ORIGINAL ARTICLE

Outcome of Inborn Compared with Outborn Very Low Birth Weight Infants Admitted to Level 3 Malaysian Nurseries

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Summary

To investigate whether a neonatal retrieval system would have any impact on the survival of infants < 1550g birthweight, data from the Malaysian Paediatric Association Very Low Birth Weight (VLBW) study were analyzed. Inborns had a significantly better survival than outborns. Outborn babies had more hypothermia, were more likely to die from hypothermia, received more blood and plasma transfusions, more exchange transfusions, and had more infections. Length of stay was significantly longer for outborns. A neonatal retrieval system could reduce the mortality of VLBW babies as well as reduce length of stay, antibiotic usage, and blood product usage.

Key Words: Neonatology, Very low birth weight infants, Neonatal nursery

Introduction

It is well established that neonatal intensive care has had an impact on mortality rates[1-6]. About 50% of neonatal deaths are in babies 1500 gm and below yet these account for only 1% of the births[1]. It is not surprising then that low birth weight babies are the main users of neonatal intensive care ventilators accounting for 60% of those ventilated[7].

The survival rate is now reported at 70 - 80 % for all babies below 1500 gm[8-10] and 50 - 60% when only those less than 1000 gm are considered[11-13]. Population based studies have been done on large regions[13-17] and several national studies have been done[8-10]. The Scottish Low Birthweight Study Group reported a survival of 75% to 28 days and 71% to $4^1/_2$ years[9]. The Netherlands Project on Preterm and Small for Gestational age infants showed a survival of 77% to 28 days and 74% to 1 year[10].

Improved survival has not been accompanied by an increase in the rate of major handicap amongst survivors. Absolute numbers of survivors and those with major handicap have increased but the proportion with handicap has not[18-20].

The birth of at risk babies should ideally be in a centre equipped to deal with a sick baby, that is, nominated by specific criteria as a level 3 intensive care nursery.[21-27] However there will always be a proportion who are born away from these centres and the mortality in this group is higher[21,26,28,29]. The National Health and Medical Research Council of Australia found that 30% of neonatal problems could only be identified when delivery was imminent or in the post-partum period[30]. Neonatal retrieval services have been developed as a means of providing skilled transport for the baby who is born away from a level 3 centre[21,22,25,27,31,32,33]. The retrieval of newborns by a skilled neonatal transport team can reduce the mortality amongst outborn babies

and even increase survival in this group so that it is not different from inborn babies[34].

Malaysia is a developing country with level 3 nurseries established throughout the country. As yet a retrieval service for newborns, born away from centres with level 3 nurseries has not been established. Multidisciplinary motor, mental, eye and hearing follow-up services to identify problems and provide intervention for the survivors have yet to be developed. The Malaysian very low birth weight (VLBW) study, a nationwide study, was conducted by the Neonatal Data Collection Group which was convened by the Malaysian Paediatric Association. The aim of the study was to examine the morbidity and mortality of VLBW babies admitted into level 3 nurseries. To identify possible preventative strategies in relation to both mortality and morbidity, in particular to investigate whether a neonatal retrieval system would have any impact on survival, data from this project was analysed to compare the outcome for inborn and outborn babies in the study population.

Materials and Methods

All babies 1500 g or less at birth who were admitted into the participating level 3 nurseries between January 1 and June 30, 1993 were studied.

Level 3 nurseries were identified from government, university and private hospital lists compiled by the ministry of health. Each level 3 nursery was invited to participate. There were 23 participating centres. These included 2 universities, 11 general hospitals, 3 district hospitals with a resident paediatrician and 5 private hospitals. Two additional participating centres were in the Kuala Lumpur General Hospital complex. One university did not participate and replies were not received from 20 private hospitals. Of these 20 private hospitals only 5 were major hospitals with comprehensive facilities. It is not known how many VLBW babies were managed in non-participating private hospitals but the numbers are likely to be very small. It is estimated that the study represents 90-95% of newborns admitted to level 3 nurseries throughout Malaysia. The study did not identify the number of babies ≤1500 g who were not admitted to a level 3 nursery.

A data centre was set up to handle the receiving and computing of all data. A standardised data sheet was sent to all participants along with a detailed protocol for completing the data sheet. The data sheet was completed at discharge or death of each baby and sent to the data centre. The technique of double data entry by 2 different operators was used and the 2 data bases were verified against each other. Incomplete data sheets were returned for completion before being entered into the central database. A code number was randomly assigned to each participating centre to ensure confidentiality between centres. Analysis of this data was used for the present study.

As the rate of post mortem is extremely low in Malaysia it was not measured in the study patients. The cause of death was classified using a modification of the British 1958 Perinatal Mortality Survey[35], intended for use when postmortem information is not available. Classification was done at the data centre by J Ho and verified by NY Boo.

