A prospective analysis of the outcomes of extremely low-birthweight neonates in Bloemfontein, South Africa

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Background. Prematurity is a leading cause of neonatal and under-5 mortality in developing countries. The mortality rate for neonates between 500 g and 999 g in South Africa (2016) was 456.2 per 1 000 live births.
Objectives. To describe the short-term outcomes of ELBW (extremely low-birthweight) neonates, including the disease profile, associated clinical characteristics and maternal characteristics.
Methods. A prospective descriptive study was conducted from 1 August 2021 to 31 July 2022 at Universitas Academic Hospital (UAH) and Pelonomi Tertiary Hospital (PTH). Neonates weighing less than 1 000 g admitted to these units were included in the study after obtaining consent from the mothers.
Results. A total of 129 neonates were enrolled (PTH: *n*=96 and UAH: *n*=33). Of these, 30 (23.3%) were discharged, 13 (10.1%) were down-referred, 80 (62.0%) died, and six (4.6%) remained admitted after the study period. Three down-referred neonates were lost to follow-up. Survival was higher at UAH (*n*=15, 50%) compared with PTH (*n*=31, 32.3%). Most deaths occurred during the early neonatal period (*n*=60, 75%), with sepsis being the leading cause of late neonatal deaths (*n*=11, 55%). One hundred and eight (83.7%) mothers received antenatal care, and 33 mothers (26.0%) did not receive antenatal steroids. Mechanical ventilation was provided to 13 neonates (10.1%), six of whom weighed less than 900 g. Sixty (47.6 %) neonates received surfactant replacement therapy.
Conclusion. Mortality and morbidity among ELBW neonates remain high, with neonatal sepsis as the leading cause. Current barriers include inadequate antenatal clinic attendance, presenting to the hospital in established labour and poor antenatal steroid coverage.

Keywords. Extremely low-birthweight; neonates; mortality; morbidity; prematurity.

S Afr J Child Health 2024;18(4):e2128. https://doi.org/10.7196/SAJCH.2024.v18i4.2128

Prematurity remains one of the leading causes of neonatal and under-5 mortality in developing countries.[1] According to the 2016 Saving Babies Report,[2] the neonatal mortality rate (NMR) for neonates between 500 - 999 g in South Africa (SA) was 456.2 per 1 000 live births, thus a more concerted effort is needed to improve the outcomes of extremely low-birthweight infants (ELBW). Addressing this high-risk group could help SA achieve the Sustainable Development Goal of reducing the NMR to 12 per 1 000 live births by 2030.[3] Advances such as antenatal steroid administration and hypothermia prevention have improved ELBW outcomes.[4-7] Ventilation and early surfactant replacement therapy have improved outcomes for ELBW neonates. However, in a resource-limited country like SA, these measures are not accessible to all infants.[8,9]

Currently, no published data exist on the outcomes of ELBW neonates in Bloemfontein, SA. Therefore, this study aimed to describe the outcomes of ELBW neonates admitted to Universitas Academic Hospital (UAH) and Pelonomi Tertiary Hospital (PTH), along with the disease profile, clinical characteristics and associated maternal characteristics. Identifying and analysing the outcomes of ELBW infants can assist relevant role-players in improving the management of these infants, thereby reducing morbidity and mortality in this very high-risk patient group.

Methods

A prospective descriptive study was conducted from 1 August 2021 to 31 July 2022 at UAH and PTH, Bloemfontein. All neonates weighing less than 1 000 g admitted to these units were included, with maternal consent obtained for participation in the study. For cases where mortality occurred before enrolment, consent was waivered by the ethics committee, as this data were retrospectively collected. A pilot study involving three neonates at each study site was conducted to test the data collection tool, following which minor changes were made. These pilot cases were excluded from the final analysis.

The study was approved by the Health Sciences Research and Ethics Committee of the University of the Free State (ref. no. UFS-HSD2022/0622/2707). Data were collected using REDCap, a secure web platform for managing databases. Information on neonates referred to other hospitals for further management was collected until their discharge.

