Sultan Qaboos University Med J, February 2015, Vol. 15, Iss. 1 pp. e91–97, Epub. 21 Jan 15
Submitted 14 Apr 14
Revision Req. 29 May 14; Revision Recd. 12 Jun 14
Accepted 3 Jul 14

Factors Responsible for the Prolonged Stay of Surgical Neonates in Intensive Care Units

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أسباب البقاء لفترات طويلة للحالات الجراحية من الأطفال حديثي الولادة في وحدات العناية المركزة

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ABSTRACT: ***Objectives:*** The length of hospital stay (HS) for patients is a major concern due to its social, economic and administrative implications; this is particularly important for neonates admitted to intensive care units (ICUs). This study aimed to determine the factors responsible for prolonged HS in surgical neonates. ***Methods:*** This retrospective study was conducted at Sultan Qaboos University Hospital, in Muscat, Oman. The medical records of 95 neonates admitted to the neonatal ICU who underwent general surgical procedures between July 2009 and June 2013 were reviewed. Mann-Whitney U and Pearson's Chi-squared tests were used for non-parametric numerical and categorical variables, respectively. A multiple regression analysis was performed to find a relationship between the variables and to detect the most important factor responsible for prolonged HS. A *P* value of <0.05 was considered statistically significant. ***Results:*** Gestational age, birth weight, number of days on a ventilator and postoperative morbidity were associated with prolonged HS. Furthermore, the age of neonates at first full enteral feed was associated with increased HS using both independent and multiple regression analyses. ***Conclusion:*** Prolonged HS can occur as a result of many factors. In this study, a number of factors were identified, including low gestational age, low birth weight, increased number of days on a ventilator and postoperative morbidity. Additionally, neonate age at first full enteral feeds also correlated with increased HS. Further research on this topic is suggested to explore this correlation in more detail and to inform future practices.

Keywords: Neonates; Neonatal Intensive Care Units (NICU); Length of Stay; Morbidity; Oman.

الملخص: الهدف: يشكل طول مدة الإقامة في المستشفى مصدر قلق كبير للمرضى ولما لها من آثار اجتماعية واقتصادية وإدارية؛ وبخاصة في الأطفال حديثي الولادة في وحدة العناية المركزة. هدفت هذه الدراسة إلى تحديد العوامل المسؤولة عن طول مدة الإقامة للحالات الجراحية في الأطفال حديثي الولادة. **الطريقة:** أجريت هذه الدراسة الاستعادية في مستشفى جامعة السلطان قابوس ، في مسقط، سلطنة عمان. تمت مراجعة 95 حالة جراحية للاطفال حديثي الولادة من السجلات الطبية الذين أدخلو وحدة العناية المركزة و خضعوا لعمليات جراحية عامة بين يوليو 2009 و يونيو 2013. استخدم اختبار مان–ويتني U واختبار بيرسون كاي للمتغيرات العددية والفئوية ، على التوالي. أجري تحليل الانحدار المتعدد لإيجاد العلاقة بين المتغيرات وللكشف عن أهم عامل مسؤول عن الإقامة لفترات طويلة. واعتبرت قيمة من $P < 0.05$ ذات دلالة إحصائية. **النتائج:** ارتبطت عوامل العمر الحملي، الوزن عند الولادة، وعدد الأيام على جهاز التنفس الصناعي والاعتلال بعد العملية الجراحية مع طول مدة الإقامة. علاوة على ذلك فإنه باستخدام كل من تحليل الانحدار المستقل والمتعدد ،ثبت ارتباط سن الوليد عند تحقيقه التغذية المعوية الكاملة بطول مدة الإقامة. **الخلاصة:** طول مدة الإقامة في المستشفى يمكن أن تحدث نتيجة لعوامل كثيرة. في هذه الدراسة، تم تحديد عدد من العوامل، بما في ذلك انخفاض العمر الحملي، وانخفاض وزن المواليد، وزيادة عدد الأيام على جهاز التنفس الصناعي والاعتلال بعد العملية. بالإضافة إلى ذلك كان سن الوليد عند تحقيقه التغذية المعوية الكاملة مرتبطا بطول مدة الإقامة ويقترح إجراء المزيد من الأبحاث حول هذا الموضوع لاستكشاف هذه العلاقة بمزيد من التفصيل في المستقبل.

