; it is accompanied by persistent infection and inflammation in the respiratory tract, with formation of viscous bronchial secretions [2, 5, 6 –8]. The first clinical symptoms usually appear in early childhood [2, 9]. A chronic, pronounced pathological process contributes to formation of bronchiectasis and development of pulmonary hypertension and cor pulmonale. However,

lower respiratory tract infection is considered to be the key factor which underlies the severity of CF and its prognosis [2, 10].

Due to modern advances in the diagnosis and treatment of CF, not only has the average life expectancy of patients increased to an average of 36.8 years, but their quality of life has also improved, and it has become possible to maintain pregnancy and childbearing [9, 11]. However, it should be understood that in women with CF, pregnancy is associated with an increased risk for disease decompensation up to death, and decompensated liver pathology can contribute to an unfavorable course of pregnancy and childbirth [4, 12, 13].

Recent studies have confirmed that fertility in women with CF is not impaired, except for cases when more viscous secretion accumulates in the cervical canal [12, 14]. Often, patients with CF are characterized by multifetal pregnancies, gestational diabetes mellitus, preterm labor, and indications for operative delivery [13, 15]. Severe respiratory disorders underlie pneumonia, with the development of acute respiratory failure and a need for invasive mechanical ventilation [13]. Nevertheless, a sufficient number of observations have shown that most pregnancies in women with CF end in spontaneous childbirth through the birth canal; caesarean section is resorted to in cases of complications associated with a risk to the health of the mother or the baby [15, 16].

Therefore, considering that CF can adversely affect the course of pregnancy, childbirth, and the health of both the mother and the child, proper management of women with CF during pregnancy and childbirth is of particular relevance. The presented clinical case is an example of competent supervision at all stages of monitoring of a patient with CF during pregnancy and childbirth.

CLINICAL CASE

Patient P., 22 years old, was routinely admitted to the pulmonology department of the Regional Clinical Hospital on October 10, 2019 for a follow-up examination and inpatient treatment and for resolving the issue of maintaining pregnancy. The pregnancy was first and desired.

From the anamnestic data: at the age of 1.5 months, the patient experienced right-sided lower lobe pneumonia; since childhood, she had been experiencing rare dry cough, sometimes with a difficulty in clearing the chest of viscous sputum, which intensified after hypothermia. She was followed up by a pediatrician with the diagnosis of chronic bronchitis. For the first time, CF was diagnosed at the age of 4 years 10 months; the examination revealed an increase in the sweat chloride level up to 119 mEq / l. The patient has been followed up at the Research Institute of Medical Genetics with the diagnosis: Cystic fibrosis, mixed form (affects the lungs and the intestines), a moderately severe, continuously relapsing course. Compound heterozygous for Dele 2.3/E92,K. Chronic pancreatic insufficiency.

In 2011, a thoracoscopic lobectomy was performed for bronchiectasis in the right lower lobe in S8–10. The patient constantly receives basic therapy: Pulmozyme (dornase alfa) 1 ampule per day using a jet nebulizer, Bramitob 300 mg 2 times a day using a jet nebulizer in courses (28-day administration / 28 day-break, the last course was completed on October 9), Kreon 25,000 IU (6,000 IU /kg of body weight), 10 capsules per day with meals, Ursofalk 250 mg, 5 capsules per day. The patient undergoes inpatient treatment 1–2 times a year and receives antibiotic therapy (ABT). The last hospitalization in the pulmonology department was in December 2018, during which the patient received another course of ABT with Co-trimoxazole, Piperacillin / Tazobactam following the microbiological examination of the sputum (*St. aureus* 10^5, *Stenotrophomonas maltophilia* 10^5).

Two weeks before the current hospitalization, the patient noted an increase in coughing with light yellow sputum in the volume of up to 20 ml per day (the amount and color of the sputum did not change), decreased exercise tolerance, low-grade body temperature in the evenings, once up to 38 °C (took Paracetamol). On October 09, 2019, a pelvic ultrasound was performed, and an early intrauterine pregnancy was detected.