Standard of care

UAH and PTH are both tertiary-level facilities that offer the same standard of care to ELBW neonates. Both hospitals are staffed by the same team of paediatric registrars and consultants, who work on a rotational basis. Neonates weighing less than 900 g are not offered intermittent positive pressure ventilation (IPPV) but may receive nasal continuous positive airway pressure (nCPAP) and surfactant therapy if needed. Mechanical ventilation for neonates below 900 g is provided at the discretion of the treating physician. This study categorised participants according to birthweight rather than gestational age because of inaccurate and uncertain gestational age assessments owing to late or no antenatal care in many cases.

Data analysis

Data analysis was performed by the Department of Biostatics at the University of the Free State. Categorical data were summarised using frequencies and percentages, while means and standard deviations (SDs) or medians and percentiles were used for numerical data. Statistical analysis of categorical variables was performed using Fisher's exact and Pearson's χ^2 tests. A p-value less than 0.05 was considered statistically significant.

Results

(*Note*: When data for individual hospitals are reported, the stated percentage is specifically for that hospital.)

The study involved 129 neonates in total (PTH: n=96, UAH: n=33). Thirty (23.3%) neonates were discharged, 13 (10.1%) were down-referred to another hospital for further management, 80 (62.0%) died and six (4.6%) remained admitted at the end of the study period. Fifteen (50%) neonates admitted to UAH survived until discharge, compared with 31 (32.3%) at PTH. The median length of stay for survivors was 65 days (interquartile range (IQR) 52 - 80), irrespective of the study site. Of the 13 neonates down-referred, three were lost to follow-up (all admitted to UAH), seven were discharged, two were transferred again to another hospital, and one died.

Sixty (75%) neonates died within the first week of life. At PTH, the leading cause of early neonatal deaths, according to the Perinatal Problem Identification Programme (PPIP), was extreme multi-organ immaturity (n=19, 38.8%). At UAH, the leading causes were equally distributed between extreme multi-organ immaturity and sepsis (both early and late-onset neonatal sepsis, excluding congenital infections) (n=3, 27.3%). At both study sites, sepsis was the leading cause of late neonatal deaths (PTH: n=8, 53.3%; UAH: n=3, 75%). Of the neonates whose final outcomes were known (n=126), 95 (73.6%) weighed less than 900 g, with the remaining 34 (26.4%) weighing between 901 - 999 g. In the less than 900 g group, 65 (69%) neonates died, compared with 15 (44.1%) in the 901 - 999 g. At PTH, 53 of the 74 (71.6%) neonates weighing less than 900 g died. At UAH, 12 of the 20 neonates (60%) weighing less than 900 g died. Among patients weighing between 900 - 999 g, 12 of the 22 (54.5%) neonates at PTH died, compared with 3 of the 10 at UAH (30%). The median gestational age was 27 weeks (IQR 26 - 28), with a median birthweight of 800 g (IQR 710 - 910). The smallest neonate was born at UAH and had a birthweight of 430 g (died) (Table 1).

Maternal characteristics

The median maternal age was 29 years (IQR 24 - 33). Thirty-nine (30.2%) mothers were HIV-positive, and 30 (76.9%) were on treatment for more than a month at delivery. None of the neonates born to mothers with HIV tested HIV-positive. Most mothers (n=32, 96.9%) who delivered at UAH received antenatal care before delivery, compared with 79.2% (n=76) at PTH. Of the mothers who received antenatal care, 39.8% (n=43) booked after 12 weeks. Sixty-one (47.3%) mothers had hypertensive disorders of pregnancy, with the majority being from UAH (n=24, 72.7%). Four (3.1%) mothers had diabetes mellitus. Ten (7.8%) mothers had a confirmed infection at the time of delivery, including urinary tract infections (n=4, 3.1%), vaginal discharge syndrome (n=1, 0.8%), chorioamnionitis (n=2, 1.6%) and syphilis (n=3, 2.3%). Eleven (8.5%) mothers had prolonged rupture of membranes, with 10 (10.4%) from PTH. Ninety-four (72.9%) mothers received antenatal steroids, with 46.5% (n=60) receiving both doses of betamethasone before delivery. Steroid coverage was better at UAH, where only 12.1% (n=4) of neonates did not receive any steroids, compared with 32.3% (n=31) at PTH. Idiopathic preterm delivery was the cause of prematurity in 48 (50%) neonates admitted at PTH and four (12.1%) at UAH (Table 2).