مفتاح الكلمات: حديثي الولادة؛ وحدة العناية المركزة للأطفال حديثي الولادة؛ طول مدة الإقامة؛ الإصابة بالأمراض؛ عمان.

Advances in Knowledge

- *The results of this study show that low gestational age, low birth weight, increased number of days on a ventilator and postoperative morbidity are factors affecting surgical neonates' length of hospital stay (HS) in a neonatal intensive care unit (NICU).*
- *In addition, an infant's age at first full enteral feed was shown to have a significant association with prolonged HS. This may encourage neonatologists to evaluate current neonatal feeding practices.*

Application to Patient Care

- *The results of this study may help to reduce the length of HS in surgical neonates by identifying certain modifiable factors that lead to prolonged NICU stays.*

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The length of hospital stay (HS) for infants in neonatal intensive care units (NICUs) is of interest for many reasons. Studies have shown that prolonged HS leads to higher costs and greater morbidity.[1,2] Moreover, in smaller NICUs with limited resources, bed availability and management can become a challenge.

Surgery in newborns is indicated either because of a primary surgical disease or other complications that have arisen in the neonatal period. Many of the factors that prolong HS in non-surgical neonates have been well studied;[1–3] however, the literature is scarce regarding the factors involved in prolonged HS among surgical neonates. Identifying such factors may help to reduce the length of HS in surgical neonates admitted to NICUs, in turn reducing related costs and improving the management and allocation of available resources. The purpose of this retrospective study was to determine the factors responsible for prolonged HS in surgical neonates admitted to the NICU of Sultan Qaboos University Hospital (SQUH), in Muscat, Oman.

Methods

This retrospective study was conducted at SQUH between July 2009 and June 2013. Newborns who required general surgical procedures and were admitted to the NICU before four weeks of age were included in the study. The medical records of all included neonates admitted to the SQUH NICU for general surgical procedures during the study period were reviewed. Prolonged HS was defined as a stay of more than 19 days, as this was the median stay in the cohort. Patients were divided into two groups based on HS: group A included neonates hospitalised for >19 days, while group B included those hospitalised for ≤19 days. The following variables were determined as possible predictors for prolonged HS: gender; source of referral (at SQUH or elsewhere); maternal comorbidities; age at admission; gestational age; birth weight; associated anomalies; age at surgery; site of surgery (e.g. thorax, abdomen or other); need for and duration of ventilatory support; postoperative complications, and age at first attaining full enteral feeds. Infants were identified as preterm if their gestational age was <37 weeks while low birth weight (LBW) was defined as a birth weight of less than 2,500 g. Full enteral feeds were defined as the necessary amount of breast milk/formula fed orally based on an infant's weight and energy requirements.

Data were analysed using the Statistical Package for the Social Sciences (SPSS), Version 16 (IBM, Corp., Chicago, Illinois, USA). The normality of numerical variables was determined using standard deviation, skewness and histograms. All variables had a skewed distribution. Mann-Whitney U and Pearson's Chi-squared tests were used for non-parametric and categorical variables to identify differences between the two groups. A multiple regression analysis was performed to determine the relationship of variables regarding length of HS. A P value of <0.05 was considered statistically significant.

This study was approved by the Medical Research & Ethics Committee of Sultan Qaboos University (MREC #656).

Results

A total of 102 surgical neonates were admitted to the NICU during the study period. However, seven cases were excluded as they were statistical outliers. These included five cases of necrotising enterocolitis (NEC), one case of jejunoileal atresia and one case of intestinal malrotation. The patient with jejunoileal atresia and one of the patients with NEC died. Out of the remaining 95 patients, 52 were male and 43 were female.

