



## ANALYSIS OF PERINATAL LOSSES IN SAINT PETERSBURG AND THE LENINGRAD REGION IN 2006–2018

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▪ **Hypothesis/aims of study.** Prevention of the most common causes of perinatal mortality provides an opportunity to reduce perinatal losses. It is customary to distinguish between maternal, fetal and placental factors, dividing them into preventable and unavoidable subfactors. Of all nosologies, intrauterine hypoxia and asphyxia of the newborn, infectious (viral and / or microbial) damage to the placenta and fetus / newborn, and placental insufficiency (acute and chronic) are most important. The aim of this study was to analyze perinatal losses most often diagnosed in Saint Petersburg and the Leningrad Region in order to assess the possibility of developing a set of measures to reduce perinatal mortality.

▪ **Study design, materials and methods.** The analysis of perinatal losses in Saint Petersburg and the Leningrad Region in 2006–2018 is based on the official reports of the Saint Petersburg State Budgetary Healthcare Institution “Medical Information and Analytical Center” and the Leningrad Regional State Budgetary Healthcare Institution “Medical Information and Analytical Center,” as well as the reports of the Leningrad Regional Pathological and Anatomical Bureau (LRP&AB).

▪ **Results.** The main causes of perinatal losses in Saint Petersburg and the Leningrad Region for 2006–2018 were: fetal hypoxia (acute and chronic), intrauterine infections, respiratory distress syndrome (for premature babies), congenital malformations, and chromosomal abnormalities. Throughout the period, intrauterine hypoxia and asphyxia of the newborn (which are the pathology manifestation, not etiology) were indicated as leading diagnoses in the conclusions of perinatal death. Moreover, according to the LRP&AB pathomorphological findings, intrauterine infections were the leading (over 60% of cases) cause of perinatal losses over the years. During the analyzed period in Saint Petersburg and the Leningrad Region, a high frequency of “individual states arising in the perinatal period” remained unchanged without determination of a specific diagnosis, which significantly complicates our analysis.

▪ **Conclusion.** For an adequate diagnosis of the etiological mechanisms of perinatal losses, it is necessary to improve histological examination of the afterbirth and pathomorphological examination of the fetus / newborn using virological and immunological tests. It is also necessary to change the structure of statistical reports, obliging medical institutions to indicate the exact cause of perinatal death, excluding whenever possible the diagnoses of intrauterine hypoxia and asphyxia in labor that indicate no etiological diagnosis explaining the occurrence of hypoxia / asphyxia.

▪ **Keywords:** perinatal loss; stillbirth; early neonatal mortality; intrauterine hypoxia; intrauterine infection; congenital malformation.

## АНАЛИЗ ПРИЧИН ПЕРИНАТАЛЬНЫХ ПОТЕРЬ В САНКТ-ПЕТЕРБУРГЕ И ЛЕНИНГРАДСКОЙ ОБЛАСТИ В 2006–2018 ГОДАХ

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■ **Актуальность.** Снизить перинатальные потери возможно путем профилактики заболеваний и состояний, служащих наиболее частой причиной смерти. Выделяют материнские, плодовые и плацентарные факторы, которые можно разделить на предотвратимые и предотвратимые. Из нозологических форм наибольшее значение имеют внутриутробная гипоксия и асфиксии новорожденного, инфекционное (вирусное и/или бактериальное) поражение плаценты и плода/новорожденного, а также плацентарная недостаточность (острая и хроническая).

**Цель** — проанализировать наиболее часто диагностируемые в Санкт-Петербурге и Ленинградской области причины перинатальных потерь для выработки комплекса мер по снижению их частоты.

**Материалы и методы исследования.** На основании официальных отчетов Санкт-Петербургского государственного бюджетного учреждения здравоохранения «Медицинский информационно-аналитический центр», Ленинградской областной государственной бюджетной организации здравоохранения «Медицинский информационно-аналитический центр» и отчетов Ленинградской областной патологоанатомического бюро проанализированы причины перинатальных потерь в Санкт-Петербурге и Ленинградской области в 2006–2018 гг.

**Результаты исследования.** Основными причинами перинатальных потерь за 2006–2018 гг. в Санкт-Петербурге и Ленинградской области были внутриутробная гипоксия плода (острая и хроническая), внутриутробные инфекции, синдром дыхательных расстройств (для недоношенных детей), врожденные пороки развития и хромосомные аномалии. В течение всего периода в заключении о перинатальной гибели наиболее часто отмечены внутриутробная гипоксия плода и асфиксия новорожденного, которые служат проявлением патологического процесса, но не указывают на этиологию. При этом, по данным Ленинградской областной патологоанатомического бюро, основанным на результатах патоморфологического исследования, ведущей причиной (более 60 % случаев) перинатальных потерь в течение ряда лет являлись внутриутробные инфекции. За анализируемый период и в Санкт-Петербурге, и в Ленинградской области сохранялась высокая частота «отдельных состояний, возникающих в перинатальном периоде» без уточнения конкретного диагноза, что существенно затрудняет анализ причин перинатальных потерь.

**Выводы.** Для адекватной диагностики этиологических механизмов перинатальных потерь необходимо усовершенствовать систему гистологического исследования послеродового патоморфологического исследования плода/новорожденного с использованием вирусологических и иммунологических тестов. Следует изменить структуру статистических отчетов, в которых организации будут фиксировать точную причину перинатальной гибели, по возможности исключая диагнозы внутриутробной гипоксии и асфиксии в родах без указания этиологического диагноза, объясняющего возникновение гипоксии/асфиксии.