Neonatal characteristics

One hundred and twelve neonates were born at the study sites. Seven (5.4%) were delivered outside a healthcare facility, and 10 (7.8%) were born at other healthcare facilities. Of the seven neonates born outside healthcare facilities, six weighed less than 900 g, and all six died. The place of delivery was not statistically significant in relation to outcomes for neonates weighing <900 g (p=0.200) or 901 - 999 g (p=0.200). All neonates born outside healthcare facilities were admitted to PTH. The overall mean (SD) admission temperature was 34.7°C (1.7). For neonates weighing <900 g who died, the mean (SD) admission temperature was 34.2°C (1.8), which was statistically significant (p=0.005). Cranial ultrasounds were performed on 99 (76.7%) of the participants. Intraventricular haemorrhage (IVH) was present in 65 participants (65.7%). Fifty neonates (50.5%) had IVH grades 1 - 2, while 15 (15.2%) participants had IVH grades 3 - 4.

All participants required respiratory support upon admission. Thirteen (10.1%) neonates were mechanically ventilated, including six weighing 850 - 900 g and seven weighing above 900 g. Only two of the six mechanically ventilated neonates weighing <900 g survived. However, these outcomes were not statistically significant for either weight group. A large proportion of neonates (n=110, 85.3%) received nCPAP, with 25 weighing above 900 g. Six (4.7%) neonates received nasal prong oxygen only. Respiratory distress syndrome (RDS) was diagnosed in 128 (99.2%) neonates, while one (0.8%) neonate was suspected to have hypoplastic lungs. Sixty (46.5%) neonates required surfactant. Of the neonates that required surfactant, 21 (35.0%) required more than one dose. Twelve neonates (20%) received two doses of surfactant, of whom three survived. None of the neonates (n=9) who received three doses of surfactant survived. Bronchopulmonary dysplasia was diagnosed in 11 (8.5%) neonates (Table 3).

The average time to achieve full-volume enteral feeds was 10 days. During the transition to full enteral feeds, 92 (71.3%) neonates received total parenteral nutrition (TPN). Necrotising enterocolitis (NEC) was diagnosed in 13 (10.1%) neonates based on clinical assessment and abdominal x-rays using modified Bell's staging. Three (2.3%) neonates had NEC stage 3B. All three were managed with abdominal drains, but none survived. Echocardiography was performed on 77 (59.7%) neonates, revealing a patent ductus arteriosus (PDA) in 37 (48.1%). Among the cases of PDA, nine (24.3%) closed spontaneously, while medical closure was attempted on 13 (35.1%), with seven (18.9%) achieving successful closure.

Fourteen (10.9%) neonates had confirmed culture-positive early-onset neonatal sepsis (EONS), occurring in 13 neonates (13.5%) at PTH and one (3.0%) at UAH. The most common organisms identified in EONS were *Acinetobacter baumannii* (n=5, 35.7%), *Serratia marcescens* (n=2, 14.8%) and *Escherichia coli* (n=2, 14.3%). Additionally, three (2.3%) neonates had congenital syphilis and six (4.7%) had congenital cytomegalovirus. Culture-proven late-onset neonatal sepsis (LONS) was diagnosed in 51 (39.5%) neonates, with an additional 25 (19.4%) suspected cases. In the <900 g group, having confirmed or suspected late onset neonatal sepsis was significantly associated with the outcome of being alive (surviving) (p<0.001). The incidence of confirmed LONS was almost similar at UAH and PTH (43.3% and 38.5%, respectively). The most commonly cultured organisms in LONS were *Acinetobacter baumanni*i (n=30, 58.8%), *Klebsiella pneumoniae* (n=13, 25.5%) and *Serratia marcescens* (n=12, 23.5%). Forty-three (48.3%) neonates had a central line at the time of sepsis diagnosis (Table 3).