Past medical history: appendectomy in 2010, removal of the lower lobe of the right lung due to bronchiectasis in 2011, removal of nasopharyngeal polyps in 2014. The patient suffered from chicken pox as a child. Menstruation started at the age of 14, is regular, moderate, pain-free; the menstrual cycle is 30 days; bleeding lasts 5 days; the patient denies menstrual irregularities.

The patient has disability group 3.

Family history of CF is positive: the middle sister (the patient is the elder sister) also has CF, she is followed up at the Research Institute of Medical Genetics.

Upon admission: the patient's condition was satisfactory. The skin was pale, clean, moist, with no cyanosis of the lips. Height – 165 cm, weight – 51 kg, BMI – 18.7, blood pressure – 100 / 60 mm Hg, pulse – 80 beats per minute, body temperature – 37.1 °C, respiratory rate – 20 breaths per minute. Oxygen saturation (SpO_2) in the ambient air was 98%, after a six-minute walk test – 96%. The chest had a cylindrical shape and was elastic upon palpation. Percussion sound was resonant and the same over symmetrical areas. Auscultation of the lungs revealed rough vesicular breathing without wheezing. The borders of cardiac dullness were not changed. Heart sounds were loud

and rhythmic. The abdomen was soft and not tender on palpation in all departments. The liver and spleen were not enlarged. No dysuria was noted. The Murphy's punch sign was negative.

Complete blood count: hemoglobin – 122 g / l, leukocytes – 17.8 x10^9 / l: band neutrophils – 6%, segmented neutrophils – 78%, eosinophils – 1%, lymphocytes – 13%, monocytes – 2%. Platelets 180 x 10^9 / l, ESR – 27 mm / h. Biochemical blood parameters were without significant deviations from the normal values: glucose – 4.25 mmol / l, total protein – 68 g / l, albumins – 33.9 g / l, bilirubin – 13.3 / 3.5 μmol / l, alanine aminotransferase (ALT) – 11.2 IU, aspartate aminotransferase – 7.1 IU, alpha-amylase – 91.6 IU / l, creatinine – 66.3 μmol / l, C-reactive protein (CRP) – 57.8 mg / l, fibrinogen – 7.4 g / l.

10.15.19. Blood culture for sterility testing revealed no growth of bacterial flora.

The microbiological examination of the sputum of 10.12.19: *Acinetobacter baumanii* 10^5 (pan-drug resistant strain, insensitivity to carbapenems); the examination of 07.15.19: *Stenotrophomonas maltophilia* 10^6, *St.aureus* 10^5, *candida albicans* 10^6 (pan-drug resistant); the examination of 10.24.19: *Stenotrophomonas maltophilia* 10^2, *candida albicans* 10^3 (pan-drug resistant).

10.12.19. Spirometry. Forced expiratory volume in one second (FEV1) – 78%, forced vital capacity (FVC) – 84%, FEV1 / FVC – 82.8. Impression: vital capacity of the lungs is within the conditional norm. Stage 0–1 obstructive ventilation abnormalities.

10.11.19. ECG: sinus tachycardia, heart rate – 92 beats per min. Right axis deviation. A turn around the longitudinal axis with the right ventricle facing forward.

10.11.19. Echocardiography: cardiac cavities were not enlarged, no hypertrophy was noted. The contractility of the left and right ventricles was within normal values. Violations of local contractility were not revealed. Left ventricular diastolic dysfunction with the pseudonormal filling pattern. The valves were unchanged. Mild tricuspid valve regurgitation, right ventricular systolic pressure was not increased. The pericardium was unchanged, no fluid was detected.

