

ORIGINAL ARTICLE

Trends in Mortality in an Australian Tertiary Surgical Neonatal Intensive Care Unit

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ABSTRACT

Aim: The aim of the study was to estimate mortality rate and trend in the neonate admitted to a surgical neonatal intensive care unit.

Methods: This study was a retrospective cohort analysis of all neonatal (from birth to <44 weeks corrected post-menstrual age) deaths that occurred in a single institution between 2000 and 2015. Mortality rate and trend over 16 years was evaluated. Mortality rates for neonates with surgical and cardiac diseases were analysed with the trend over a fifteen year period reported.

Results: There were a total of 8994 admissions with 425 deaths during the study period, of whom 328 infants met inclusion criteria. In this group 18.9% (n=62) were admitted for a surgical condition, 35.4% (n=116) for cardiac disease and 45.7% (n=150) for other reasons. The median birth weight was 2715g (IQR 1890g-3220g) and the median gestational age was 37 weeks (IQR 33-39 weeks). The inter-quartile range for length of stay was between 2 to 20 days. The overall mortality rate was 3.6% over 16 years. There was a decline in mortality rate from 5.9% in 2000 to 3.5% in 2015 (p=0.06). Female infants accounted for 41% of the deaths. On multivariate analysis only very low birth weight was an independent predictor of mortality for surgical and cardiac deaths compared to deaths by other cause.

Conclusions: There has been an overall decline in mortality in the surgical neonatal population from 2000 to 2015.

Key words: Neonatal surgery; Cardiac surgery; Congenital heart disease; Mortality

INTRODUCTION

Changes in neonatal care and obstetric care including antenatal corticosteroids for women at risk of preterm delivery, surfactant for respiratory distress syndrome and postnatal steroids for chronic lung disease have been associated with decrease in neonatal mortality especially among very low birth weight infants in the 1990s [1]. The steady decline in neonatal mortality has continued in the last decade across neonatal cohorts from United States and Europe [2-6]. With advances in neonatal practice, surgical techniques and anaesthesia, there appears

to be a general declining trend in mortality associated with neonatal surgery [7]. The improved survival over the years seems to be related to combination of different factors which include advances in paediatric surgery and paediatric anaesthesia; advances in neonatal intensive care including mechanical ventilation, parenteral nutrition, antibiotics, better understanding of neonatal physiology and technological advances [7].

A literature search for mortality in neonatal surgical units identified one study which examined in-hospital mortality for non-cardiac surgery in 2000

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and 2003 (Search items- Newborn, mortality, surgery, congenital cardiac anomaly) [8]. The estimated mortality for full-term neonates was 2% (n=11,287) and for pre-term infants 10.5% (n=3,991) [8]. The clinical variables that improved prediction of in-hospital mortality were prematurity, serious respiratory problems, necrotising enterocolitis, neonatal sepsis and congenital heart disease [8]. A similar prospective study looking at prognostic factors determining mortality in surgical neonates showed that early gestational age, respiratory distress and shock at presentation were poor prognostic factors [9]. Risk factors for mortality after congenital heart disease surgery has been well documented based on Risk adjustment in congenital heart surgery score (RACHS-1) and other preoperative risk factors [10-14]. Although there are prognostic classifications for individual surgical conditions none can be individually applied to the neonatal surgical cohort [15-18].

In New South Wales, mortality rates for children needing neonatal surgery was 3% during the period from July 1996 to June 1998 [19]. Australian & New Zealand Neonatal Network [ANZNN] 2013 report showed a mortality of 4.7% for ANZNN registrants who underwent major surgery. Among the infants who had major surgery in the ANZNN 2013 cohort, 6.5% had surgery for proven Necrotising enterocolitis (NEC) with a mortality rate of 26.8% for those with definite NEC [20].

Perinatal death classification systems including Perinatal society of Australia and New Zealand neonatal death classification (PSANZ-NDC) aide in identifying a single most important foetal, maternal or neonatal factor causing neonatal death or still-birth [21-23]. However it is difficult to obtain in-hospital mortality data in neonates admitted for surgical or cardiac conditions after they are 28 days of age using current classification systems and we have to rely on individual death certificates to get a complete picture. A better understanding of the factors that impact mortality is critical for continual practice improvement as well as assisting families in making informed decisions regarding treatment strategies [24]. This study was undertaken in order to address the lack of contemporary data by evaluating the mortality patterns in a tertiary neonatal surgical unit in New South Wales, Australia.

MATERIALS AND METHODS

Study Objectives: The primary objective of this study was to report the mortality rate and trend in neonates admitted to a tertiary surgical neonatal intensive care unit from 2000 to 2015. The second-

ary objective was identification of factors which may have impacted on mortality over different epochs.