■ **Ключевые слова:** перинатальные потери; мертворождение; ранняя неонатальная смертность; внутриутробная гипоксия; внутриутробные инфекции; врожденные пороки развития.

Perinatal losses can be reduced by preventing diseases and conditions that most commonly cause death most. There are maternal, fetal, and placental factors that are subdivided into preventable and unavoidable factors [1–5]. In the range of nosological forms, intrauterine hypoxia and neonatal asphyxia, infectious (viral and/or microbial) lesion of the placenta and fetus/newborn, as well as placental insufficiency (acute and chronic) are of the greatest importance.

**This study aimed** to analyze the causes of perinatal losses that are commonly diagnosed in St. Petersburg and the Leningrad Region in order to develop a set of measures to reduce their frequency.

## Materials and methods

Based on the official reports of the St. Petersburg Medical Information and Analytical Center (MIAC SPb), the Leningrad Medical Information

and Analytical Center (MIAC LR), and reports of the Leningrad Regional Anatomicopathological Bureau (LRAPB), the dynamics of the causes of perinatal losses in St. Petersburg and the Leningrad Region from 2006 to 2018 was analyzed. The LRAPB data for the period of 2006–2016 was presented because starting from 2017, the LRAPB report was compiled based on the diagnoses presented in the medical documentation, which duplicates the MIAC LR report.

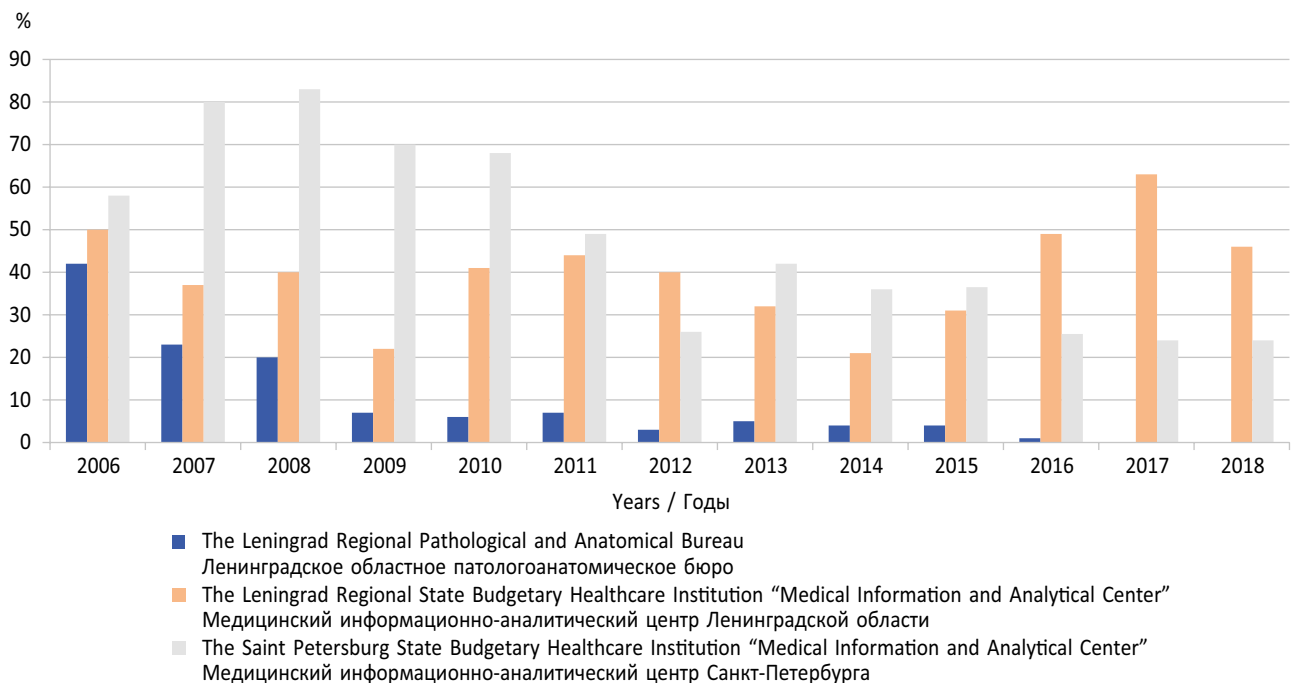
## Results

Intrauterine hypoxia (ICD-10 code is P20) and birth asphyxia (ICD-10 code is P21) are symptomatic diagnoses that represent a whole group of pathological conditions leading to perinatal losses. These include acute hypoxia (premature abruption of a normally located placenta, umbilical cord prolapse, etc.), chronic hypoxia in case of chronic placental insufficiency (CPI) (regardless

of its cause), and all undiagnosed conditions (including infectious lesions) that caused antenatal losses. Accordingly, the true cause of death is often identified when a more detailed study of the retained products and fetus/newborn is performed; although the main clinical manifestations were hypoxia and asphyxia, these conditions are less often diagnosed as the cause of death. For example, patient M., 30 years old, had a final diagnosis of premature second delivery at a term of 31 weeks; hydramnious; premature abruption of a normally located placenta; and antenatal fetal death. The diagnosis established for the stillborn child was acute intrauterine fetal hypoxia and birth asphyxia (P20, P21). The histological examination of the placenta revealed acute placental insufficiency with hematogenous viral placentitis; the postmortem examination of the fetus showed congenital herpetic infection, myocarditis, and intra-alveolar pneumorrhagia. Thus, it was indicated that the stillbirth was caused by hypoxia/asphyxia, although the death was actually caused by an infectious factor.

