A retrospective study on the prevalence, severity and outcomes of intraventricular haemorrhage in infants with a low birth weight in a quarternary hospital in a low- to middle-income country

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Background. Intraventricular haemorrhage (IVH) is a serious complication in infants with a low birth weight (LBW).
Objective. To study the prevalence, severity and outcomes of IVH in LBW infants admitted to a neonatal intensive care unit (NICU).
Methods. This was a retrospective cohort study of LBW infants admitted to the NICU at a quarternary hospital between January and December 2012. Neonates with recorded cranial ultrasound scans were included and followed up to between 18 and 24 months of age for neurological outcomes.
Results. An overall IVH prevalence of 44.3% (95% confidence interval 40 - 50) was observed in the study population (*N*=210). The prevalence of IVH in infants with a very low birth weight (VLBW) was 67.0%. Multivariable logistic regression showed risk factors for IVH to be VLBW, extreme prematurity, exposure to HIV, outborn delivery and receipt of a blood transfusion. Moderate to severe IVH was more common in VLBW and extremely premature infants. Severe IVH was associated with high mortality. At follow-up, 18.8% of the subjects showed signs of neurodevelopmental delay, while 6.3% were diagnosed with epilepsy. The overall all-cause mortality rate was 15.7% at discharge. Mothers' antenatal clinic attendance and caesarean delivery were protective factors.
Conclusion. Improved perinatal care for women in preterm labour, especially in rural areas in South Africa, could lead to better outcomes in infants. A screening schedule could contribute to timeous detection of brain injury in at-risk babies to facilitate appropriate medical management and detection of lesions associated with adverse long-term neurodevelopmental outcomes.

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Despite global improvements in perinatal care, the incidence of prematurity remains high.[1] Intraventricular haemorrhage (IVH) is a serious complication in infants with a very low birth weight (VLBW).[2,3] The more severe grades of IVH are associated with severe neurological sequelae, including death.[3,4] IVH occurs when bleeding in the subependymal germinal matrix spreads through the ventricular system.[3] Studies in low- and middle-income countries indicate a decreasing prevalence of IVH in VLBW infants (from 50% to 34%) over the past 30 years owing to improved perinatal care.[1,4,5]

The pathogenesis of IVH in infants with a low birth weight (LBW) is multifactorial and encompasses haemodynamic fluctuations, respiratory compromise and tenuous anatomical support of the affected area.[6] In a neonatal intensive care unit (NICU), a diagnostic screening test is required to detect cranial abnormalities that could affect acute and long-term care and also prognosis among premature neonates.[7] The risk of IVH is inversely correlated with gestational age. When premature delivery cannot be avoided, steps must be taken to ensure that delivery occurs at a centre with a NICU to facilitate effective management of the premature infant and reduce complications.[6,8,9]

Ultrasound scans of the cranium are reliable, safe and relatively affordable. Such scans can identify the severity of IVH, although it has been noted that parenchymal injury, such as mild white matter injury, may be missed.[10] Alternative investigations include computerised tomography (CT) scans and magnetic resonance imaging (MRI), which both yield excellent images but require a sick neonate to be transported to a radiology unit. CT scanning also involves considerable radiation exposure. MRI provides more extensive information about the brain substance and development and is the gold standard for diagnosing brain lesions.[11]

The most widely used grading system for IVH is based on that devised by Papile *et al.*[12] and modified by Volpe.[2]

Previous studies have indicated that 90% of all haemorrhages can be detected with a scan by the fourth postnatal day.[2] In ~20 - 40% of cases, the lesion can progress later, with maximal extent usually reached within 3 - 5 days of initial diagnosis, warranting a subsequent scan.[2] The American Academy of Neurology endorsed the practice of routine cranial ultrasound scanning in all infants born at <30 weeks' gestation.[7] A recent meta-analysis revealed that both mild and severe grades of IVH are associated with higher odds of death or moderate to severe neurodevelopmental impairment.[10] Most survivors with grade III lesions develop progressive ventricular dilatation.[13] Periventricular leukomalacia (PVL) is an ischaemic injury to the white matter that often accompanies grade III to IV IVH and is associated with multiple neurological abnormalities. With increasing survival of LBW infants, assessing the factors that contribute to the development of IVH may help to delineate preventable factors or highlight an area for management or treatment focus.

