

Research Article

Duration of Hospital Stay and Factors Associated with Prolonged Hospital Stay in Very Low Birth Weight Infants Surviving to Hospital Discharge

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Abstract

Background: Ongoing care of surviving very low birth weight infants (VLBWI) is associated with increases in medical costs. Thus, knowing their length of hospital stay (LHS) will assist in counselling parents and budgeting for their neonatal care.

Objective: To determine the LHS among VLBWI surviving to hospital discharge and factors associated with prolonged LHS.

Methods: This was a retrospective analytic study performed at Chris Hani Baragwanath Academic Hospital, South Africa. Records of VLBWI who

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survived to hospital discharge between January 2015 and October 2016 were reviewed. Data on maternal and infant characteristics, morbidities and LHS were recorded. Comparison between those with and without prolonged LHS as defined by being discharged beyond 41 weeks of postmenstrual age was performed.

Results: Records of 435 VLBWI who survived to hospital discharge were reviewed. Their mean birth weight and gestational age were 1234 ± 192 grams and 30 ± 2 weeks respectively. The median duration of LHS was 39 days, with a range of 11 to 183 days. The LHS increased proportionally with decreasing gestational age

or birth weight. Thirty-four VLBWI (7.82%) had prolonged duration of hospital stay. On multiple logistic regression analysis factors associated with prolonged LHS were gestational age (OR: 2.01; 95% CI 1.6-2.61), chronic lung disease (OR: 9.40; 95% CI 2.53-34.72), and healthcare associated infections (OR: 31.86; 95% CI 6.75-150.3).

Conclusions: The median LHS stay for the VLBWI was noted to be 5.5 weeks (39 days) and neonates with morbidities, namely chronic lung disease and healthcare associated infections are more likely to have prolonged LHS.

Keywords: Duration; Hospital stay; Very low birth weight infants

Abbreviations: ANC-Antenatal care; BBA-Born before arrival; BPD-Bronchopulmonary dysplasia; CHBAH-Chris hani baragwanath academic hospital; CLD-Chronic lung disease; CMV-Conventional mechanical ventilation; Cpap-Continuous positive airway pressure; DBM-Donor breastmilk; EBM-Expressed Breastmilk; ELBW-Extreme low birthweight; EONS-Early onset neonatal sepsis; GA-Gestational age; HIC-High income country; HFOV-High frequency oscillation ventilation; HIE-Hypoxic ischaemic encephalopathy; IQR-linterquartile range; KMC- Kangaroo mother-care; LHS-Length of hospital stay; LMIC-Low middle income country; LONS-Llate onset neonatal sepsis; NEC-Necrotising enterocolitis; NICU-Neonatal intensive care unit; SD-Standard deviation; TPN-Total parenteral nutrition; VLBW-Very low birth weight; VLBWI-Very low birth weight infants; PHS-Prolonged length of hospital stay

1. Introduction

Survival of very low birth weight infants (VLBWI) (birthweight <1500 grams) or infants born preterm has

improved over the years [1]. Though survival rates of VLBWI are higher in high income countries (HIC) than in low middle income countries (LMIC), both groups of countries have shown an improvement in overall survival of VLBWI over the years [2]. The ongoing care of surviving VLBWI is associated with high medical costs [3]. These high medical costs cause stress and anxiety to families and place more financial demands to the health system. Thus, both parents and health systems are interested in knowing upfront the financial costs of caring for surviving VLBWI till hospital discharge. The LHS has been used as a surrogate for assessing the medical costs, therefore knowing the average LHS of VLBWI will assist in budget planning and in counselling parents.

Numerous factors have been reported to influence LHS and these include gestational age, birth weight, neonatal morbidities like chronic lung disease, necrotizing enterocolitis and healthcare-associated infections [4]. Local hospital practices or protocols, namely the weight used to discharge VLBWI have been reported to influence the LHS [5-7]. Many studies have reported on average LHS of VLBWI, but most of them are from HIC [8]. One study reported the median LHS for VLBW infants to be 44 (28-66) days in UK, a HIC and it was longer for extreme low birth weight (ELBW) (birth weight less than 1000 grams) at 86 (65-102) days [9]. The LHS vary from country to country even in HIC. Length of hospital stay in Italy was reported to be 46.2 (95% CI 44.5-47.8) days while in Sweden it was reported to be 61.0 (95% CI 60.0-62.0) days during the same period, 2006 to 2008 [10]. The LHS in LMIC may differ from those reported in HIC, because of differences in local practices. Therefore, in this study, we sought to determine the LHS amongst the VLBWI born and admitted to a public hospital in a LMIC and to determine factors associated with prolonged LHS.