Fig. 1 presents the incidence of fetal hypoxia detection (intrauterine hypoxia and birth asphyxia; P20, P21).

According to LRAPB, the frequency of this pathology has been steadily decreasing over the



**Fig. 1.** Frequency of intrauterine hypoxia and asphyxia as a cause of perinatal death in 2006–2018

**Рис. 1.** Частота выявления внутриутробной гипоксии и асфиксии как причины перинатальной гибели плода в 2006–2018 гг.

period of 2006–2016. This can be explained by the fact that for many years, the bureau thoroughly worked to establish the true causes of perinatal losses by searching for an etiological factor (infectious, genetic, hematological, etc.), and not the pathogenetic mechanism of its implementation (intrauterine hypoxia, intranatal asphyxia etc.).

In obstetric institutions, as a rule, when premature detachment of the normally located placenta as a result of viral hematogenous placentitis occurs, the stillborn is diagnosed with intrauterine fetal hypoxia or birth asphyxia (P20, P21). It does not matter what exactly caused the placental detachment which led to asphyxia; viral placentitis, a prolonged period without amniotic fluid, bacterial chorioamnionitis, and polyhydramnios, which developed in the presence of a congenital malformation, or iatrogeny, namely improper labor induction or stimulation. In cases where the diagnosis of a viral lesion is verified only after the patient is discharged, the main medical documentation is filled out without taking this factor into account. If the patient does not seek to get the results of the pathomorphological study in the future, she will not know the cause of the perinatal loss, which complicates the prevention of this pathology.

Since chronic and acute fetal hypoxia during the entire period analyzed caused perinatal losses

most often according to the official statistics, the prevention and timely diagnosis of this pathology must be performed using cardiotocography and Doppler studies, and depending on the obstetric situation, it must be conducted once every 2 weeks or more often in the third trimester of pregnancy, as well as through prolonged and continuous cardiotocography during labor.

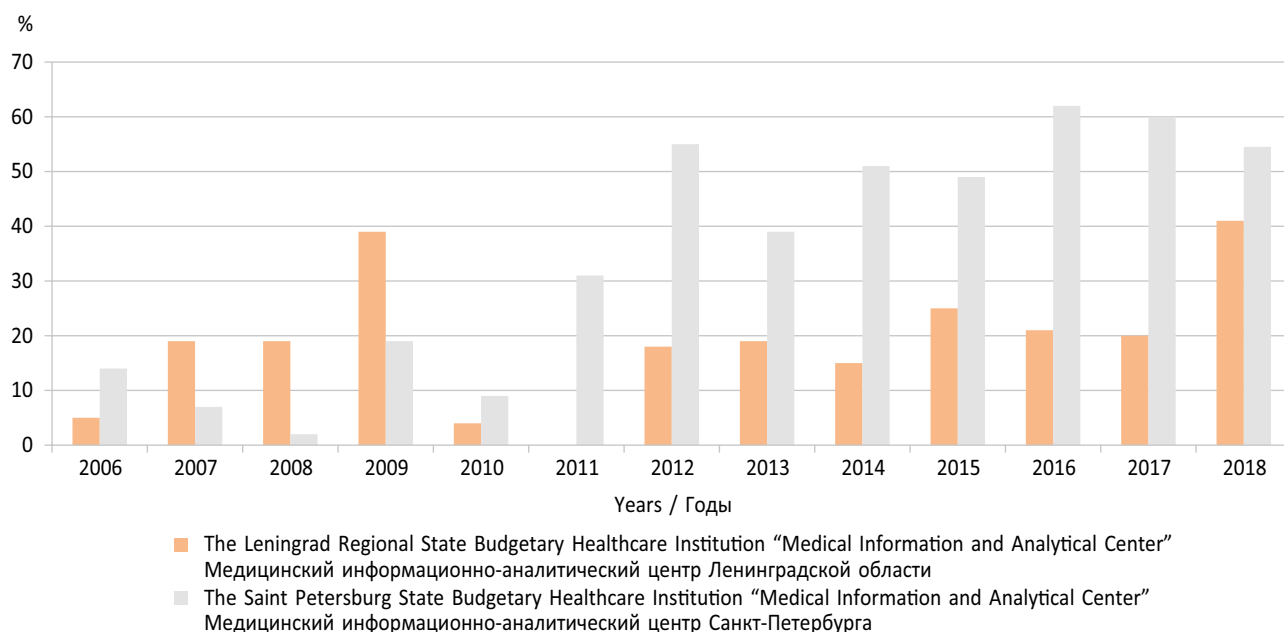
In St. Petersburg, fetal hypoxia and birth asphyxia are the most frequent causes of perinatal losses, and there has been a tendency toward a decrease in the level of these pathologies in recent years. This tendency can presumably be associated with the improvement in the quality of histological examinations performed after birth and postmortem examinations of fetuses/newborns and in the identification of the true etiology of the perinatal death, or with improved medical care. However, this trend is unfortunately due to another reason.

