Birth weight recovery among very low birth weight infants surviving to discharge from Charlotte Maxeke Johannesburg Academic Hospital

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Background. The recommended growth velocity (GV) of very low birth weight (VLBW) infants is 15 g/kg/day. Several factors have been associated with poor postnatal weight gain.
Objective. To provide current information on the postnatal growth of VLBW infants at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).
Methods. This was a longitudinal study of VLBW infants surviving to discharge from CMJAH neonatal unit from August to October 2013.
Results. Sixty-nine infants were included in the study. The mean GV was 13.2 g/kg/day, the median weight loss was 7.69% and the median time for regaining birth weight was 16 days. Fifty-one infants (73.9%) regained their birth weight at or before 21 days. There was a decrease in mean *z*-scores for weight (ZSWs) from –0.32 (standard deviation 1.25) at birth to –1.94 (1.35) at discharge. A multiple linear regression showed a negative association between ZSW at discharge and number of days nil per os without parenteral nutrition (PN). Antenatal steroids were associated with poor GV. There were no factors associated with regaining birth weight after 21 days on multiple logistic regression.
Conclusion. This study showed a GV in VLBW infants approaching recommended standards. Number of days without PN and use of antenatal steroids were associated with poor postnatal growth.

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Very low birth weight (VLBW) infants are those born weighing less than 1 500 g. VLBW infants comprise between 1% and 2% of all live births, but contribute significantly to neonatal mortality and morbidity.[1,2] Birth weight is a general index of the health of a newborn baby.[3] The growth of a newborn baby and specifically a VLBW infant reflects the development of its brain, liver, heart, muscles and other organs of the body.[3] After regaining their birth weight, VLBW infants have a target of adding 15 g/kg of weight daily.[4] The goal is to achieve a postnatal growth rate that approximates that of a normal foetus.[5]

Poor postnatal weight gain in VLBW infants is associated with prolonged hospital stay, increased cost of care and an increased risk of nosocomial infection.[4] This is of major importance in overcrowded neonatal units in resource-poor settings. There is also an association between retinopathy of prematurity and poor weight gain.[4,6] Many factors affect postnatal weight gain in VLBW infants, including necrotising enterocolitis (NEC), feeding intolerance, parenteral nutrition (PN), type of enteral feed, chronic lung disease and neonatal sepsis.[4,7-9] Ideally, VLBW infants should receive PN to ensure adequate nutrition, because these infants receive low volumes of enteral feeds in the first days of their life in order to prevent NEC. Uhing reported that preterm infants below 30 weeks' gestation accumulate an energy deficit in the first 5 weeks.[10] Uhing also documented an improved weight gain when PN is started early and aggressively. In addition, breastmilk provided to these infants should be fortified.[10] Preterm milk (obtained from mothers of preterm infants) is often low in protein, sodium, calcium and phosphorus; therefore, preterm infants receiving expressed breastmilk need human milk fortifiers.[5] South Africa (SA) is a country with limited health resources, and PN is used on a limited basis to reduce costs. Breastfeeding of VLBW infants is suboptimal in many units, partly related to the HIV epidemic. In addition, breastmilk fortifiers may not be used routinely. Kangaroo care is widely practised and has been shown to improve postnatal weight gain in VLBW infants.[5,11]

There are limited data regarding postnatal growth of VLBW infants in sub-Saharan Africa. A study from Groote Schuur Hospital (Cape Town, SA) showed that the growth velocity (GV) of extremely low birth weight infants (<1 000 g at birth) in this unit was close to the internationally accepted norms.[12] The objective of the present study was to provide current information on the postnatal growth of VLBW infants at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), to inform future nutritional policy for VLBW in this unit.

Methods

This was a retrospective, longitudinal study of VLBW infants admitted to CMJAH neonatal unit within 72 h of birth and surviving to discharge between August and October 2013.

In order to have a representative sample of the VLBW population at CMJAH, the sample size was calculated as follows, based on a prevalence of VLBW infants of 4.7% of live births (personal communication, D E Ballot):

$$\text{Sample size (SS)} = [Z^2 \times P \times (1 - P)] \div C^2$$

where: SS = required sample size; Z = 95% confidence interval (standard value of 1.96); P = estimated prevalence of VLBW in the project area; and C = 5% margin of error (standard value of 0.05).

A sample size of 69 infants was calculated. Patient information of VLBW infants discharged from CMJAH was reviewed from 1 August 2013 until the desired sample size was achieved. Infants whose records were unobtainable or incomplete, and those infants who died or were transferred to other units were not included.

