Neonatal mortality in singleton pregnancies: a 20-year retrospective study from a tertiary perinatal unit in Hong Kong

Genevieve PG Fung, SL Lau, Annie SY Hui, Sani TK Wong, WT Tse, PC Ng, DS Sahota, HS Lam, TY Leung *

ABSTRACT

Introduction: The global neonatal death (NND) rate has been declining in recent decades, but there are no comprehensive data concerning the characteristics of NNDs in Hong Kong. This study investigated the trends and aetiologies of NNDs among singleton pregnancies in Hong Kong.

Methods: This study included all cases of NND from singleton pregnancies in a tertiary hospital in Hong Kong between 2000 and 2019. The rates, clinical characteristics, and aetiologies of NND were compared between the first (2000-2009) and the second (2010-2019) decades.

Results: The NND rate decreased from 1.66/1000 livebirths (97 cases) in the first decade to 1.32/1000 livebirths (87 cases) in the second decade. Congenital or genetic abnormalities (82 cases) caused 44.6% of all NNDs. There was a significant reduction from 0.82/1000 livebirths in the first decade to 0.52/1000 livebirths in the second decade (P=0.037). Other causes of NND were prematurity (69 cases; 37.5%), sepsis (16 cases; 8.7%), hypoxic-ischaemic encephalopathy (15 cases; 8.2%), and sudden infant death syndrome (2 cases; 1.1%). Gestational age-specific neonatal mortality for moderately preterm neonates (31-33 weeks of gestation) significantly decreased from 34.73/1000 in 2000-2009 to 8.63/1000 in 2010-2019 (P=0.001), but there were no significant changes in neonatal mortality for other gestations.

Conclusion: The NND rate in Hong Kong is among the lowest worldwide. Neonatal deaths in our centre declined over the past two decades, mainly because of improvements in the prenatal diagnosis and treatment of congenital or genetic abnormalities, as well as an improved survival rate among moderately preterm neonates.

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New knowledge added by this study

- The rate of neonatal mortality among singleton pregnancies in Hong Kong decreased from 1.66/1000 livebirths in 2000-2009 to 1.32/1000 livebirths in 2010-2019.
- The decline in the neonatal mortality rate mainly resulted from improvements in the prenatal diagnosis and treatment of congenital or genetic abnormalities, as well as an improved survival rate among moderately preterm neonates (31-33 weeks of gestation).

Implications for clinical practice or policy

- Future improvements in the neonatal mortality rate should focus on in utero treatment, expanded carrier screening of genetic abnormalities, and the prevention of preterm birth and pre-eclampsia.

Introduction

Perinatal and neonatal mortality rates are important measures of the quality of medical care during pregnancy, childbirth, and the neonatal period. Although the global neonatal death (NND) rate has demonstrated a decreasing trend over the past 30 years, from 37/1000 livebirths to 17/1000 livebirths between 1990 and 2020,[1] NND rates considerably vary among regions. According to the 2020 report by the World Health Organization, the NND rates were the highest in Africa (27/1000 livebirths), Eastern Mediterranean (25/1000 livebirths) and South-East Asia (18/1000 livebirths); the NND rates were the lowest in Americas (7/1000 livebirths), Western Pacific (5/1000 livebirths) and Europe (4/1000 livebirths).[1] In Hong Kong, territory-wide statistics indicated NND rates of 1.2/1000 and 1.0/1000 livebirths in 2004 and 2014, respectively[2];

these rates are lower than the rates in most regions, according to the above report by the World Health Organization. However, there have been few in-depth studies concerning the trends and underlying causes of NND in Hong Kong. Our group recently published two epidemiological studies regarding singleton pregnancies in Hong Kong, which revealed a decreasing trend in the rate of stillbirths among singleton pregnancies from 3.61/1000 in 2000-2009 to 3.09/1000 in 2010-2019.[3] The rate of perinatal mortality in multiple pregnancies also decreased from 5.52/1000 to 4.59/1000 during the same period.[4] These improvements in mortality rates have mainly occurred because of advances in the prenatal diagnosis and management of fetal malformations and genetic diseases, as well as improvements in the antenatal management of multiple pregnancies. The present study investigated the trends of NNDs among singleton pregnancies in the largest tertiary perinatal centre in Hong Kong, as well as changes in the characteristics and aetiologies of NND over the past two decades, with the goal of improving perinatal care in Hong Kong.

