

# Perinatal injury of the central nervous system in Lithuania from 1997 to 2014

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**Background.** Perinatal CNS injuries are significant for the health of neonates and for child development at a later period. The aim of this study was to evaluate the dynamics of the frequency of perinatal CNS lesions (corresponding to ICD 10 code P91) over a 20-year period, using the data collected from the Lithuanian Medical Data of Births (Registry of Births).

**Material and methods.** In total, data of 559,164 newborns were analyzed.

**Results.** During the period from 1997 to 2014, the frequency of term newborns with perinatal CNS injury decreased almost two times, from 20.4/1000 live births in 1997 to 15.5/1000 live births in 2014, or from 3.12% (95% CI 2.95; 3.31) to 1.46% (95% CI 1.32; 1.61). In 18 years, the rate of infant mortality from perinatal CNS injury decreased by more than four times and in 2014 it was 0.3/1000 births; it accounts for 11% of neonatal mortality (2.6/1000 live births). The largest decrease of CNS injury was seen after a caesarean birth (from 13.7% in 1999 to 1.7% in 2014) and breech delivery (from 9.7% in 1999 to 0.8% in 2014). Analysis of the dynamics of perinatal CNS injury in preterm births in selected groups did not identify a significant positive shift during the period. When evaluating the level of childbirth services in different-level maternity hospitals, CNS injury is undoubtedly diminished in 2B-level maternity hospitals (regional). Also, positive dynamics was observed in the data of 2A-level maternity hospitals, while in 3-level maternity hospitals (university hospitals), which deal with the most complicated obstetrical pathology and preterm newborns, positive dynamics was not observed. It is estimated that the frequency of hypoxic-ischemic encephalopathy was 0.63/1000 live births in Lithuania in 1993.

**Conclusions.** The frequency of perinatal CNS injury and its positive dynamics in over 18 years shows a progressive and scientifically-based perinatal health care organization in Lithuania.

**Keywords:** neonates, central nervous system, perinatal injury, frequency in Lithuania

## INTRODUCTION

The outcomes of perinatal injury of the central nervous system (CNS) manifest themselves in many different clinical forms and can cause intellectual disabilities (1). Although diagnosing these lesions with the help of ultrasound, MRI, EEG, and other modern methods is no longer a problem, the pathogenesis, the course of disease, and some other aspects are widely discussed among physicians and remain an important medical and social problem. It is reflected in the classification and terminology of these lesions. However, so far there have been no unified criteria for the characterization of these injuries: hypoxic-ischemic encephalopathy (HIE), perinatal asphyxia, neonatal encephalopathy (NE), etc. In recent years, two main forms of CNS lesions in newborns are mostly known.

“Neonatal encephalopathy” (NE) has emerged as the preferred term to describe a dysfunction of the central nervous system in the newborn period (2). The terminology does not imply a specific underlying pathophysiology, which is appropriate since the nature of brain injury causing neurologic impairment in a newborn is poorly understood. NE is a clinical outcome of a cerebral dysfunction, which can cause death, cerebral palsy, epilepsy, and other significant cognitive, developmental, and behavioural disturbances (3). In term newborns, the symptoms of NE develop during the first days of their life: breathing insufficiency, decreased tonus and reflexes, changes in consciousness, seizures, and some other symptoms (4). When neonatal encephalopathy is due to hypoxic-ischemic (anoxic) brain injury, it is appropriate to use the term hypoxic-ischemic encephalopathy (HIE) (5). HIE refers to the acute clinical syndrome seen in babies following an acute severe hypoxic-ischaemic (asphyxial) event that is typically perinatal in timing (6).

Although estimated 30% of cases of NE in developed countries are associated with the evidence of intrapartum hypoxic ischemia (3), it is important to stress that NE symptoms can occur without hypoxia: in preterm newborns NE can occur when an intrauterine infection is present (7). Important initial considerations in trying to describe the epidemiology of NE and HIE are a lack of a universally agreed definition of both of these terms. The epidemiological data of perinatal and newborn CNS lesions is contradictory and depends on research type (prospective or

retrospective), population (newborn population, maternity hospital patients, or hospital patients), economical factors, and other factors.

The aim of this study was to evaluate the dynamics of the frequency of perinatal CNS injury (corresponding to ICD 10 code P91) over a 20-year period, using data collected at the Lithuanian Medical Data of Births (Registry of Births) (8).