The number of neonates admitted to the NICU from other SQUH departments (n = 48) was almost equal to those transferred from other hospitals in Oman (n = 47). The age of the neonates at admission ranged from 1–28 days, with a median age at admission of one day. The infants' gestational ages varied from 26–42 weeks (mean: 36.38 ± 3.50 weeks; median: 38 weeks). Of those included in the study, 64 neonates were considered term while 31 were preterm. The median birth weight was 2,770 g (range: 800–3,900 g). A total of 36 neonates (37.9%) were considered to have a LBW.

There were 22 cases of maternal comorbidities, including gestational diabetes mellitus (n = 10), pregnancy-induced hypertension (n = 8), non-insulin-dependent diabetes mellitus (n = 1), twin pregnancy (n = 1), systemic *lupus* erythematosus (n = 1) and haemolysis/elevated liver enzymes/low platelet (HELLP) counts syndrome (n = 1). Echocardiography was performed on 69 neonates, with 22 showing normal results. In the remaining 47 patients 58 anomalies were detected. Patent *ductus arteriosus* in isolation or combined with other cardiac defects was the most common finding (n = 31; 66%). Other cardiac anomalies included pulmonary hypertension (n = 8), atrial septal defects (n = 6), ventricular septal defects (n = 7), septal hypertrophy (n =2), dextrocardia (n = 2) and peripheral arterial hypertension (n = 2). The most common chromosomal anomaly was trisomy 21 (n = 5, 5.3%).

Table 1: Differences in the mean rank of numerical variables of the surgical neonates by duration of intensive care unit stay (N = 95)

Numerical Variables	Groups A = >19 days (n=45) B = ≤19 days (n=50)	Median (Range)	Mean rank*	U-Value*	*P* value
Age at admission (Days)	A	1 (1–30)	45.02	991	0.27
	B	2 (1–30)	50.68		
Gestational age (weeks)	A	36 (26–42)	38.91	716	<0.001
	B	38 (28–41)	56.18		
Birth weight (Grams)	A	2,400 (800–3,900)	3,734	645	<0.001
	B	2,955 (990–3,900)	5,759		
Age at surgery (Days)	A	3 (1–45)	44.38	962	0.21
	B	4 (1–37)	51.26		
Duration of ventilatory support (Days)	A	6 (0–40)	56.79	729	<0.001
	B	2 (0–30)	40.09		
Age at full enteral feeds(Days)	A	20 (1–88)	65.29	347	<0.001
	B	8 (0–17)	32.44		

**Test of significance using Mann-Whitney U.*

The neonates median age at surgery was three days (range: 1–45 days). Surgical procedures included 51 abdominal, 29 thoracic and 15 other surgeries. The most common procedure was a tracheoesophageal *fistula* repair (n = 18). Ventilatory support was required in 80 infants (85.3%) and was maintained for a median of four days (range: 1–40 days). Postoperative morbidity was seen in 22 patients (23%) and included sepsis (n = 10), wound infections (n = 2), pneumothorax (n = 2), diarrhoea (n = 2), postoperative adhesions (n = 2), lung collapse (n = 1), disseminated intravascular coagulation (n = 1), bowel gangrene due to abdominal compartment syndrome (n = 1) and hypotension (n = 1). There were 10 fatalities (10.5%).

The length of HS ranged from 3–79 days (median: 19 days). The maximum stay of 79 days was due to a case of gastroschisis repair while the mimimum stay of three days resulted from a case of an imperforated anus. Neonates with NEC had a median stay (53 days; range: 2–60 days) greater than that of neonates undergoing other types of surgery. Neonates with anterior abdominal wall (AWD) defects had a shorter HS (median: 35 days; range: 20–79 days). Neonates with congenital diaphragmatic hernia had a median HS of 22 days (range: 6–48 days).

