Neonatal outcomes of preterm or very-low-birth-weight infants over a decade from Queen Mary Hospital, Hong Kong: comparison with the Vermont Oxford Network

YY Chee *, Mabel SC Wong, Rosanna MS Wong, KY Wong

A B S T R A C T

Introduction: There is a paucity of local data on neonatal outcomes of preterm/very-low-birth-weight infants in Hong Kong. This study aimed to evaluate the survival rate on discharge and morbidity of preterm/very-low-birth-weight infants (≤29+6 weeks and/or birth weight <1500 g) over a decade at Queen Mary Hospital in Hong Kong, so as to provide centre-specific data for prenatal counselling and to benchmark these results against the Vermont Oxford Network.

Methods: Standardised perinatal/neonatal data were collected for infants with gestational age of 23+0 to 29+6 weeks and/or birth weight of <1500 g who were born at Queen Mary Hospital between 1 January 2005 and 31 December 2014. These data were compared with all neonatal centres in the Vermont Oxford Network in 2013. The Chi squared test was used to compare the categorical Queen Mary Hospital data with that of Vermont Oxford Network. A two-tailed P value of <0.05 was considered statistically significant.

Results: The overall survival rate on discharge from Queen Mary Hospital for 449 infants was significantly higher than that of the Vermont Oxford Network (87% versus 80%; P=0.0006). The morbidity-free survival at Queen Mary Hospital (40%) was comparable with the Vermont Oxford Network (44%). At Queen Mary Hospital, 86% of infants had respiratory distress syndrome, 40% bronchopulmonary dysplasia, 44% patent ductus arteriosus, 7% severe intraventricular haemorrhage, 5% necrotising enterocolitis, 10% severe retinopathy of prematurity, 10% late-onset sepsis, and 84% growth failure on discharge. Rates of respiratory distress syndrome, intraventricular haemorrhage, necrotising enterocolitis, and severe retinopathy of prematurity were similar in the two populations. At Queen Mary Hospital, significantly more infants had bronchopulmonary dysplasia (P=0.011), patent ductus arteriosus (P=0.015), and growth failure (P=0.0001) compared with the Vermont Oxford Network. In contrast, rate of late-onset sepsis was significantly lower at Queen Mary Hospital than the Vermont Oxford Network (P=0.0002).

Conclusions: Mortality rate and most of the morbidity rates of our centre compare favourably with international standards, but rates of bronchopulmonary dysplasia and growth failure are of concern. A regular benchmarking process is crucial to audit any change in clinical outcomes after implementation of a local quality improvement project.

Hong Kong Med J 2017;23:381–6
DOI: 10.12809/hkmj166064

YY Chee *, FHKAM (Paediatrics)
MSC Wong, FHKAM (Paediatrics), FHKCPaed
RMS Wong, FHKAM (Paediatrics)
KY Wong, FHKAM (Paediatrics)

Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, Pokfulam, Hong Kong

* Corresponding author: yychee@hotmail.com

New knowledge added by this study
* Mortality rate and most of the morbidity rates at our centre compare favourably with international standards.
* Significantly more preterm/very-low-birth-weight infants had bronchopulmonary dysplasia and growth failure at our centre compared with the Vermont Oxford Network. Identification of these areas for improvement could facilitate the development of a quality improvement project.

Implications for clinical practice or policy
* Local survival and morbidity rates provided by this study can be used for prenatal counselling about preterm delivery.
* The baseline data (growth failure rate upon discharge) obtained in the present study can be used to audit a future quality improvement project in the local community (standardised nutritional pathway for very-low-birth-weight infants).

Introduction
There has been a substantial improvement in the outcomes for preterm infants over the past few decades. This improvement reflects the advances made in antenatal, perinatal, and neonatal care. It is crucial to audit and benchmark local data on clinical outcomes with international standards. One of the largest neonatal databases, the Vermont Oxford

This article was published on 7 Jul 2017 at www.hkmj.org.
Hong Kong Med J 2017 Aug;23(4):382-393

Methods

Study population and clinical outcomes

The study was conducted at QMH, Hong Kong, which is a tertiary referral perinatal centre with an annual delivery rate of approximately 3500 to 4500. The hospital provides care for preterm infants who are predominantly of Chinese ethnicity. This study was done in accordance with the principles outlined in the Declaration of Helsinki.