10.12.19. Abdominal ultrasound: the liver was not enlarged, the contours were even, the edge was sharp, echogenicity was within normal values, the structure was homogeneous, the bile ducts were not dilated, the walls were dense, the vascular pattern was without irregularities; the portal vein – 8 mm. Gallbladder: dimensions: 80 x 30 mm, wall density 3 mm, biliary sludge was detected. The pancreas was not enlarged, the contours were even, the echogenicity was normal, the structure was homogeneous. The pancreatic duct – 1 mm. The spleen was not enlarged, the structure was homogeneous. The kidneys were not enlarged, the thickness of the renal parenchyma was normal, the contours were even, the mobility was preserved, the position was normal, the structure of the parenchyma was homogeneous, the boundaries of the renal sinuses were fuzzy, no signs of urodynamic disturbances were noted. Impression: signs of chronic cholecystitis. Moderate diffuse changes in the kidneys.

10.14.19. Thyroid and parathyroid ultrasound. Impression: no pathology detected.

The patient categorically refused to undergo a chest X-ray, despite the physician's explanation of its necessity and safety.

17.12.18. Spiral computed tomography of the chest. Impression: Condition after right-sided lower lobe lobectomy. Infiltrative areas, focal infiltrative changes in the lungs with interstitial thickening along the contour in the lobes of the lungs on both sides. Bronchial wall thickening. Small saccular bronchiectasis, a few calcified pulmonary nodules on both sides. Small areas of stringy fibrosis on both sides.

Taking into account chronic excretion of *Pseudomonas aeruginosa* from the sputum in the past medical history, the presence of other non-fermenting gram-negative bacteria (*Acinetobacter baumannii, Stenotrophomonas maltophilia*) in the bacteria culture tests, the presence of clinical and laboratory signs of exacerbation of bronchopulmonary infection, and an unfavorable prognosis in the absence of ABT, ABT was prescribed for health reasons. The prescription of ABT and further management of the patient were carried out taking into account pregnancy, with an informed consent obtained from the patient. The prescribed initial therapy (Meronem 1.0 g, 3 times a day via intravenous drip infusion) had no effect: the body temperature remained low-grade, leukocytosis was up to 21.3 x 10^9 / l with a left shift. Therefore, ABT was changed to a combination of Cefoperazone / Sulbactam 6 g (Cefoperazone 3 g + Sulbactam 3 g) per day via intravenous drip infusion and Fosfomycin 2.0 2 times a day via intravenous drip infusion. In the context of the therapy, the patient's condition improved: the body temperature did not exceed 37 °C, the volume of yellow sputum was about 15 ml per day. In the CBC, a positive trend was observed – a decrease in leukocytosis (as of 24.10.2019, leukocytes – 9.43 x 10^9 / l: band neutrophils – 6%, segmented neutrophils – 71%, eosinophils – 0.5%, lymphocytes – 16.8%, monocytes – 5.7%; the level of CRP decreased to 4.3 mg / l.

A consultation was held with the participation of pulmonologists, geneticists, and obstetricians – gynecologists in order to choose further treatment strategy and decide on the possibility of maintaining pregnancy.

Taking into account the patient's condition, the features of the clinical presentation of CF were the following: moderate course, no significant changes in the pulmonary ventilation parameters (they are close to normal values), no signs of respiratory failure (SpO2 in the ambient air – 98%), no pulmonary hypertension, and right ventricular hypertrophy, childbearing is possible. At the same time, the presence of vital indications for massive ABT at the present time (the first trimester of pregnancy) is associated with a risk of negative effects on the fetus. The patient and relatives were informed about this in order to make a decision. In addition, they were explained that after birth, given the condition of the patient, she may be hospitalized and may need help in caring for the baby. The patient decided to maintain the pregnancy.

Obstetric and gynecological status upon admission. 10.12.19. Examination by a gynecologist. The external genital organs are developed correctly, without pathological changes. The vaginal mucosa is not changed, the cervix is not visually changed. The cervix is positioned posteriorly from the pelvic axis, it is not shortened, its shape is cylindrical, the consistency is normal, the cervical os is closed, the uterus is enlarged up to 5–6 weeks of pregnancy; the uterus is normotonic, mobile, and not tender. At the time of examination, there are no data for acute obstetric pathology. The patient is 6–7 weeks pregnant.