The prevalence of IVH and its associated risk factors is unknown in the LBW preterm neonate population at the NICU of Inkosi

Albert Luthuli Central Hospital (IALCH). The current study therefore explored the epidemiology, risk and outcomes of IVH in LBW infants at this unit. The objectives were to assess (*i*) the prevalence of IVH in this population, (*ii*) the timing and outcome of IVH in these infants, and (*iii*) the risk factors for IVH and their association with morbidity and mortality.

Methods

This was a retrospective descriptive study conducted at IALCH, a quaternary referral hospital with a 14-bed NICU. This unit is staffed by neonatologists and paediatric registrars and is the only quaternary NICU in KwaZulu-Natal, South Africa (SA).

All LBW infants (<2 500 g) admitted to the NICU between 1 January and 31 December 2012 were included in the study. Infants were excluded if no cranial ultrasound scan had been performed or if the scan showed abnormalities other than IVH (e.g. congenital hydrocephalus, periventricular flaring, echogenic posterior horns, intracerebral haemorrhage other than grade IV IVH, an echogenic cerebellum, basal ganglia enhancement, and caudothalamic and choroid plexus cysts not associated with IVH).

Demographic data collected included: place of delivery (inborn or outborn); gestational age; birth weight; the presence of intrauterine growth restriction; noted asphyxia (based on an Apgar score of ≤6 at 1 minute and 5 minutes, associated with metabolic acidosis at birth), and the need for resuscitation at birth (such as intermittent positive pressure ventilation or chest compressions). Other parameters included: suspected early sepsis (based on a raised white cell count or high C-reactive protein level), blood transfusion(s), and the presence of patent ductus arteriosus (PDA) and associated therapy. Maternal details recorded included booking status at an antenatal clinic, mode of delivery and HIV status.

Standard coronal and parasagittal images were obtained through the anterior fontanelle using a portable Siemens Acuson X300 ultrasonographic scanner with a curvilinear 8.5 mHz transducer. The severity of IVH was graded according to the modified Papile grading system and sequelae such as PVL and hydrocephalus were noted. Cranial ultrasound scans are performed at the bedside in high-risk infants according to a set protocol. In this unit, the protocol is as follows: all admitted infants are scanned at least once; infants weighing <1 500 g are scanned on admission, 24 hours later, on the third and seventh day of life, and weekly afterwards; and all infants weighing >1 500 g are scanned on admission and then weekly or as clinically indicated. Follow-up by a neonatologist at the neonatal clinic continues until 18 - 24 months of age and includes a full neurological examination.

Statistical analysis

Data were exported from the electronic database at IALCH and analysed using STATA (version 13.1). At an assumed IVH prevalence of 50%, a sample size of 170 was required to detect a difference of 18% or more with at least 80% power when assessing determinants of IVH. Continuous variables (gestational age; time to developing IVH) were summarised using means and standard deviations. Categorical variables (weight category, grade of IVH) were summarised using frequency (contingency) tables. Subjects were assigned to discrete weight categories and grouped according to gestational age. The prevalence of IVH was estimated as the number of infants with IVH across the total number of infants included in the study and expressed as a percentage. The association of mortality with IVH was assessed with a standard Pearson's χ^2 test. The risk factors for IVH and their association with severity, morbidity or mortality were assessed using Pearson's χ^2 tests, or Fisher's exact test in the case of a small number of subjects in a particular stratum. A significance level of $p<0.2$ was used for inclusion in the adjusted multivariable model. The adjusted effect of risk factors for IVH was assessed according to a logistic regression model that included the variables identified in the univariate analysis. Goodness of fit of the multivariable logistic model was assessed. An odds ratio (OR) with a 95% associated confidence interval (CI) was also calculated from the logistic regression model. A significance level of $p<0.05$ was used. At follow-up, neurological development was assessed according to medical history, anthropometry and standardised neurological examination. Motor function, cognitive skills, behavioural problems and visual or auditory impairment were noted.