Fig. 2 presents the cases of perinatal death due to an unknown cause. According to the official MIAC reports of the Leningrad Region and St. Petersburg, the number of verified diagnoses is always less than the total number of perinatal deaths. The fact is that upon discharge from the hospital, the cause of the perinatal loss is not indicated in some cases. As a result of the widespread use of the diagnosis “intrauterine fetal death” (O36.4 in ICD-10), the analysis of the causes

of perinatal losses based on report forms No. 32 is significantly complicated. The cause of death was not indicated in approximately half of the cases; this figure exceeded 60% in some years. Consequently, according to the data of the St. Petersburg MIAC, the frequency of the pathogenetic diagnoses of “intrauterine hypoxia” (P20) and “birth asphyxia” (P21), and cases with an unspecified cause of death exceeded 80% for almost the entire monitoring period (Fig. 3).

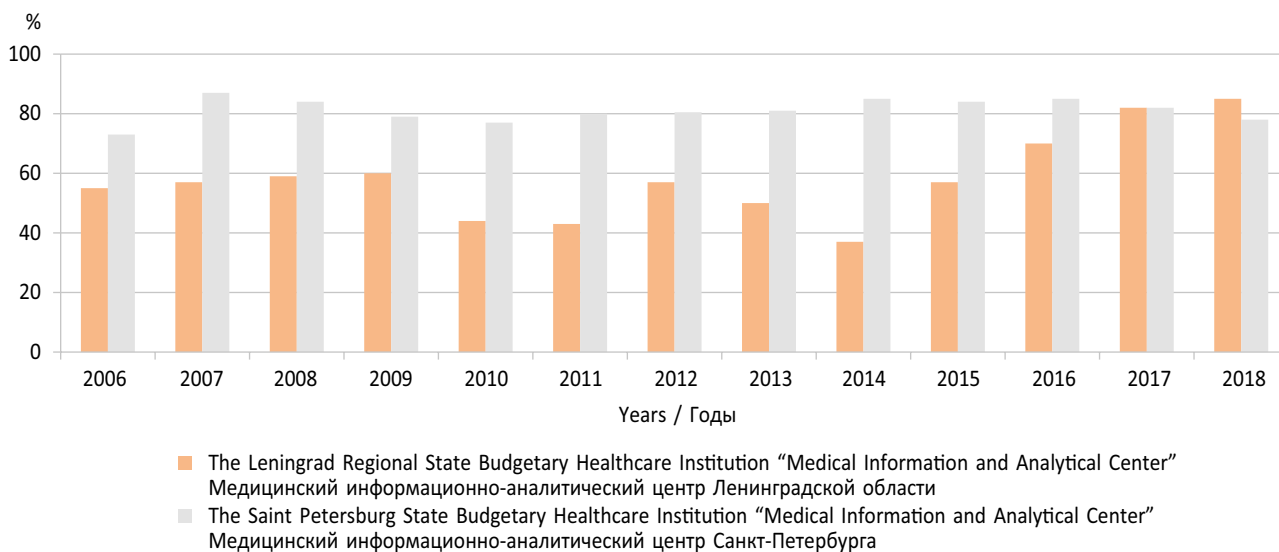
The incidence of CPI as a cause of perinatal losses (most often stillbirths) over the period analyzed was quite stable and according to LRAPB, it amounted to approximately 30% (11%–44%), and according to MIAC (St. Petersburg and the Leningrad Region), it did not exceed 1%–2%. In LRAPB, the diagnosis was established when hypoxic cardiopathy was detected during the autopsy; it develops with long-term hypoxia in CPI and causes fetal death antenatally and intranatally with decompensation, and it less often causes newborn death. Obstetricians establish the diagnosis of CPI *in utero* and immediately after delivery based on fetal/newborn undernutrition (Fig. 4).

According to official reports, fetal undernutrition rarely leads to perinatal death (no more than 2% for the entire period). Therefore, establishing the real role of CPI in perinatal losses is impossible due to the postulate that hypotrophy is the