單胎妊娠新生兒死亡率：香港公立醫院產科20年回顧性研究

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引言：近幾十年來，全球的新生兒死亡率一直呈下降趨勢。然而，目前還沒有關於香港新生兒死亡率的詳細數據。本項研究調查了香港單胎妊娠中新生兒死亡率的趨勢和病因。

方法：本研究涵蓋了2000年至2019年間香港一所教學醫院所有單胎妊娠的新生兒死亡病例，並比較了第一個十年（2000-2009）和第二個十年（2010-2019）的新生兒死亡率、死亡臨床特徵和死亡病因。

結果：研究發現，單胎新生兒死亡率在第一個十年為1.66/1000（97例），及後在第二個十年降低到1.32/1000（87例）。其中先天性或基因異常導致的新生兒死亡病例數（82例）佔總新生兒死亡病例數的44.6%。在第一個十年，先天性或基因異常導致的新生兒死亡率為0.82/1000，而在第二個十年，該死亡率顯著減低至0.52/1000（P=0.037）。新生兒死亡的其他原因包括早產（69例，37.5%）、敗血症（16例，8.7%）、缺氧缺血性腦病（15例，8.2%）和嬰兒猝死綜合症（2例，1.1%）。中度早產新生兒（胎齡31-33週）的特定年齡組妊娠死亡率從2000至2009年的34.73/1000顯著降低至2010至2019的8.63/1000（P=0.001），但是對於其他胎齡的新生兒，其死亡率並無顯著改變。

結論：香港的新生兒死亡率是全球最低之一。在過去二十年，本院的新生兒死亡率下降，主因是本院在先天性或基因異常的產前診斷和治療方面有所改進，以及中度早產兒存活率上升。

Methods

Study setting

This retrospective study included all singleton pregnancies that delivered at the Prince of Wales Hospital from 1 January 2000 to 31 December 2019. The STROBE reporting guideline was followed when writing this manuscript. The Prince of Wales Hospital is affiliated with The Chinese University of Hong Kong and serves a large population of 1.7 million in the New Territories East region of Hong Kong; the hospital's annual delivery rate is 6000 to 7000 (approximately one-sixth of the total births in all public hospitals in Hong Kong, and one-ninth of the total births in Hong Kong). Both the obstetric unit and the neonatal unit are the largest in Hong Kong. The neonatal unit is a Level III centre that consists of a 22-bed neonatal intensive care unit (NICU). The staff of the neonatal unit worked closely with the staff of the obstetric unit to manage high-risk deliveries from complicated pregnancies, as well as pregnancies that required fetal intervention after referral from other hospitals.

Perinatal and neonatal management

Complicated pregnancies were discussed in weekly perinatal meetings attended by the staff of both the obstetric unit and the neonatal unit; discussions of these pregnancies focused on management plans and the optimal timing of delivery. Relevant disciplines (eg, paediatric surgery, cardiology, neurosurgery, radiology, or otolaryngology) were included as appropriate. In cases where a specialist service outside of Prince of Wales Hospital (eg, cardiothoracic surgery) was anticipated after delivery, specialists from other centres were invited to participate in management planning. Active resuscitation was provided for all viable neonates delivered at ≥24 weeks. For extremely premature neonates with borderline viability (ie, delivered at 22-23 weeks of gestation), considering the high risks of mortality and long-term morbidity, comprehensive counselling was provided to affected families, which allowed them to select active resuscitation or no resuscitation at birth. In accordance with the departmental protocol, the paediatric unit was requested to prepare for rapid management of deliveries that involved specific maternal or fetal conditions (eg, prematurity, fetal distress, instrumental deliveries, and antenatally diagnosed severe congenital abnormalities). Neonates were managed in the NICU in accordance with the standard unit protocols and guidelines. These protocols were updated regularly according to the latest evidence-based consensus guidelines and recommendations established by clinicians in Hong Kong and other nations. In accordance with departmental guidelines, comprehensive investigations were performed to determine the cause of death in all cases of NND. All NNDs were referred for autopsy unless the cause of death was clearly identified (eg, trisomy 13 or 18 confirmed

by genetic tests). If the cause of NND could not be identified, the case was reported to the coroner. If NND was caused by multiple pathologies, the most clinically significant pathology that contributed to death was selected for analysis.