2. Patients and Study Methods

2.1 Study design

This was a retrospective analytic study.

2.2 Study setting

The study was conducted at Chris Hani Baragwanath Academic Hospital (CHBAH), a public tertiary hospital, in South Africa. The hospital conducts about 22000 births per annum and is a referral centre for 8000 births per annum conducted at the local clinics. It has 185 neonatal beds, of which 66 beds are Level 3 or acute care nurseries. The hospital protocol is that all neonates requiring resuscitation at birth are offered resuscitation, but because of limited resources non-invasive ventilation is offered only to those weighing ≥ 750 grams and invasive ventilation only to those weighing ≥ 900 grams. All VLBWI are offered in-hospital continuous Kangaroo Mother Care once they weigh ≥ 1000 g, on full feeds and not requiring any treatment. During the study period, the weight used to discharge VLBWI was 1650 grams.

2.3 Study population

All VLBWI born and/or admitted at CHBAH from January 2015 up to October 2016 inclusive and survived to hospital discharge were included in this study. Infants excluded were those transferred out of the CHBAH neonatal unit to another hospital and did not return to CHBAH or came back after more than a week or died before discharge.

2.4 Data collection

All data collected was entered into an electronic data base using Microsoft Excel (Microsoft Seattle, WA, USA). Maternal and neonatal data were gathered from patients' hospital notes. Maternal data collected included age, parity and gravidity as well as the HIV status, and neonatal data included gestational age, birthweight, place of delivery, diagnosis and

management namely, need for mechanical ventilation, milk feed types, insertion of central lines, parenteral nutrition and whether the infant received phototherapy or not. Those who received mechanical ventilation were categorised into those who received non-invasive mechanical ventilation that is continuous positive airway pressure (CPAP) only and those who received invasive ventilation. The milk feed types were divided into exclusive breast milk, formula feeds and mixed feeds. Information on time to full enteral feeds and the duration on parenteral nutrition, neonatal complications namely chronic lung disease or, necrotizing enterocolitis, and sepsis were collected. Chronic lung disease was defined as need for supplemental oxygen for more than 28 days. Sepsis was defined as growth of an organism considered to be a pathogen from blood and/or cerebrospinal fluid. Healthcare associated infection was defined as infection diagnosed after 72 hours of being admitted to the hospital.

2.5 Data analysis

Infants were stratified according to gestational age in weeks from ≤ 26 to ≥ 35 weeks and according to birth weight in 100 grams from <900 grams to 1400-1499 grams. Categorical variables were summarized and presented as frequencies and percentages. Summary of continuous data were presented as means with standard deviation and median with interquartile ranges. In comparing the group of those with prolonged LHS and those who did not, categorical variables were compared using Pearson chi-square or Fisher exact test, and continuous variables were compared using Student t-tests or Mann-Whitney U test. In assessing factors associated with prolonged LHS, comparison was assessed using multivariable logistic regression. Differences that had a p-value <0.05 were considered statistically significant. All statistical analysis were performed using STATA MP version 13.0 StataCorp LLC, Texas, USA.

2.6 Ethics

Permission to conduct the study was acquired from the hospital management and ethical approval was given by the University of the Witwatersrand Human Research Ethics Committee (Medical) (Clearance number M161170).

2.7 Sample size estimation

Sample of VLBWI planned to be enrolled in the study was 448, calculated based on the assumption that the standard deviation for the duration of hospital stay will be 27 days similar to that reported by Bannwart et al. [4], with a precision of 2.5 days and level of confidence of 95%. Selection of patients was that of a convenient sampling based on the first 448 files of VLBWI who survived to hospital discharge.