## MATERIALS AND METHODS

A retrospective analysis of the data from the Health Information Centre of the Institute of Hygiene (Lithuania) from the period of 1995 to 2014 was performed. In total, data on 639,201 newborns were analyzed. 559,164 newborns were included in the study; the data of 1995–1996 was rejected because of incomplete information.

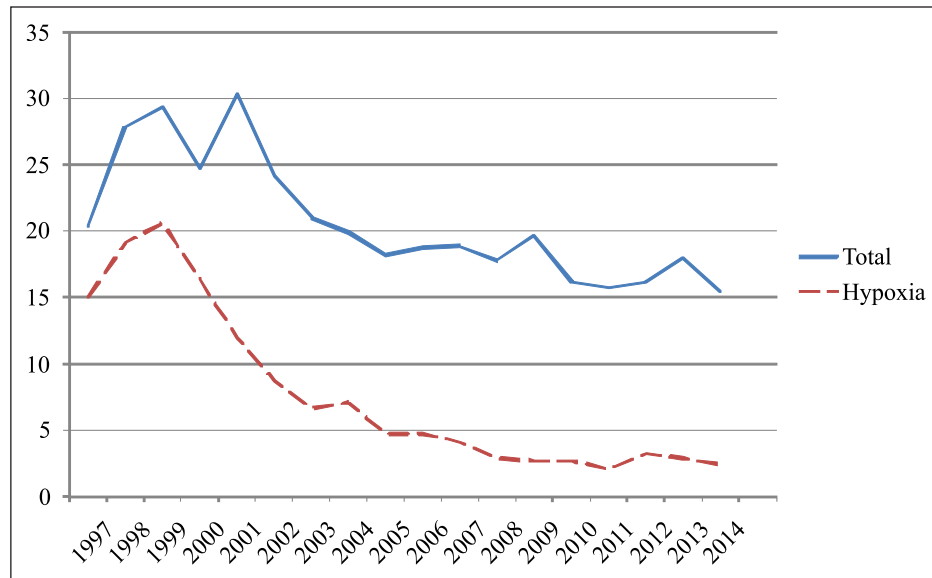
Diagnosis of perinatal CNS lesions in Lithuania is based on the data on the evaluation of morphological changes (i. e., congenital defects, intracranial trauma), the APGAR score after five minutes, results of estimation of pH of the umbilical cord blood, sonography, the EEG data, and other diagnostic methods.

In this study the frequency of CNS injury was evaluated from the point of view of pregnancy pathologies (maternal infection), breech birth, and delivery type (a vaginal delivery or a caesarean section). Though many reasons can cause perinatal CNS lesions (obstetric, genetic, social, and other factors), we used only the data given in the unified questionnaire of the Lithuanian Medical Data of Births. Also we evaluated the relationship between perinatal CNS lesions and the level of services in maternity hospitals (birthplace).

Although special verification of the Medical Data of Births was not performed, in 2001–2002 parallel research into the influence of socio-economic factors and health behaviour on the risk of stillborns and low birth weight infants in Lithuania was conducted (9). Results of this research were compatible with the Medical Data of Births results, and that can be considered as partial confirmation of data validity.

## RESULTS

The frequency of perinatal lesions of CNS among term newborns is shown in Fig. 1.