VLBW infants admitted to the neonatal unit were managed according to the unit protocol. Babies were kept nil per os (NPO) for the first 24 h and given an intravenous infusion of 10% dextrose water with electrolytes, starting at 80 mL/kg/day. Orogastric feeds were then introduced at a volume of 20 - 30 mL/kg/day. Breastmilk was the preferred feed. If maternal

breastmilk was not available, babies were fed a premature formula (PreNan; Nestlé, SA). Donor breastmilk was not available during the study period. Enteral feeds were advanced daily at a rate of 20 - 30 mL/kg/day up to a maximum of 160 - 180 mL/kg/day based on the baby's clinical condition and evidence of feeding tolerance. PN was only provided to those infants with surgical conditions of the gastrointestinal tract or NEC. Breastmilk was fortified (FM85; Nestlé, SA) once a volume of 20 mL per feed was achieved. Babies were weighed twice weekly on designated days. Basic demographic and clinical data were obtained from the computerised neonatal database. Neonatal data are collected and managed using REDCap electronic data capture tools hosted at the University of the Witwatersrand.[13] This is done as ongoing clinical audit. Data information not included in the database, including twice-weekly weights and days of NPO, were obtained from patients' files. In the current study, duration of NPO and NPO without PN were considered rather than the time to establish full enteral feeding. The information was thereafter captured in a Microsoft Office Excel version 2007 spreadsheet, and imported to Stata version 13 (StataCorp, USA) for analysis.

Infants' weights were plotted using Fenton's growth charts.[4] Those with birth weights below the 10th percentile were classified as small for gestational age (SGA) and those above the 90th percentile were classified as large for gestational age. The Fenton chart (http://www.peditools.org/fenton2013/) was also used to calculate a *z*-score for weight (ZSW) at birth and at discharge, and a ZSW every week until 63 days, using the corrected gestational age, as only few babies were hospitalised for >63 days. GV was calculated for every infant by two-point models average weight, as shown in the following formula:

$$GV = [1\,000 \times (W_n - W_1)] \div \{(D_n - D_1) \times [(W_n + W_1)/2]\}$$

where: W = weight in grams; D = day; 1 = beginning of time interval in days; n = end of time interval in days (discharge time).

The starting time taken was 7 days of life, and if there was no weight recorded at day 7 of life, the closest next weight was taken. Two babies had the next weight close to the discharge weight; in those two infants the birth weight was taken as W_1. Seven days was taken as the starting point as previous studies have shown that this is the time weight loss has reached its nadir.[12,14]

Feeding intolerance was defined as a gastric residual volume of more than 50% of volume of the previous feed or total gastric residual volume >20% of the total volume of feed on the previous day. Bile-stained gastric residuals, vomiting and abdominal distension were considered to be evidence of feeding intolerance or possible NEC. Resuscitation at birth was defined as the need for assisted ventilation, chest compressions or the administration of adrenaline. Babies who were given supplemental oxygen alone at birth were not classified as needing resuscitation. NEC was defined as stage 2 or 3 using modified Bell's criteria.[15] The need for assisted ventilation after initial resuscitation was defined as requiring either conventional mechanical ventilation or high-frequency ventilation. During the study period, babies with respiratory failure were initially treated with nasal continuous positive airways pressure (NCPAP); only those babies failing NCPAP would be ventilated. Owing to limited resources, babies with a birth weight of between 750 g and 900 g were offered NCPAP but not assisted ventilation, while those weighing <750 g did not get NCPAP.

Table 1. Characteristics of very low birth weight in infants and their mothers (*N*=69)

Variable	*n* (%)
Maternal HTA (chronic or pregnancy induced)	16 (23.2)
Antenatal steroid received	27 (39.1)
Mode of delivery	
Caesarean section	49 (71.0)
NVD	20 (29.0)
AGA at birth	51 (73.9)
LGA at birth	6 (8.7)
SGA at birth	12 (17.4)
Time of initiation of feeding ≤48 h	64 (92.8)
Feeding intolerance	24 (34.8)
NEC	3 (4.3)
NCPAP	47 (68.1)
Assisted ventilation	12 (17.4)
PDA	10 (14.5)
Anaemia requiring blood transfusion	29 (42.0)
Neonatal jaundice requiring phototherapy	48 (69.6)
HMD	56 (81.2)
O_2 requirement at 28 days' chronological age	13 (18.8)
Time of regaining birth weight ≤21 days	51 (73.9)
Type of feeding at discharge	
Fortified breastmilk	3 (4.4)
Breastmilk	19 (27.5)
Breastmilk and formula	5 (7.2)
Formula only	42 (60.9)
Good GV (>14 g/kg/day)	26 (37.7)
Appropriateness of weight for CGA at discharge	
Appropriate	30 (43.5)
<10th percentile	39 (56.5)