Data collection and analysis

All cases of NND in livebirths of singleton pregnancies during the study period were retrieved using the Hospital Authority's Clinical Data Analysis and Reporting System. Cases of NND in livebirths of multiple pregnancies were excluded. The included cases of NND were divided into two groups according to the decade of birth. The first group (ie, first decade) included cases of NND among singleton pregnancies that delivered between 1 January 2000 and 31 December 2009. The second group (ie, second decade) included cases of NND among singleton pregnancies that delivered between 1 January 2010 and 31 December 2019. Obstetric data including maternal demographics (maternal age, maternal illnesses, antenatal complications, and treatment) and birth history (gestation, mode of delivery, sex, birth weight, Apgar scores, and neonatal resuscitation) were collected from the Obstetric Specialty Clinical Information System. Neonatal data comprising neonatal diagnoses, interventions, and length of survival were retrieved from the Hospital Authority's Clinical Management System. When further details were needed, individual case records were retrieved for analysis.

All NNDs were categorised as early NND (within 7 days after birth) or late NND (within 8-28 days after birth). Early, late, and total rates of NND, as well as baseline demographics, were compared between the two groups. Causes of death were divided into four main categories: prematurity, hypoxic-ischaemic encephalopathy (HIE), congenital abnormalities, and sepsis. Congenital abnormalities were defined by characteristic features on physical examination, confirmed by either genetic tests, diagnostic investigations, or autopsy. Sepsis was defined on the basis of positive cultures established using samples of blood, urine, cerebrospinal fluid, or tissue from the affected neonate. Hypoxic-ischaemic encephalopathy was diagnosed in accordance with criteria derived from international guidelines.[5]

Statistical analysis

The analysis was performed using data that overlapped with a previous study.[3] Categorical variables were compared by the Chi squared test or Fisher's exact test. The threshold of statistical significance was defined as a two-sided P value of <0.05. Data analysis was performed with the SPSS software (Windows version 22.0; IBM Corp, Armonk [NY], United States).

TABLE 1. Neonatal mortality in singleton pregnancies during 2000-2009 and 2010-2019

	Total, n=124 281	2000-2009, n=58 442	2010-2019, n=65 839	P value†
No. of NND (rate /1000 livebirths)*				
Total NND	184 (1.48)	97 (1.66)	87 (1.32)	0.122
Early NND	136 (1.09)	74 (1.27)	62 (0.94)	0.084
Late NND	48 (0.39)	23 (0.39)	25 (0.38)	0.901

Abbreviation: NND = neonatal death

* Early NND = within 7 days after birth; late NND = within 8-28 days after birth; total NND = sum of early and late NND

† P values determined by Pearson's Chi squared test

TABLE 2. Distribution of gestational age among all livebirths (including neonatal deaths) at time of delivery during 2000-2009 and 2010-2019*

Gestational age, wk	Total	2000-2009	2010-2019	P value†
24-27	328 (0.3%)	148 (0.3%)	180 (0.3%)	0.237
28-30	475 (0.4%)	220 (0.4%)	255 (0.4%)	
31-33	1242 (1.0%)	547 (0.9%)	695 (1.1%)	
34-36	5820 (4.7%)	2764 (4.7%)	3056 (4.6%)	
≥37	116 416 (93.7%)	54 763 (93.7%)	61 653 (93.6%)	
Total	124 281 (100%)	58 442 (100%)	65 839 (100%)	

* Data are shown as No. (%), unless otherwise specified

† P value determined by Pearson's Chi squared test

Results

Overall and gestational age-specific neonatal mortality

There were 124 281 livebirths from singleton pregnancies between 2000 and 2019 (Table 1). The number of livebirths increased by 12.7% from 58 442 in the first decade (2000-2009) to 65 839 in the second decade (2010-2019). There were 184 NNDs (1.48/1000 livebirths) between 2000 and 2019, including 97 in the first decade (1.66/1000 livebirths) and 87 in the second decade (1.32/1000 livebirths). Overall, there were 136 cases (73.9%) of early NND and 48 cases (26.1%) of late NND.