Regarding statistical analysis for responsible factors, Table 1 shows the difference in medians, ranges, mean ranks, Mann-Whitney U values and *P* values of the two groups by duration of ICU stay, i.e. group A (HS >19 days) and group B (HS ≤19 days). It is evident that low gestational age, LBW, prolonged ventilatory support and older age at first full feed were associated with increased HS. However, age at admission or age at surgery did not significantly affect the length of HS. Among the categorical variables, preterm status, LBW and morbidity were associated with increased HS, while gender, maternal comorbidities, associated cardiac or non-cardiac anomalies and the site of surgery did not significantly affect HS [Table 2]. All of the variables which were found to significantly increase HS were subjected to regression analysis. According to the multiple regression analysis, the infants' age at first full feed was found to be the most important factor prolonging HS [Table 3]. Table 4 shows the neonate's surgical conditions in relation to their median and maximum ages at full feeds and discharge, respectively.

Discussion

This study aimed to identify possible factors responsible for prolonged HS in surgical neonates. The overall morbidity (23%) and mortality (10.5%) rates were higher than those mentioned in the Western literature (6–13%)[4,5] but lower than those reported from Africa (up to 30%).[6,7]

Regarding HS, neonates with NEC had a greater median stay compared to those undergoing other types of surgery. This was shorter than that reported by Moss *et al*. from a multicentre randomised clinical trial for perforated NEC neonates who underwent laparotomies (116 ± 56 days).[8] However, the neonates in the clinical trial all had birth weights of <1,500 g

Table 2: Differences in the categorical variables of the surgical neonates by duration of intensive care unit stay*

Categorical variable		Duration of hospital stay			OR†	*P* value
		>19 days	≤19 days	Total		
Referral source	Internal	20	28	48	0.74	0.47
	Elsewhere	23	24	47		
Gender	Female	19	24	43	0.92	0.84
	Male	24	28	52		
Maternal comorbidities	Present	8	14	22	0.62	0.33
	Absent	35	38	73		
Gestational age	Preterm	23	8	31	6.32	<0.001
	Term	20	44	64		
Birth weight	LBW	25	11	36	5.17	<0.001
	NBW	18	41	59		
Associated non-cardiac anomalies	Present	5	7	12	0.84	0.78
	Absent	38	45	83		
Associated cardiac anomalies	Present	10	12	22	0.79	0.66
	Absent	24	23	47		
Site of surgery	Thorax	14	15	29	1.19	0.69
	Abdomen/other	29	37	66		
Postoperative complications	Present	14	8	22	2.94	0.02
	Absent	29	44	73		

OR = odds ratio; LBW = low birth weight; NBW = normal birth weight.
**Test of significance using Pearson's Chi-squared test; †confidence interval = 95%*

while birth weights varied from 700–2,500 g in the current study. Similarly, the length of HS for neonates with congenital diaphragmatic hernia in the current study was shorter than that reported by Skarsgard *et al*. (22 versus 36 days).[9] However, the length of HS in this study was comparable to that of Skarsgard *et al*.'s study with regards to cases of anterior AWD (35 versus 39 days).[9]

Preterm status and LBW were independent risk factors for prolonged HS. Both are well-known risk factors for poor outcomes.[10] Surgery in such patients increases the duration of HS due to the time required for recovery and for the infant to gain weight, as the preterm infant's weight should be similar to that of an infant born at term prior to discharge. The traditional approach to treating infants with NEC is a laparotomy and resection of the necrotic bowel in addition to *stoma* formation.[11] The resulting short bowel syndrome may increase HS due to the need for parenteral nutrition. Moreover, neonates requiring subsequent surgeries (e.g. *stoma* reversals) are not discharged until after these procedures have been performed. Similarly, mechanical ventilation appeared to prolong the duration of HS in the current study. A possible explanation for this could be due to morbidities associated with of ventilatory support, such as respiratory tract infections, lung barotrauma, brain injuries or cardiovascular instability.[12] These conditions lead to delayed recovery from surgery and, therefore, prolonged HS. Likewise, postoperative complications increased the duration of HS in the present study for obvious reasons. The most common complications found in the current study were

