Nutritional practices and growth of preterm infants in two neonatal units in the UK and Malaysia: a prospective exploratory study

Haslina Abdul Hamid, Lisa Szatkowski, Helen Budge, Fook-Choe Cheah, Shalini Ojha

ABSTRACT

Objective To explore differences in nutritional practices and growth outcomes among preterm infants in neonatal units in Malaysia and the UK.

Design Prospective exploratory study of infants born at <34 weeks gestational age (GA).

Setting Two neonatal units, one in Malaysia and one in the UK (May 2019 to March 2020).

Methods Data collected from birth until discharge and compared between units.

Results From 100 infants included, median GA (IQR) was 31 (30–33) and mean±SD birth weight was 1549±444 g. There were more small-for-gestational age infants in Malaysian unit: 12/50 (24%) vs UK: 3/50 (6%), p=0.012 and more morbidities. More Malaysian infants received breast milk (Malaysia: 49 (88%) vs UK: 38 (76%), p=0.001), fortified breast milk (Malaysia: 43 (86%) vs UK: 13 (26%), p<0.001) and exclusive breast milk at discharge (Malaysia: 26 (52%) vs UK: 16 (32%), p=0.043). There was higher parenteral nutrition use among Malaysian infants (40/50 (80%) vs UK (19/50 (38%)) (p<0.001) with higher protein intake (mean±SD Malaysia: 3.0±0.5 g/kg/d, p=0.004) in weeks 1–4 and smaller cumulative protein deficits (mean±SD Malaysia: 11.4±6.1 g/kg; UK: 15.4±8.0 g/kg, p=0.006). There were no significant differences in short-term growth between units and more than half of the infants in both units had ≥1.28 changes in weight-for-age Z-score at discharge (p=0.841).

Conclusions An exploratory comparison of practices showed differences in patient characteristics and nutritional practices which impacted growth. Future studies with larger sample sizes and detailed analysis of maternal characteristics and infants’ outcomes are needed for improving care of preterm infants in all settings.

INTRODUCTION

Growth is one of the most important outcomes in determining the well-being of a preterm infant, and provision of optimal nutrition is a modifiable independent factor that could facilitate growth. Factors such as clinical traditions and resource limitations in hospitals may influence the adoption of effective feeding practices. Internationally, nutritional recommendations have been created and growth studies were evaluated among preterm populations in the UK, USA and other high-income settings. However, there is a paucity of studies in this area among low-income, middle-income and upper-middle-income countries, despite the growing availability of neonatal intensive care in these settings. Malaysia, as an upper-middle income country, has one of the lowest Neonatal Mortality Rates (NMR) in ASEAN countries at 5 per 1000 live births in 2019, in line with its advancement in neonatal care services, which is comparable to the UK’s NMR of 3 per 1000 live births. A study on nutritional practices and growth outcomes from a neonatal unit in...
Malaysia was last performed in 2011, showing that more than 80% of very low birthweight infants had a >1 SD decline in weight-for-age Z-score (WAZ) by 36 weeks corrected gestational age (GA).

Methods

The study was carried out in the neonatal units of the Royal Derby Hospital (RDH), UK and the Hospital Canselor Tuanku Muhriz (HCTM), Malaysia, from May 2019 to March 2020. The UK unit is a local neonatal unit (level II) routinely caring for infants born at >25 weeks GA. More immature infants and those requiring surgical care are transferred to appropriate centres. The Malaysian unit is a tertiary neonatal unit (level IIIb), which also provides surgical support on-site (except for cardiac surgery). In RDH, the neonatal unit has 24 neonatal cots and caters for 6000–7000 birth per year, while in HCTM, its neonatal unit has 26 cots and also caters for approximately 6000 birth per year. With an exception for not providing inhouse surgical support in the UK unit, both units provide similar types of care which comprises of care for the stable to intensive care infants. Both hospitals follow similar discharge criteria including weight of at least 1800 g, not needing any additional medical support and fully milk fed.

Infants <34 weeks’ GA who were admitted to either unit were recruited consecutively and followed to discharge until the sample size of 50 was reached at each site. Infants were included if admitted within 24 hours of birth, not transferred out for any part of their care and had length of stay of ≥14 days. Infants with major congenital anomalies, genetic abnormalities or missing records for ≥3 days were excluded. As this was an exploratory study, the sample size was determined based on the usual monthly admissions and length of stay at the respective units. Therefore, collection of data from 50 infants from each unit (total of 100) was deemed to be feasible within the time and resources available for the study.