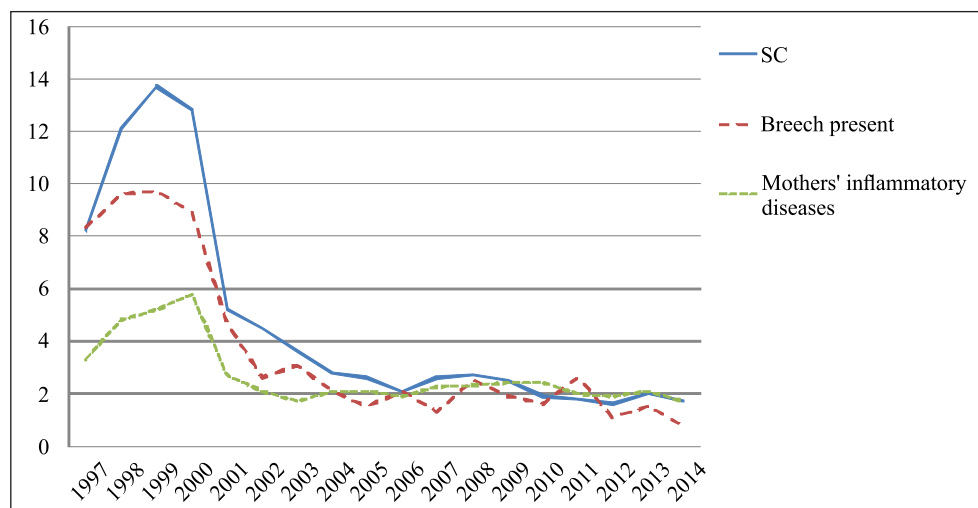


**Fig. 1.** The perinatal CNS injury rate (%) among term newborns in 1997–2014

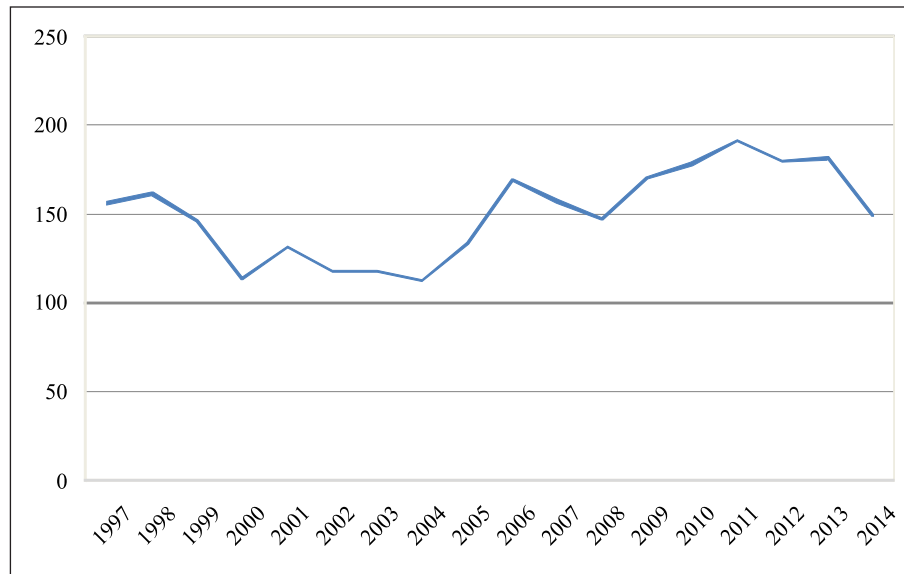
During the period of 1997 to 2014, perinatal injury of CNS in term newborns decreased almost twice in Lithuania: from 20.4 per 1000 newborns in 1997 to 15.5/1000 newborns in 2014, or from 3.12% (CI 95% 2.95; 3.31) to 1.46% (CI 95% 1.32; 1.61).

When evaluating the frequency of perinatal CNS lesions in the group of term newborns by peculiarities of the delivery type, we found that lesions of the CNS decreased from 13.7% in 1999 to 1.7% in 2014 after a caesarean section. Also, CNS lesions of term newborns decreased from 9.7% in 1999 to 0.8% in 2014 after breech deliveries (Fig. 2).

Changes in the frequency of perinatal CNS injury due to the mother's infection are almost identical to the overall positive dynamics, especially in the early period (1997–2002) of the reorganization of perinatal care in Lithuania. The dynamics of perinatal CNS injuries of preterm newborns differs clearly from that of term newborns, both in the overall frequency of term and in the frequency in selected groups: a significant positive shift has not been determined (Fig. 3). In 1997, it was 156/1000 live births, in 2014 149/1000 live births, or 15.75% (95% CI: 13.99, 17.68) and 14.88% (95% CI: 13.00, 16.95) newborns, respectively.



**Fig. 2.** The relationship of the rate (%) of perinatal CNS injury among term newborns with the mode of delivery and inflammatory diseases of mother



**Fig. 3.** Rate (%) of perinatal CNS injury among preterm newborns in 1997–2014

The frequency of perinatal CNS injuries by births given in maternity hospitals of different levels (secondary A and B, tertiary level) of obstetric and neonatal services is shown in Fig. 4. The graphs in this chart reflect any pathological lesion: perinatal CNS injury as a main disease and other accompanying diseases or syndromes. Two, three, or even four ICD P.91 codes may be attributed to one sick newborn, therefore the statistical incidence of pathological injury of CNS per 1000 births is high with positive tendencies. The positive dynamics of the frequency of injury were observed in maternity

hospitals of level 2A (the lowest level of perinatal care), while in perinatal centres (tertiary level, university hospitals) that concentrated on complicated obstetric pathology and where premature infants are mainly born, there is no positive dynamics.

For the assessment of the severity of perinatal CNS injury we established a neonatal mortality rate related with such injuries: neonatal mortality due to perinatal CNS injury has fallen by more than 4 times in the last 18 years; in 2014, this indicator was 0.3/1000 births (Fig. 5). This corresponds to 11% of infant mortality (2.6/1000) (8).