The maternal demographic characteristics of all singleton pregnancies during the study period were reported in our previous paper.[3] The distribution of gestational age among all livebirths did not differ between the two decades (P=0.237) [Table 2]. The highest rate of NND (195.12/1000 livebirths) was observed in extremely preterm neonates (≤27 weeks of gestation) [Table 3]. The rate of NND decreased with increasing gestational age, such that NND rates were 48.42/1000, 20.13/1000, 4.98/1000, and 0.37/1000 for neonates delivered at gestational ages of 28-30 weeks, 31-33 weeks, 34-36 weeks, and ≥37 weeks, respectively. Compared with the first

decade, there was a significant reduction (75.2%) in the rate of NND among neonates delivered at 31-33 weeks of gestation during the second decade (34.73/1000 vs 8.63/1000; P=0.001); however, there were no significant differences in the rates of NND among neonates in other gestational groups.

Causes of neonatal death

The primary causes of NND in the two decades are shown in Table 4. Congenital or genetic abnormalities was the most common cause of NND (82 of 184; 44.6%) during the 20-year study period. Other common causes of NND were prematurity (69 cases; 37.5%), sepsis (16 cases; 8.7%), and HIE (15 cases; 8.2%) [online supplementary Fig].

Chromosomal abnormalities caused 18.3% (15 of 82) of NNDs related to congenital or genetic abnormalities; all of these abnormalities were trisomy 13 or 18. Structural abnormalities caused 63.4% (52 of 82) of NNDs related to congenital or genetic abnormalities, and respiratory system abnormalities were the most common causes in both decades (22 cases). These respiratory system abnormalities included congenital diaphragmatic hernia (13 cases), pulmonary hypoplasia (5 cases), alveolar capillary dysplasia (2 cases), and tracheal stenosis or atresia (2 cases). The next most common causes were congenital cardiac abnormalities (8 cases), including transposition of the great arteries (2 cases), total anomalous pulmonary venous drainage (2 cases), endocardial cushion defect (2 cases), hypoplastic left heart syndrome (1 case), and congenital heart block (1 case); central nervous system abnormalities (8 cases), including anencephaly (3 cases), central nervous system malformation (4 cases), and brain tumour (1 case); and musculoskeletal abnormalities (7 cases), including fetal akinesia syndrome with arthrogryposis (3 cases), spinal muscular atrophy (2 cases), and skeletal dysplasia (2 cases). There were two cases of gastrointestinal abnormalities (volvulus and bowel atresia with meconium peritonitis), two cases of sacrococcygeal teratoma, two cases of multiple abnormalities, and one case of bilateral renal agenesis (a urogenital abnormality). There were also nine cases of haemoglobin Barts disease and six cases of idiopathic hydrops. There was a statistically significant decline in the rate of NND caused by congenital or genetic abnormalities, from 0.82/1000 livebirths in the first decade to 0.52/1000 livebirths in the second decade (P=0.037).

There were no significant differences in the rates of NND caused by prematurity, sepsis, or HIE between the two decades. Cases of NND due to sepsis were mainly caused by Group B Streptococcus in the first decade and *Escherichia coli* in the second decade. The majority of HIE cases (67.7%) were related to acute intrapartum events, including placenta abruption (5 cases), uterine rupture (2 cases), vasa praevia (1 case), cord accident (1 case), and chorioamnionitis (1 case).

TABLE 3. Gestational age-specific neonatal mortality during 2000-2009 and 2010-2019*

Gestational age, wk	Total No. (/1000)	2000-2009 No. (/1000)	2010-2019 No. (/1000)	P value†
24-27	64 (195.12)	26 (175.68)	38 (211.11)	0.420
28-30	23 (48.42)	14 (63.64)	9 (35.29)	0.151
31-33	25 (20.13)	19 (34.73)	6 (8.63)	0.001
34-36	29 (4.98)	12 (4.34)	17 (5.56)	0.509
≥37	43 (0.37)	26 (0.47)	17 (0.28)	0.078
Total	184 (1.48)	97 (1.66)	87 (1.32)	0.122