Anonymised data were extracted from paper or electronic medical records (accessed from BadgerNet (Client V.2.9.1.0) in the UK, and the Caring Hospital Enterprise System in Malaysia).

Baseline and feeding data

Infant and maternal characteristics including sex, GA at birth, maternal age and parity as well as infants’ clinical characteristics were collected prospectively. In the Malaysian unit, GA was determined by using early first trimester ultrasound or by estimation based on last menstrual period for those who presented in later pregnancy. In the UK unit, GA was determined by early first trimester ultrasound. These records were retrieved from both paper and electronic medical records. For feeding data, daily nutritional intakes including parenteral nutrition (PN) and enteral nutrition (EN) were recorded. Volume of breast milk intakes was recorded only from bottle feeding (expressed breast milk) as units do not routinely record before and after feeding weight for direct breast feeding. The nutritional content of EN and PN (protein, lipid and carbohydrate content) was calculated based on the manufacturers’ literature while the composition of breast milk was based on current evidence. Nutrient deficits were calculated as the difference between actual intake and the minimum intake recommended by The European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) (2010) guidelines.

Similar feeding protocols are used in both units. Generally, minimal enteral feeding (5–15 mL/kg/day) is started within the first 24 hours. The units have guidelines on advancing feeds, promoting the use of mother’s milk and the use of breast milk fortification and micronutrient supplementation.

Growth measures

The Fenton growth chart was used as a reference for all growth assessments in both units in determining Z-scores. We used the same charts for both groups to enable a comparison of postnatal growth trajectories. The Fenton chart was chosen for this study for its advantage of using more recent and larger sample of preterm infants’ data from many countries which link to the WHO growth data. It is routinely used in the Malaysian unit. In this study, only weight and head circumference (HC) measurements were assessed, as length is not routinely measured in the UK unit.

The marker for growth used in this study is the change in WAZ from birth to discharge which was determined by subtracting the WAZ at birth from the WAZ at discharge. This was used due to the better sensitivity of weight than HC measurements in determining short term growth and Z-score as the best system for the presentation and evaluation of anthropometric data especially in indicating change over time. Postnatal growth failure was defined as a decrease in WAZ between birth and discharge of ≥1.28 as used in previous studies. Small-for-GA (SGA) was defined as birth weight <10th centile for birth weight.

Statistical analysis

All statistical analyses were performed using STATA V.16.0 (StataCorp). Descriptive statistics were used to summarise the demographic and clinical characteristics of infants and their mothers. Infants’ EN, PN and combined intakes in weeks 1–4 and weeks 5–8 and the cumulative deficits accrued in this period were analysed. Growth outcomes and other variables collected at discharge were also compared. The characteristics of infants and mothers, feeding practices as well as growth outcomes in

the UK and Malaysia cohorts were compared using the Student’s t-test or Mann-Whitney U test for continuous variables and by χ² or Fisher’s exact tests for categorical variables, as appropriate. Mean or median difference and 95% CIs were calculated for nutritional intakes and growth outcomes value comparison between sites.

No parental consent was sought as this was a prospective exploratory study using routinely recorded clinical data and this approach received no objection from the Ethics Committee in both study sites.

**Patient and public involvement**

Patients or the public were not involved in the design, conduct, reporting or distribution plans of our study.

**RESULTS**

In this study, infants in Malaysia and the UK units were of similar GA, but Malaysian infants were lighter and had a lower WAZ and length-for-age Z-scores at birth although the HC Z-scores were not different (table 1). There were more SGA infants in Malaysia (12/50; 24%) compared with the UK unit (3/50; 6%) (p=0.039). In Malaysia unit, there were fewer multiple births, more morbidities, mothers were older and had had more previous births (table 1).