Table 1. Neonatal outcomes (*N*=129)

	Overall (*N*=129), *n* (%)	PTH (*n*=96), *n* (%)	UAH (*n*=33), *n* (%)
Place of delivery			
Inborn	112 (86.8)	80 (83.3)	32 (97.0)
Outborn*	10 (7.8)	9 (9.4)	1 (3.0)
BBA	7 (5.4)	7 (7.3)	0
Mode of delivery			
NVD	67 (51.9)	62 (64.6)	5 (15.2)
Caesarean section	62 (48.1)	34 (35.4)	28 (84.8)
Outcome†			
Survived‡	46/126 (36.5)	31/96 (32.3)	15/30 (50)
Died	80/126 (63.5)	65/96 (67.7)	15/30 (50)
Early neonatal death	60/80 (75)	49/65 (75.4)	11/15 (73.3)
Late neonatal death	20/80 (25)	16/65 (24.6)	4/15 (26.7)
Length of stay for survivors (days), median (IQR)	65 (52 - 80)	65 (52 - 81)	65 (54 - 72)
Sex, n			
Male	57 (44.2)	46 (47.9)	11 (33.3)
Female	72 (55.8)	50 (52.1)	22 (66.7)
Gestational age (weeks), median (IQR)	27.0 (26.0 - 28.0)	26 (26.0 - 28.0)	28.0 (26.0 - 28.0)
Birthweight (g), median (IQR)	800 (710 - 910)	795 (718 - 892)	875 (700 - 950)

PTH = Pelonomi Tertiary Hospital; UAH = Universitas Academic Hospital; BBA = born before arrival (born outside a healthcare facility); NVD = normal vaginal delivery; IQR = interquartile range.
* Outborn: born at a healthcare facility other than one of the study sites.
†Three neonates lost to follow-up/unknown final outcome after being down-referred.
‡For reporting purposes, the six neonates still admitted at the end of the study period were included in the survivors' group.

Discussion

This study found an 18% difference in ELBW neonate survival rates between UAH and PTH (50% v. 32%, respectively). Despite the same team of doctors rotating between the two hospitals and providing the same level of care, differences in patient characteristics identified in this study may explain the variation in outcomes. Both antenatal clinic attendance and steroid coverage were better at UAH. Antenatal care and steroid administration are well-documented factors contributing to improved neonatal outcomes.[6,10]

The survival rate of ELBW neonates at PTH (32.6%) in the present study was comparable with that of Leratong Hospital (33.3%).[11] However, direct comparisons are limited, as the Leratong Hospital study included all neonatal admissions and only 15 had ELBW. At UAH, the survival rate of 50% matched that of Steve Biko Academic Hospital (50.7%) but was lower than the survival rate at Tygerberg Hospital (63.3%).[12,13]

Overall, 63.6% of neonates in the present study died, similar to the mortality rates of ELBW neonates in Brazil (60.1%).[14] Of the neonates in the present study, 73.6% had a birthweight <900 g, with a mortality rate of 68.4%. Statistically significant factors associated with mortality in the <900 g group included mean admission temperature, median APGAR scores at 1 and 5 minutes, mean admission pH and LONS. Studies show that mortality increases with decreasing birthweight.[12,13] Similarly, a study at Grey's Hospital found that 68.6% of their sample weighed <900 g, with a mortality rate of 61.1%.[15]

Studies from the USA and Japan reported mortality rates of 22% and 55%, respectively, in neonates with birthweights <500 g.[16,17] The lower mortality in high-income countries may be attributed to a lower birthweight threshold for neonatal intensive care unit (NICU) admission and access to mechanical ventilation. In the present study, most deaths occurred within the first week of life, consistent with studies from other SA sites.[12,13] The importance of *in-utero* transfer for premature neonates is highlighted by the high mortality rates observed in neonates born outside healthcare facilities in our study (*n*=6/7 died) and at other healthcare facilities (*n*=5/9 died). However, these findings were not statistically significant in either weight group.[10]

In the present study, 83.7% of mothers received antenatal care, aligning with other SA studies, which varied from 68.6% to 92.1%.[12,13,18] However, our study was conducted amidst the COVID-19 pandemic, which could have negatively affected antenatal clinic attendance. Antenatal steroid coverage at UAH (87.9%) was higher than at Tygerberg Hospital (82.4%) and Steve Biko Academic Hospital (67.8%).[12,13] Hypertension was the most common comorbidity among mothers in the current study, consistent with other SA studies.[13,15,18]

In the present study, the mean admission temperature of neonates weighing <900 g who died was 1°C lower than those who survived, a statistically significant finding. Laptook *et al.*[19] reported that for every 1°C drop in admission temperature, mortality increased by 28%. Admission hypothermia in our study may be attributed to low environmental temperatures in Bloemfontein, especially during winter, and the long distance between the labour ward and the neonatal unit at PTH. Prevention of hypothermia needs to be addressed continuously to prevent morbidity and mortality.[20]