* Mortality determined based on the number of livebirths in each gestational age category shown in Table 2

† P values determined by Pearson's Chi squared test

TABLE 4. Causes of neonatal death in singleton pregnancies during 2000-2009 and 2010-2019*

Cause of neonatal death	Total	2000-2009	2010-2019	P value
Total neonatal deaths	184	97	87	
Total livebirths	124 281	58 442	65 839	
Congenital/genetic abnormalities	82 (0.66)	48 (0.82)	34 (0.52)	0.037†
Chromosomal	15	8	7	
Trisomy 13	6	6	0	
Trisomy 18	9	2	7	
Structural	52	29	23	
Respiratory	22	13	9	
Cardiac	8	5	3	
Central nervous	8	4	4	
Musculoskeletal	7	3	4	
Gastrointestinal	2	0	2	
Sacrococcygeal teratoma	2	1	1	
Multiple abnormalities	2	2	0	
Urogenital	1	1	0	
Haematological (all haemoglobin Barts)	9	6	3	
Hydrops fetalis (idiopathic)	6	5	1	
Prematurity	69 (0.56)	32 (0.55)	37 (0.56)	0.914†
Sepsis	16 (0.13)	10 (0.17)	6 (0.09)	0.322‡
Hypoxic-ischaemic encephalopathy	15 (0.12)	5 (0.09)	10 (0.15)	0.422‡
Sudden infant death syndrome	2 (0.02)	2 (0.03)	0	0.221§

* Data are shown as No. (No./1000 livebirths), unless otherwise specified

† P values determined by Pearson's Chi squared test

‡ P values determined by Chi squared test with continuity correction

§ P value determined by Fisher's exact test

Discussion

The NND rate in our tertiary centre is consistent with the rate of 1.2/1000 livebirths in the territory-wide report[2] and lower than the rates in many developed

countries (eg, the United States, Australia, and nations located in Europe; neonatal mortality rates of 2-3/1000 livebirths).[1,2] The global NND rate has been decreasing over the past two decades because of advances in perinatal care.[2] Our overall NND rate decreased by 20%, from 1.66/1000 in the first decade to 1.32/1000 in the second decade. This decrease is mainly the result of a decrease in NNDs related to congenital or genetic disorders, as well as a decrease in NNDs among neonates delivered at 31-33 weeks of gestation.

Neonatal death due to congenital abnormalities

Similar to our previous report, which showed a reduction in the rate of congenital or genetic abnormality-related stillbirths,[3] the present study showed that the rate of congenital or genetic abnormality-related NNDs decreased from 0.82/1000 livebirths in the first decade to 0.52/1000 livebirths in the second decade. This decline was presumably because of improvements in antenatal screening and the early detection of lethal congenital abnormalities, which resulted in termination of pregnancy before 24 weeks of gestation. Universal first trimester combined screening for Down syndrome was implemented by the Hospital Authority in 2010.[6] In 2011, non-invasive cell-free fetal DNA tests for common trisomies, as well as chromosomal microarrays for the diagnosis of chromosomal microdeletion syndromes, became available in the private sector.[7,8] Expanded antenatal screening of inborn errors of metabolism was launched in the private sector in 2013; this expanded screening has gradually become available in the public sector since 2018.[9] Although we expected a decline in the rate of trisomy-related NNDs after universal aneuploidy screening became available in 2011, there was an increase in the rate of trisomy 18–related NNDs (from 2 cases to 7 cases). A review of the individual cases revealed that the rate of trisomy 13–related NNDs decreased from six cases in the first decade to none in the second decade. Conversely, five of the seven cases of trisomy 18–related NND in the second decade were in pregnancies that had not received any screening; all of these five cases occurred during the period from 2010 to 2013. The other two cases of trisomy 18–related NND were diagnosed during prenatal screening, but the parents chose conservative management rather than termination of pregnancy. To further reduce mortality associated with hereditary genetic disorders such as spinal muscular atrophy and fetal akinesia syndrome (which caused NND in 5 cases), there is a need for expanded carrier screening of parents, particularly in families with a history of consanguineous marriage.[10,11]

