Socioeconomic inequity in survival for deliveries at 22–24 weeks of gestation

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ABSTRACT

Objective Guidelines recommend individual decision making on resuscitating infants of 22–24 weeks' gestational age (GA) at birth. When the decision not to resuscitate is made, infants would likely die soon after delivery, and under some circumstances such neonatal deaths may be registered as stillbirths occurring during delivery (intrapartum stillbirth). Thus we assessed whether socioeconomic factors are associated with peridelivery deaths (during or within 1 hour of delivery) of infants delivered at 22–24 weeks' gestation.

Methods We analysed 14 726 singletons of 22–24 weeks' GA using the 2003–2011 Japanese vital statistics, and assessed how maternal characteristics influence risk of peridelivery death as well as intrauterine fetal death (IUFD) and death after 1 hour of age until 40 weeks postmenstrual age.

Results Living in a municipality with low-average income (lowest tertile (risk ratio 1.32, 95% CI 1.20 to 1.44), middle tertile (risk ratio 1.08, 95% CI 0.98 to 1.19)), younger maternal age (age <20 (risk ratio 1.43, 95% CI 1.17 to 1.75), age 20–34 (risk ratio 1.14, 95% CI 1.03 to 1.27)) and having previous live births (risk ratio 1.08, 95% CI 1.01 to 1.17) increased risk of peridelivery deaths, but did not increase risk of IUFD or deaths after 1 hour of age. Peridelivery death was twice as likely to occur in births to multiparous teenage mothers in a low-income municipality, compared with those of older primiparous mothers in a wealthier municipality.

Conclusions Socioeconomic factors substantially influence whether births of 22–24 weeks' GA survive delivery and the first hour of life. Such disparities may reflect the impact of socioeconomic situations on decision making for resuscitation.

What is already known on this topic?

- Institutional factors influence decision making for the resuscitation of extremely low-gestational-age infants at delivery.
- However, it has not been reported how parental social factors play a role.

What this study adds?

- Japanese vital statistics showed socioeconomic factors influenced whether singleton births at 22–24 weeks of gestation survive delivery and the first hour of life.
- However the same factors did not increase mortality in utero or after the first hour.
- The results imply a potential socioeconomic discrepancy in decision making on whether to resuscitate periviable births.

INTRODUCTION

Perinatal care of preterm deliveries at the periviable gestation of 22–24 weeks requires a multidisciplinary approach by an experienced perinatal team including obstetricians, neonatologists, midwives, nursing staff and the parents, as the discussion would focus on intensive care requirements and on whether intensive care should be provided in the first place. While there is a general consensus to provide active care or resuscitation for infants at ≥25 weeks' gestational age, large variation exists in guidelines both internationally and within countries regarding whether to provide active care to more premature infants at 22–24 weeks' gestational age,[1] acknowledging that their mortality and severe impairment rate are high compared with higher gestations. Multiple guidelines recommended 'individualized care', where the provision of active care or the withholding of life-saving treatment would be justified based on the best interests of the unborn infants in shared decision making by the parents and clinicians.[2 3] If an antenatal decision not to provide resuscitation is made, fetuses and infants at 22–24 weeks' gestation would likely die shortly after birth or even during delivery, as obstetric management would not aim to ensure fetal survival. Furthermore, as infants who die shortly after birth are live births by definition, some of these deaths could be registered as stillbirths (intrapartum deaths), especially if they have a gestational age of borderline viability.[4–6] Antenatal decision making before delivery is a major factor affecting peridelivery mortality during delivery or shortly after the birth of fetuses and infants at 22–24 weeks' gestation.[4 7]

The decision-making process to provide or not provide care to maximise odds of survival to births at borderline viability, including both obstetric interventions (antenatal corticosteroids, antenatal transfer and caesarean section for fetal indication) and neonatal interventions (active resuscitation at birth), often requires extensive discussion between parents and clinicians, taking into account various clinical prognostic factors (such as gestational age, estimated fetal weight, multiplicity and any underlying diseases of the mother or child).[8] Parents are often informed that their infants have a high risk of in-hospital death, and that even if they do survive there is a large possibility that the infant may have

severe impairment and chronic diseases later in life. In light of this depressing prospect, socioeconomic factors may play a major role in such decision making because they are related to the family's perception about whether their economical and societal circumstances would allow them to raise a child who needs continuous medical support, or the parents' wish to have a child despite any disability. Thus it is likely that mortality occurring in the few hours before and after birth is more caregiver-driven than clinically driven compared with mortality later in life.