Ethical considerations

The study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (ref. No. BE278/14) and by the provincial Department of Health (ref. no. HRKM168/15).

Results

A total of 210 infants were enrolled in the study (Fig. 1). Birth weights ranged from 750 g to 2 500 g and 60% of the cohort was male. Baseline characteristics of the study population are outlined in Table 1. Of the cohort, 93 infants (44.3%) had ultrasonic evidence of IVH, but it was moderate to

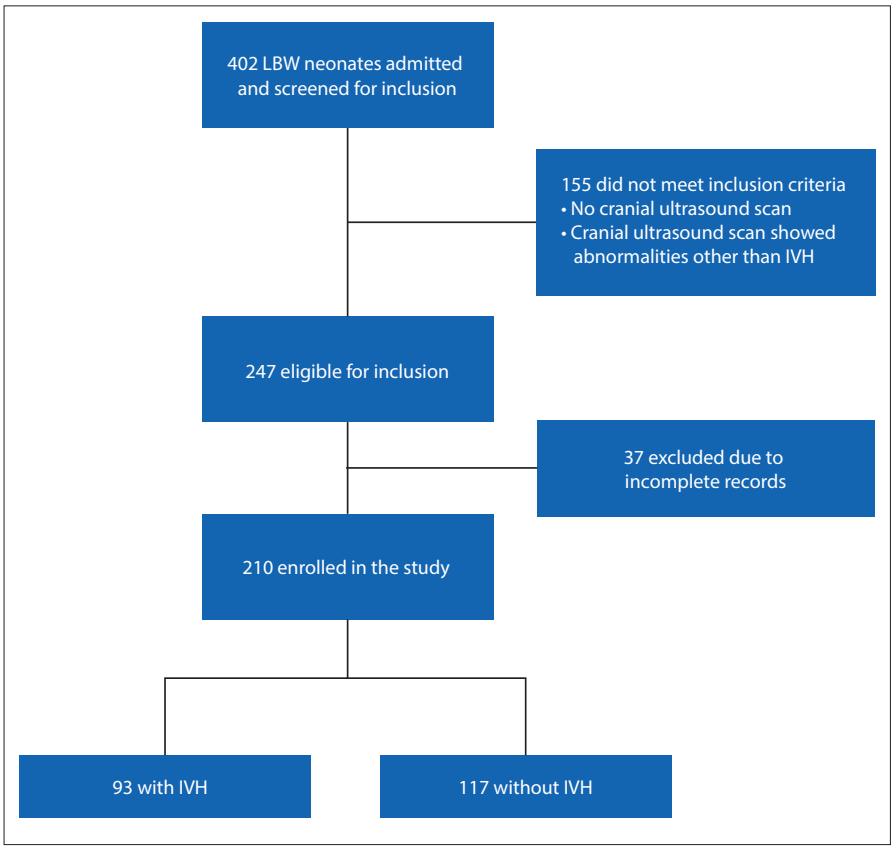

Fig. 1. Selection of participants to the study.
LBW = low birth weight; IVH = intraventricular haemorrhage.

severe (grade III or IV) in only 20 of these cases. The prevalence of IVH for infants weighing <1 500 g (i.e. VLBW infants) and those born at <32 weeks' gestation was 67.0% and 68.2%, respectively.

Only 194 infants' mothers (92.4%) had attended antenatal clinics. Not attending an antenatal clinic was a significant risk factor for the infant developing IVH (OR 10.2; 95% CI 2.2 - 46.1; $p<0.001$), as shown in Table 2. Only 22.6% of the infants who developed IVH were inborn. According to the multivariable model, outborn delivery was a highly significant risk factor for IVH (OR 4.8; 95% CI 2.1 - 11.1; $p<0.001$). The prevalence of intrauterine growth restriction was similar between the IVH and non-IVH groups ($p=0.8$).