Statistics

Statistical analysis was performed using the software statistical package Epi Info. The chi squared statistic was applied and results expressed in odds ratios (OR) with 95% confidence intervals (95% CI). A p value of <0.05 was accepted as significant. For data not normally distributed, a Mann-Whitney U test was applied.

Definitions

For this study, a level 3 nursery was defined as a nursery which ventilates newborns and is under the control of a paediatrician.

An inborn baby was defined as a baby born in the hospital where the level 3 nursery was situated. An outborn baby was defined as born at home, on the way to hospital or in another hospital and transferred postnatally to the hospital with the level 3 nursery. This also included horizontal transfer between level 3 nurseries.

The following clinical definitions were applied: hypothermia, skin temperature below 36°C; hyaline

membrane disease (HMD), respiratory distress with supportive xray findings; hypoglycaemia, blood sugar or rapid enzymatic method (Reflolux) of < 2.2mmol/l; hypocalcaemia, < 1.8mmol/l; jaundice, any clinical jaundice necessitating a bilirubin level; pulmonary airleak, any type. Confirmed infection was clinical infection with a postive blood, urine or CSF culture and suspected infection referred to clinical evidence only. Necrotising enterocolitis (NEC) was classified according to Bells critieria[36] and positive NEC was defined as Bells criteria stage 2 or 3.

Results

Data from 868 babies from 23 centres were analysed. Two centres admitted only inborns and two centres admitted only outborns. Three centres did not have any VLBW admissions during the study period. Inborns accounted for 636 (73%) of admissions while 232 (27%) were outborn. There was no significant difference between the two groups with respect to birthweight, and maternal gravida. There was a significantly lower gestation and maternal age in the outborn group. (Table I).

Place of Birth

The place of birth was classified into one of 8 categories (Table II). A total of 670 (77%) were born in a major government hospital with a resident paediatrician, while 32 babies (4%) were born in the private sector. Of these, 18 were born in hospitals with a level 3 nursery. Of these 18 babies, only 2 were cared for fully in a private hospital level 3 nursery. Sixty-three (7%) deliveries were conducted in the mothers own home and 72 (8%) were born in government hospitals without a specialist. The remaining 31 (4%) were born in other places, the majority being on the way to hospital.

Age on Admission

A total of 829 of the 868 (96%) babies were admitted within the first 24 hours of life. For inborns, 48% were admitted within 1 hour of life and 93% by 2 hours of life, whereas only 4% of outborns were admitted within 1 hour and 20% by 2 hours. The mean age on admission for those admitted within 24 hours was 0.7 hours (SD=1.24) for inborns and 4.2 hours (SD=4.59) for outborns (p«0.001).

Overall Mortality

The overall survival to discharge was 543 (63%). Inborn survival was 415 of 636 (65%) and outborn survival was 128 of 232 (55%), OR=1.53 (95% CI 1.11-2.10).

Cause of Death

HMD and its complications accounted for 48% of deaths. Infection, either antepartum or post-partum accounted for 22%. Pulmonary immaturity accounted for 14%. (Table III). The interobserver variability between the 2 classifiers was 3.4%.

Length of Stay

The mean duration of stay was 27.7 days for the whole population, 38.9 days for survivors and 9.2 days for those who died. Outborn survivors had a significantly longer duration of stay, $p < 0.001$ (Table IV).

Incidence of Hypothermia and Mortality

Hypothermia was significantly more common in outborns and the mortality was higher although this just failed to reach significance. It was seen on admission in 201 of 631 inborns (32%) admitted within the first 24 hours and in 79 of 193 outborns (41%), OR=1.48 (95% CI 1.05 - 2.10). Five babies did not have skin temperature taken on admission. Of the 201 inborn babies with hypothermia, 79 (39%) died as compared with 41 of the 79 (52%) outborn babies, OR=1.67 (95% CI 0.95-2.93).

Incidence of Hypotension

Hypotension was seen significantly more commonly in outborns. Of 632 inborns who had their blood pressure recorded 78 (12%) had hypotension and 47 of 231 outborns (20%), OR=1.81(1.19-2.76). 5 babies did not have their blood pressure recorded. The mortality in those with hypotension was not significantly different between the 2 groups.

Other Significant Morbidity Results

A significantly higher number of inborns were intubated at birth, OR=0.60 (95%CI 0.38-0.93). Exchange transfusion was performed on a higher proportion of outborns, OR=2.13 (95% CI 1.11 - 4.05) and mortality was higher in outborns who recieved exchange transfusion, OR=5.31(1.27- 23.49).