**Fig. 4.** The rate (%) of perinatal CNS injury (among term and preterm newborns) by place of birth (level of services in maternity hospitals)

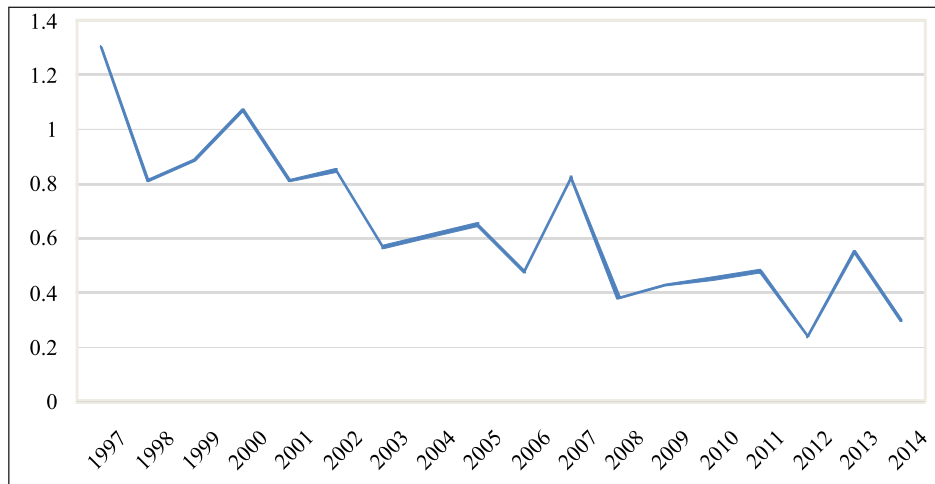


Fig. 5. Newborn mortality rate (%) due to CNS injury

## DISCUSSION

Possible inaccuracies in the assessment of the epidemiological data of perinatal CNS injury are related to the formulation of the diagnosis (NE, or HIE, or others), classification of diseases (ICD code), accounting data, and interpretations of the changes that occur over a longer period of time. They also depend on methodological problems: what kind of data will be analyzed and evaluated (for example, hospital-based studies or population studies), what period of time is evaluated, etc. In general, hospital-based incidence figures tend to be higher than population-based results. Perinatal asphyxia severe enough to cause moderate-to-severe encephalopathy occurs in about 1–2/1000 birth in resource-rich countries, with over a tenfold rate in the countries with limited resources (10).

It is indicated that HIE incidence in developed countries is 1.5/1000 births, while in developing countries from 2.3 to 26.5/1000 live births (11). There is a high risk of death and cerebral injury in survivors. It is an important public health problem globally, with high opportunity costs for the affected families and health services which leads to major litigation claims (12).

A comprehensive epidemiological data summary of HIE and NE states that according to the neonatal population survey (Derby, UK) the frequency of this kind of pathology among term newborns (gestational age more than 37 weeks) decreased from 7.6/1000 live births in 1970 to 1.9/1000 live births in 1990 (3). When

evaluating only the term newborns data it was determined that during the period of 1992 to 1996, the incidence of HIE (diagnosed according to criteria of Levene et al.) (13) was 1.94/1000 live births (14), while NE incidence in one of the regions of London from 1993 to 1995 was 2.63/1.000 live births (15). Studies based on the data of maternity hospitals indicated a significantly higher frequency of HIE: between 1970 and 1988, various authors stated the incidence ranging from 3.32 to 7.61/1.000 live births (3). The American College of Obstetricians and Gynecologists and the American Academy of Pediatrics summed up the population data in 2002 and stated that the frequency of NE ranged from 1.9 to 3.8/1000 live births (16). Thus, the assessment of various authors and sources of data shows that NE is approximately 3.0/1000, and HIE is 1.5/1000 live births (3); in such a case, the overall frequency of such type of CNS pathology is about 4.5/1000 births.

Diagnostic of CNS lesions in both maternity hospitals and neonatal pathology departments in Lithuania is currently based on neurological examination (Levene criteria), ultrasound, and other imaging techniques and is sufficiently objective. The medical database of births, which covers more than 500,000 births over the analyzed period and is based on maternity hospitals data, indicates that the total term newborns with perinatal CNS lesions frequency over the last 16 years decreased almost two times (from 29.4/1000 to 15.5/1000 births). These positive changes are primarily concerned with the high quality of childbirth assistance, especially when delivery is finalized by



a caesarean section or fetal breech delivery. Infant mortality data due to CNS injury in Fig. 5 shows that life incompatible CNS lesions are very rare.