10.14.19. Transvaginal ultrasound of the uterus and appendages. The uterus is positioned in the center and is retroverted; the contours of the uterus are even; the structure of the myometrium is homogeneous; in the uterine cavity, a fetal egg (d 24 mm) is visualized; pregnancy 6 weeks and 3 days. Cervix: the structure is not changed; no masses projected at the uterine appendages are detected. There is no free fluid in the posterior cul-de-sac. Impression: Pregnancy 6 weeks and 3 days.

10.21.19. Gynecological status. The external genitalia are developed correctly. Female pattern hair growth. The vagina is narrow, the folds are preserved. The cervix is posterior, up to 3.0 cm long, dense; the cervical os is closed. The uterus is enlarged because of pregnancy (up to 8 weeks), spherical in shape, soft, and not tender. Appendages on both sides are without pathology.

Dynamic transvaginal ultrasound of the uterus and appendages: 10.21.19. Following fetometry, the patient is 7 weeks 3 days pregnant.

The patient was discharged against medical advice on 31.10.19.

Diagnosis at discharge: 9 weeks pregnant. Cystic fibrosis, mixed form (affects the lungs and the intestines), a moderately severe, continuously relapsing course. Compound heterozygous for Dele 2.3/E92,K. Chronic infection of the respiratory tract with *St. aureus, Pseudomonas aeruginosa, Stenotrophomonas maltophilia, Acinetobacter baumannii*. Chronic bronchitis. Bronchiectasis of both lungs, condition after thoracoscopic lobectomy for bronchiectasis in the right lower lobe (03.04.2011). Fibrosis of the upper lobe of the right lung. Chronic pansinusitis. Exocrine pancreatic insufficiency. Chronic erosive antral gastritis, duodenitis HP(-), insufficiency of the gastric cardia. Gastroesophageal reflux disease (GERD). Bacterial overgrowth syndrome. Secondary intestinal dysbiosis. Asthenic syndrome.

Pregnancy follow-up was carried out in the Regional Perinatal Center from 13 weeks pregnant. The follow-up was carried out by an obstetrician – gynecologist together with a pulmonary internist. The patient's high adherence to follow-up and treatment was noted.

There were no exacerbations of the disease that required ABT prescription. No significant negative trend in spirometry parameters and oxygen saturation values was noted.

During pregnancy, shortness of breath on exertion, most pronounced in the last trimester of pregnancy, nausea, and repeated vomiting were common.

During pregnancy, in accordance with the recommendations, the patient received: vaginal Utrogestan 200 mg 1 time per day, vitamin D 2,000 IU, Calcemin Advance 1 capsule per day (500 mg calcium), Ursofalk 5 capsules per day in 2 doses, Kreon 10 capsules per day in 3 doses, Pulmozyme inhalations 1 time per day, Iodomarin 200 mcg / day, Tobramycin inhalation (28-day therapy – 28-day break), on-demand Salbutamol inhalation.

Weight gain during pregnancy was 9 kg.

The following ultrasound screenings were carried out:

1. 12 weeks pregnant (Research Institute of Medical Genetics) – no pathology was detected.

2. 19.6 weeks pregnant (Research Institute of Medical Genetics) – no pathology was detected.

3. 30 weeks pregnant (Regional Perinatal Center) – no pathology was detected.

At 35.2 weeks pregnant, the patient was admitted to antenatal hospital unit to resolve the issue of delivery. A plan for childbirth was drawn up: high degree of risk (15 points), estimated fetal weight was 2,600 g +\- 26 g.

Due to the appearance of shortness of breath on minimal exertion and the gestational age close to full term (35.2 weeks), a decision was made on elective operative delivery on 04.30.2020. The patient agreed with the strategy. Regional anesthesia with antibiotic prophylaxis were planned: Ampicillin + Sulbactam 1.5 g parenterally, further prescription of ABT according to indications.