The other main congenital abnormalities that caused NND in our cohort were cardiorespiratory and neuromusculoskeletal disorders, among which congenital diaphragmatic hernia was the most common. Although survival was common among neonates with mild to moderate congenital diaphragmatic hernia, neonates with severe congenital diaphragmatic hernia had a survival rate of 10% to 20% because of pulmonary hypoplasia. A recent large randomised controlled trial showed that fetoscopic endoluminal tracheal occlusion can improve the survival rate to 40% to 50%.[12] In our unit, a baby survived after treatment with fetoscopic endoluminal tracheal occlusion in 2020.[13] Pulmonary hypoplasia caused by hydrothorax or lung tumours can also be effectively and safely treated before birth with newly designed instruments such as the Somatex® shunt for pleuro-amniotic shunting, and radiofrequency ablation of the tumour feeding artery, respectively.[14,15] Fetal tumours such as sacrococcygeal teratoma, placental chorioangioma, and lung tumours remain challenging to manage because the rapid growth of tumours in utero increases the risk of preterm birth and leads to impaired neonatal cardiac function. We have demonstrated improvements in survival after in utero embolisation of chorioangioma using cyanoacrylate, and after in utero radiofrequency ablation of lung sequestration.[15,16] Although spinal muscular atrophy has no cure, it can be prevented by accurate parental carrier screening using genomic technology and prenatal diagnosis.[10]

Neonatal death due to hydrops fetalis

The rate of idiopathic hydrops fetalis–related NND decreased from 5.2% in the first decade to 1.1% in the second decade. Advances in antenatal diagnostic techniques in recent years have identified the underlying causes of many conditions which may have previously been regarded as 'idiopathic hydrops fetalis'.[17] The early diagnosis of treatable conditions in the antenatal period can prevent the development of severe hydrops fetalis and subsequent NND.[17,18] Intrauterine blood transfusion for fetal anaemia and anti-arrhythmic treatment[19] has significantly reduced the rate of hydrops fetalis, resulting in improved survival and long-term outcomes.

Neonatal death due to prematurity

Our study showed a significant (75.2%) decrease in the rate of NND among moderately preterm neonates (31-33 weeks of gestation) from 34.73/1000 in 2000-2009 to 8.63/1000 in 2010-2019; however, the rate of NND did not change in other gestational groups (Table 3). The decrease in mortality among moderately preterm neonates could be attributed to the implementation of multiple approaches for the management of such neonates since 2010, including improved ventilation strategies with early extubation to non-invasive ventilation, new

methods for surfactant administration (eg, the 'less invasive surfactant administration' method), and improvements in NICU care through continuous quality improvement programmes. The rate of NND among extremely preterm neonates (24-27 weeks of gestation) was 175-211/1000, which is comparable with the rates in other developed countries (139-326/1000).[20] It is difficult to reduce the rate of NND among extremely preterm neonates. Research is ongoing regarding artificial placenta and womb technology, and the results may improve the survival of extremely preterm neonates in the future.[21]

The rate of prematurity-related NND can be reduced by preventing preterm delivery; however, this prevention remains a challenging goal. Although our overall preterm delivery rate of 7% is lower than the rates in other developed countries,[1,22] it has remained at this level for the past two decades, and there has been no variations in gestation age-specific neonatal mortality among preterm categories. In a previous study, we demonstrated that measurements of cervical length can help to identify pregnant women who are at higher risk of preterm delivery, although the risk prediction values for Chinese women in Hong Kong are lower than the corresponding values for women in non-Asian countries.[23] Additional methods to predict the onset of labour (eg, cervical elastography, immune markers, and genetic markers) should be explored to improve accuracy.[24,25] Prophylactic progesterone is effective in reducing the risk of preterm delivery among women who have a short cervix.[26] Although the use of a cervical ring pessary reportedly had a similar effect in a Spanish study,[27] this result was not confirmed by a randomised controlled trial in Hong Kong[28] or by subsequent meta-analysis.[29] Pre-eclampsia is a common complication that requires medically induced preterm delivery. First trimester screening of pre-eclampsia, followed by prophylactic aspirin treatment in high-risk cases, is a proven strategy to effectively delay the onset of pre-eclampsia and the associated preterm births.[29] Our recent study confirmed the accuracy of a screening programme for pre-eclampsia.[30] Reductions in pre-eclampsia–related preterm births and mortality may be achieved by the implementation of a universal screening programme in the future.

