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Original article

Temporal trends in perinatal mortality and cerebral palsy: A regional population-based study in southern Japan

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Abstract

Aim: The prevalence of cerebral palsy (CP) has not decreased in developed countries over the past 30 years. We examined gestational age-specific trends in the prevalence of CP.

Methods: This unselected, population-based study was conducted in Miyazaki prefecture, Japan (10,000 deliveries annually), where 102,999 deliveries were registered between 2001 and 2010. Of these, 312 were stillbirths ($\geqslant$22 weeks of gestation), 126 were neonatal deaths (<28 days of birth), and 214 infants were determined to be at risk of CP at peer-review conferences. Survival and neurological damage were compared for two 5-year periods, 2001–2005 and 2006–2010, and infants were classified according to gestational ages.

Results: Stillbirths and neonatal deaths decreased significantly during both periods. Likewise, the number of registered high-risk cases of CP decreased by 30.2%, from 126 to 88 cases. After excluding congenital anomalies, the corrected CP prevalence was 1.5 per 1000 (78/51,889) and 1.3 per 1000 (67/51,110), for the two periods, which was not a significant difference. The number of extremely preterm infants (22–25 weeks) did not change over the 10-year period, whereas that of moderately preterm infants (26–36 weeks) increased, and that of term infants significantly decreased ($p < 0.01$). In term infants, asphyxia decreased from 18 to 7 cases ($p < 0.05$).

Conclusions: Perinatal deaths and CP decreased in prevalence during both 5-year periods, and the CP prevalence was 2.1 per 1000 births. Furthermore, fewer term infants were at high risk for CP mainly because of the reduced prevalence of asphyxia.

Keywords: Cerebral palsy; Perinatal mortality; Population-based study; Periventricular leukomalacia; Asphyxia

1. Introduction

Several case-control and population-based cohort studies have been conducted to elucidate the relationship between cerebral palsy (CP) and perinatal risk factors [1–10]. The prevalence of CP in developed countries has not decreased over the past 30 years, despite a 5-fold increase in the rate of cesarean births. Clark et al. [5] mentioned that CP was unpreventable given our current state of technology.

In the population-based study from Western Australia [2], Canada [6], and Japan [7,8], the sustained prevalence is possibly due to the improved survival rate for extremely preterm infants, who are at particular risk of neurological damage and reduced CP prevalence in term infants. In recent studies, no decreases in CP preva-

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lence in low birth weight infants were reported since1990's [9,10].

As mentioned above, the risk factors of CP are still uncertain. To verify this suspicion, we need update the etiology of perinatal mortality and brain damage that occurs during the perinatal period. It is important to investigate the risk factors of CP in relation to perinatal death, because some factors are independent and persistent from perinatal death to neurological damage [11].

This study aimed to assess the overall gestational age-specific chronological trends in the rate of CP in southern Japan, where the perinatal mortality rate is among the lowest in the world, 3.0 per 1000 births. This study would also provide some information to ascertain the future direction of perinatal and neonatal care.

2. Materials and methods

We conducted an unselected, population-based cohort study in Miyazaki prefecture, Japan (10,000 deliveries/year), where 102,999 deliveries were registered between 2001 and 2010. During this period, we held peer-review audit conferences to examine all 312 stillbirths (⩾22 weeks of gestation), 126 neonatal deaths, and 214 infants with CP. Infants were classified into three groups according to gestational age: term (⩾37 weeks); moderately preterm (26–36 weeks); and extremely preterm (22–25 weeks). The infant survival rate and prevalence of neurological damage were compared between two 5-year periods, 2001–2005 and 2006–2010.

In Miyazaki prefecture, we have been taking a leading role in perinatal and neonatal medicine in efforts to reduce perinatal mortality and neonatal neurological damage. Details of our work have been reported previously [12–15]. Briefly, we have 34 primary obstetrical clinics, seven secondary perinatal centers, and one tertiary center across four medical districts in Miyazaki. Each district has at least one secondary center, and all but two primary clinics are within 30 min of the nearest perinatal center. Nearly 80% of women were low risk and delivered mainly in the primary clinics, while the remaining 20% were referred with high risk factors to secondary or tertiary centers.

The Miyazaki Perinatal Data Group holds a peer-review audit conference twice a year, which is attended by perinatal specialists from our eight perinatal centers who discuss the clinically associated factors of the perinatal deaths and neurological complications that have occurred. Specialists from the divisions of maternal-fetal medicine, neonatal medicine, and pediatric neurology also participate in the conference. Our criteria for registering high-risk infants with neurological damage are listed in Table 1. The definition for asphyxia is listed in Table 2, modified from international consensus statement on CP [16]. When there was no umbilical cord blood gas available, at least 3 of the 5 risk factors needed to be present (Table 2). Congenital anomalies include chromosomal disorders, neurological anomalies, myopathies, metabolic diseases, hydrops fetalis, known anomaly syndromes, and intrauterine exposure to teratogenic substances.

Table 1
Inclusion criteria of the neurological high-risk infants.

1	Umbilical arterial pH < 7.0 or base deficit ⩾12 mmol/l
2	Abnormal neurological findings during the neonatal period
	a. Seizure activity
	b. Hypertonia or hypotonia
	c. Abnormal reflex
	d. Irritability or hyperexcitability
	e. Poor sucking and swallowing reflexes
	f. Shallow, irregular respirations
	g. Apnea (not caused by prematurity)
3	Abnormal neurological images during the neonatal period
	a. Intraventricular hemorrhage (grade 3–4)
	b. Periventricular leukomalacia
	c. Hydrocephalus
	d. Congenital CNS anomalies
	e. Hypoxic-ischemic encephalopathy
4	Congenital infection which may cause neurological damage
5	Severe IUGR (<-3SD)

IUGR, intrauterine growth restriction.

Perinatal deaths consist of stillbirth ⩾22 weeks of gestation and neonatal deaths <28 days of age. Infant mortality rate is the total number of deaths among infants under one year of age per 1000 live births.

The Chi-squared and Fisher's exact tests were used to compare proportions, and significance was taken as $p < 0.05$. The study protocol was approved by the institutional review board of the Faculty of Medicine, University of Miyazaki.

3. Results

3.1. Overall trends

Perinatal deaths (including stillbirth and neonatal death) decreased significantly from 236 in 2001–2005 to 183 in 2006–2010 ($p < 0.03$, Chi-squared test), which is from 4.6 per 1000 to 3.7 per 1000 by perinatal mortality rate. Although stillbirths did not decrease significantly, neonatal deaths decreased significantly from 79 to 47 ($p < 0.01$) (Fig. 1). The infant mortality rate also decreased from 3.12 to 2.34 per 1000 [17]. The number of CP infants also decreased significantly from 126 in 2001–2005 to 88 in 2006–2010 ($p < 0.02$, Chi-squared test). The overall prevalence of brain damage was 2.1 per 1000 deliveries (214/102,999).

3.2. Etiology of cerebral palsy

Among the 214 infants with CP, 129 (60%) were born preterm between 22 and 36 weeks of gestation and the