Data were organised according to discrete categories for birth weight (250 g increments) and gestational age. The odds of IVH decreased with increasing gestational age ($p<0.05$ for all) and

Table 1. Baseline characteristics of the study population and prevalence of intraventricular haemorrhage

Characteristics	All (*N*=210), *n* (%)	With IVH (*N*=93), *n* (%)	Without IVH (*N*=117), *n* (%)	*p*-value
Birthweight <1 500 g	91 (43.3)	61 (67.0)	30 (33.0)	<0.001
Gestational age <32 weeks	88 (41.9)	60 (68.2)	28 (31.8)	<0.001
Inborn	86 (41.0)	21 (24.4)	65 (75.6)	<0.001
Intrauterine growth restriction	61 (29.0)	26 (42.6)	35 (57.4)	0.629
Booking at antenatal clinic	194 (92.4)	79 (40.7)	115 (59.3)	<0.001

IVH = intraventricular haemorrhage.

Table 2. Factors associated with intraventricular haemorrhage (adjusted multivariable logistic regression model) (*N*=93)

		Unadjusted model		Multivariable model	
Variable	*n* (%)	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Birthweight					
<1 500 g	61 (65.6)	5.5 (3.0 - 10.0)	<0.001	3.6 (1.4 - 9.2)	0.007
≥1 500 g	32 (34.4)	ref			
Gestational age					
<32 weeks	60 (54.6)	5.8 (3.2 - 10.5)	<0.001	2.6 (1.0 - 6.5)	0.04
≥32 weeks	33 (35.5)	ref			
Inborn					
Yes	21 (22.6)	ref			
No	72 (77.4)	4.3 (2.3 - 7.9)	<0.001	4.8 (2.1 - 11.1)	<0.001
Intrauterine growth restriction					
Yes	25 (26.9)	ref	0.8	Not included	
No	68 (73.1)	1.1(0.6 - 2.0)			
Antenatal booking					
Yes	78 (83.9)	ref	<0.001		0.4
No	15 (16.1)	10.2 (2.2 - 46.1)			
Received blood transfusion					
Yes	60 (64.5)	7.0 (3.8 - 13.1)	<0.001	3.9 (1.9 - 7.9)	<0.001
No	33 (35.5)	ref			
HIV status					
Exposed	48 (51.6)	1.6 (0.9 - 2.9)	0.08		0.2
Unexposed	45 (48.4)	ref			
Presence of asphyxia					
Yes	23 (24.7)	1.9 (0.9 - 3.9)	0.06		0.4
No	70 (75.3)				
Mode of delivery					
Caesarian section	50 (53.8)	ref	<0.001		0.1
Normal vaginal delivery	43 (46.2)	3.2 (1.7 - 5.8)			
Resuscitation required					
Yes	53 (57)	1.7 (0.9 - 2.9)	0.07		0.7
No	49 (52.7)	ref			
Suspected sepsis					
Yes	88 (94.6)	7.8 (2.9 - 20.9)	<0.001	2.9 (0.9 - 9.3)	0.08
No	5 (5.4)	ref			
Medical treatment of PDA					
Yes	17 (18.3)	8.5 (2.4 - 30.0)	<0.001		0.6
No	76 (81.7)	ref			

OR = odds ratio; CI = confidence interval; PDA = patent ductus arteriosus; ref = 1.

generally also with increasing birth weight. The distribution of the severity of IVH is shown according to gestational age in Fig. 2A and weight categories in Fig. 2B. The highest prevalence of IVH was seen in infants with a birth weight <1 000 g (87.5%), whereas the lowest prevalence was seen in the group with a birth weight ≥1 500 g (26.3%). The prevalence of IVH was similar in the groups weighing 1 000 - 1 249 g and 1 250 - 1 499 g (62.8% and 63.6%, respectively).