HTA = hypertension; NVD = normal vaginal delivery; AGA = appropriate for gestational age; LGA = large for gestational age; SGA = small for gestational age; NEC = necrotising enterocolitis; NCPAP = nasal continuous positive airways pressure; PDA = patent ductus arteriosus; HMD = hyaline membrane disease; GV = growth velocity; CGA = corrected gestational age.

Statistics

Data were described using standard statistical methods. Categorical variables were described using frequency and percentage, while continuous variables were described using mean and standard deviation or median and range, depending on the distribution of the data. Birth weight recovery at ≥21 days and GV >14 g/kg/day were used to separate babies into two

Table 2. Growth and other characteristics of very low birth weight in infants (*N*=69)

Variable	Median (IQR) or mean (SD)*
Age of the mother (years)	28 (23 - 33)
Gestational age at birth (weeks)	30 (27 - 32)
ZSW at birth	–0.37 (1.25)*
Birth head circumference (cm)	28 (26 - 29)
Birth weight (g)	1 210 (1 030 - 1 390)
Time of initiation of feeding (h)	25 (19 - 32)
Days NPO without total PN (days)	1 (1 - 3)*
Days NPO with PN (days)	2 (0 - 3)*
Weight loss (%)	7.69 (3.14 - 13.4)
Time of regaining birth weight (days)	16 (12 - 22)
Duration of ventilation (days) (*n*=12)	6.5 (4.5 - 13)
Number of transfusions (*n*=29)	2 (1 - 3)
CGA at discharge (weeks)	35 (2.5)*
ZSW at discharge	–1.94 (1.35)*
GV (g/kg/day)	13.2 (4.24)*
Duration of hospital stay (days)	35 (25 - 53)

IQR = interquartile range; SD = standard deviation; ZSW = *z*-score for weight; NPO = nil per os; PN = parenteral nutrition; CGA = corrected gestational age; GV = growth velocity.
*Median and IQR are presented except otherwise specified.

Table 3. Multiple logistic regression of factors associated with good GV

Variable	Odds ratio	*p*-value	95% CI
Antenatal steroids	0.18	0.005	0.05 - 0.60
Feeding intolerance	0.56	0.33	0.17 - 1.79
Constant	1.44	0.35	0.66 - 3.13

GV = growth velocity; CI = confidence interval.

Table 4. Multiple linear regression of factors associated with ZSW at discharge

Variable	Coefficient	*p*-value	95% CI
Gestational age	–0.23	0.399	–0.97 - 0.51
Time of initiation of feeding (h)	0.03	0.177	–0.02 - 0.09
NPO without PN (days)	–0.63	0.047	–1.24- –0.02
NPO on PN (days)	–0.38	0.206	–1.13 - 0.37
Duration of ventilation (days)	0.21	0.101	–0.07 - 0.49
Number of transfusions	–0.54	0.103	–1.29 - 0.20
Constant (intercept)	6.36	0.399	–14.25 - 26.97

ZSW = *z*-score for weight; CI = confidence internal; NPO = nil per os; PN = parenteral nutrition.

groups. Univariate analysis was done using the Pearson χ^2 test and Fisher's exact test for categorical variables, while a Student's *t*-test was used for continuous variables. Parameters with $p<0.1$ on univariate analysis were included in a multivariate analysis. In multivariate analysis, a 95% confidence interval (CI) was reported.

Simple linear regression was done for normally distributed continuous variables, and logistic regression analysis for binary variables, to determine factors associated with good GV and those associated with birth weight recovery after 21 days. Multiple linear and logistic regression was then done, considering the same outcomes.

The study was approved by the human research ethics committee (medical) of the University of the Witwatersrand (clearance certificate no. M130226).