Perinatal/neonatal data of all infants born alive at QMH with GA of 23+0 to 29+6 weeks and/or birth weight of <1500 g between 1 January 2005 and 31 December 2014 were collected. These infants were part of the VON database. Infants born outside of QMH were not included in this study. Data were collected retrospectively from the Clinical Management System and Clinical Information System and entered into the VON database by members of the QMH neonatal team.

Definitions for maternal and infant characteristics were provided in the manual “Nightingale Data Definitions” by the VON. In this study, GA was determined as the best obstetric age (GA), was determined using growth charts published as birth weight of <10th percentile for gender and gestational age during pregnancy. GA was estimated by postnatal neonatal assessment. Intrauterine growth restriction, defined as birth weight of <10th percentile for gender and GA, was determined using growth charts published by Fenton and Kim. Maternal obstetric data included data on antenatal steroid use, presence of chorioamnionitis, and mode of delivery. Antenatal steroid therapy was considered to be given if it was provided to the mother during pregnancy at any time prior to delivery. Chorioamnionitis was diagnosed on histopathological findings.

The survival rate was defined as neonates who survived to the time of discharge. Surfactant was used as early rescue therapy for infants with respiratory distress syndrome (RDS), defined by the presence of clinical and radiological features within the first 24 hours of life. Conventional mechanical ventilation use at any time was defined as intermittent positive pressure ventilation through an endotracheal tube with a conventional ventilator at any time after leaving the delivery room. Rescue postnatal steroids were used beyond 2 weeks of age at our centre to facilitate extubation of ventilator-dependent neonates with oxygen requirement of >40% and significant radiological features of persistent lung disease. Data on infants discharged with oxygen were also collected.

Early-onset sepsis was defined as blood or cerebrospinal fluid culture–positive bacterial sepsis occurring within 72 hours of life. Haemodynamically significant patent ductus arteriosus (PDA) on two-dimensional echocardiography was treated with...
intravenous ibuprofen (only data from 2010 to 2014 were collected as ibuprofen was used as medical treatment for PDA at QMH since 2010) or surgical ligation if medical treatment was unsuccessful or contra-indicated. Severe retinopathy of prematurity was defined as stage III or above according to international classification.5

The major morbidities included severe neurological injury (defined as grade 3 or 4 intraventricular haemorrhage [IVH], or periventricular leukomalacia [PVL]), bronchopulmonary dysplasia (BPD; defined as supplemental oxygen use at a postmenstrual age [PMA] of 36 weeks), pneumothorax (defined as extrapleural air diagnosed by chest radiograph or needle aspiration), necrotising enterocolitis (NEC; defined as stage ≥2 of Bell’s criteria), and late-onset infection (defined as bacterial or fungal infection after day 3 of life).

Data from QMH were compared with those of all neonatal centres in the VON database in a single year in 2013, the latest data available at the time of the study.

**Statistical analysis**

The Chi squared test was used to compare the categorical QMH data with that of VON. All P values were two-tailed, and a P value of <0.05 was considered statistically significant.

**Results**

**Study group**

A total of 449 infants with GA of 23+0 to 29+6 weeks and/or birth weight of 345 g to 1890 g who were born at QMH between 1 January 2005 and 31 December 2014 were included in this study. This study compared survival rate and morbidity of these infants from QMH against 38754 infants in the VON database in 2013. A significantly greater proportion of infants was delivered at 23 weeks of gestation in the VON group compared with the QMH group, which is contrary to the two groups at 27 and 29 weeks (P=0.0002). The proportion of infants born at 24 to 26 weeks and 28 weeks was similar for both groups (Table 1).