**Enteral feeding**

Milk feeding was started on median day of life (DOL) of 2 (p=0.833) in both units. Full milk feeds (defined as 150 mL/kg/day EN with no PN) was reached on median (IQR) DOL 9 (7–12) in Malaysia and DOL 8 (7–10) in the UK, p=0.400 (table 2).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Infants in the Malaysian unit, n=50</th>
<th>Infants in the UK unit, n=50</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>21 (42)</td>
<td>22 (44)</td>
<td>0.84</td>
</tr>
<tr>
<td>Gestational age at birth (weeks) median (IQR)</td>
<td>32 (29 to 32)</td>
<td>31 (30 to 33)</td>
<td>0.736</td>
</tr>
<tr>
<td>Birth weight (g) mean (SD)</td>
<td>1448 (458)</td>
<td>1649 (409)</td>
<td>0.022</td>
</tr>
<tr>
<td>Birth weight-for-age z-score mean (SD)</td>
<td>−0.53 (0.93)</td>
<td>−0.10 (0.70)</td>
<td>0.009</td>
</tr>
<tr>
<td>Small for gestational age, n (%)</td>
<td>12 (24)</td>
<td>3 (6)</td>
<td>0.012</td>
</tr>
<tr>
<td>HC at birth (cm), mean (SD)</td>
<td>28 (2.68)</td>
<td>28.9 (2.35)</td>
<td>0.106</td>
</tr>
<tr>
<td>HC-for-age z-score at birth, median (IQR)</td>
<td>−0.26 (−0.98 to 0.59)</td>
<td>0.06 (−0.57 to 0.59)</td>
<td>0.310</td>
</tr>
<tr>
<td>Length at birth (cm) mean (SD)</td>
<td>38.4 (3.65)</td>
<td>41.9 (4.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length at birth-for-age z-score mean (SD)</td>
<td>−0.92 (1.05)</td>
<td>0.21 (1.23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Singleton birth, n (%)</td>
<td>45 (90)</td>
<td>34 (68)</td>
<td>0.007</td>
</tr>
<tr>
<td>Mother’s age (years) mean (SD)</td>
<td>32 (5)</td>
<td>29 (5)</td>
<td>0.009</td>
</tr>
<tr>
<td>Parity, median (IQR)</td>
<td>3 (1–4)</td>
<td>0 (0–1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Caesarean section, n (%)</td>
<td>37 (74)</td>
<td>32 (64)</td>
<td>0.280</td>
</tr>
<tr>
<td>Apgar score at 5min, median (IQR)</td>
<td>9 (8–10)</td>
<td>9 (9–9)</td>
<td>0.844</td>
</tr>
<tr>
<td>Antenatal steroid use, n (%)</td>
<td>47 (94)</td>
<td>42 (84)</td>
<td>0.194</td>
</tr>
<tr>
<td>Received positive pressure ventilation, n (%)</td>
<td>21 (42)</td>
<td>27 (54)</td>
<td>0.230</td>
</tr>
<tr>
<td>Late onset sepsis (confirmed)*, n (%)</td>
<td>13 (26)</td>
<td>4 (8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Necrotising enterocolitis (suspected)*, n (%)</td>
<td>6 (12)</td>
<td>3 (6)</td>
<td>0.243</td>
</tr>
<tr>
<td>Intraventricular haemorrhage*, n (%)</td>
<td>36 (72)</td>
<td>2 (4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Retinopathy of prematurity*, n (%)</td>
<td>4 (8)</td>
<td>1 (2)</td>
<td>0.181</td>
</tr>
<tr>
<td>Periventricular leukomalacia*, n (%)</td>
<td>7 (14)</td>
<td>0</td>
<td>0.006</td>
</tr>
<tr>
<td>Chronic lung disease*, n (%)</td>
<td>10 (20)</td>
<td>3 (6)</td>
<td>0.036</td>
</tr>
<tr>
<td>Patent ductus arteriosus*, n (%)</td>
<td>16 (32)</td>
<td>6 (12)</td>
<td>0.014</td>
</tr>
</tbody>
</table>

P values for comparisons between the two groups were determined by the Student’s t-test or Mann-Whitney U test for continuous variables and by χ² or Fisher’s exact tests for categorical variables, as appropriate.

*Diagnoses were noted from clinical records: late onset sepsis (culture proven sepsis after 72 hours of birth); necrotising enterocolitis (based on clinical or radiological features that needed at least 5 days of withheld feeding and antibiotics); retinopathy of prematurity (any stage diagnosed on screening examination); periventricular leukomalacia (any lesion reported on cranial ultrasound); chronic lung disease (infants requiring respiratory support including any supplemental oxygen at 36 weeks’ corrected gestational age) and patent ductus arteriosus (diagnosed on echocardiography).

HC, head circumference.
More infants in Malaysia received any mother’s own milk (MOM) during admission (Malaysia: 98% vs UK: 76%, p=0.001) and more infants in the UK received formula milk (Malaysia: 80% vs UK: 94%, p=0.037).