The prevalence of moderate to severe IVH (grades III or IV) was 31.3% for infants weighing <1 000 g, 14.0% for those weighing 1 000 - 1 249 g, and 18.2% for the group weighing 1 250 - 1 499 g (Fig. 2B). The prevalence of moderate to severe IVH was 40.0% for infants born at <28 weeks' gestation and 12.3% for those born between 28 and 32 weeks. Again, the lowest prevalences (2.5% and 0%) were seen for infants with a birth weight ≥1 500 g and a gestation period >37 weeks, respectively. Birth weight ≥1 500 g was associated with significantly lower odds of IVH compared with a birth weight <1 000 g (OR 0.06; 95% CI 0.01 - 0.26; $p<0.001$). There was no statistically significant difference between the weight categories 1 000 - 1 249 g and 1 250 g - 1 499 g for either the IVH or the non-IVH group ($p=0.101$ and $p=0.119$, respectively).

According to the unadjusted logistic model (Table 2), the following factors were identified as being associated with IVH: VLBW, extreme prematurity (<28 weeks), outborn delivery, the mother not having attended an antenatal clinic, blood transfusion, vaginal delivery, suspected sepsis, and treatment for PDA. The multivariable logistic regression showed the following factors to be significantly associated with the development of IVH: VLBW ($p=0.007$), prematurity (<32 weeks) ($p=0.04$); outborn delivery ($p<0.001$), and the infant having received blood ($p<0.001$).

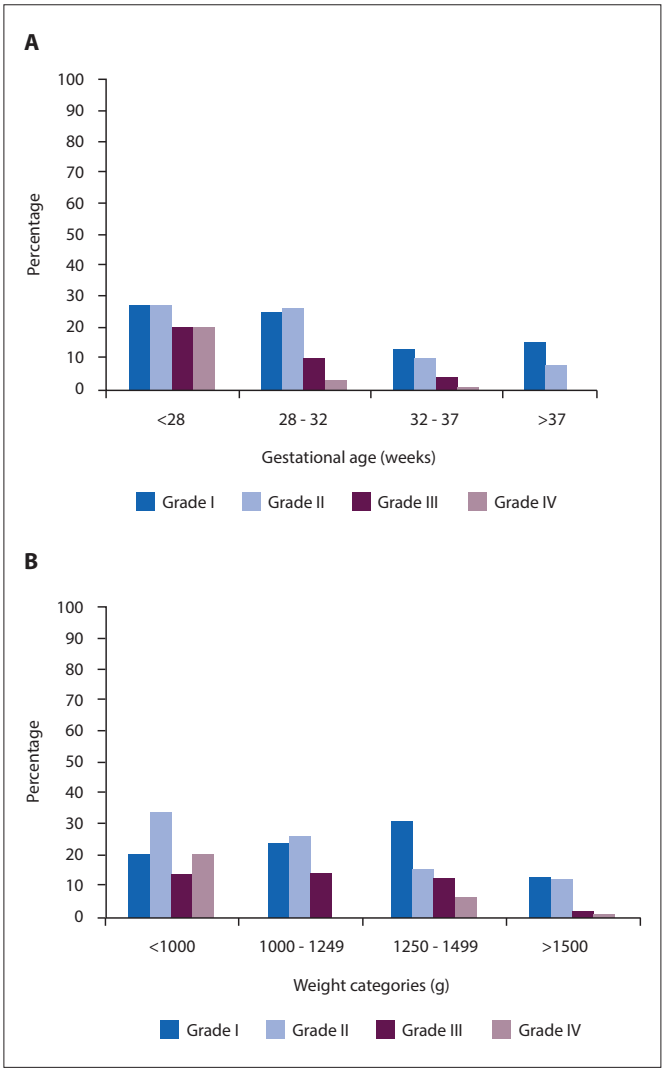

Fig. 2. Prevalence of different severities of intraventricular haemorrhage grouped according to (A) gestational age and (B) birthweight.