Study Population: All admissions from 2000 to 2015 were included in the source population. Neonatal deaths were defined as deaths occurring from birth to 44 weeks corrected post-menstrual age.

Inclusion criteria: All deaths occurring within the neonatal unit during the study period.

Exclusion criteria: Neonatal deaths occurring outside the unit in infants that were previously admitted; and neonatal deaths occurring beyond 44 weeks PMA.

Study Design: A retrospective cohort analysis of all neonatal deaths that occurred between 2000 and 2015 was conducted. The study site was the neonatal nursery of a tertiary referral hospital where neonates with serious cardiac and surgical disorders are admitted for treatment as well as neonates who require multidisciplinary speciality review. Hospital neonatal database and Australian and New Zealand neonatal network (ANZNN) database was searched to obtain all relevant data across the study period. Data was extracted and independently reviewed by a co-author for accuracy. The data was de-identified. Prior approval was obtained from the local ethics committee for this study.

The primary reason for admission was recorded and classified as surgical, cardiac or other cause by the author and reviewed independently by two co-authors. Surgical admissions included gastroschisis, omphalocele, trachea-oesophageal fistula, necrotising enterocolitis as well as congenital diaphragmatic hernia. Cardiac admissions included congenital heart disease as well as cardiomyopathy and cardiac rhythm abnormalities. Other cause included Hypoxic ischemic encephalopathy, Central nervous system malformations, congenital malformations, chromosomal anomalies, sepsis and metabolic conditions. Cause of death was taken from hospital death certificate and categorised into surgical, cardiac and other by two co-authors. The immediate cause and underlying cause of death for all cases was extracted from individual death certificates. The underlying cause of death was considered as the primary cause of death in this study as it was the single most important factor preceding death.

Definitions: Surgical death was defined as death where primary cause of death was underlying surgical condition. Cardiac death was defined as death where primary cause of death was underlying car-

diac condition. Other death was defined as death where underlying cause was a non-surgical and non-cardiac condition.

Mortality rate and trend over 16 years was calculated. Mortality rate was compared to national neonatal mortality data. The mortality characteristics over three different epochs- 2000-2004, 2005-2009 and 2010-2015 were analysed. Gestational age, sex and birth weight were analysed among the three epochs to identify any significant factors influencing mortality.

Statistical Methods: Univariate analysis was undertaken with descriptive statistics of continuous data reported as mean (standard deviation) or median (interquartile range (IQR)) depending on the normality of the data. Categorical data was summarised using frequency distributions. Chi square test or Fischer's exact test was used for evaluation of categorical variables. Wilcoxon rank sum test was used when the outcome data was continuous had a skewed distribution. All *p*-values were two-tailed. A nominal significance level of 0.05 was applied. All statistical analyses were conducted with SAS statistical software package.

Table 1- Surgical and cardiac deaths compared to deaths by other cause.

		Surgical and cardiac deaths (%)	Deaths by other causes (%)	p-value
Sex	Male	90 (46.6)	103 (53.4)	0.84
	Female	61 (45.5)	73 (54.5)	
G	<28 wks	10 (29.4)	24(70.6)	0.05
	28-32 wks	17(37.8)	28(62.2)	
	33-36 wks	28(43.8)	36(56.3)	
	>37 wks	96(52.2)	88(47.8)	
BW	<1500g	24(42.1)	33(57.9)	0.91
	1500-2499g	39(48.1)	42(51.9)	
	2500-3999g	80(46.8)	91(53.2)	
	>4000g	8(44.4)	10(55.6)	

G: gestational age; BW: Birth weight

RESULTS

There were a total of 8994 admissions and 425 deaths between 2000 and 2015. 328 deaths fitted the inclusion criteria with an overall mortality rate of 3.6% over the study period (Figure 1).

Mortality: There was an overall decline in mortality rate from 5.9% in 2000 to 3.5% in 2015 (Figure 2). Female infants accounted for 41% of the deaths

and males accounted for 59% of the deaths. The median birth weight was 2715g (IQR 1890-3220g) and the median gestational age was 37 weeks (IQR 33-39 weeks). The median duration of stay was 16 days (IQR 2-20 days).