Neonatal death due to hypoxic ischaemic encephalopathy

Despite advances in NICU management of HIE and the use of therapeutic hypothermia since 2011, the rate of HIE-related NND did not improve during the study period. Approximately 67% of HIE-related NNDs were caused by acute and unpredictable perinatal events such as cord prolapse, uterine rupture, vasa praevia, or placental abruption. We previously reported an infant death secondary to severe cerebral palsy as a result of prolonged shoulder dystocia, which occurred during the first study decade.[31] Therefore, team-based training for the above perinatal events is needed to ensure that the obstetric team can respond appropriately and efficiently so that the risk of HIE and associated perinatal mortality can be reduced. During these situations that involved irreversible peripartum hypoxia, we showed that umbilical cord arterial pH decreased as the length of the bradycardia-to-delivery interval increased.[31-33] With appropriate training, we were able to achieve a median bradycardia-to-delivery interval of 10 minutes and a median decision-to-delivery interval of 11 minutes,[32] which was effective in preventing peripartum mortality. Furthermore, we showed that during umbilical cord prolapse, the knee-chest position is the most effective approach for relieving fetal compression of the prolapsed cord[34]; we also formulated an algorithm for acute resolution of cord prolapse.[35] Shoulder dystocia is associated with macrosomia, but the optimal fetal weight cut-off for prophylactic elective caesarean delivery has not been established. Our previous study suggested a cut-off of 4.2 kg may help to prevent shoulder dystocia.[36] With effective training and correct use of manoeuvres such as posterior arm delivery, we recently showed that the head-to-delivery interval can be shortened and the Apgar scores can be improved.[37,38] We also proposed a modified posterior axillary sling technique to relieve severe shoulder dystocia.[39]

Neonatal death due to sepsis

The rate of severe sepsis-related NND is low and has been decreasing over the past two decades. Since the implementation of universal Group B Streptococcus screening and peripartum antibiotic prophylaxis in 2012, the rate of early onset Group B Streptococcus infection has significantly decreased from 1/1000 to 0.24/1000 births.[40] Despite the reduced risk of neonatal Group B Streptococcus infection, recent reports have shown an increase in *Escherichia coli*–related early-onset neonatal sepsis.[41] Clinicians should remain vigilant concerning the presence of chorioamnionitis and risk factors for sepsis.

To our knowledge, this is the largest and most comprehensive analysis of neonatal mortality during a 20-year period in Hong Kong. Nevertheless, there were a few limitations in this study. First, it was performed in a single large centre, rather than in a large segment of the population. Because the Prince of Wales Hospital is the main centre for fetal intervention in Hong Kong, many high-risk pregnancies are referred from adjacent hospitals, which may have led to an over-representation of complex cases and a bias towards worse outcomes. Second, some case details were not available for analysis because of the retrospective nature of the

study. Third, our study excluded cases of NND among neonates with borderline viability (gestational age: 22-23 weeks and 6 days) because such NNDs are regarded as miscarriages based on the legal definition in Hong Kong. Although some parents of neonates with borderline viability requested resuscitation, the survival rate in this small group was zero according to a recent study in our centre.[42] Finally, because the rate of NND is very low in Hong Kong, this study could have been strengthened by including data regarding the rates of major morbidities (eg, cerebral palsy). Nonetheless, our findings provide a basis for future territory-wide reviews of perinatal outcomes.

Conclusion

Hong Kong has one of the lowest rates of NND worldwide. The neonatal mortality in our centre has decreased from 1.66/1000 livebirths to 1.32/1000 livebirths over the past two decades, mainly because of improvements in the prenatal diagnosis and treatment of congenital or genetic abnormalities, as well as an improved survival rate among moderately preterm neonates. Future improvements should focus on in utero treatment, expanded carrier screening for genetic abnormalities, and the prevention of preterm birth and pre-eclampsia.

Author contributions

Concept or design: GPG Fung, TY Leung.
Acquisition of data: All authors.
Analysis or interpretation of data: GPG Fung, TY Leung.
Drafting of the manuscript: GPG Fung, TY Leung.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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Ethics approval

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