Detection of intraventricular haemorrhage

Of the infants with a birth weight <1 500 g, 67% developed IVH. Detection in this group was evaluated from 59 cranial ultrasound scans taken between day 1 and day 77 of life. With the current imaging protocol in this unit, 50% of IVH cases were detected by day 5 of admission. Most scans were performed on day 2 (13.3%) and day 4 (18.3%) of life. Both initial scans and repeat scans were analysed, which showed the progression of IVH. Timing to IVH could not be extrapolated accurately as results from referral centres were not considered.

Mortality

The overall mortality among the cohort (irrespective of IVH) was 15.7%. The mortality among infants with IVH was 31.2% compared with 3.4% in those with normal ultrasound scans. Mortality increased significantly with increasing severity of IVH ($p=0.008$ between grades I and IV; $p=0.05$ between grades II and IV; $p=0.043$ between grades III and IV). The mortality rate was 46.7% in extremely premature infants (born at <28 weeks). Mortality among VLBW infants was 19.8% (Table 3). The odds of death decreased with increasing gestational age. Birth weight, attendance at an antenatal clinic, intrauterine growth restriction, HIV exposure, need for resuscitation, suspected sepsis and treatment of PDA were not significant contributors to mortality. In contrast, normal vaginal delivery was associated with greater odds of death (OR 4.5; 95% CI 1.5 - 13; $p=0.007$) in this group, as was asphyxiation at birth (OR 3.2; 95% CI 1.0 - 10; $p=0.04$) and having received a blood transfusion (OR 5.1; 95% CI 1.4 - 19; $p=0.009$). Also of significance is that 66.7% of deaths were outborn.

Morbidity

Among the 177 survivors (84.3%) who were discharged, 64 (36.2%) presented with IVH and required intense follow-up to determine signs of neurological impairment. With reference to severity of IVH, 31 infants (81.6%) classified as grade I survived to hospital discharge, 22 (71.4%) of those classified as grade II, 9 (69.2%) who were classified as grade III and 2 (28.6%) classified as grade IV. One-third of the IVH cohort was noted to have comorbidities, which ranged from dilated ventricles to epilepsy. Six infants with IVH had coexisting PVL. Nine infants with IVH (9.7%) had evidence of dilated ventricles, of whom only two (22.2%) developed persistent posthaemorrhagic ventricular dilatation that required surgical intervention before discharge. A quarter of the infants with IVH who survived to discharge were not followed up at IALCH; they were transferred to peripheral hospitals for weight gain and were to be followed up there. The remainder ($n=48$) were given follow-up dates on discharge. On follow-up, nine (18.8%) of these infants showed signs of neurodevelopmental delay, whereas three (6.3%) were diagnosed with epilepsy. Twenty-five (52.1%) infants in this group were lost to follow-up.

Discussion

We found an overall IVH prevalence of 44.3% in LBW neonates, with the majority presenting with a mild grade. The prevalence of IVH in VLBW infants was 67.0%, which is higher than what has recently been reported in Zambia, a country regarded as being of similar economic status to SA.[5] Our study revealed short gestation periods, LBW, HIV exposure, outborn delivery and receiving a blood transfusion as risk factors for IVH. Protective factors against IVH

Table 3. Univariate analysis of risk factors for mortality in all infants with a very low birthweight (*N*=91)