Among infants who were fed their MOM, 86% infants had breast milk fortifier (BMF) added on median (IQR) DOL 118–16 in Malaysia when they were receiving a median (IQR) milk volume of 154 (149-164) ml/kg/day while...
In this study, we observed more Malaysian infants received breast milk as compared with UK infants. This is consistent with each country’s national reports that record a higher rate of breast feeding among Malaysian infants. The higher rate of breast feeding among Malaysian infants could be attributed to the cultural and societal practices in Malaysia that promote breast feeding.

Nutritional intakes

There was no significant difference in energy intakes in weeks 1–4 between the two units (p=0.238). However, Malaysian infants received more protein (Malaysia: 3.0±0.5 g/kg/day vs UK: 2.7±0.6 g/kg/day, p=0.004) and had smaller cumulative energy and protein deficits over this period, than the UK infants (Malaysia (energy): 191.6±129.8 vs UK: 254.5±152.0 kcal/kg, p=0.028 and Malaysia (protein): 11.4±6.1 vs UK: 15.4±8.0 g/kg, p=0.006). Protein energy ratio was also higher in the Malaysia unit (Malaysia: 3.03±0.31 g/100kcal/day vs UK: 2.61±0.48 g/100kcal/day, p<0.001).

For those infants who remained in the hospital in weeks 5–8 of life (Malaysia: n=28, UK: n=23), better energy intakes were shown in both units although energy intakes were lower than in weeks 1–4. Infants in the UK unit had marginally lower energy intakes than infants in Malaysia. The difference in energy intakes between the two units was significant (Malaysia: 126±19 kcal/kg/day vs UK: 109±17 kcal/kg/day, p=0.031) as was the difference in protein intakes (Malaysia: 17.1±5.8 g/kg/day vs UK: 11.6±4.6 g/kg/day, p=0.001). There was no significant difference in total fluid intake between the two units in weeks 5–8 (Malaysia: 141.4±32.4 mL/kg/day vs UK: 153.9±33.4 mL/kg/day, p=0.077).

Postnatal growth

There were no significant differences in growth outcomes at discharge from the two units. The mean±SD change in WAZ between discharge and birth was similar between the two units (Malaysia: −0.62±1.03 vs UK: −0.91±1.16, p=0.250). However, Malaysian infants had a lower cumulative energy deficit than UK infants (Malaysia: −105±25 kcal/kg, p=0.028). The magnitude of the deficit was also lower in the Malaysia unit (Malaysia: −1.2±0.3 g/kg/day vs UK: −1.7±0.4 g/kg/day, p=0.004).

Discussion

In this study, we observed more Malaysian infants received breast milk as compared with UK infants. This is consistent with each country’s national reports that record a higher rate of breast feeding among Malaysian infants. The higher rate of breast feeding among Malaysian infants could be attributed to the cultural and societal practices in Malaysia that promote breast feeding.
Malaysian infants is possibly related to older maternal age and higher parity among mothers, as shown in many studies. Experienced mothers may have an easier start to breast feeding and their previous experiences could help with continuation of breast feeding in the unit. Cultural differences in attitudes to breast feeding between the UK and Malaysia, where breast feeding is the norm and the prevalence is increasing may also underlie some of the differences between breastfeeding rates in the two units. The Malaysian unit has an established accreditation as Baby Friendly Hospital, which is favourably related to the high rate of initiation and continuation of breast feeding. The UK unit has achieved stage 1 of BFI accreditation and is building towards a stage 2.

Supplementation of breast milk with BMF or protein supplements was more frequent in the Malaysian unit while BMF was used more selectively in the UK unit. The standard protocol recommends the addition of BMF at 75–100 mL/kg/day milk feeds in Malaysian unit while in the UK unit, protocol suggests the addition of BMF when feeding reaches 150–180 mL/kg/day but only at clinician’s discretion when there are significant concerns about growth. The majority of infants who were fed breast milk in the Malaysian unit received some fortification, while the majority of infants who received breast milk in the UK unit received some supplemental formula feeding instead. Interestingly, in the Malaysian unit, infants on mixed feeds, that is, who had breast and formula milk, continued fortification if predominantly breast milk fed while most mixed fed infants in the UK unit did not receive BMF.