3. Results

There were 2204 VLBWI delivered at CHBAH from January 2015 to October 2016. Among these 1661 survived to hospital discharge, giving a survival rate of 80%. A total of 435 hospital records were retrieved for the study. Majority of mothers of infants enrolled in this study were of age group 20-35 years, 28.5% were primigravida, and 29.9% were HIV positive (Table 1). Most of mothers (90.6%) gave birth in hospital with only 3.4% giving birth outside a healthcare facility and 92.0% had attended antenatal care.

Characteristics of VLBWI enrolled in the study and diagnosis on admission are presented in (Table 2). The average birth weight and gestational age of infants were 1234 ± 192 grams and 30 ± 2 weeks respectively. Less than 20% of infants weighed less than 1000 grams or were of gestational age less than 28 weeks, with 85.1% weighing between 1000 and 1499 grams and 76.6% having a gestational age of 28-32 weeks. Fifty five percent of infants were males. In addition to being VLBW, respiratory system diagnoses were found to be

the most common primary reason for admission to the neonatal unit with 335 (77.0%) of infants being admitted with a diagnosis of respiratory distress syndrome and 75 (17.2%) with transient tachypnoea of the newborn.

Sixty five percent of VLBW required mechanical ventilation, with the common mode of ventilation used being nCPAP (196/284; 69.1%) (Table 3). Only 53.6% were exclusively breast fed on discharge from hospital. Fifty-five percent received parenteral nutrition at some stage during their stay in hospital. The average time to full feeds was $11 (\pm 6)$ days and the average duration on parenteral feeds was 6 days. Proportion of infants who developed different morbidities during their stay are reported in (Table 3). About a third of patients (152/435; 34.9%) had late onset sepsis and of these patients there was a total of 125 culture confirmed episodes of sepsis with some patients having more than one episode during their hospital stay whilst others were presumed to have late onset sepsis and treated as such but did not have any positive cultures. There were 49 patients (11.3%) who had necrotizing enterocolitis and 32.0% developed chronic lung disease.

Median LHS amongst VLBWI was 39 (29-53) days and average LHS was $45 (\pm 25)$ days. Duration of hospital stay was inversely proportional to the birth weight and gestational age (Tables 4 and 5). Each birth weight increase of 100 grams was associated with a reduction of LHS by 4.3 days and each gestational age increase of one week being associated with a decrease in LHS by 0.4 days.

On univariate analysis prolonged hospital stay was associated with lower birth weight ($p < 0.001$), need for ventilation ($p = 0.012$) or parenteral nutrition ($p = 0.009$), and having been diagnosis with necrotizing enterocolitis ($p = 0.002$) or healthcare associated infections ($p < 0.001$)

and chronic lung disease (p<0.001) (Table 6). On multiple logistic regression analysis, factors associated with prolonged LHS were gestational age (OR: 2.01; 95% CI 1.6-2.61), having a diagnosis of chronic lung

disease (OR: 9.40; 95% CI 2.53-34.72), and healthcare associated infections (OR: 31.86; 95% CI 6.75-150.3) (Table 6).

Variable	Number	Percentage
Maternal Age		
<20	35	8.0
20-35	348	80.0
>35	52	12.0
HIV status		
Positive	130	29.9
Negative	305	70.1
Parity		
<1	124	28.5
1-4	305	70.1
>4	6	1.4
Place of Delivery		
Inborn	394	90.6
Local Clinic	20	4.6
Other hospitals	6	1.4
Home	15	3.4
Antenatal care		
Yes	400	92.0
No	35	8.0

Table 1: Maternal Characteristics.

Variable	Number	Percentage
Birthweight(g) Categories		
<1000	65	14.9
1000-1499	370	85.1
Gestational age (weeks)		
<28	50	11.5
28-30	223	51.3
31-32	110	25.3
33-44	52	12.0

Gender		
Male	238	54.7
Female	197	45.3
Admission diagnosis (1)		
Respiratory distress syndrome	335	77.0
Transient tachypnoea of the newborn	75	17.2
Very Low birthweight	17	3.9
Intrauterine growth restriction	4	0.9
Congenital Pneumonia	3	0.7
Congenital Anaemia	1	0.2

Table 2: Infant Characteristics.