Table I
Comparison of gestation, birthweight, and maternal age and gravida between inborn and outborn babies. The Standard Deviation (SD) is given in parenthesis

	Inborn	Outborn	p Value
Mean birthweight in gm (range 550-1500)	1221.5 (230.5)	1226.4 (200.4)	ns
Mean gestation in weeks (range 21-42)	31.01 (3.3)	30.06 (2.9)	p<0.05
Mean maternal age in years (range 13-49)	28.6 (6.64)	26.4 (6.02)	p<0.001
Mean gravida (range 1-15)	3.2 (2.7)	2.8 (2.1)	ns

Table II
Place of birth

Place of Birth	Number (%)
University or Institute	183 (21%)
Government General Hospital	402 (46%)
Government District Hospital with Paediatrician	85 (10%)
Government District Hospital without Paediatrician	72 (8%)
Private Hospital	18 (2%)
Private Maternity Home	14 (2%)
Own Home	63 (7%)
Other	31 (4%)
Total	868 (100%)

Table III
Cause of death
(Abbreviated from Hey EN, Lloyd DJ, Wigglesworth JS.[33])

Cause of Death	Inborn	Outborn	Total (%)
Congenital Malformations	18	2	20 (6)
Asphyxia	5	2	7 (2)
Pulmonary immaturity	39	7	46 (14)
HMD	95	61	156 (48)
Intraventricular haemorrhage	2	1	3 (1)
NEC	8	5	13 (4)
Antepartum and intrapartum infection	8	4	12 (4)
Post partum infection	40	19	59 (18)
Miscellaneous	6	3	9 (3)
Total	221	104	325

Blood transfusion was given to significantly more outborns than inborns, OR=1.58 (95% CI 1.15-2.17). Plasma transfusion was also more common in outborns, OR=1.33 (95% CI 0.96-1.84). Infection, confirmed either by a positive culture or defined clinically occurred significantly more often in outborns, OR 1.93 (95% CI 1.41 - 2.65). A summary of significant results is shown in Table V.

Results not reaching significance

There was no significant difference between the 2 groups with respect to duration of ventilation, incidence of hypoglycaemia, hypocalcaemia, clinical patent ductus arteriosus, NEC, congenital pneumonia, jaundice, airleak, use of exogenous surfactant, use of parenteral nutrition, or the presence of intraventricular haemorrhage determined by either clinical or ultrasound means. The incidence of these conditions is shown in Table VI.

Table IV
Median duration of stay. Quartiles given in parenthesis

	Inborn	Outborn	p Value
Median duration of stay (days)	27 (6-40)	25 (4-44)	ns
Median duration of stay for survivors (days)	36 (26-46)	40 (32-52)	<0.01
Median duration of stay non-survivors (days)	2 (1-9)	3 (1-12)	ns

Table V
Summary of results
(Statistical significance is expressed in terms of odds ratios and 95% confidence intervals are given)

	Inborns (n=636)	Outborns (n=232)	Statistical significance
Overall survival	415 (65%)	128 (56%)	1.53 (1.11-2.10)
Median length of stay for survivors (days)	36	40	p<0.01
Frequency of intubation at birth	134 of 628 (21%)	32 of 230 (14%)	0.60 (0.38-0.93)
Frequency of hypothermia	201 of 631 (32%)	79 of 193 (41%)	1.48 (1.05-2.93)
Mortality from hypothermia	79 of 201 (40%)	41 of 79 (52%)	1.67 (0.95-2.93)
Frequency of hypotension	78 of 632 (12%)	47 of 231 (20%)	1.81 (1.19-2.76)
Frequency of exchange transfusion	27 (4%)	20 (9%)	2.13 (1.11-4.05)
Frequency of plasma transfusion	223 (35%)	97 (42%)	1.33 (0.96-1.84)
Frequency of blood transfusion	226 (36%)	108 (47%)	1.58 (1.15-2.17)
Frequency of infection	237 (37%)	124 (53%)	1.93 (1.41-2.65)

Discussion

The Malaysian Paediatric Association VLBW study, provides good representative data on the outcome of VLBW babies admitted to Level 3 Malaysian nurseries. It is the first available data of its kind in Malaysia thus providing a baseline for future comparison. It also gives individual hospitals an opportunity to compare their mortality and morbidity with other centres. Such comparison has limitations but is still useful. The adoption of a severity score index used for assessing the status of newborns admitted to level 3 nurseries would improve the meaning of such comparisons and its further exploration into this is recommended.

These results show that outborn babies admitted to Malaysian level 3 nurseries are at least one and a half times more likely to die than inborn babies. It is likely that the mortality amongst outborns may be even higher since a proportion may have never reached the

nursery, either dying in transit or not referred at all because of poor prognosis. No record is available of the number of babies this may have involved.