Although many previous studies have investigated clinical[8 9] and institutional[10 11] factors related to resuscitation practices and mortality at the extremely low gestational ages, few studies have investigated the influence of parental social factors on such.[4] Thus, we investigated which parental factors were associated with death in the peridelivery period (from the onset of delivery to 1 hour after delivery) at 22–24 weeks' gestation using a large national database with complete stillbirth registration. Intrapartum stillbirths were included in the outcome, as live birth infants who died shortly after birth due to an antenatal decision not to resuscitate may be registered as intrapartum fetal deaths, although they should be registered as live births.[4–6 12]

METHODS

We used data on stillbirths and live births (linked to infant mortality data) from the period 2003–2011 registered in the Japanese national vital statistics database provided by the Ministry of Health, Labour and Welfare. Using unique identifiers, we linked these data with average annual income figures calculated by municipal (town, city or village) tax data from year of birth collected by the Ministry of Internal Affairs and Communications.

Japan obligates registration of all live births, stillbirths and termination of pregnancies above 12 weeks. Termination of pregnancies above the limit of viability (defined to be 22 completed weeks of gestation since 1990) for any reason has been prohibited with strict regulations that make it extremely difficult to procure an illegal abortion. Thus, under-reporting of stillbirths and termination of pregnancies are considered minimal.

In our database, maternal age, marital status, number of previous live births and stillbirths, place of birth (hospital, birth centre, home, other) and multiplicity, best clinical estimate of gestational age and birth weight were available for both live birth and stillbirths. Time of stillbirth (categorised as termination of pregnancy, intrauterine fetal death (IUFD), intrapartum fetal death (IPFD)) was available for stillbirths. Time from delivery to death (in days if the infant survived more than 24 hours, and hours and minutes if the infant died within 24 hours) was available for all infant deaths. We categorised municipal annual income into tertiles: highest (3.3–6.5 million yen), middle (2.9–3.3 million yen) and lowest (1.9–2.9 million yen). Maternal age was categorised into three categories: under 20 years, 20–34 years, and 35 years and above. Small for gestational age (SGA) was defined as a birth weight below the 10th percentile for infants of the same gestational age, parity and sex according to the Japanese birth weight reference.[13] This study considered younger maternal age (especially teenage pregnancy), maternal marital status, income tertile and having had previous live births (likely having a child) as social factors that may have a potential effect on decision making for providing resuscitation.

To assess the impact of parental social factors on the decision not to resuscitate extremely preterm infants, this study defined the primary outcome as mortality at the peridelivery period (from the onset of delivery to 1 hour after delivery). The upper limit of 1 hour of age was used because infants at 22–24 weeks' gestational age are likely to die shortly after birth without resuscitation.[14] We included intrapartum deaths (deaths during delivery) in the primary outcome as the distinction between intrapartum deaths and deaths shortly after live births at perivable gestation (22–24 weeks) can be artificial depending on the birth and death registration practices of the physicians or institutions involved.[4–6 12] This study also assessed IUFD before onset of delivery and neonatal deaths after 1 hour of age (until 40 weeks' corrected age) as secondary outcomes. These secondary outcomes were included in order to investigate whether the effect of social factors as well as biological factors on the primary outcome differed from those of the secondary outcomes.

Analysis was limited to singletons born at 22–24 completed weeks of gestation delivered at hospitals and with complete data on maternal characteristics; after excluding 166 deliveries at home or birth centres, 31 withmissing birth weight information and 1 with missing maternal age. Marital status, number of previous live births and stillbirths, place of birth and municipal annual income were available for all births (as all births were successfully linked to their municipal data). We used Poisson regression with robust error variance including all social and biological factors as covariates to estimate risk ratios (RR) of maternal and infant characteristics on mortality at three intervals: IUFD, peridelivery death and death after 1 hour of age. For the latter two intervals, the analyses excluded infants who already died at previous time intervals. For example, the analyses for peridelivery deaths excluded IUFD cases. All analyses were conducted using Stata V.13 SE. This study was approved by the ethical committee of the National Center for Child Health and Development in Tokyo, Japan.