Results

A total of 69 patients were reviewed. The majority were female (52.2%) and most babies were singletons (78.3%). Antenatal clinic attendance among the mothers was good (75.4%). Twenty-two (31%) of the mothers were primiparous. Only one mother had syphilis during pregnancy, while 18 mothers (26.1%) were HIV-positive. There was no maternal tuberculosis or maternal diabetes among the study population. The majority of patients (*n*=56 (81.2%)) were born with a 5-min Apgar >5. Most of the babies (*n*=49 (71%)) were born by caesarean section. Forty-eight infants (69.6%) received kangaroo mother care (KMC); among them, 30 patients (43.5%) had continuous KMC while 18 patients (26.1%) had intermittent KMC. Most babies were fed formula (*n*=42 (60.9%)). The remaining patient characteristics are shown in Tables 1 and 2, which report categorical and continuous variables, respectively.

Enteral feeds were initiated within 48 h in the majority of babies (92.8%) and birth weight was recovered within 21 days in 51 infants (73.9%). The median time of initiation of enteral feeds was 25 h (range 19 - 32), the median time of regaining birth weight was 16 days (12 - 22) and the median percentage weight loss was 7.69% (3.14 - 13.4%). The median time for the 24 (34.8%) infants who had feeding intolerance was 3 days (1.5 - 4.5) without PN and 2 days (0 - 5) with PN.

Univariate analysis showed a statistically significant association between birth weight recovery after 21 days and the following factors: feeding intolerance (p=0.031), sepsis (p=0.06), and oxygen requirement at 28 days (p=0.086). There was no statistically significant association between birth weight recovery after 21 days and any of the other variables. A multiple logistic regression analysis showed no significant association between regaining birth weight after 21 days and feeding intolerance, sepsis or oxygen requirement at 28 days.

Mean GV was 13.2 (SD 4.24) g/kg/day. In a simple linear regression, GV was negatively associated with the number of days NPO without PN (p=0.005), number of days NPO with PN (p=0.026), duration of ventilation (p=0.033), number of transfusions (p=0.001), duration of hospital stay (p=0.007) and administration of antenatal steroids (p=0.02). A multiple linear regression, however, did not show any of the above factors to be significant. Good GV (>14 g/kg/day) showed a significant association with antenatal steroids (p=0.004) and the type of feeding at discharge (p=0.051) by univariate analysis. A multiple logistic regression was done to look for factors associated with good GV. Administration of antenatal steroids had a negative effect on the GV; this was the only statistically significant

factor associated with good GV (odds ratio 0.18, 95% CI 0.05 - 0.60) (Table 3).

Mean ZSW at birth was –0.37 (SD 1.25) and –1.94 (1.35) at discharge. A simple linear regression showed a negative association between ZSW and gestational age (p<0.0001), time of initiation of feeding (p=0.037), number of days NPO without PN (p<0.001), number of days NPO with PN (p=0.002), duration of ventilation (p=0.018) and number of transfusions (p=0.001). A multiple linear regression of these factors associated with ZSW at discharge on univariate analysis showed that only the number of days NPO without PN remained statistically significant (p=0.047). See Table 4.

There was an overall decline in ZSW during hospital stay (Fig. 1), and a statistically significant decrease in ZSW from birth to discharge (paired t-test p<0.0001) (Fig. 2).

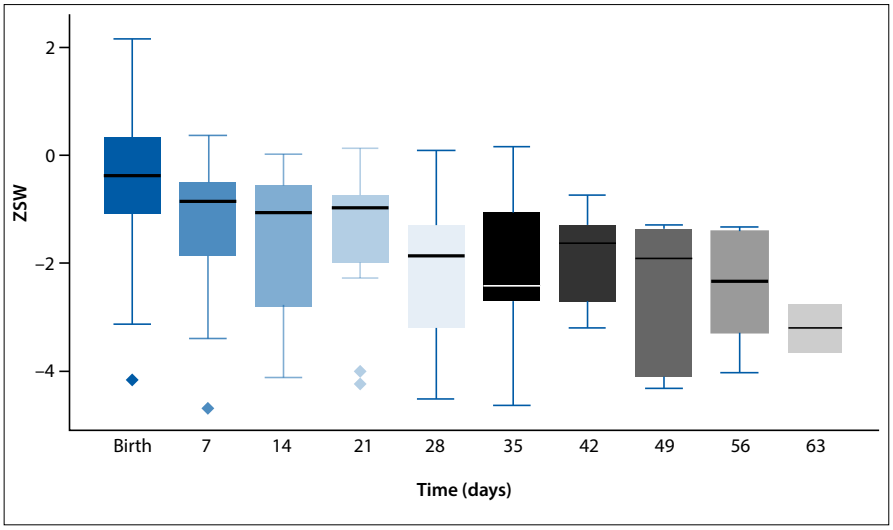

Fig. 1. ZSW during hospital stay. (ZSW = z-score for weight.)