In the present study, all but one of the neonates had a diagnosis of RDS, a higher incidence than other SA sites, where RDS was reported in 71 - 83.2% of cases.[13,21] This discrepancy might be attributed to RDS being overdiagnosed at the study sites. The usage of nCPAP in SA varies between 54.3 - 93% and could be attributed to differences in the level of airway support offered to ELBW neonates at different centres.[12,13,15] nCPAP was used in 85.3% of cases in the current study, similar to the 84.7% usage reported in the Steve Biko Academic Hospital study. However, surfactant administration in the current study was lower than in the Steve Biko Academic Hospital (46.5% v. 75.8%).[12] Administering additional doses of surfactant did not appear to improve survival, which is in keeping with the findings of other

Table 2. Maternal characteristics (*n*=129)

	Total (*N*=129), *n* (%)	PTH (*N*=96), *n* (%)	UAH (*N*=33), *n* (%)
Age, years			
≤18	1 (0.8)	1 (1.0)	0
19-34	102 (79.1)	77 (80.2)	25 (75.8)
≥35	25 (19.4)	18 (18.8)	7 (21.2)
Unknown	1 (0.8)	0	1 (3.0)
HIV status			
Positive	39 (30.2)	27 (28.1)	12 (36.4)
Negative	86 (66.7)	66 (68.8)	20 (60.6)
Unknown	4 (3.1)	3 (3.1)	1 (3.0)
HIV-positive mothers			
On treatment for more than 4 weeks	30/39 (76.9)	21/27 (77.8)	9/12 (75.0)
HIV viral load <1 000	22/39 (56.4)	13/27 (48.1)	9/12 (75.0)
Received antenatal care	108 (83.7)	76 (79.2)	32 (96.9)
Booking after 12 weeks	43/108 (39.8)	30/76 (39.4)	13/32 (40.6)
Rupture of membranes for more than 18 hours	11 (8.5)	10 (10.4)	1 (3.0)
Antenatal steroids			
None	35 (27.1)	31 (32.3)	4 (12.1)
1 dose	34 (26.3)	26 (27.0)	8 (24.2)
2 doses <24 hours from delivery	20 (15.5)	10 (10.4)	10 (30.3)
2 doses >24 hours from delivery	40 (31.0)	29 (30.2)	11 (33.3)
Maternal co-morbidities			
Hypertensive disorders	61 (47.3)	37 (38.25)	24 (72.7)
Maternal infection	10 (7.8)	7 (7.3)	3 (9.1)
Obesity	6 (4.7)	5 (5.2)	1(3.0)
Diabetes mellitus	4 (3.1)	3 (3.1)	1 (3.0)
Anaemia	2 (1.6)	2 (2.1)	0
COVID-19 positive within 10 days of delivery	6 (4.7)	4 (4.2)	2 (6.1)
Alcohol use in pregnancy	2 (1.6)	1 (1)	1 (3)
Smoking during pregnancy	2 (1.6)	0	2 (6.1)
Idiopathic preterm delivery	52 (40.3)	48 (50)	4 (12.1)

PTH = Pelonomi Tertiary Hospital; UAH = Universitas Academic Hospital; COVID-19 = Coronavirus disease of 2019.

SA studies.[12,21] Owing to increased morbidity and mortality rates as well as resource constraints, IPPV is not offered to all neonates <900 g. Administering ventilation to six neonates <900 g did not result in a decrease in mortality, and the finding was not statistically significant (p=0.800). In other SA studies, IPPV was also associated with increased mortality.[15,21] The prevalence of bronchopulmonary dysplasia (BPD) (8.8%) in our study was similar to findings from the Western Cape (8.2%).[13] A systemic literature review conducted between 2006 and 2017 revealed a BPD global incidence of 10 - 89%. However, no studies from Africa were included in this analysis. Possible reasons for differences in the incidence of BPD include low survival rates (which may result in lower incidence of BPD) as well as variations in the case definition of BPD.[22] The incidence of NEC grades 2 and 3 was 10.3%, similar to that reported in a systemic review conducted by Ramaswamy *et al.*[23] in developing countries (7 - 10%).