The overall survival for VLBW infants of 63% is below that of developed countries where it is generally around 70 - 80%. However a number of hospitals have survival rates similar to those quoted in the literature from developed countries. These figures reflect the state of economic development in Malaysia which is high for a developing country but below that of industrially developed countries. Exogenous surfactant has resulted in a visible reduction of mortality in the US since 1990, not only for VLBW infants, but also in the neonatal mortality rate and the infant mortality rate. Surfactant was not available during the study period but was given to 16 babies on an experimental basis.

Outborns are more likely to have hypothermia on admission and if hypothermia is present are more likely to die than hypothermic inborn babies. They are also more likely to have hypotension. If they survive outborns stay longer in hospital and receive more blood transfusions, more plasma transfusions, more exchange transfusions and have more infections.

If a neonatal transport system were to be introduced and the mortality in outborns brought down to the same level as in inborns, there would be a significant improvement in the survival of VLBW babies. Access to skilled neonatal transport may result in a further reduction in mortality in the group of babies who at present never reach a level 3 nursery.

It is also likely that the duration of stay, usage of antibiotics and blood transfusions may be reduced, thus reducing costs. This saving would cover part of the cost of a retrieval system. However it is likely that a retrieval system will increase the cost of neonatal care, as it will not only improve access to neonatal intensive care - opening it up to more babies, but it will also increase the number of survivors in those already with access.

It is disturbing that almost half of the inborns were

Table VI
Incidence of conditions not reaching statistical significance

	Inborn (n=636)	Outborn (n=232)	Overall (%)
Patent ductus arteriosus	99	33	132 (15)
Necrotising enterocolitis	18	7	25 (3)
Congenital pneumonia	20	10	30 (3)
Jaundice	427	160	587 (68)
Airleak	44	22	66 (8)
Exogenous surfactant	13	3	16 (2)
Use of parenteral nutrition	76	32	108 (12)
Hypoglycaemia	189 of 631	54 of 228	243 (28)
Hypocalcaemia	42 of 577	25 of 214	67 (8)
Ultrasound periventricular haemorrhage	69 of 170	24 of 62	93 (40)
Clinical periventricular haemorrhage	61	30	91 (10)

admitted more than an hour after birth. If true, such unwarranted delay in the stabilisation of a VLBW neonate and the implied delay in mechanical ventilation, arterial lines, intravenous access and adequate and early treatment of hypoxaemia and acidosis suggests this is a most important target strategy to improve outcome. Skilled internal transport of an inborn neonate is just as necessary.

A retrieval system could create a network between level 3 nurseries making it possible to move babies to a nursery experiencing a low occupancy rate. Wide fluctuations in bed requirements can occur throughout the year. At present a level 3 nursery is forced to maintain sufficient ventilator beds to cater for the heaviest admission periods which may actually be for only short periods of a year. A retrieval network could make it possible to reduce the number of beds in a region by averaging bed requirements over a wider area. Funding for a retrieval system is similar to the funding of an additional neonatal intensive care bed and could actually be viewed as a mobile intensive bed. Thus a reduction by 2 - 3 beds in a region would fund a retrieval service.

Retrieval services have found that the number of VLBW outborns has been reduced with time.[34] This is attributed to both increased awareness and education between the retrieval service and the referring hospital. Such a service would also lead to improvement in the preventable morbidities lisited in Table V. Education on appropriate resuscitation, prevention of hypothermia and hypoglycaemia, acid-base management, oxygenation and ventilation should also lead to decreased morbidity and better intensive treatment. An improvement in the in utero transfer rate would also result in better obstetric management for most of these high risk babies. For example, the increased use of antenatal steroids, a simple and inexpensive antenatal treament, would lead to a reduced incidence in HMD death from HMD, intraventricular haemorrhage, and NEC[36,37].

No data is available yet comparing the outcome of inborn and outborn term babies. It is possible that skilled transport of term babies may result in a reduction in post-resuscitation asphyxia. It is recommended that this be studied.

Neonatal intensive care in Malaysia has progressed rapidly over a 10 year period and very little data exists on its outcome. Because at present no national data is available, an excellent opportunity exists to develop a properly designed national network of data collection. This would provide well defined, comparable data, collected independently but transferable to a national data base. This could be part of the function of a retrieval network. Long term outcome of level 3 nursery graduates should also be monitored as survival is not the only endpoint. This is particularly important in Malaysia where delayed referral of both pregnant mothers and outborn babies are variable, depending on the geographic location and socio-economic development. Various severity scores have been developed[38,39] and validated such as the CRIB score[39]. These are now being applied both within countries and between countries[40].

Very low birth weight babies account for a large proportion of admissions to level 3 nurseries and prematurity is the commonest cause of death in infancy[41]. Any reduction in the mortality of this group is likely to have an impact on both national perinatal and neonatal mortality rates.

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