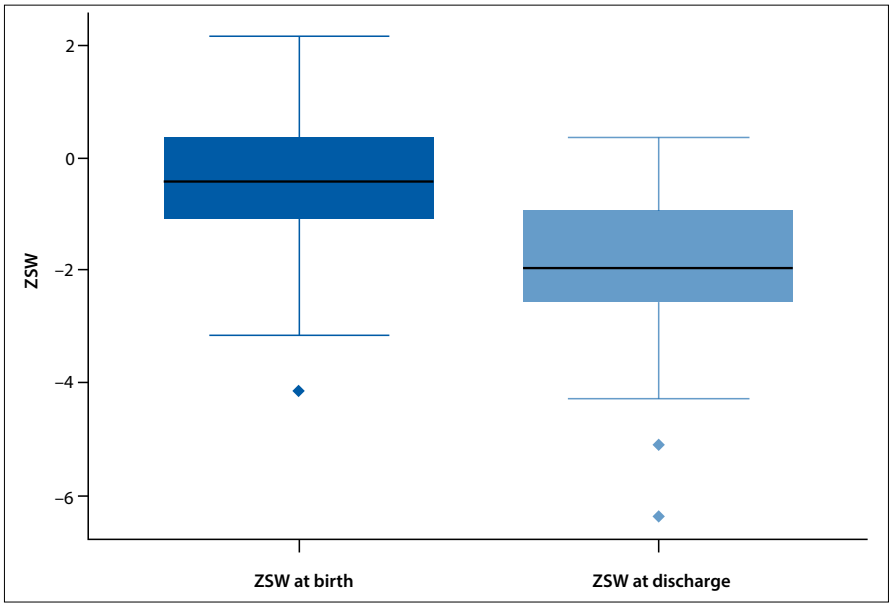

Fig. 2. ZSW at birth and at discharge. (ZSW = z-score for weight)

Discussion

This study is one of few that has evaluated growth in hospitalised preterm infants in sub-Saharan Africa. Infants were predominantly appropriate for gestational age (73.9%), which is slightly above the finding of a study done by Lima *et al.*[9] The median gestational age was 30 weeks, which is comparable with the findings of Lima *et al.*[9]

The results showed that 92.8% of babies were fed at or before 48 h, and median time of initiation of feeding was 25 h, in accordance with the unit protocol. At birth, the mean ZSW was –0.37 (SD 1.25), which decreased to –1.94 (2.5) at discharge. This is similar to findings in other reports: in a study done by Saluja *et al.*[16] the mean ZSWs were –1.17 at birth and –2.16 at discharge, whereas Lima *et al.*[9] documented a drop of mean ZSW from –0.96 to –1.54 from birth to discharge. In the current study, the prevalence of SGA at birth was 17.4%, but increased to 56.4% at discharge. De Curtis and Rigo[17] documented that 22% of VLBW infants were SGA at birth, whereas at 36 weeks corrected age, 97% had growth failure.

The median time for regaining birth weight in this study was 16 days (range 12 - 22), whereas Ehrenkranz[18] documented a time of regaining birth weight of 11 - 18 days. In the current study, the median percentage of weight loss was 7.69 (range 3.14 - 13.4), which is less than that reported by Senterre and Rigo.[19]

The only factor associated with poor ZSW at discharge was the number of days NPO without PN. This confirms reports that an aggressive nutrition starting PN on the first day of life prevents growth failure.[20]

The mean GV of the present study was 13.2 g/kg/day, which is close to that of other reports,[12,16] but below the recommended 15 g/kg/day.[12] The recommended value is a GV of babies after having gained their birth weight.[4] GV in the current study was calculated using day 7 as the baseline, rather than the day birth weight was regained, as weight loss has reached its nadir. This is in keeping with other reports.[12] Using the day of regaining birth weight would possibly give a GV closer to the recommended value.

The study showed a negative effect of antenatal steroids on growth, compared with the findings of Kumar and Seshadri,[21] who found an increased incidence of infants with weight below the 10th percentile at discharge after multiple doses of antenatal steroids.

Conclusion

The current study showed a GV approaching the recommended GV of VLBW. In a resource-limited setting where an aggressive PN is not feasible, the study showed an extrauterine growth failure at discharge and an association between ZSW at discharge and number of days NPO without PN. This study also showed a negative effect of antenatal steroids on good GV of VLBW infants. More liberal use of PN may improve postnatal growth in this VLBW population.

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