To evaluate the severity of the perinatal CNS disease, from 1998 the available data was carefully examined every five years (1998, 2003, 2008, 2013) and it was found that 61–73% of term newborns had the mildest form of CNS – a brain-derived neonatal irritability (P91.3 in ICD classification). This means that in 30–40% of newborn CNS injury may be considered from mild to moderate.

In 2013 neonatal HIE (P91.6) was 3.5% among all term newborns with brain disorders (CNS lesions). The evaluation of the overall rate of term newborns with perinatal CNS injury in 2013 (18/1000 live births) concludes that in 2013 the frequency of HIE in Lithuania was 0.63/1000 births. Such frequency of perinatal CNS injury among term infants reflects well-organized perinatal care.

The epidemiological data on the injury of CNS among preterm newborns are discussed less often in literature, because the grouping and evaluation of premature newborns is expressively different in developing and developed countries. It is argued that in preterm newborns, perinatal CNS pathology occurs at least ten times more often than in term newborns. In this way, the assessment for Lithuania is expected to be around 20/1000 live births.

## CONCLUSIONS

The presented data show that the frequency of term newborns with perinatal CNS injury over a 20-year period dropped by almost two times and the frequency of hypoxic ischemic encephalopathy (HIE) (0.63/1000 births) is in line with the data from developed countries. This reflects progress in obstetric and neonatal care in Lithuania over the last 20 years and outlines future challenges of perinatology in order to reduce neonatal and infant morbidity, especially the frequency of nervous system disorders.

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#### PERINATALINIAI CNS PAŽEIDIMAI LIETUVOJE 1997–2014 METAIS

##### *Santrauka*

**Tikslas.** Nustatyti perinatalinių CNS pažeidimų dažnumą ir pagrindinius juos lemiančius veiksnius Lietuvoje.

**Medžiaga ir metodai.** Išnagrinėti Sveikatos statistikos centre 1997–2014 m. sukaupti duomenys apie

559 164 gimdymo stacionaruose gimusius naujagimius.

**Rezultatai.** 1972–2014 m. išnešiotų naujagimių perinatalinių CNS pažeidimų dažnis Lietuvoje sumažėjo beveik 2 kartus: nuo 20,4/1 000 gimusiųjų 1997 m. iki 15,5/1 000 gimusiųjų 2014 m., arba nuo 3,12 % (PI 95 % 2,95; 3,31) iki 1,46 % (PI 95 % 1,32; 1,61). Naujagimių mirtingumas dėl perinatalinių CNS pažeidimų per 18 metų sumažėjo daugiau kaip 4 kartus ir 2014 m. buvo 0,3/1 000 gimusiųjų; tai sudaro 11 % bendro naujagimių mirtingumo (2,6/1 000 gimusiųjų). Labiausiai perinatalinių išnešiotų naujagimių CNS pažeidimų dažnis sumažėjo po cezario pjūvio (nuo 13,7 % 1999 m. iki 1,7 % 2014 m.) ir gimusiųjų sėdmeninėje pirmiejoje (nuo 9,7 % 1999 m. iki 0,8 % 2014 m.). Neišnešiotų naujagimių perinatalinių CNS pažeidimų dinamikos pagal pasirinktas analizės grupes didesnio teigiamo poslinkio per nagrinėjamą laikotarpį nenustatyta.

Antrinio B lygio stacionaruose gimusių naujagimių grupėje perinatalinių CNS pažeidimų skaičius neabejotinai sumažėjo. Teigiama dažnumo dinamika stebima ir antrinio A lygio paslaugas teikiančiuose akušerijos ir neonatologijos stacionaruose, o tretinio lygio paslaugas teikiančiuose stacionaruose, kuriuose koncentruojami sudėtingiausi akušerinės patologijos atvejai ir dažniausiai gimsta neišnešioti naujagimiai, teigiamos dinamikos nenustatyta. Apskaičiuota, kad hipoksinės-išeminės encefalopatijos dažnumas Lietuvoje 1993 m. sudarė 0,63/1 000 gimusiųjų.

**Išvada.** Perinatalinių CNS pažeidimų dažnis ir teigiama dinamika per 18 metų rodo pažangią ir mokliškai pagrįstą perinatalinės pagalbos organizavimą Lietuvoje.

**Raktažodžiai:** naujagimiai, centrinė nervų sistema, pažeidimai, dažnis Lietuvoje