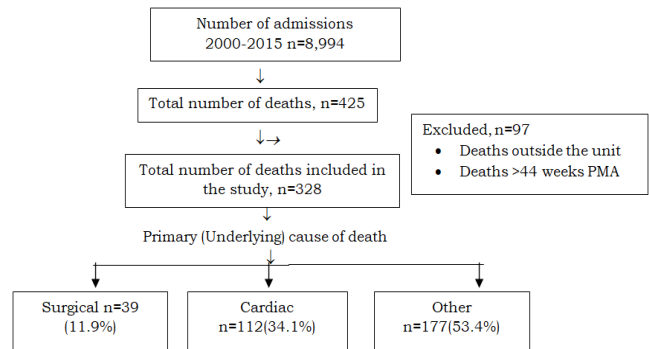


Figure 1- Flow chart depicting study design and outcome

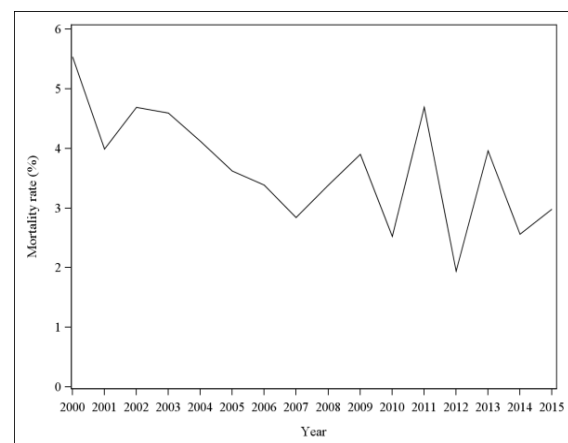


Figure 2- Mortality trend in tertiary surgical unit from 2000-2015

Reason for admission: The primary reason for admission was surgical in 18.9% (n=62), cardiac in 35.4% (n=116) and other in 45.7% (n=150) of the cases. The admissions for 'Other' causes were mainly Central nervous system conditions including Hypoxic ischemic encephalopathy (14.3%), respiratory conditions (8.8%), metabolic conditions (7%), congenital malformations (6.1%) chromosomal anomalies (5.5%) and sepsis (1.5%). Figure 3 shows the pattern of admissions over the last 16 years.

Cause of death: The immediate cause of death was surgical in 19.8% (n=65), cardiac in 35.7% (n=117) and other 44.5% (n=146) of the deaths. The primary (underlying) cause of death was surgical in 11.9% (n=39), cardiac in 34% (n=112) and other causes in 54% (n=177) of the deaths. The primary cause of death was the surgical disease in 54.8% (n=34) cases who were admitted for a surgical reason. The primary cause of death was the cardiac disease in 87.9% (n=102) of the cases who were admitted for a

cardiac disease. Figure 4 shows the pattern of deaths by primary cause over the study period.

Co-morbidity was present in 77.4% (n=48) of the surgical admissions, 39.7% (n=46) of the cardiac admissions and 56.7% (n=85) of admissions for other cause. In the study group 16.4% (n= 54) died post-surgery of whom 5.5% (n=4) were post general surgery and 87% (n=47) were post cardiac surgery.

In view of higher number of deaths due to other causes, we did an exploratory analysis to see if there were any gestational age, birth weight or gender differences between surgical and cardiac deaths versus deaths due to other causes (Table 1). There was a significant proportion (p=0.015) of preterm babies <28weeks who died of other causes com-

pared to term babies. On multivariate analysis only very low birth weight (<1500grams) was an independent predictor of mortality among babies who died because of surgical and cardiac conditions.

Mortality over different epochs: The mortality rate for the epochs 2000-2004, 2005-2009 and 2010-2015 shows a downward trend with mortality rate being 4.6%, 3.4% and 3.1% respectively (p=0.002). Table 2 summarizes the salient characteristics among the different epochs. Mean gestational age at admission, birth weight and sex were not different over the three epochs. The length of stay increased significantly over the study period. Presence of co-morbidity however did not increase over the study period.

Table 2- Mortality pattern across three epochs.