**Fig. 2.** Frequency of the unknown cause of death in the Forms of Statistical Report No. 32 in 2006–2018

**Рис. 2.** Частота неустановленной причины смерти в отчетных формах № 32 в 2006–2018 гг.

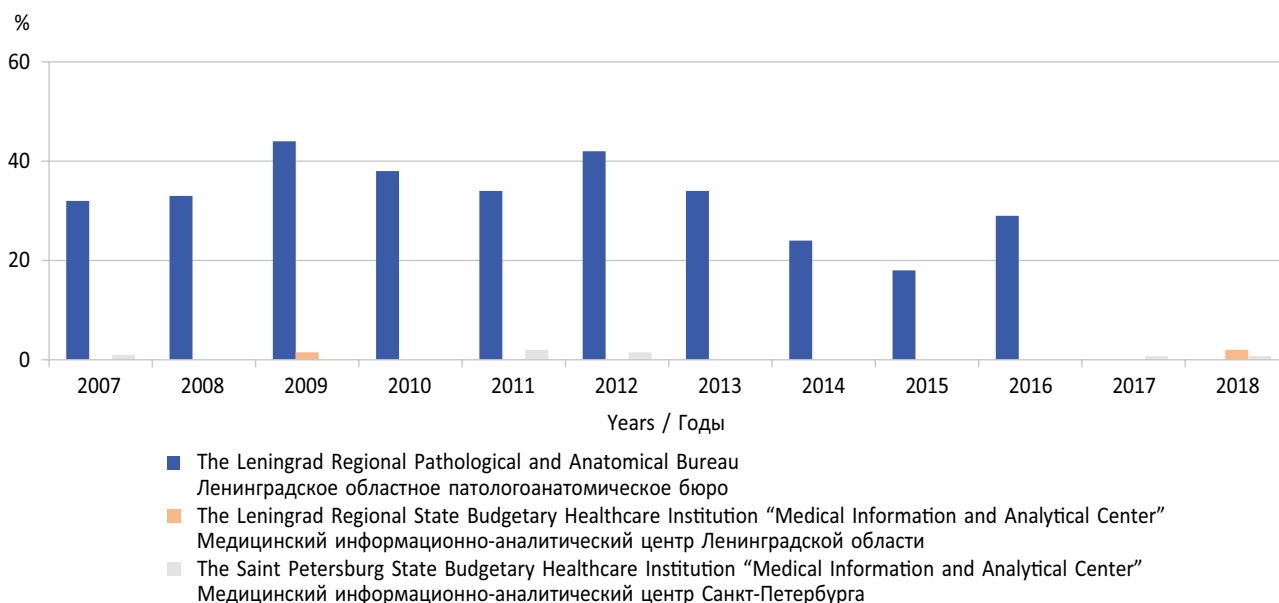


**Fig. 3.** Cumulative frequency of cases in which the cause of death is not specified, and the diagnoses of P20 and P21

**Рис. 3.** Совокупная частота случаев, в которых причина смерти не указана, и диагнозов P20 и P21

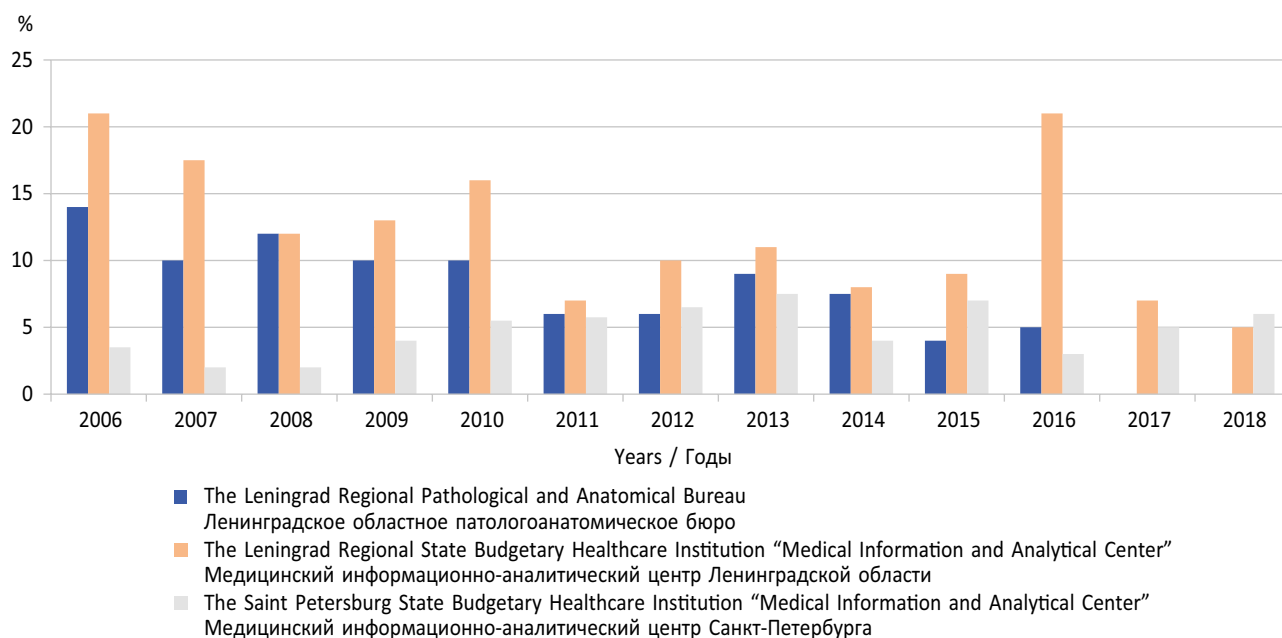
primary and possibly the only symptom of CPI. Thus, a very important mechanism of perinatal (mainly antenatal) death, which in this case can be prevented, is underestimated. The underestimation of undernutrition as a cause of perinatal losses partly explains the high incidence of intrauterine hypoxia or birth asphyxia. The extremely low incidence of fetal undernutrition deserves very close consideration, since it casts a doubt on the generally accepted opinion [1] that CPI is the cause of perinatal losses. Perhaps this is due to

the fact that CPI as an isolated factor does not always cause perinatal death. The opinion about the high frequency of this pathology is based on the overdiagnosis of this condition by obstetricians who establish decompensated CPI for all fetuses that died antenatally. As a result, the placental complex pathology is life-threatening on one hand and there is a problem of overdiagnosis on the other. In this situation, it is necessary to develop a system for diagnosing CPI, which would enable the identification of this condition with a high



**Fig. 4.** Frequency of chronic placental insufficiency / fetal malnutrition as a cause of perinatal death in Saint Petersburg and the Leningrad region