**Antenatal, maternal, and neonatal demographics**

Overall, 31.0% of the cohort subjects at QMH were multiple births (no difference between the QMH and VON group; P=0.061). Fewer infants in the QMH group were delivered by caesarean section compared with the VON group (58.6% vs 68.2%; P=0.0001). Antenatal steroids were given to 90.4% of mothers in QMH; rate of prenatal steroid use increased with increasing GA, from 73% at 23 weeks, to 82%-89% between 24 and 25 weeks and 90%-96% between 26 and 29 weeks. There was no significant difference in prenatal steroid use between the two groups (P=0.065). Chorioamnionitis was confirmed by placental histology in 24.3% of mothers at QMH, which was significantly more than that in the VON group (17.9%; P=0.0006).

Infants at QMH were predominantly born to Asian (mainly Chinese) mothers whereas the majority of the VON group were of White origin (P<0.001). In QMH, 11.8% of the neonates were born small for GA, similar to the VON group (9.2%, P=0.07) [Table 2].

In QMH, 78% of the infants were being intubated for delivery room resuscitation. At 23 weeks, all infants underwent intubation in the delivery room. Around half of the infants delivered at 29 weeks and 20% at 28 weeks did not need intubation in the delivery room, whereas 83%-97% of infants born between 24 and 27 weeks needed intubation at birth. Compared with infants with GA of ≥26 weeks, the proportion of infants with GA of <26 weeks with Apgar score of ≤3 at 1 minute was higher. Only 16% of the infants were able to achieve a target core temperature of 36.5°C to 37.5°C upon admission to the neonatal intensive care unit (vs 51% in the VON group; P<0.0001).

**Survival rate on discharge and major morbidities**

In QMH, 87% of the 449 infants survived to discharge. Rates of survival increased with increasing GA, from 27% at 23 weeks to 96% at 29 weeks. Overall survival rate of the QMH group was significantly higher than that in the VON group (87% vs 80%; P=0.0006). In QMH, morbidity-free survival rate increased from 0% at 23 weeks to 65% at 29 weeks (Table 3). Survival without major morbidity was similar when comparing the QMH and VON data (40% vs 44%; P=0.105) [Table 3].

In QMH, 86% of infants experienced RDS and...
83% needed surfactant therapy. Rate of mechanical ventilation at any time decreased from 100% at 23 weeks to 69% at 29 weeks. There was no significant difference in the incidence of RDS between QMH and VON groups (P=0.808). Significantly more infants in the QMH, however, were given surfactant therapy for RDS and put on mechanical ventilation, compared with VON (83% vs 74%; P=0.0001). The overall frequency of pneumothorax was similar in both groups (P=0.57).

Use of postnatal steroids for BPD was lower in QMH compared with VON (3% vs 14%; P=0.0001) although the QMH rate for BPD was higher (40% vs 34%; P=0.011) and rate of home oxygen use was lower (10% vs 18%; P=0.0001) [Table 4].

In QMH, rates of early- and late-onset sepsis were 3% and 10%, respectively. No significant difference was noted in the incidence of early-onset sepsis of Table 2. Demographic features and perinatal information of infants born at Queen Mary Hospital and Vermont Oxford Network

<table>
<thead>
<tr>
<th>Variable</th>
<th>Queen Mary Hospital (n=449)</th>
<th>Vermont Oxford Network (No. of subjects/total No.)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male infant</td>
<td>248 (55.2)</td>
<td>18 087/34 255 (52.8)</td>
<td>0.328</td>
</tr>
<tr>
<td>Race or ethnic group of mother</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black</td>
<td>3 (0.7)</td>
<td>9165/33 696 (27.2)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>32 (7.1)</td>
<td>16 208/33 696 (48.1)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>413 (92.0)</td>
<td>1921/33 696 (5.7)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (0.2)</td>
<td>6402/33 696 (19.0)</td>
<td></td>
</tr>
<tr>
<td>Antenatal steroids to mother</td>
<td>406 (90.4)</td>
<td>27 067/30 969 (87.4)</td>
<td>0.065</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>263 (58.6)</td>
<td>23 361/34 254 (68.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Multiple gestation</td>
<td>139 (31.0)</td>
<td>9218/34 269 (26.9)</td>
<td>0.061</td>
</tr>
<tr>
<td>SGA</td>
<td>53 (11.8)</td>
<td>3150/34 243 (9.2)</td>
<td>0.070</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>109 (24.3)</td>
<td>6069/33 905 (17.9)</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