RESULTS

Among 14 726 deliveries at 22–24 weeks' gestation (8159 stillbirths and 6567 live births), there were 6616 IUFDs (45% of all deliveries), 1797 peridelivery deaths (22% of infants alive at onset of delivery) and 1964 deaths after 1 hour of age until 40 weeks' corrected gestational age (31% among infants alive at 1 hour of age).

Table 1 shows mortality in three periods by maternal and infant characteristics. After adjusting for biological factors, all social factors assessed were significantly associated with the risk of the primary outcome (peridelivery deaths) (table 2). Younger maternal age (teenage pregnancy (RR 1.43, 95% CI 1.17 to 1.75), age 20–25 years (RR 1.14, 95% CI 1.03 to 1.27)), lower municipal average income (lowest tertile (RR 1.32, 95% CI 1.20 to 1.44), middle tertile (RR 1.08, 95% CI 0.98 to 1.19)), being unmarried (RR 1.49, 95% CI 1.33 to 1.67) and having a previous live birth (RR 1.08, 95% CI 1.01 to 1.17) significantly increased risk of peridelivery death. In contrast, none of the social factors were significantly associated with deaths after 1 hour of age. Although unmarried status and maternal age of 20–34 years (compared with 35 years or older) were associated with increased risk of IUFD, lower annual income and having a previous live birth had rather negative associations, and teenage pregnancy was not associated with IUFD.

For biological risk factors, maternal history of stillbirth was a risk factor for peridelivery death (RR 2.48, 95% CI 2.26 to 2.73) and IUFD (RR 1.43, 95% CI 1.37 to 1.50) but was not associated with later survival. Infant male sex had a significant risk of mortality after 1 hour of age (RR 1.11, 95% CI 1.04 to 1.18) but was unrelated to peridelivery death or IUFD. Lower gestational age and SGA were strongly associated with death at

Table 1 Mortality rates in three periods for 14 726 births delivered at 22–24 weeks of gestation, by social and infant characteristics

	Intrauterine fetal deaths (n=6616)		Peridelivery deaths (n=1797)		Deaths after 1 hour of age (n=1964)	
	n	%*	n	%†	n	%‡
Social factors						
Municipal annual income						
Lowest	2122	43	738	27	629	29
Middle	2133	45	566	21	664	30
Highest	2359	47	492	19	670	30
Maternal age						
<20	186	45	74	33	47	30
20–34	5261	45	1433	23	1521	30
≥35	1169	43	290	19	396	30
Marital status						
Not married	706	54	241	40	130	33
Married	5910	44	1556	21	1834	30
Previous live births						
Yes	3061	41	1041	23	1074	30
No	3555	49	756	21	890	30
Biological factors						
Previous stillbirths						
Yes	889	68	271	64	51	32
No	5727	43	1526	20	1913	30
Gestational age						
22 weeks	2425	57	949	53	534	55
23 weeks	2197	44	594	21	760	33
24 weeks	1994	36	254	7	670	20
Infant sex						
Male	3245	43	960	22	1095	32
Female	2869	43	816	22	869	28
Small for gestational age						
Yes	3377	79	239	27	309	45
No	3239	31	1558	22	1655	28

Peridelivery deaths defined as antepartum stillbirths and neonatal deaths occurring within 1 hour from birth.
The percentages in the tables show the mortality rates of fetuses or infants in three periods: before delivery (intrauterine deaths), from onset of delivery to 1 hour of age (peridelivery deaths) and after 1 hour of age.
*Among all deliveries.
†Among all fetuses alive at onset of delivery (excluding intrauterine fetal death).
‡Among births alive at 1 hour of age.

all stages; however, the effect of gestational age was strongest for peridelivery death, while the effect of SGA was smallest for peridelivery death (RR 1.24, 95% CI 1.11 to 1.39).

DISCUSSION

This study found maternal social background was strongly associated with peridelivery deaths (from onset of delivery to 1 hour of age) of fetuses and infants at 22–24 weeks' gestation. Mothers of younger age (especially teenage pregnancies) with experience of a previous live birth (likely to have a child) or with lower income were more likely to experience a peridelivery death for births at 22–24 weeks' gestation. The lack of similar associations with IUFD and infant deaths after 1 hour of age indicated that these social factors may affect peridelivery mortality by influencing the decision to provide active resuscitation. Unlike these social factors, gestational age and SGAs (biological factors) were associated with mortality in all three periods.