Variable	Number	Percentage
Management		
Ventilation (N=435)		
Yes	284	65.3
No	151	34.7
Ventilation Type (N=284)		
Non invasive	196	69.1
Invasive	88	31.0
Feed Type (N=435)		
Expressed Breast Milk	233	53.6
Formula	65	14.9
Mixed	137	31.5
Parenteral Nutrition (N=435)		
Yes	239	54.9
No	196	45.1
Central Line (N=435)		
Yes	109	25.1
No	326	74.9
Complications		
Chronic Lung Disease (N=435)		
Yes	139	32.0
No	296	68.0
Chronic Lung Disease by Gestation (N=139)		
<32 weeks	125	89.9

≥ 32 weeks	14	10.1
Early Onset Sepsis (N=435)		
Yes	26	6.0
No	409	94.0
Late Onset Sepsis (N=435)		
Yes	152	34.9
No	283	65.1
Necrotising Enterocolitis (N=435)		
Yes	49	11.3
No	386	88.7
Neonatal Jaundice (N=435)		
Yes	271	62.3
No	164	37.7

Table 3: Management and Complications.

Birth weight in grams	Number	Median (25th -75th centile)	Mean ± SD
<900	28	68 (58-92)	80 ± 36
900-999	37	59 (51-82)	68 ± 24
1000-1099	39	50 (45-62)	54 ± 17
1100-1199	59	44 (39-62)	54 ± 26
1200-1299	83	37 (30-46)	42 ± 22
1300-1399	85	32 (27-39)	36 ± 14
1400-1499	104	32 (27-39)	30 ± 15
All	435	39 (29-53)	45 ± 25

Table 4: Median and Average Length of Hospital Stay According to Birthweight.

Gestational age in weeks	Number	Median (25th -75th centile)	Mean ± SD
≤ 26	27	64 (50-74)	71 ± 38
27	23	49 (41-58)	55 ± 27
28	64	47 (34-79)	59 ± 32
29	74	43 (35-53)	47 ± 21
30	85	38 (30-53)	42 ± 16
31	62	35 (25-41)	35 ± 15
32	48	31 (27-39)	35 ± 16
33	24	27 (23-32)	35 ± 27

34	11	27 (23-30)	30 ± 16
≥ 35	17	30 (15-57)	38 ± 27
All	435	39 (29-53)	45 ± 25

Table 5: Median and Average Length of Hospital Stay According to Gestational Age.

	Total	Not Prolonged	Prolonged	Association tests	Multivariate analysis
Gestational Age (weeks)	N=435 n (%)	N=401 n (%)	N=34 n (%)	p-value	OR (95% CI)
Mean ± SD	30 ± 2	30 ± 2	31 ± 4	0.065	2.0 (1.6-2.6)
Birthweight (grams) Mean ± SD	1230 ± 190	1240 ± 190	1110 ± 200	<0.001	0.99 (0.99-1)
Male	238 (54.7)	222 (55.4)	16 (47.1)	0.350	1.2 (0.5-3.3)
Chronic Lung disease	139 (32.0)	112 (27.9)	27 (79.4)	<0.001	9.4 (2.5-34.7)
Ventilation	286 (65.7)	257 (64.1)	29 (85.3)	0.012	0.7 (0.2-3)
Healthcare-Associated Infections	152 (34.9)	123 (30.7)	29 (85.3)	<0.001	31.9 (6.8-150.3)
Necrotizing Enterocolitis	49 (11.3)	42 (10.5)	7 (14.3)	0.002	2.1 (0.8-6)
Parenteral Nutrition	239 (54.9)	213 (53.1)	26 (76.5)	0.009	0.5 (0.2-2)

Table 6: Factors Associated with Prolonged Length of Stay.

4. Discussion

In this study, we report on LHS of VLBWI from a LMIC, where discharge weight is much lower than that used in HIC. The findings in this study have shown that the LHS vary with gestational age and birth weight and is inversely related to these anthropometric measurements. Overall the average LHS of VLBWI was found to be 45 days, with a median of 39 days. One week increase in gestational age resulted in a decrease in LHS by 0.4 days. A 100 g increase in birth weight

was associated with 4.3 days decrease in LHS. Factors associated with prolonged LHS were gestational age at birth, a diagnosis of chronic lung disease and healthcare associated sepsis.