On 04.30.2020, elective operative delivery was performed. A premature boy was born (weight 2,620 g, height 49 cm, the Apgar score of 8/8). During the operation, delayed umbilical cord clamping was performed. Amniotic fluid was light (400 ml). Blood loss was 600 ml.

The caesarean section went without technical difficulties.

The postoperative period proceeded without complications. The new mother was discharged on day 13 (delay in discharge due to the condition of the child). The newborn was in the Neonatal Intensive Care Unit for 7 days and in the Neonatal and Premature Infant Pathology Unit for 10 days. Primary diagnosis: late preterm baby (35.3 weeks). Postconceptional age 37.4 weeks. Secondary diagnosis: newborn respiratory distress syndrome of moderate severity. Incomplete ureteral duplication in the left kidney. Premature infant jaundice. Right-sided choroid plexus cyst.

The condition at birth was severe due to respiratory disorders. The Silverman Andersen Respiratory Severity Score of 4–5 points. Infusion therapy and respiratory support were carried out (6 days): nCPAP was performed in the delivery room, CPAP with positive dynamics and phototherapy were carried out in the intensive care unit for newborns (increased jaundice, unconjugated hyperbilirubinemia). A positive trend was noted in the context of the therapy. The condition at discharge was satisfactory. The neurological status corresponded to the gestational age.

Bottle-feeding with expressed breast milk. Attachment to the breast.

Nasal breathing was free, the pharynx was not irritated. The skin was subicteric, pink, and clean. The umbilical wound was epithelialized. Breath sounds were heard throughout all lung fields, no wheezing was heard. Heart sounds were clear and rhythmic. The abdomen was soft and not tender on palpation. The liver and spleen were not enlarged. Urination. No vaccinations were given.

Currently, the child is followed up in the pediatric hospital: he develops according to age, no abnormalities and developmental delays have been identified.

CONCLUSION

Modern advances in pulmonology, obstetrics, and neonatal and anesthetic services have enabled women with CF to have successful pregnancies without apparent significant impairment of their lung function. When considering the use of drugs during pregnancy, the known and unknown risks of the effects of drug treatment on the fetus must be weighed against the risk to the mother's health resulting from discontinuation of therapy. The choice of a method for delivering a baby is determined by the state of the mother's health, and in case external respiration deteriorates, a decision can be made to perform a caesarean section.

A number of conditions underly a successful pregnancy and successful delivery in this clinical case: firstly, the patient was diagnosed with CF in childhood, she has been followed up by pulmonologists and geneticists for her disease for a long time; secondly, the patient had no disorders of external respiration at early stages of pregnancy and no obstetric and gynecological diseases in the past medical history; and, thirdly, the coordinated work of specialists (pulmonologists, obstetrician – gynecologists, and neonatologists) in patient's management and delivery support.