Abbreviation: SGA = small for gestational age

Table 3. Overall survival and morbidity-free survival rates at Queen Mary Hospital and Vermont Oxford Network according to gestational age

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Queen Mary Hospital, No. (%) of infants</th>
<th>Vermont Oxford Network, No. of subjects/total No. (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 (n=15)</td>
<td>4 (27)</td>
<td>27 311/33 927 (80)</td>
<td>0.0006</td>
</tr>
<tr>
<td>24 (n=39)</td>
<td>25 (64)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 (n=44)</td>
<td>32 (73)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 (n=52)</td>
<td>47 (90)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>27 (n=92)</td>
<td>86 (93)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 (n=80)</td>
<td>75 (94)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29 (n=127)</td>
<td>122 (96)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (n=449)</td>
<td>391 (87)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Pulmonary morbidities according to gestational age at Queen Mary Hospital and Vermont Oxford Network

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Queen Mary Hospital, No. (%) of infants</th>
<th>Vermont Oxford Network, No. of subjects/total No. (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 (n=15)</td>
<td>14 (93)</td>
<td>27 858/32 431 (86)</td>
<td>0.808</td>
</tr>
<tr>
<td>24 (n=39)</td>
<td>39 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 (n=44)</td>
<td>43 (98)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 (n=52)</td>
<td>49 (94)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>27 (n=92)</td>
<td>85 (92)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 (n=80)</td>
<td>70 (88)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29 (n=127)</td>
<td>88 (69)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (n=449)</td>
<td>388 (86)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Abbreviations:
- BPD = bronchopulmonary dysplasia
- CMV = continuous mechanical ventilation
- RDS = respiratory distress syndrome

83% needed surfactant therapy. Rate of mechanical ventilation at any time decreased from 100% at 23 weeks to 69% at 29 weeks. There was no significant difference in the incidence of RDS between QMH and VON groups (P=0.08). Significantly more infants in the QMH, however, were given surfactant therapy for RDS and put on mechanical ventilation, compared with VON (83% vs 74%; P=0.0001). The overall frequency of pneumothorax was similar in both groups (P=0.57).

Use of postnatal steroids for BPD was lower in QMH compared with VON (3% vs 14%; P=0.0001) although the QMH rate for BPD was higher (40% vs 34%; P=0.01) and rate of home oxygen use was lower (10% vs 18%; P=0.0001) [Table 4].

In QMH, rates of early- and late-onset sepsis were 3% and 10%, respectively. No significant difference was noted in the incidence of early-onset sepsis.
sepsis between QMH and VON (P=0.792) although QMH had a significantly lower rate of late-onset sepsis (10% vs 16%; P=0.0002) [Table 5].

In QMH, NEC developed in 5% of infants (≥stage 2) and 10% of infants were diagnosed as having severe retinopathy of prematurity (≥stage 3). The overall frequencies of NEC and severe retinopathy of prematurity were similar in the QMH and VON groups (P=0.693 and P=0.100, respectively) [Table 5].

In QMH, PDA was diagnosed in 44% of infants, of whom 36% were treated with ibuprofen (in 2010-2014), and 7% with surgical closure. For management of PDA, QMH had higher rates of ibuprofen treatment than the VON group (36% vs 12%; P=0.0001), whereas the rates of PDA ligation were similar (P=0.936) [Table 5].

In QMH, 7% of sonograms indicated severe IVH (grade 3 or 4); PVL was observed in 3% of infants. There were no significant differences in the incidence of severe IVH or PVL between QMH and VON groups (P=0.070 and P=0.963, respectively; Table 5).

In QMH, the length of hospital stay among survivors decreased with increasing GA, from 19 weeks at GA 23 weeks to 8 weeks at GA of 29 weeks. Similarly, PMA at discharge decreased from 42 weeks for surviving infants born at GA of 23 weeks, to 41 weeks at GA of 24 weeks, 39 to 40 weeks at GA of 25 to 27 weeks, 38 weeks at GA of 28 weeks, and 37 weeks at GA of 29 weeks.