Due to improved survival of the preterm infant, research is now focused on models that can be used to predict LHS in this population of patients. Birthweight, gestational age, antenatal and perinatal factors are known to influence the LHS and can be used to estimate

LHS [4, 9, 11]. There is a paucity of data reporting on the LHS of the VLBWI in the LMIC. The median LHS in VLBWI delivered in Brazil [4], a LMIC, from January 1992 to December 1993, was reported as 45 (35-62) which was just 6 days longer than our observed median LHS of 39 (29-53) and similar to findings in Salford UK whose median LHS for the same population of patients over April 1986 and November 1990 was 44 (28-66) [9]. Differences between our study and that in Brazil were most notable among the extremely premature neonates. The mean LHS was 92.2 (\pm 26.7) in infants weighing <1000 g in Brazil compared to 73.1 (\pm 30.3) in our study. Infants in our study were discharged home once they were \geq 1650 g and feeding well with no other complications whereas those in Brazil were discharged once they reached a weight of \geq 2000 g [4]. This would account for the longer LHS in the Brazilian study a LMIC similar to South Africa in addition to differences in hospital practices as well as availability and distribution of resources. Similarities were observed when one assessed the overall relationship between birthweight and LHS. The infants born with lower birthweights had longer LHS overall as compared to the babies that higher birthweights in both studies.

A study conducted in HIC including 10 European regions, reported that average LHS of infants with gestational ages between 22+0 and 31+6 was 63.1 (\pm 36) days with a median LHS of 55 (interquartile range 40-75) [12]. Variation in patient clinical characteristics, patient populations, in hospital morbidities and planning/organisation of discharge as well as lack of availability of home care and step down facilities, resource limitations directing hospital policies may explain the difference on LHS between HIC and LMIC [13]. There is evidence that being SGA will increase the odds of having shorter LHS [14]. In our study, we did not assess for SGA because of unreliability of

gestational age. HIC offer advanced interventions like invasive mechanical ventilation to almost all VLBWI and discharge infants when they achieve weights of \geq 1800 grams, whereas in our study settings, invasive ventilation is only offered to those weighing above 900 grams and infants are discharged at weights \geq 1650 grams because of limited resources. Offering advanced care to all weight groups results in more smaller infants surviving and using higher weights to discharge are the most likely explanations for longer LHS in HIC compared to LMIC. It has been reported that the extremely premature infants have a high risk of mortality and those who survive have a six fold risk of increase in LHS [15] and thus mortality has been inversely correlated to the risk of having prolonged LHS [16].

One of the objectives of our study was to investigate factors associated with prolonged LHS. Knowing that most extremely preterm infants are discharged by 42 weeks postmenstrual age (PMA) [16], we defined prolonged LHS as discharge beyond 41 weeks PMA. Gestational age at birth, development of chronic lung disease or bronchopulmonary dysplasia (BPD) and healthcare-associated infections was associated with PHS. Gestational age has previously been reported to be a strong predictor of LHS [5, 9, 17, 18] with one study reporting that each day of increase in gestational age was associated with a one day decrease in LHS [5]. BPD (oxygen dependency at \geq 28 days) is known to prolong LHS in the premature neonate. In Israel over a 9-year period (1995 to 2003) the relationship between BPD and LHS in the VLBWI was investigated and they reported that LHS was prolonged if the infant had BPD [19]. It was reported that the adjusted mean LHS of infants <999 g without BPD was 89.8 days and 112.9 days for those with BPD. The adjusted mean for LHS for VLBW infants with BPD overall was 84.1 days and 58.1 days for those without BPD. In our study patients