Risk factor	*N*	Mortality, *n* (%)	OR (95% CI)*	*p*-value
Weight (g)				0.8
<1 000	15	4 (26.7)		
1 000 - 1 249	43	8 (18.6)		
1 250 - 1 499	33	6 (18.2)		
Mode of delivery				0.01
Normal vaginal delivery	30	11 (36.7)	4.5 (1.5 - 13)	
Caesarian section	61	7 (11.5)		
Place of delivery				0.4
Inborn	39	6 (15.4)		
Outborn	52	12 (23.1)		
Gestation (weeks)				
<28	15	7 (46.7)		
28 - 32	59	10 (16.9)	0.2 (0.07 - 0.8)	0.02
32 - 37	16	1 (6.3)	0.08 (0.008 - 0.7)	0.03
>37	1	0 (0.0)		
Antenatal booking				0.09
Yes	81	14 (17.3)		
No	10	4 (40.0)		
IVH	61	18 (29.5)		
Intrauterine growth restriction	36	7 (19.4)		0.9
HIV-exposed	43	11 (25.6)		0.2
Presence of asphyxia	19	7 (36.8)	3.2 (1.0 - 10)	0.04
Resuscitation required	57	14 (24.6)		0.2
Suspected sepsis	78	17 (21.8)		0.2
Blood transfusion received	51	15 (29.4)	5.1 (1.4 - 19)	0.01
Medical treatment of PDA	16	2 (12.5)		0.4

*Not calculated if *p*-value was not significant.
OR = odds ratio; CI = confidence interval; IVH = intraventricular haemorrhage; PDA = patent ductus arteriosus.

included the mother attending an antenatal clinic and caesarean delivery. A lower gestational age was associated with severe IVH, which in turn was associated with higher mortality.

Data from the Neonatal Research Network VLBW registry (National Institute of Child Health and Human Development, USA) show an overall IVH prevalence of ~29% and a 22% prevalence of severe IVH between 1997 and 2002.[14] The prevalence of severe IVH seen in our study is slightly higher (26.3%). The higher prevalences seen in this study can be attributed to the NICU being a referral centre for the smallest and sickest premature infants. More than half the cohort (59%) were outborn and required transfer to the NICU before receiving vital perinatal care. Findings from our study support the American Academy of Neurology's recommendation that screening should be routinely performed on all infants of <30 weeks' gestation; this has been the case in most NICUs in SA for the past decade.[7]

Of the patients with IVH, 50% were identified by day 5 of admission. The 2002 recommendation of the American Academy of Neurology is that screening ultrasound scans should be performed at 7 - 14 days of age and ideally repeated at 36 - 40 weeks postmenstrual age, as severe grades of IVH can develop as late as the third postnatal week.[7] Volpe recommends two scans in the first week, with timing of subsequent scans determined by initial clinical findings.[2] Earlier scanning may prove useful in the SA context, given the generally poor attendance rates at antenatal clinics.

In KwaZulu-Natal, the survival of VLBW infants has increased over the last two decades. We recorded 19.8% mortality compared with 32% recorded in a similar study of babies born in 1991 - 1992.[1] The reduction can be attributed to vast improvements in perinatal care, including antenatal corticosteroid use, which has become a standard of care in SA. A recent Cochrane review found antenatal corticosteroid use to protect against the development of IVH (relative risk 0.55; 95% CI 0.40 - 0.76).[15]

Most of the risk factors for IVH are linked with prematurity and the primary endpoint therefore is to prevent premature birth. An aggressive perinatal approach to prolong gestation and allow normal maturation of the germinal matrix has not shown consistent benefit in so-called at-risk pregnancies.[8] In our study, more infants with IVH were outborn and a low attendance rate at antenatal clinics was observed, which suggests a reduced likelihood of mothers receiving antibiotics, tocolysis and antenatal steroids. Future studies (including animal studies, multicentre randomised prevention trials and follow-up studies) will contribute to our understanding of how to reduce the incidence of IVH and improve the outcome of premature infants.

LBW babies born vaginally had an increased risk of developing IVH compared with those born by caesarean section (OR 3.2; 95% CI 1.7 - 5.8). The potential value of caesarean delivery has been noted in previous studies, but more data are required to delineate the specific clinical circumstances that could lead to a recommendation for elective caesarean section.[6,8] The NEOPAIN trial showed that location of delivery was an important contributory factor to the development of severe IVH,[16] attributed to mothers probably being less likely to receive antenatal steroids if delivery is outborn. This factor was not investigated further in our study.