		2000-2004	2005-2009	2010-2015	p-value
Total deaths (%)		125 (38.1)	98 (29.9)	105 (32)	
Total admissions (%)		2723 (30.2)	2871 (32)	3400 (37.8)	
Mortality rate (%)		4.6	3.4	3.1	0.002
Mean GA \pm SD		34.8 \pm 5.1	35.8 \pm 4.3	36 \pm 3.8	0.11
Birth wt. in g \pm SD		2386 \pm 1027	2675 \pm 1014	2616 \pm 887	0.17
Male Sex (%)		70 (56.5)	54 (55.1)	69(65.7)	0.23
LOS in days \pm SD		14 \pm 21	15 \pm 24	19 \pm 24	0.01
Primary admission (%)					
	Surgical	22.4	20.4	13.3	0.33
	Cardiac	30.4	37.8	39	
	Others	47.2	41.8	47.7	
Immediate cause of death (%)					
	Surgical	24	22.5	12.4	0.09
	Cardiac	28.8	38.8	41	
	Others	47.2	38.8	46.6	
Underlying cause of death (%)					
	Surgical	13.6	10.2	11.4	0.16
	Cardiac	26.4	35.7	41.9	
	Others	60	54.1	46.7	
Presence of co-morbidity (%)		60	54.1	48.6	0.22
		2000-2004	2005-2009	2010-2015	p-value
Total deaths (%)		125 (38.1)	98 (29.9)	105 (32)	
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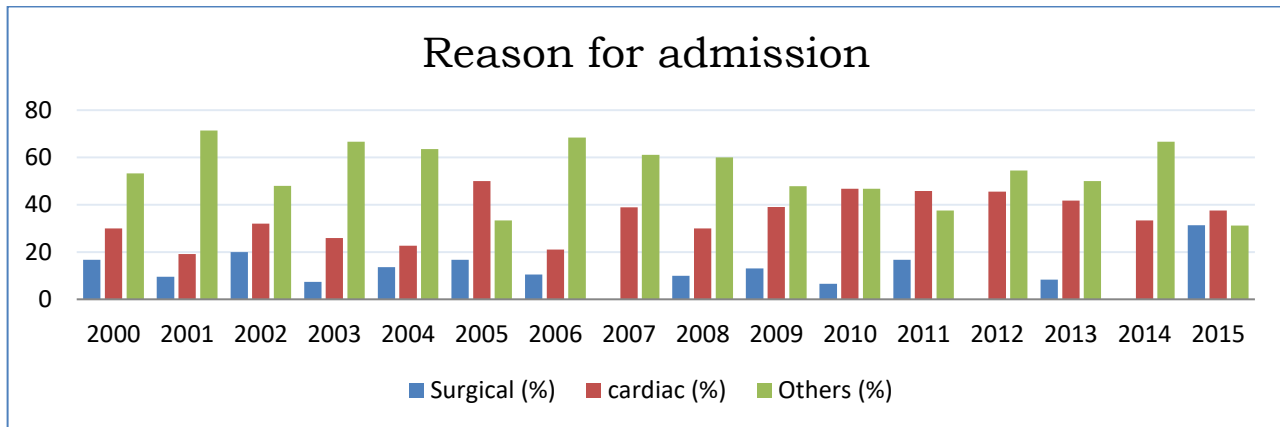


Figure 3- Trends in cause for admission.

DISCUSSION

As far as we are aware this is the only Australian study reporting neonatal mortality for cardiac and surgical neonates admitted to a surgical neonatal unit. The neonatal mortality rate in Australia for 2015 was reported to be 2.3% [25]. The overall neonatal mortality rate of 3.6% in our study is not comparable to national neonatal mortality statistics because the denominator in our study was the total number of admissions per year. The declining trend in mortality was reflective of the overall decline in neonatal mortality with improvement in neonatal care. In a study of neonates undergoing surgery in various centres across New South Wales, mortality rate was estimated to be 3% which is similar to our results [19].

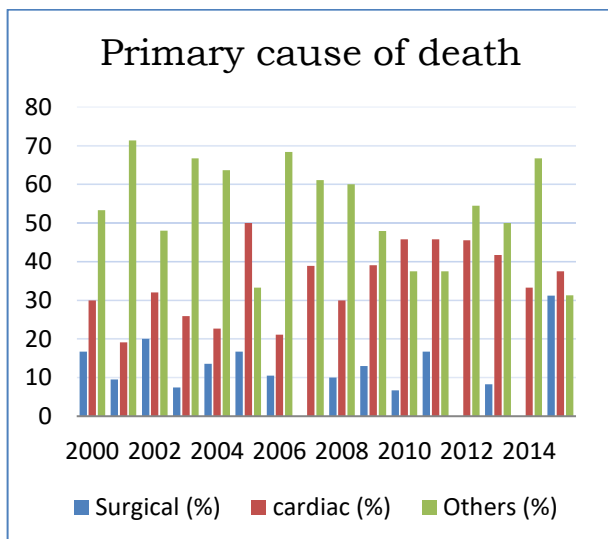


Figure 4- Trends in primary cause of death over the study period

Lillehei et al estimated in-hospital mortality for neonates undergoing non-cardiac surgery as 2% in term infants and 10.5% in preterm infants [8].