Based on our estimates, a periviable infant born to a teenage mother who lives in a municipality with the lowest income tertile and who already has a child has only half the chance of surviving the peridelivery period after the decision to provide resuscitation is made, compared with a child with the same risk born to a wealthier mother of advanced age who does not have a child. Our results suggest that social characteristics in combination with gestational age may strongly influence the decision making as to whether the infant is resuscitated. As clinical data directly measuring the decision-making process were not available in our database, we used peridelivery mortality as a proxy for the decision not to provide resuscitation. It is possible that the observed association between social factors and peridelivery deaths may not be due to the social factors influencing the decision making, but may rather reflect the baseline regional disparity in access to high-quality perinatal care, or maternal characteristics (eg, smoking, obesity) related to the risk of obstetrical complications and morbidity of their offspring. The lack of similar associations between social factors and IUFD or deaths after 1 hour of age in this study opposed such a possibility; however, future research should consider such possibilities as well as possible influences of other regional disparities (such as incidences of emergency situations).

Our results highlight the difficulties parents face when told that their child may survive with a severe impairment, even if provided with the most intensive treatment, and that social factors play a large role in such recipiency. Although our study

Table 2 Association between social and infant characteristics with fetal/infant mortality in three periods among infants delivered at 22–24 weeks of gestation

	Primary outcome	Secondary outcomes	
	Peridelivery deaths† Adjusted RR (95% CI)	Intrauterine fetal deaths‡ Adjusted RR (95% CI)	Death after 1 hour of age§ Adjusted RR (95% CI)
Social factors			
Municipal annual income			
Lowest tertile	1.32 (1.20 to 1.44)***	0.95 (0.91 to 0.99)*	1.01 (0.93 to 1.10)
Middle tertile	1.08 (0.98 to 1.19)	0.95 (0.91 to 0.99)*	1.00 (0.92 to 1.08)
Highest tertile	1 (reference)	1 (reference)	1 (reference)
Maternal age			
<20	1.43 (1.17 to 1.75)***	1.10 (0.98 to 1.23)	1.09 (0.85 to 1.39)
20–34	1.14 (1.03 to 1.27)*	1.08 (1.03 to 1.13)**	0.99 (0.91 to 1.08)
≥35	1 (reference)	1 (reference)	1 (reference)
Not married	1.49 (1.32 to 1.69)***	1.26 (1.19 to 1.34)***	1.14 (0.97 to 1.33)
≥1 Previous live born	1.11 (1.02 to 1.21)*	0.89 (0.86 to 0.92)***	1.06 (0.99 to 1.14)
Biological factors			
≥1 Previous stillbirth	**2.48 (2.26 to 2.73)*	1.43 (1.37 to 1.50)***	1.07 (0.86 to 1.33)
Gestational age			
22 weeks	6.43 (5.66 to 7.30)***	1.49 (1.43 to 1.56)***	3.05 (2.80 to 3.32)***
23 weeks	2.88 (2.52 to 3.30)***	1.18 (1.13 to 1.23)***	1.70 (1.56 to 1.85)***
24 weeks	1 (reference)	1 (reference)	1 (reference)
Male infant	1.03 (0.95 to 1.11)	0.97 (0.93 to 1.00)	1.11 (1.04 to 1.19)***
Small for gestational age	1.24 (1.11 to 1.39)***	2.40 (2.32 to 2.48)***	1.69 (1.54 to 1.84)***
Year of birth (/year)	0.92 (0.91 to 0.94)***	0.99 (0.98 to 0.99)***	0.93 (0.92 to 0.94)***

†Among all deliveries.
‡Among all fetuses alive at onset of delivery (excluding intrauterine fetal death).
§Among births alive at 1 hour of age.
*p<0.05, **p<0.01, ***p<0.001.
RR, risk ratio.

is the first to investigate the role of social factors in decision making for resuscitation at birth of infants of the extremely lower gestations, studies in the UK have shown that socioeconomic variations exist in decision making for the termination of pregnancy after antenatal detection of Down syndrome[15] and other congenital anomalies.[16] Our finding that such social disparities do not influence infant survival after the first hour of life also matches findings from the UK showing that survival of very preterm births (22–31 weeks' gestational age) was unrelated to neighbourhood income.[17]

Our study raises the concern that making decisions about a child's life may strongly depend on their parents' social background, as well as infants' biological characteristics. If 'individual' decision making of whether or not to resuscitate[1] is related to socioeconomic inequity, it may mean that 'selection of life' is based on socioeconomic factors rather than the biological viability of fetuses and infants. Although it is reasonable to consider the social situations of parents and families to provide appropriate individualised care to their children, making a decision of life or death based on socioeconomic situations of parents and families may not be justifiable. The findings of this study highlight the need for increased social support after delivery for parents and families with social difficulties, such as teenage mothers or low-income families. Furthermore, caregivers should make sure such families are well informed of the social welfare that would be available if their children become handicapped, before they make the decision on delivery.