Our findings show that receipt of a blood transfusion increased an infant's odds of developing IVH, which is in line with recent studies showing that a blood transfusion is an independent risk factor for IVH. However, interpretation of this finding is complicated by the multifactorial reasons for a blood transfusion and the observation

that the smallest and most critical babies are those most likely to receive a transfusion.[17]

IVH in the premature neonate continues to be a cause of morbidity and mortality in NICUs worldwide. The outcome of these infants depends predominantly on the severity of associated parenchymal injury and the degree of prematurity. Our study highlighted the relationship between the severity of IVH and neurological outcome. Mortality was found to have increased significantly with increasing grades of IVH, which is comparable with results from a recent meta-analysis that revealed severe IVH to be associated with higher odds of death or moderate to severe neurodevelopmental impairment than in the case of mild IVH.[10]

Poor long-term follow-up was observed at IALCH, despite follow-up bookings being made. Further research on neurological outcomes is required, as the long-term complications contribute to prognostication and affect future resource utilisation owing to possible readmissions and increased healthcare costs. The availability of care resources contributes to the survival rate of preterm infants. With a survival rate of 80.2% among VLBW infants at IALCH, which is higher than most resource-limited centres in SA, a higher demand for care associated with medical and neurodevelopmental complications of prematurity is expected at this centre.[17,18]

Strengths of the study

This is the first study of IVH prevalence at the NICU of IALCH. The strengths of the study include that clear inclusion and exclusion criteria were used and that the sample size met the prospective calculated requirement for adequate power. The findings may contribute to guidelines for monitoring and follow-up of high-risk infants to achieve optimal survival and neurodevelopmental outcomes.

Study limitations

The retrospective design and the inability to track the outcome of all subjects owing to loss to follow-up were limitations in this study. Controls (i.e. infants without IVH) were not representative of the general population and thus prone to selection bias. Confounding was a major issue, as complications of prematurity are intricately linked. Many infants who presented with higher grades of IVH may have had coexisting pathologies such as haemodynamic instability, which is associated with IVH, neurodevelopmental impairment and death. These conditions have a poor prognosis and infants may have died in the NICU or life-sustaining therapy may have been withdrawn owing to the poor predicted outcome. The temporal relationship between receiving a blood transfusion and developing IVH could not easily be analysed retrospectively.

This study originally hoped to also explore the neurological outcomes of infants with IVH at this centre. However, no validated toolkit was used to assess this at follow-up. There is a need for the use of validated assessment tools such as the Gross Motor Functional Classification Scale for Cerebral Palsy and the Bayley Scales of Infant Development Mental Developmental Index to assess neurodevelopmental impairment.[8,10] Long-term outcomes could include analysing school performance and IQ, which can assist with counselling in the acute phase.[8,10]

Finally, as IALCH caters for high-risk deliveries and referrals from all other hospital nurseries in the province, it is possible that selection was biased towards sicker infants. Selection bias was seen in the analysis as the survivors did not represent the entire population first diagnosed with IVH. In addition, a large number of subjects were lost to follow-up after referral to local hospitals and hence further analysis of neurological outcomes was not possible.

Conclusion

Risk factors for IVH were low gestational age, LBW, outborn delivery and receipt of a blood transfusion. Protective factors against IVH included mothers' antenatal clinic attendance and caesarean delivery. Education around the value of antenatal attendance can be reinforced.

VLBW and extremely premature infants had a high likelihood of developing moderate to severe IVH. Severe IVH was associated with high mortality. Improved perinatal care, specifically focused on timeous transfer from rural areas if a woman is in preterm labour, could lead to a better outcome in the infant.

USA guidelines recommend routine cranial ultrasound screening at 7 - 14 days of age in all infants with a gestational age <30 weeks, which should ideally be repeated at 36 - 40 weeks postmenstrual age.[7] This would ensure timeous detection of brain injury in at-risk babies and so facilitate appropriate medical management and detection of lesions associated with long-term adverse neurodevelopmental outcome. Our findings suggest that this schedule could facilitate the detection of a considerable proportion of brain injuries in the at-risk neonatal population and so contribute to continued improvement in perinatal care in SA.

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