Acinetobacter baumannii and *Serratia marcescens* were the most common pathogens in early and late-onset neonatal sepsis. In this study, EONS was described as the onset of neonatal sepsis within the first 72 hours of life. Our findings regarding EONS were inconsistent with published data.[24,25] Further research is needed to determine the sources of early-onset gram-negative sepsis in neonates. In contrast, the prevalence of *Acinetobacter baumannii* and *Serratia marcescens in* LONS is in keeping with data from other SA studies.[26,27] A recent multi-centred SA study found that *Klebsiella pneumonia* was the most common pathogen in LONS,[27] differing from our findings, where *Acinetobacter baumannii* was predominant.

Strengths and limitations

The prospective design of the study minimised missing data by addressing gaps in records. Other key strengths included: (*i*) a focus on ELBW only, whereas other studies focused on very low birthweight neonates; (*ii*) follow-up on neonates after transfer to other facilities (*iii*) data collection from two study sites, enabling outcome comparisons. However, the study had limitations: (*i*) long-term follow-up of survivors was not possible owing to time constraints and (*ii*) participants were grouped according to birthweight rather than gestational age, as done in some studies.

Recommendations

Neonatal sepsis remains a major contributor to mortality. At the hospital level, more needs to be done to limit hospital-acquired infections in ELBW neonates. More attention should be given to mothers who have hypertension in pregnancy. It remains crucial that these women are followed up post-natally to ensure that those who

Table 3. Neonatal characteristics (*N*=129)

		<900 g			901 - 999 g		
	Overall (*N*=129)†	Alive (*n*=29)	Died (*n*=65)	*p*-value	Alive (*n*=17)	Demised (*n*=15)	*p*-value
Place of delivery, *n* (%)				0.20			0.20
Inborn	112 (87.3)	28 (96.6)	54 (83.1)		13 (76.5)	15 (100)	
Outborn*	10 (7.1)	1 (3.4)	5 (7.7)		3 (17.6)	0	
BBA	7 (5.6)	0	6 (9.2)		1 (5.9)	0	
Mode of delivery				<0.001			0.50
NVD	67 (53.2)	7 (24.1)	47 (72.3)		5 (29.4)	8 (53.3)	
C-section	59 (46.8)	22 (75.9)	18 (27.7)		12 (70.6)	7 (46.7)	
Admission temp (°C), mean (SD)	34.7 (1.7)	35.2 (1.5)	34.2 (1.8)	0.005	35.6 (0.9)	35.3 (1.2)	0.50
APGAR							
1 minute, median (IQR)	5 (3 - 7)	6 (5 - 7)	4 (3 - 6)	0.003	6 (4 - 7)	7 (5 - 8)	0.30
5 minute, median (IQR)	8 (6-9)	8 (8 - 9)	6 (5 - 8)	0.004	9 (6 - 9)	8 (7 - 9)	>0.90
Glucose at admission (mmol/L), mean (SD)	4.4 (4.8)	5.3 (6.5)	4.1 (4.0)	>0.9	4.7 (5.4)	3.3 (2.5)	0.40
Admission pH, mean (SD)	7.22 (0.13)	7.26 (0.10)	7.19 (0.13)	0.011	7.23 (0.16)	7.24 (0.10)	0.50
Admission BE, mean (SD)	−8.2 (5.8)	−6.7 (6.6)	−9.7 (5.2)	0.070	−6.3 (4.8)	−6.6 (6.3)	0.80
Admission lactate (mmol/L), mean (SD)	5.2 (4.0)	4.9 (3.6)	6.4 (4.3)	0.10	3.7 (3.29)	2.8 (2.83)	0.12
Total CRUS	99 (76.7)	26/29 (89.7)	41/65 (63.0)		16/17 (94.1)	14/15 (93.3)	
IVH grade 1 - 2	50/99 (50.5)	17/26 (65.3)	21/41 (51.2)		7/16 (43.8)	5/14 (35.7)	
IVH grade 3 - 4	15/99 (15.2)	0	9/41 (22.0)		1/16 (6.3)	5/14 (35.7)	
Type of resp support				0.8			0.12
IPPV	13 (10.1)	2 (6.9)	4 (6.2)		2 (11.8)	5 (33.3)	
nCPAP	110 (85.3)	25 (86.2)	59 (90.8)		14 (82.4)	10 (66.7)	
Nasal prongs	6 (4.7)	2 (6.9)	2 (3.1)		1 (5.9)	0	
RDS	128 (99.2)	29 (100)	65 (100)		17 (100)	14 (93.3)	
Number of SFT doses				0.3			0.14
1	39/60 (65.0)	12/14 (85.7)	17/29 (58.6)		6/7 (85.7)	3/9 (33.3)	
2	12/60 (20.0)	2/14 (14.3)	6/29 (20.7)		1/7 (14.3)	3/9 (33.3)	
3	9/60 (15.0)	0	6/29 (20.7)		0	3/9 (33.3)	
NEC Stage				>0.9			0.071
2	9 (7.0)	3 (10.3)	5 (7.7)		1 (5.9)	0	
3	4 (3.1)	0	1 (1.5)		1 (5.9)	2 (13.3)	
Total cardiac echocardiograms	77 (59.7)	28	19		17	10	
Normal heart	35/77 (45.5)	15/28 (53.6)	5/19 (26.3)		9/17 (52.9)	3/10 (30.0)	
PDA	37/77 (48.1)	12/28 (42.9)	12/19 (63.2)		6/17 (35.3)	7/10 (70.0)	
ASD	5/77 (6.5)	1/28 (3.6)	2/19 (10.5)		2/17 (11.8)	0	
EONS				0.2			0.20
Confirmed EONS	14 (10.9)	4 (13.8)	9 (13.8)		0	1 (6.7)	
Suspected EONS	13 (10.1)	2 (6.9)	7 (10.8)		3 (17.6)	1 (6.7)	
No EONS	102 (79.1)	23 (79.3)	49 (75.4)		14 (82.4)	13(86.7)	
LONS				<0.001			0.60
Confirmed LONS	51 (39.5)	15 (51.7)	15 (23.1)		12 (70.6)	8 (53.3)	
Suspected LONS	25 (19.4)	9 (31.0)	10 (15.4)		3 (17.6)	3 (20.0)	
No LONS	53(41.1)	5 (17.2)	40 (61.5)		2 (11.7)	4 (26.7)	