Table 3: Multiple regression analysis of variables significantly increasing the duration of intensive care unit stay for surgical neonates (N = 95)

Variables	B coefficient	*P* value
Constant*	11.06	<0.001
Age at first full enteral feed	0.91	<0.001
Days of ventilatory support	0.65	0.71
Gestational age†	−5.02	0.13
Birth weight‡	0.11	0.97
Morbidity§	5.03	0.10

**Predictors in combination; †Term/pre-term; ‡ low birth weight/ normal birth weight; §Present/absent.*

Table 4: Surgical conditions of the neonates in relation to age at first full enteral feed and discharge from the intensive care unit

Surgical condition	n	Age in days at first full enteral feed		Age in days at discharge	
		Median	Maximum	Median	Maximum
NEC	6	21	45	53	60
Intestinal malrotation	3	30	70	41	73
Anterior AWD	6	13	39	35	79
Congenital diaphragmatic hernia	14	14	42	22	48
Duodenal atresia	9	11	29	19	37
TEF	18	10	29	18	37
NAD	3	15	20	15	51
Hirschsprung's disease	17	8	42	14	69
Jejunoileal atresia	3	26	47	14	50
Non-specific intestinal perforation	7	8	12	13	34
Anorectal malformation	5	3	6	5	7

NEC = necrotising entercolitis; AWD = abdominal wall defect; TEF = tracheoesophageal fistula; NAD = no abnormality detected.

surgical site infections and sepsis. Local and systemic infections in surgical patients tend to increase stress by shifting the balance towards a catabolic state, which leads to prolonged recovery time and an increase in the duration of HS.[13]

Many factors were not found to affect length of HS in the current study. Literature on these factors is either controversial, contradictory or scarce. The presence of cardiac anomalies as a risk factor is an example of the first. Although studies such as that of Kassa *et al*. have reported no association between cardiac anomalies and HS, Berry *et al*. and Payne *et al*. have both identified this factor as a predictor of longer HS.[14–16] One possible reason that cardiac abnormalities were not observed to affect HS in the current study could be due to the minor nature of the cardiac anomalies observed, with no cases requiring surgical intervention. Other factors that were determined to be contradictory to findings in the literature were gender, source of referral and the presence of maternal comorbidities. The male gender has been reported as a risk factor for poor outcomes in premature infants born at <27 gestational weeks.[17] However, no significant difference was found in the duration of HS between male and female neonates in the present study. Nevertheless, it is worth noting that the calculation of gender-based duration of HS in the current study did not include stratification of gestational age.

Another factor with contradictory evidence is the source of referral to the NICU. Source of referral has been reported to affect outcomes in certain surgical neonate subgroups (e.g. neonates with congenital diaphragmatic hernias or gastroschisis).[14,18] In the present study, there was no statistically significant difference in the duration of HS between neonates born at SQUH and those born elsewhere. It may be assumed that these findings differed from those of other researchers due to centre-specific referral and case acceptance practices and the individual nature

Table 5: Protocol for neonatal minimal enteral feeds with expressed breast milk

Age of neonate in days	Required volume and schedule
1–2	0.5 mL every six hours
3–4	0.5 mL every four hours
5–6	0.5 mL every two hours
7	1.0 mL every two hours

Adapted from: Sultan Qaboos University Hospital. Neonatal Protocols. Muscat, Oman: Sultan Qaboos University Hospital, 2010.