Our results also suggest the potential existence of an argument in the decision-making process of resuscitation. Does the extent to which parents are involved in the process change by social background? Would the practitioners present information to the families differently, and would they be more willing to try to convince the parents not to ask for intensive care, according to their personal negative perception of the family's current status? As institutional and societal support should aim for such children and their families to make best use of their potential, future studies to understand and how the current decision-making process is and should be conducted are required.

These problems may have been negligible previously when the chances of such infants surviving were slim. However, in our study, moderate proportions of infants at 22, 23 and 24 weeks' gestational age lived if they survived the initial 1 hour after birth, which was likely due to active resuscitation (survival rates of 45%, 67% and 80%, respectively) (table 1). Reports from Japan,[18] Sweden[19] and Germany[20] showed that survival rates without major complications or disabilities can be as high as 9%–12%, even for infants born at 22 weeks if provided with active resuscitation, and has given rise to intensive debate on how care should be provided to periviable deliveries at these extremely low gestational ages.[11 21]

The main strengths of our study include its complete population coverage including those on stillbirths, as well as separate reporting of intrauterine and intrapartum stillbirths. As mothers facing delivery would choose different institutions based on whether they would want their child resuscitated or not, institution-based studies including larger hospitals with a well-equipped neonatal intensive care unit would underestimate the rate of non-resuscitated infants; thus, a population-based study is required for such an analysis. Neonatal deaths in the early hours of life have been

misclassified as stillbirths in many settings, especially in the lower gestational ages,[4] which has been a barrier to studying survival rates at these lower gestations. However, as such misclassification is more likely to occur for IPFDs rather than antepartum fetal deaths, we used the term 'peri-delivery deaths', which combines IPFDs and neonatal deaths within 1 hour of life, and is less prone to such misclassification.

Our study has several limitations. First, the income data were not available at the individual level and the municipal average was used as a surrogate. However, although area-level estimates do not necessarily agree with individual-level incomes, they can be used as a proxy when individual income data are not available,[22 23] as carried out in previous studies on socioeconomic inequalities and perinatal outcomes.[16 17] Second, as we lacked detailed clinical data and were not able to investigate other direct measures of active resuscitation such as provision of antenatal steroid, caesarean delivery for fetal indication or intubation and other invasive procedures,[7 11 24] we were not able to observe the relationship between social factors and provision of active care directly. To interpret our findings, we had to compare how the same factors were related to IUFD and infant survival later in life, which are more likely to be biological. The same limitation is applied to interpreting the risk factors observed for IUFD, for which the interpretation should be limited to 'risk factors for IUFD *among* those delivered at 22 to 24 weeks of gestation', and not 'risk factors for IUFD *at* 22 to 24 weeks of gestation', as the latter should be based on births at all gestational ages above 22 weeks rather than limited to those at 22–24 weeks. (Such an analysis has been conducted in the online supplementary appendix as a sensitivity analysis. It also showed that annual income was most strongly associated with deliveries at 22–24 weeks that ended in peridelivery death, compared with IUFD or delivery of live births surviving the first hour at 22–24 weeks.) However, we believe our study may stimulate further research to assess the role such factors play in this decision-making process. Third, our study was conducted in Japan, where care provided to infants at the extremely low gestational ages is generally more intensive and survival rates are higher compared with other populations[18 25]; thus, the effect of social disparity in resuscitation may be more prominent than elsewhere. However, we believe this will become a significant problem with advances in neonatal care in other populations, even where palliative care is currently the standard for births at these extremely low gestational ages.

CONCLUSION

Social risk factors significantly increase the mortality of an infant born at 22–24 weeks' gestation during delivery and the first hour after delivery, although they do not increase mortality in utero or after the first hour of birth. This implies a potential social discrepancy in decision making on whether to resuscitate an infant with borderline viability.

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