REFERENCES

1. Bucher J., Oualha M., Dupic L., Lebourgeois M., Lesage F., Renolleau S. et al. 312 Outcomes and factors associated with poor outcome of children with cystic fibrosis admitted to the intensive care unit. *Journal of Cystic Fibrosis.* 2015;14(1):138. DOI: 10.1016/S1569-1993(15)30486-0.
2. Chen Q., Shen Y., Zheng J. A review of cystic fibrosis: basic and clinical aspects. *Animal Model Exp. Med.* 2021;4(3):220–232. DOI: 10.1002/ame2.12180.
3. Shteinberg M., Haq I.J., Polineni D., Davies J.C. Cystic fibrosis. *Lancet.* 2021;397(10290):2195–2211. DOI: 10.1016/S0140-6736(20)32542-3.
4. Clinical guidelines on cystic fibrosis. Union of Pediatricians of Russia, Association of Medical Geneticists, Russian Respiratory Society, Russian Transplant Society, Association of Pediatricians of the Moscow Region. 2021 (in Russ.).
5. Hao S., Roesch E.A., Perez A., Weiner R.L., Henderson L.C., Cummings L. et al. Inactivation of CFTR by CRISPR/Cas9 alters transcriptional regulation of inflammatory pathways and other networks. *Journal of Cystic Fibrosis.* 2020;19(1):34–39. DOI: 10.1016/j.jcf.2019.05.003.
6. Elborn J.S. Cystic Fibrosis. *Lancet.* 2016;388(10059):2519–2531. DOI: 10.1016/S0140-6736(16)00576-6.
7. Deschamp A.R., Hatch J.E., Slaven J.E., Gebregziabher N., Storch G., Hall G.L. et al. Early respiratory viral infections in infants with cystic fibrosis. *Journal of Cystic Fibrosis.* 2019;18(6):844–850. DOI: 10.1016/j.jcf.2019.02.004.
8. Krasovsky S.A., Chernyak A.V., Amelina E.L., Nikonova V.S., Voronkova A.Yu., Samoilenko V.A. et al. Survival trends in cystic fibrosis patients in Moscow and Moscow region in 1992–2001 and 2002–2011. *Russian Pulmonology Journal.* 2012;(3) 79–86 (in Russ.). DOI: 10.18093/0869-0189-2012-0-3-79-86.
9. Kashirskaya N.Yu., Kondrat'eva E.I., Krasovsky S.A., Starinova M.A., Voronkova A.Yu., Amelina E.L. et al. Register of patients with cystic fibrosis in the Russian Federation. 2019. M.: Medpraktika-M, 2021:68 (in Russ.).
10. Khan T.Z., Wagener J.S., Bost T., Martinez J., Accurso F.J., Riches D.W. Early pulmonary inflammation in infants with cystic fibrosis. *Am. J. Respir. Crit. Care Med.* 1995;151(4):1075–1082. DOI: 10.1164/ajrccm/151.4.1075.

11. Kashirskaya N.Yu., Krasovsky S.A., Chernyak A.V., Sherman V.D., Voronkova A.Yu., Shabalova L.A. et al. Trends in life expectancy of cystic fibrosis patients in Moscow and their association with the treatment received: retrospective study for 1993–2013. *Voprosy Sovremennoi Pediatrii.* 2015;14(4):503–508 (in Russ.). DOI: 10.15690/vsp.v14.i4.1390.
12. McArcdle J.R. Pregnancy in cystis fibrosis. *Clin. Chest. Med.* 2011;32(1):111–120. DOI: 10.1016/j.ccm.2010.10.005.
13. Patel E.M., Swamy G.K., Heine R.P., Kuller J.A., James A.H., Grotegut C.A. Medical and obstetric complications among pregnant women with cystis fibrosis. *Am. J. Obstet. Gynecol.* 2015;212(1):98.E1–E9. DOI: 10.1016/j.ajog.2014.07.018.
14. Shteinberg M., Taylor-Cousar J.L., Durieu I., Cohen-Cymberknoh M. Fertility and Pregnancy in Cystic Fibrosis. *Chest.* 2021;160(6):2051–2060. DOI: 10.1016/j.chest.2021.07.024.
15. Reynaud Q., Jablonski C.R., Poupon-Bourdy S., Denis A., Rabilloud M., Lemonnier L. et al. Pregnancy outcome in women with cystic fibrosis and poor pulmonary function. *Journal of Cystic Fibrosis.* 2020;19(1):80–83. DOI: 10.1016/j.jcf.2019.06.003.
16. Jaina R., Kazmerski T.M., Zuckerwisec L.C., West N.E., Montemayor K., Aitken M.L. et al. Pregnancy in cystic fibrosis: Review of the literature and expert recommendations. *Journal of Cystic Fibrosis.* 2021;21(3):1569–1993. DOI: 10.1016/j.jcf.2021.07.019.