More Malaysian infants received PN which could be related to more SGA infants and higher rates of comorbidities in this unit. Although they were given some enteral feeds, they were also started on PN possibly due to anticipation of feed intolerance and slower advancement of milk feeds. PN was used in this scenario possibly, with a view to boost nutrition while milk feeds were established. Additionally, PN support was provided for a longer duration. Infants in the UK unit were larger and less unwell and hence more likely to establish enteral feeding quicker and hence PN use was restricted. However, this study showed no difference between units with reference to the postnatal age when full feeds were established. The more frequent and longer use of PN and BMF resulted in significantly higher protein intake among the Malaysian infants when compared with those in the UK unit.

Despite the high use of formula milk which has more protein than that estimated for breast milk, average protein intakes in the UK unit did not meet the recommended intake of 3.5 g/kg/day. Previous studies showed that protein intakes aimed at >3.5 to 3.8 g/kg/day could decrease cumulative deficits and achieve better growth. Fortifying breast milk can increase protein intake although this would also involve cow’s milk protein exposure and interfere with exclusive human milk feeding. Additionally, any change to feeding strategies for the individual infant would also, understandably, be a response to infants’ clinical conditions which might not be detected in this study.

Despite notable differences in intake, there were no significant differences in the short-term growth at discharge between the units. Throughout admission, the UK infants were observed to have consistently higher weekly weight Z-score than Malaysian infants, although both groups had a decline in growth trajectories. The differences in infant characteristics, possibly birth weight and comorbidities, may explain this. Baseline anthropometric assessment showed that there was a significantly higher proportion of SGA infants in the Malaysian unit. This is possibly due to the centre acting as a referral hospital for high-risk obstetric cases involving mothers with pre-eclampsia, diabetes and fetal growth restriction. In addition, the Fenton growth chart that was used in this study may not represent the Asian population as much as it was constructed based on mostly a Caucasian population, which could also lead to higher SGA infants classified in the Malaysian unit. Studies showed that there were significant deviations in the assessments of growth depending on the growth charts used.

Infants in the Malaysian unit were also challenged with a higher incidence of comorbidities such as chronic lung disease and patent ductus arteriosus that likely necessitated the restriction of total fluid intake which could affect growth. However, any interpretation for ‘optimal growth’ outcome should explore factors other than weight only, including longer-term growth, neurodevelopmental and metabolic outcomes in later life. Studies show that preterm infants fed mainly breast milk have better long-term outcome despite slower weight gain in early life.

The strengths of this study are that it is the first attempt to explore comparison of nutritional practices between two centres in different settings. Prospective collection of details of daily actual nutrient intake and weekly growth allowed a comprehensive analysis of nutritional practices. However, as this is an exploratory study, the sample size was small and not powered for differences.
in outcomes. A larger sample size is needed for evaluating the reasons for the differences observed in this study affecting growth failure. Estimation of nutritional intakes in breastfed infants cannot be accurate as intakes were analysed by using the best available estimates and may not reflect the true nutritional composition of the milk received. Maternal details including her nutritional status, clinical conditions and antenatal care should also be considered as these are vital determinants of fetal nutrition and infants’ outcomes including SGA status.

Despite these limitations, studies comparing nutritional intakes and growth outcomes are feasible to do in these two countries. Malaysia is an upper-middle-income country with similar government-funded healthcare system and NMR as the UK. The nutritional protocols used in these two units were based on the similar international guideline but were applied differently perhaps due to differences in patient characteristics and cultural differences making such comparisons an interesting area of study. Studies with an adequately powered sample, collection of more data on maternal characteristics and infants’ longer-term outcomes and the use of a more representative growth chart would provide evidence to ensure that preterm infants receive adequate nutrition, hopefully, in all care settings globally.

CONCLUSION

In our exploratory analyses, there were variations in nutritional practices between the two units included in this study. Current nutritional practices often do not meet recommended intakes, especially for protein in preterm infants. We found that with international collaboration, future comparison studies involving units in varied income settings are feasible and may provide evidence to support equity in care of preterm infants.

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Contributors HAH, SQ, LS, HB and F-CC conceptualised and designed the study and reviewed and revised the manuscript. HAH performed the data collection in the UK unit, completed the data analysis in both units and drafted the initial manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval Ethical approval was obtained from the Health Research Authority (HRA) and Health and Care Research Wales (HCRW) Approval (UK) (IRAS project ID: 258817, Protocol number: 19 012) and Research Ethics Committee, Universiti Kebangsaan Malaysia (UKM) (Malaysia) (JEP-2019-325).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Data are available on request, from the corresponding author.

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