**Рис. 4.** Частота выявления хронической плацентарной недостаточности/гипотрофии плода как причины перинатальной гибели плода в Санкт-Петербурге и Ленинградской области



**Fig. 5.** Frequency of respiratory distress syndrome and intraventricular hemorrhage as a cause of perinatal death in Saint Petersburg and the Leningrad Region

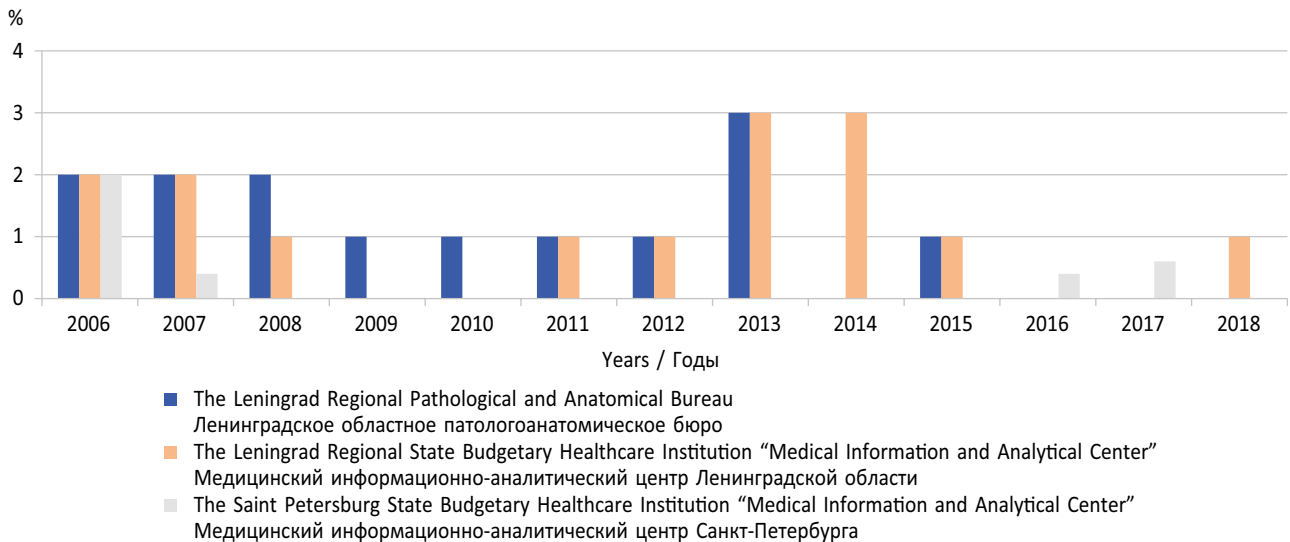
**Рис. 5.** Частота выявления синдрома дыхательных расстройств и внутрижелудочковых кровоизлияний как причины перинатальной гибели плода в Санкт-Петербурге и Ленинградской области

degree of accuracy. At the same time, the other extreme aspect is very dangerous, which is denial of the problem of undernutrition and CPI, based on official statistics.

Intraventricular hemorrhage and respiratory distress syndrome (Fig. 5) are the major causes of early neonatal death in premature infants. It turned out that with the introduction in 2012 of the live birth criteria recommended by the World Health Organization, the dynamics of these indicators for the analyzed period changed insignificantly, especially in the Leningrad Region, where the maximum contribution of intraventricular hemorrhages and respiratory distress syndrome to perinatal mortality was recorded in 2006 and 2016 (more than 20%). In other years, the incidence of this cause of perinatal losses ranged from 7% to 17% without clear dynamics. According to LRAPB, the indicators of these causes of newborn deaths obviously decreased over the period of 2006–2012 (from 14% to 6%); there was an increase in 2013 (9%), and a gradual decline to 5% in 2016. In St. Petersburg, the frequency of the respiratory distress syndrome and intraventricular hemorrhage ranged from 2% to 8% (the maximum rate was registered in 2013). The number of cases of this pathology can be reduced by preventing premature births.

Hemolytic disease of the fetus and newborn (Fig. 6) is not the leading cause of perinatal losses either in the Leningrad Region or in St. Petersburg; in addition, the development of this pathology can currently be prevented. A system for the prevention of Rh sensitization as the main cause of hemolytic disease of the fetus and newborn has been developed for the exclusion of transfusion of foreign rhesus blood, prevention of abortion, and use of anti-rhesus immunoglobulin. At the same time, the peak of the incidence of this pathology was noted in 2013 and 2014 (3%) in the Leningrad Region, and it was noted in 2006 (2%) in St. Petersburg. This fact is extremely important, since this problem can be eliminated with the proper conduct of sanitary and educative activities among the population, including the need to address the problem of toxic effects on the fetus (consumption of alcohol, drugs, smoking), which is rarely indicated as the cause of perinatal death (preventable factor).