Authors contribution

Teteneva A.V. – conception and design, analysis of the nosology. Chernyavskaya G.M., Skorokhodova T.V., Stepanov I.A., Karmanova A.V., Golubyatnikova E.V., Ustyuzhanina E.A., Varfolomeeva I.A., Radionov D.I., Kalyuzhina E.V., Romanov D.S., Radionova E.V. – analysis of the clinical case, selection of the material. Bespalova I.D. – editing of the article, communication with the editorial board. Koshchavtseva Yu.I. – work with the reference list, translation of the article.

Authors information

Teteneva Anna V. – Dr. Sci. (Med.), Deputy Chief Physician for Medicine, Medical and Sanitary Hospital No. 2; Professor, Division of Introduction into Internal Diseases with a Course in Therapy, Siberian State Medical University, Tomsk, anna.dubodelova@mail.ru, http://orcid.org/0000-0002-4323-2798

Chernyavskaya Galina M. – Dr. Sci. (Med.), Professor, Division of Advanced-Level Therapy with a Course in Physiotherapy, Rehabilitation and Sports Medicine, Siberian State Medical University, Tomsk, chernyavskayag@gmail.com, http://orcid.org/0000-0003-0105-2307

Bespalova Inna D. – Dr. Sci. (Med.), Head of the Division of Introduction into Internal Diseases with a Course in Therapy, Siberian State Medical University, Tomsk, innadave@mail2000.ru, http://orcid.org/0000-0002-4513-6329

Skorokhodova Tatyana V. – Cand. Sci. (Med.), Deputy Chief Physician for Clinical and Expert Work, Regional Perinatal Center; Associate Professor, Obstetrics and Gynecology Division, Siberian State Medical University, Tomsk, itv7@yandex.ru

Ustyuzhanina Elena A. – Cand. Sci. (Med.), Head of the Pulmonology Department, Tomsk Regional Clinical Hospital, Tomsk, u_elan@mail.ru

Varfolomeeva Irina A. – Pulmonologist, Tomsk Regional Clinical Hospital, Tomsk, varfolomeeva.irina@lust.ru

Koshchavtseva Yuliya I. – Teaching Assistant, Division of Introduction into Internal Diseases with a Course in Therapy, Siberian State Medical University, Tomsk, kossy09@mail.ru, http://orcid.org/0000-0001-5260-4832

Radionov Denis I. – Post-Graduate Student, Division of Introduction into Internal Diseases with a Course in Therapy, Siberian State Medical University, Tomsk, radionovdenis12@gmail.com.

Kalyuzhina Elena V. – Dr. Sci. (Med.), Professor, Division of Advanced-Level Therapy with a Course in Physiotherapy, Rehabilitation and Sports Medicine, Siberian State Medical University, Tomsk, kalyuzhina.e@mail.ru, http://orcid.org/0000-0002-7978-5327.

Romanov Dmitriy S. – Post-Graduate Student, Division of Introduction into Internal Diseases with a Course in Therapy, Siberian State Medical University, Tomsk, romanovds92@yandex.ru

Radionova Ekaterina V. – Resident, Division of General Medical Practice and Polyclinic Therapy, Siberian State Medical University, Tomsk, Opoldnik@yandex.ru

Stepanov Igor A. – Cand. Sci. (Med.), Chief Physician, Regional Perinatal Center, Tomsk, stepanovopc@mail.ru

Karmanova Alla V. – Cand. Sci. (Med.), Deputy Chief Physician for Obstetric and Gynecological Care, Regional Perinatal Center, Tomsk, karmanovaav@opc.tomsk.ru

Golubyatnikova Ekaterina V. – Obstetrician-Gynecologist, Regional Perinatal Center, Tomsk, ketrintomsk@mail.ru

(✉) **Bespalova Inna D.,** innadave@mail2000.ru

Received 17.05.2022;
approved after peer review 21.07.2022;
accepted 08.09.2022