BBA = born outside a healthcare facility; NVD = normal vaginal delivery; C-section = Caesarean section; SD = standard deviation; IQR = interquartile range; BE = base excess; CRUS = cranial ultrasound; IVH = intraventricular haemorrhage; IPPV = intermittent positive pressure ventilation; nCPAP = nasal continuous positive airway pressure; RDS = respiratory distress syndrome; SFT = surfactant; NEC = necrotising enterocolitis; PDA = patent ductus arteriosus; ASD = atrial septal defect; EONS = early-onset neonatal sepsis; LONS = late-onset neonatal sepsis.
*Outborn: born at a healthcare facility other than one of the study sites.
†Three neonates lost to follow-up were only included in the overall column (and not with final outcome of alive or demise, *n*=126).

go on to develop chronic hypertension are identified timeously to prevent complications in future pregnancies. Further studies should be conducted investigating the long-term follow-up of surviving ELBW babies, with a specific focus on their neurodevelopmental outcomes.

Conclusion

The mortality and associated morbidity rates among ELBW neonates remain high. This study identified hypothermia and sepsis, especially in neonates weighing less than 900 g, as significant contributing factors. Key obstacles to improved neonatal outcomes include

limited antenatal clinic attendance, deliveries outside healthcare facilities and inadequate antenatal steroid coverage. Access to IPPV is scarce in SA, highlighting the need for more research into the poor outcomes of ELBW neonates receiving mechanical ventilation. Continuous efforts are needed to improve maternal and neonatal healthcare services. This requires combined efforts by all parties involved in management and policy-making in maternal and neonatal healthcare.

Declaration. This manuscript was submitted in partial fulfilment of CRP's M. Med Paeds degree at the University of the Free State.

Acknowledgements. We thank Dr JB Sempa (Department of Biostatistics, University of the Free State) for his assistance with data analysis.

Authors' contributions. CRP was the principal investigator, responsible for data collection and manuscript preparation. JJvR was responsible for the supervision and conceptualisation of the study, as well as revising the manuscript. OK revised and edited the article.

Funding. None.

Data availability statement. The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.

Conflict of interest. None.

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Received 16 April 2024. Accepted 9 October 2024