During the period analyzed, there was no clear dynamics of the rate of incidence of intrauterine infections (IUI) as the cause of death in the perinatal period in St. Petersburg (from 1 to 12%). In the Leningrad Region, statistics on this pathology had been changed significantly, as over 10 years, the role of IUIs has been rethought and the frequency of their detection has increased by approximately



**Fig. 6.** Frequency of hemolytic disease of the fetus and newborn in Saint Petersburg and the Leningrad region

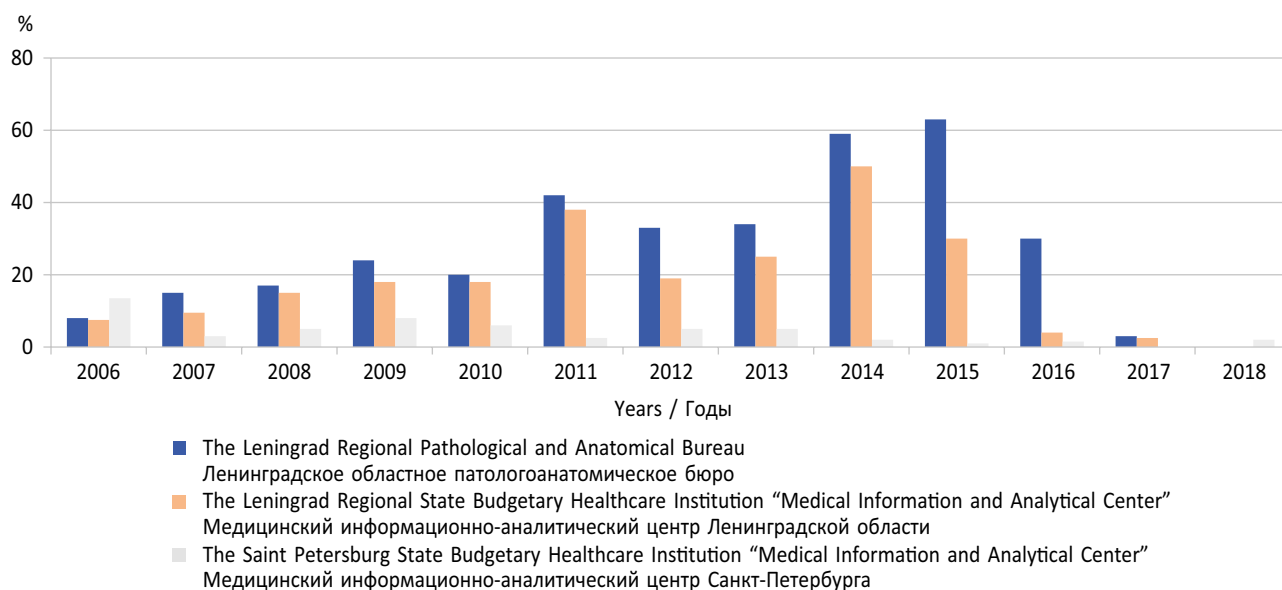
**Рис. 6.** Частота выявления гемолитической болезни плода и новорожденного в Санкт-Петербурге и Ленинградской области

10 times. The IUI was used to explain both antenatal and early neonatal death, which necessitated the development and implementation of a system for diagnosing and treating infection in patients from risk groups. The approach to the diagnosis of a number of conditions has changed, and such diagnoses as viral antral myocarditis, often associated with lesions of the pacemaker in the right atrium in case of herpes infection, have appeared. The methodology for diagnosing these conditions was developed at LRAPB and introduced into the practice of all anatomic pathology departments of the Leningrad Region. Over the past 2 years, the incidence of IUI as a cause of death in the perinatal period has decreased 3 times. This can be explained by the introduction into practice of a system for the detection and treatment of infection of patients from risk groups, especially those hospitalized in the pregnancy pathology department of the Leningrad Regional Clinical Hospital. According to the initiative of the doctors of this institution, a total examination of pregnant women hospitalized in the gynecological hospitals of the Leningrad Region was implemented for the presence of antibodies to types 1 and 2 Human herpesvirus, as well as determination of the avidity index with further (according to indications) antiviral treatment (in the trimester II of pregnancy). In St. Petersburg, this diagnostic technique, in particular the targeted examination of the pacemaker area in the right atrium, has not been introduced, and accordingly,

the diagnosis of IUI, including antral myocarditis, is established much less frequently (Fig. 7).

In the general population of infants who died perinatally, it is difficult to assess the role of one virus or another and one localization of the lesion or another, since in the presence of two or more localizations of the lesion and/or two or more pathogens, these data cannot be entered into the report. Accordingly, the better the diagnostics of IUI-related problems is performed, the more often the report indicates "unspecified intrauterine infection." In addition, intrauterine pneumonia is a disease in which infectious etiologic agents are of a major importance. According to the official report, it relates to the group of respiratory disorders, which leads to an underestimation of the importance of the infectious factor. That is why, on the basis of official reports, it is impossible to draw a conclusion about the role of any particular pathogen in the genesis of perinatal losses, as well as about the specific localization of the pathological process in fetuses and newborns. Such a denial of the role of IUI is not only irrational, but also dangerous for the life of not only infants, but also the mothers due to the high incidence of chorioamnionitis [6, 7].