Table 6: Protocol for neonatal minimal enteral feeding and increases in feed volume

Length of gestation in weeks	Minimal enteral feeds	Feed volume
<29	Required	Increase by 20 mL/kg/day from day eight
29–32	May be required if health concerns are identified	Increase by 25 mL/kg/day
33–36	Not required	Increase by 30 mL/kg/day

Adapted from: Sultan Qaboos University Hospital. Neonatal Protocols. Muscat, Oman: Sultan Qaboos University Hospital, 2010.

of diseases requiring surgery. Maternal comorbidity is another factor for which the current findings were not in accordance with the literature. Many maternal comorbidities, including multiple gestation pregnancies, pregnancy-induced hypertension and gestational diabetes mellitus, have been identified as predictors of NICU admission and longer HS.[19] However, no significant association between maternal comorbidities and length of HS was determined in this study.

Certain factors which have rarely been studied in the literature were investigated in the current study but were not found to affect the length of HS. For instance, the site of the surgery had no significant relationship with prolonged HS. Possible reasons for this could include the low number of thoracic procedures among the studied infants, with tracheoesophageal *fistula* repairs being the only procedure done via thoracotomy. On the other hand, abdominal surgeries included both minor and major procedures. Similarly, infant age at surgery did not appear to affect the duration of HS. While older age was expected to reduce HS by decreasing recovery time, it was in fact associated with an increased stay in most cases. This is because the duration of HS was calculated from the day of admission to the NICU and not from the day of surgery and most infants underwent surgery after admission.

The age of neonates at first full enteral feed is of special concern. It is well documented that the early initiation and attainment of full feeds in postoperative neonates improves their outcome and decreases HS.[20,21] It is usually recommended that postoperative neonates begin early enteral nutrition (5–20 mL of breast milk/kg/hour) within 12 hours of the surgery, even in cases of intestinal *anastomosis* after abdominal surgery.[22] Results of the current study found that an older age at first full feed was a risk factor for prolonged HS both through independent and multiple regression analyses. This may be because of variations in institutional feeding practices or intolerance to feeds due to the severity of the illness.

At SQUH, feeding practices are based on recommended guidelines and the gestational age, health and operative status of the neonate. Feeding procedures for postoperative patients are planned according to their gestational age.[22] Generally, the goal of neonatal nutrition is a weight gain of 15–20 g per day on full enteral feeds. Expressed breast milk is the preferential option for enteral feeding. If this is not available, however, term formula is used for all babies until they reach full enteral feeds. At a later stage, preterm/high-calorie formula is used according to infants' weight-gain patterns. All neonates who are <32 weeks or <1.5 kg are started on total parenteral nutrition on their first day. The time-frame for the commencement of enteral feeding depends on the infants' gestational age. All neonates who are <28 weeks or <32 weeks with health concerns are started on minimal enteral feeds according to neonatal feeding protocols [Tables 5 and 6].

While neonate age at full feed was found to be the most important factor prolonging HS in the present study, it is difficult and potentially misleading to conclude that feeding practices are the only factor responsible for prolonged HS. The late attainment of full feeds could be attributable to illness severity or other variables. While this study suggests that a surgical neonate's age at full feed prolongs their NICU stay, identifying the reasons behind the late attainment of full feeds, especially the severity of illness, should be assessed by future prospective studies.

There were several limitations to this study. The first limitation was that the postoperative neonates who died were not excluded from the study. Secondly, a severity score index was not used to classify the neonates. The major reason for this was the lack of a scoring system incorporating surgery as a factor in the score calculation. The third limitation was that most of the neonates were operated on using an open surgical technique. Hence, the results are not applicable to infants who underwent minimal access surgery.[23] The results of this study should therefore be interpreted in the light of the above limitations.

Conclusion

Prolonged ICU stay in surgical neonates has major consequences in terms of morbidity, costs and bed management. A number of factors resulting in prolonged HS were identified through independent analysis, including low gestational age, LBW, number of days on a ventilator and postoperative morbidity. Infant age at first full enteral feed was found to increase HS both through independent and multiple regression analyses. The implications of this finding require further research in order to determine if current neonate feeding practices should be revised.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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