Growth failure (body weight <10th centile for age and sex) was evident in 84% of infants at QMH (vs VON 42%; P=0.0001) upon discharge.

### Discussion
This study reports the mortality and morbidity in the neonatal intensive care unit in QMH over a 10-year period (2005-2014). As the only intensive care centre from China participating in the VON, QMH data provide an important source of local epidemiological information. Data recorded at QMH were compared with the entire VON database. This allows the benchmarking of our neonatal care and clinical outcomes for preterm infants internationally. Local centre–specific information about preterm infants based on GA facilitates parental counselling about high-risk infants and aids decision making.

Our study revealed that the survival rate on discharge of preterm/VLBW infants (≤29+6 weeks and/or birth weight of <1500 g) from QMH was higher than that from VON, with comparable morbidity-free survival. The higher survival rate on discharge from QMH may be partly explained by the higher proportion of 23-week GA infants in the VON (3.3% vs 6.5%; P=0.0002). Advances in perinatal and neonatal care have contributed to improved survival among preterm infants. The goal in the care of these babies should be to improve intact survival without morbidities. Among the key morbidities (severe IVH, PVL, BPD, NEC, pneumothorax, any late infection), BPD was the only clinical entity with a significantly higher incidence at QMH compared with VON (40% vs 34%; P=0.011). Reducing the risk of BPD will have a great impact on morbidity-free survival in our population. Of note, BPD is a condition with multifactorial causes and preterm infants are predisposed to lung injury.
including ventilator-induced lung injury, infection, and inflammation. The higher rate of BPD in QMH compared with VON could be related to the higher prevalence of chorioamnionitis, a known risk factor that inhibits alveolar development. As we were ventilating more infants than VON (as evidenced by the higher rate of surfactant use for RDS and use of conventional mechanical ventilation at any time), the risk of ventilator-associated lung injury was increased. Haemodynamically significant PDA was present in a greater proportion of infants at QMH compared with VON (44% vs 39%; P=0.015); PDA increases pulmonary blood flow and causes interstitial oedema. The mechanical ventilator setting and oxygen requirement increase as a result and provide a foundation for BPD. The risk of BPD is also influenced by growth restriction. Growth failure upon discharge was present in 84% of our infants. With poor nutrition in these infants, normal lung growth, maturation, and repair are inhibited. Postnatal steroid was used less frequently in QMH compared with VON (3% vs 14%), and may explain in part the decreased incidence of BPD in VON.

In order to reduce the incidence of BPD in our population, modifiable risk factors need to be reduced. In recent years, our unit has been managing RDS more with continuous positive airway pressure support with subsequent selective surfactant administration—that is, INSURE (INtubation, SURfactant administration, then Extubation)—in order to avoid unnecessary or prolonged ventilation, thereby reducing ventilator-associated lung injury and BPD. Targeted oxygen saturation has also been used in our centre to minimise oxygen toxicity associated with BPD.

We had a significantly higher proportion of infants who were small for GA upon discharge compared with the VON group (84% vs 42%; P=0.0001). Apart from affecting lung growth and maturation, postnatal growth failure is associated with poor long-term neurocognitive outcome. One possible explanation for growth failure in our population is the lack of guidelines about preterm infant nutrition (eg timing of feeding initiation and milk volume advancement, prescription of total parenteral nutrition etc.). Without such guidelines, a preterm infant’s caloric intake may be suboptimal with consequent compromise of growth. In order to improve the growth of our preterm infants, a standardised nutritional pathway for the VLBW infants has been in use since 2015. Its effect has yet to be evaluated.

A limitation of our study is the lack of adjustment for potential confounding factors. The two groups, QMH and VON, were not directly comparable, for instance, the higher survival rate of preterm infants in our centre could be partly affected by the lower proportion of GA of 23 weeks in our study population.

Conclusions

The majority of neonatal outcomes for preterm/ VLBW infants at QMH were comparable with VON, with the exception of BPD and growth failure upon discharge. Regular auditing and benchmarking of clinical outcomes will help ensure quality improvement with implementation of new interventions and projects in our unit.

Declaration

All authors have disclosed no conflicts of interest.

References