The incidence of congenital malformations (CM) and chromosomal abnormalities, identified as the cause of perinatal losses, was approximately the same during the analyzed period and amounted to approximately 10% (2%–16% in the Leningrad

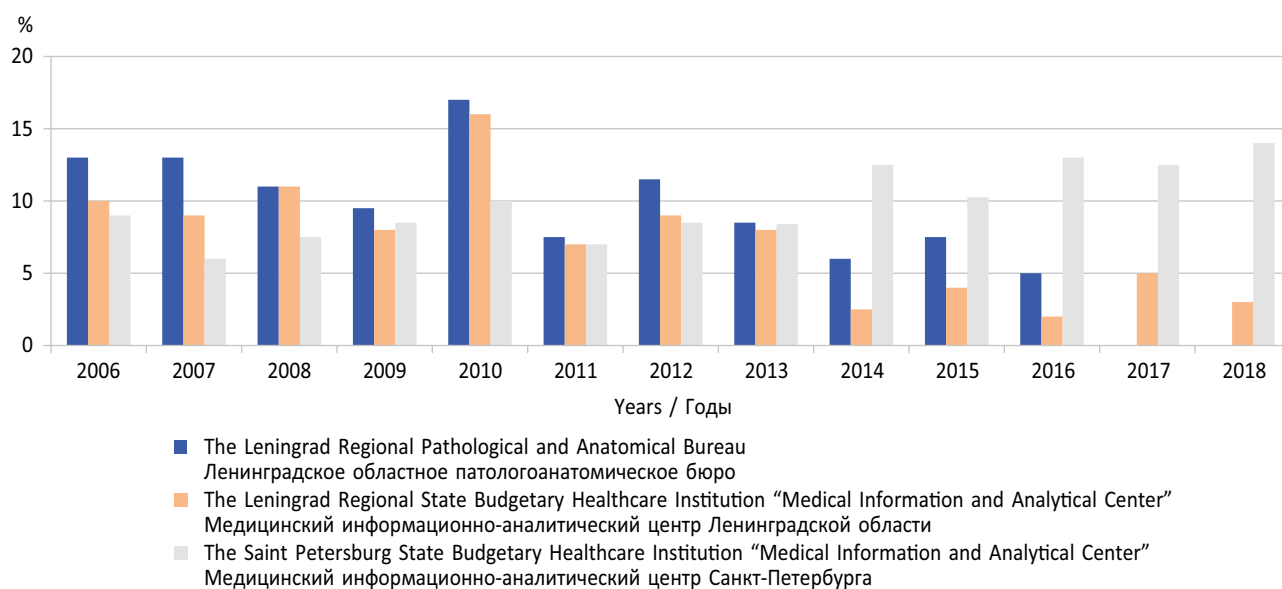


**Fig. 7.** Frequency of intrauterine infections as a cause of perinatal death in Saint Petersburg and the Leningrad region

**Рис. 7.** Частота выявления внутриутробных инфекций как причины перинатальной гибели плода в Санкт-Петербурге и Ленинградской области

Region, 6%–13% in St. Petersburg) (Fig. 8). The CMs of the central nervous system, cardiovascular system, multiple CMs, and chromosomal abnormalities such as Patau syndrome were diagnosed most frequently. These defects are lethal in most cases, whereas, malformations of the gastrointestinal tract do not always cause perinatal death, although they occur quite often in the newborn population.

Such pathologies can also be combined with heart defects that do not lead to lethal hemodynamic disorders. Thus, in 2016, one of the fetuses that died antenatally from an unspecified viral infection had a small-sized ventricular septal defect. The congenital heart disease probably had a viral etiology, but its role in the genesis of perinatal death is questionable.



**Fig. 8.** Frequency of congenital malformations and chromosomal abnormalities as a cause of perinatal death in Saint Petersburg and the Leningrad region

**Рис. 8.** Частота выявления врожденных пороков развития и хромосомных аномалий как причины перинатальной гибели плода в Санкт-Петербурге и Ленинградской области



On one hand, CMs represent an unavoidable cause of perinatal losses, while on the other hand, lethal CMs and chromosomal abnormalities should be diagnosed in a timely manner, namely in the first trimester of pregnancy, when it can be terminated prior to the period of fetal viability. Unfortunately, there are still cases of children born weighing more than 1000 g with fatal CMs, namely holoacrania with rachischisis. Accordingly, it is necessary to improve the performance of ultrasound and biochemical screenings.

### Conclusions

1. The main causes of perinatal losses from 2006 to 2018 in St. Petersburg and the Leningrad Region were intrauterine fetal hypoxia (acute and chronic), IUIs, respiratory distress syndrome (for premature babies), CMs, and chromosomal abnormalities.
2. Throughout the period, intrauterine fetal hypoxia and birth asphyxia were indicated as the leading diagnoses in the conclusion of the perinatal death; however, they are manifestations of a pathological process, and do not reflect its etiology.
3. According to LRAPB, based on the results of pathomorphological studies, IUI were the primary cause (more than 60%) of perinatal losses for a number of years.
4. For the period of 2006–2018, both in St. Petersburg and in the Leningrad Region, a high frequency of “isolated conditions arising in the perinatal period” persisted, without specifying an accurate diagnosis, which complicates significantly the analysis of the causes of perinatal losses.
5. For the adequate diagnosis of the etiological mechanisms of perinatal losses, the system of the histological examination of the retained products and pathomorphological study of the fetus or newborn using virological and immunological tests needs to be improved.
6. The structure of statistical reports need to be changed, so that organizations will be required to indicate the accurate cause of perinatal death, if possible, excluding diagnoses of intrauterine hypoxia and birth asphyxia without specifying an etiological diagnosis explaining the occurrence of hypoxia or asphyxia.

7. Perinatal losses can be reduced by developing a set of measures for the timely diagnosis and rational treatment of the major conditions causing fetal and newborn death newborn.

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