with CLD or BPD had mean LHS of 55 days and those without had mean LHS of 39 days. In our study, the odds of having PHS were nine-fold higher if a VLBWI had CLD. Another factor that was found to be associated with an increase in risk of prolonged LHS was healthcare-associated infection with its presence increasing the odds of having PHS by 32 folds. The association between infections and PHS has been reported previously [4]. Necrotizing enterocolitis, one of relatively common morbidities of infections has also been reported with PHS [20]. Parenteral nutrition was significantly associated with prolonged LHS in univariate analysis ($p=0.009$) but not in multivariate analysis (OR 0.52 ; 95% CI; 0.15-1.82). This may be due to the increased risk of infection when on parenteral nutrition or perhaps the infants were already too sick to take oral feeds and therefore required parenteral nutrition. We did not compare the risks of morbidity in those that were exclusively breastfed against those that received cow's milk formula or mixed feed in this study though this has been studied elsewhere [21]. However, the inconsistent breastmilk supplies with prolonged length to full feeds together with parenteral nutrition may be factors that could have predisposed our patient population to healthcare associated infections which was the most significant determinant of LHS in our study together with BPD.

The LHS in LMIC countries has not been well studied and what this study adds is information in an area where there is paucity of published data in the literature. The information that we have gathered in this study will allow parents to better understand the approximate date of discharge of their premature infants. Continued counselling can be given to parents whose infants may have any morbidities as these parents and caregivers can be counselled about the high likelihood that their infant may have a more prolonged length of stay than as originally estimated. This will allow them to plan

accordingly and will allay any anxiety or fear that the parents may have should their infant not be discharged around the timeframe initially advised. Hospital managers can now plan according to these findings and will direct budgets towards prevention and treatment of morbidities associated with prolonged LHS.

The strength of this study was that it was conducted at one tertiary centre which has a large number of VLBWI who stay in the same centre from admission to discharge with negligible outward transfer rates and has uniform policy with regards to labour room practices, management protocols and discharge criteria so this enabled us to make the assessment of LHS without having to account for variations that may be seen in different units that may have differing practices and protocols to our neonatal unit. Our study population was a good representation of the VLBWI that one encounters in a LMIC as it is a state hospital. We were able to explore for factors associated with PHS. The LHS in LMIC countries has not been well studied and what this study adds is information in an area where there is paucity of published data in the literature.

Limitations to our study was the fact that it was a retrospective study. Files were manually retrieved from the archives and this was a lengthy exercise, thus we were not able to enrol the calculate sample size of 448 as the study period came to an end, but we were able to retrieve 97% of the files. Again, being a retrospective study, it was difficult to determine as to how was the gestational age determined as the method of determination was not recorded, thus unable to rely on its accuracy. The other limitation is that maternal details were often incomplete, and literature has shown that including in-hospital comorbidities with antenatal and perinatal factors in estimation of LHS gives more clinically applicable and accurate data to determine

LHS for future hospital planning and parental counselling [15].

5. Conclusion

The median LHS stay for the VLBWI in this study was 39 days (5.5 weeks) with a range of 11 to 183 days and the average LHS of 45 days. Birthweight can be used as a predictor of LHS, but gestational age may not be so accurate in our setting. Neonates with morbidities stay longer in the hospital. Chronic lung disease and healthcare associated infections are significantly associated with prolonged LHS. More attention is required to prevent chronic lung disease and healthcare associated infections in order to reduce LHS of VLBWI and related costs. This information should enable nurses and doctors to counsel the mothers regarding the expected duration of stay based on their infants' birth weight. Hospital management can use this information as part of calculating costs towards taking care of VLBWI, but more information is still required to do this, for example, how much time these infants spend in level 3 versus level 1 nursery or the number of interventions they require as costs or interventions will vary depending on the level of care required.

Ethics Approval

Permission to conduct the study was acquired from the hospital management and ethical approval was given by the University of the Witwatersrand Human Research Ethics Committee (Medical) (Clearance number M161170).

Competing Interests

There are no competing interests.

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Authors Contribution

Both Authors are responsible for the reported research and have participated in the concept and the design of the study. Dr Mahovo collected data, analysed and interpreted data, wrote the first draft on the manuscript, revised and approved manuscript for submission. She has conducted this research as part of her master's in medicine research report. Dr Sithembiso Velaphi interpreted data, reviewed and revised the manuscript and approved its submission.

Availability of Data

Upon request.

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