Lillehei et al categorised infants who underwent surgery to one of sixty six procedure codes and assigned them to a risk category to calculate mortality rate. This made it difficult to compare the non cardiac mortality subset directly to our study[8]. The median age at admission was 37 weeks with a significant proportion being term at admission. About one-third of our admissions were for a cardiac condition. Neonates with congenital heart disease have been shown to deliver at term and with a higher mean birth weight [26]. This may well be the reason for median near-term gestational age at admission. Our finding of higher mortality in male infants resonates with the limited reported data. In a study from Badawi et al., almost two thirds of all neonatal surgery was in male infants [19]. Higher mortality in male infants with congenital heart disease has also been noted in a study from the U.S. [27]. On multivariate analysis only very low birth weight was an independent predictor of mortality for surgical and cardiac deaths compared to deaths by other cause. This is in contrast to a prospective study on mortality in surgical neonates which showed that increased mortality occurred with early gestational age, respiratory distress and shock at presentation [9].

There seems to be a changing trend in the primary cause of admission with a decreasing number of surgical admissions [22% of all admissions in epoch 1 versus 13% in epoch 3], increasing cardiac admissions [30% of all admissions in epoch 1 versus 39% in epoch 3] while admissions for other causes have remained steady. High rates of prenatal diagnoses of congenital heart disease and the state-wide guideline mandating birth of neonates with antenatal diagnosis of heart defects in a co-located perinatal centre could be one of the reasons for this trend [28-30]. It has been postulated that efforts to improve prenatal diagnosis and delivery close to a

cardiac surgical unit significantly improves survival in neonates with Hypoplastic left heart [31]. The reason for decline in admissions for surgical causes is not clear. However a study by Loh et al showed there was no significant difference in overall mortality of infants with Necrotising enterocolitis managed in non-surgical unit when compared to surgical unit [32]. There is also a possibility that more complicated surgical cases diagnosed antenatally are terminated thereby reducing number of surgical admissions. A population based survey on congenital diaphragmatic hernia (CDH) in Western Australia showed that only 40% of the total cases of CDH reach a tertiary surgical centre and up to 49% of prenatally diagnosed fetuses underwent elective termination of pregnancy [33].

Among the cardiac admissions, significant majority of them (87.9%) died because of primary cardiac cause whereas among surgical admissions only around half (54.8%) died because of a primary surgical cause. This may be because high proportion (77.4%) of surgical admissions had another co-morbidity compared to cardiac admissions (39.7%). Presence of two or more system anomalies and severity of associated anomalies have been noted to influence mortality in oesophageal atresia [34]. Among babies with congenital diaphragmatic hernia (CDH) presence of additional anomaly and preterm delivery were among the factors associated with increased mortality [35].

The overall mortality rate is showing a declining trend over the three different epochs from 5.04% in 2000 to 3.2% in 2015 ($p=0.06$). There is also a trend towards increasing mean gestation and birth weight at admission over the different epochs. The median length of stay (or duration of survival) has gone up from 14 days to 19 days and is statistically significant ($p=0.01$) which may reflect improvements in neonatal intensive care. This trend is consistent with a changing pattern of neonatal mortality in Australia [26]. Prolongation of survival could also mean that certain infants survive beyond 44 weeks corrected age and would be missed in our study.

Improved survival among neonatal surgical patients has been attributed to growth in paediatric surgery, anaesthesia and neonatal practices along with advances in mechanical ventilation, use of parenteral nutrition and effective use of antibiotics [7]. Although it is difficult to quantify the role of each of these factors it can be fair to assume that combination of all these factors have had a significant role in decreasing mortality rates over the different epochs.

There are some limitations to our study. This was a retrospective analysis. Although the mortality rates in our study are generally low, they include death within the hospital and do not include palliated cases that may have died in other hospitals or in hospice. In this study we have not looked specifically at factors which have been shown to influence mortality in surgical neonatal population including APGAR scores, gestational age, sex, birth weight and physiological parameters at admission [9]. Review of admission risk factors could have provided more insight of mortality risk across different epochs. Grouping of surgical conditions based on surgical conditions could also have been useful to develop surgical risk categories. Mortality risk models exist for congenital heart disease surgeries which adjust for variables including age, primary procedure, weight, co-morbidities and preoperative factors [12, 36].

There could be a potential non-uniformity in recording immediate and underlying cause of death. Variations in coding cause of admissions can impede comparison of neonatal surgical outcomes across different networks.

CONCLUSION

There has been a general decline in mortality in the surgical neonatal population from the year 2000 to 2015. Our review also highlights the changing profile of the 'surgical' neonate over this time period. There is a need for developing risk adjusted models for evaluation of in-hospital mortality for both cardiac and surgical neonates across Australasia.

Authors' contribution: All authors equally contributed in concept, design, manuscript writing, and approved final version.

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