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Factors affecting nursery survival of very low birth weight infants

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1 Introduction

Recent improvement in the survival of very low brithweight (VLBW) infants, i.e. with birthweights ≤ 1500 g, has been well documented [14, 15, 20]. The impact of the VLBW infants on neonatal mortality is dependent both upon the incidence of VLBW infants born and upon survival of these infants. While factors related to the incidence of VLBW infants have been related to socioeconomic status, maternal health and pregnancy problems [1, 5, 7, 21], the survival within specific birthweight (BW) categories was found to be related to perinatal care and infant maturity [4, 6, 9–12, 16, 17, 19].

Despite increasing numbers of Hispanic immigrants there is little information regarding the recent incidence of birth and survival of the VLBW infants among the Hispanics. Los Angeles County-University of Southern California Medical Center, Women's Hospital is a tertiary perinatal center with greater than 16000 deliveries per year. The patient population is 87% Hispanic, highly mobile, of low socio-economic status with no alternative health care resource. More than half are immigrants who speak no English.

A prospective study from January 1982 in December 1983 was done to determine the incidence and survival rate of the VLBW infants, separated into groups by birth weight and gestational age, and to determine causes of death as well as identify factors influencing outcome of these infants.

2 Methods

All inborn live births with BW 500–1500 g, born between January 1, 1982 and December 30, 1983, were included in the study. Survival was determined by discharge from the nursery rather than by the neonatal period of life. Ges-

Curriculum vitae

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tational age (GA) was determined from the first day of the last normal menstrual period (LMP). A clinical estimate of GA by the BALLARD assessment method [2] was used when LMP was unknown or varied by more than two weeks from the estimated GA.

Unless specified, all infants with death due to congenital anomalies were excluded from the analysis. Information was obtained from parent interviews, hospital records, autopsy reports and by ongoing recording of the infant's nursery course. Results were analyzed by chisquare test to compare frequency. Yates correction was used when observed frequency in one cell was less than 10. Student's t-test was used to compare means of normally distributed data.

The primary clinical cause of death was determined according to the criteria of HEINS and BROWN [9], including:

1) Congenital anomalies, when the condition was believed to be incompatible with life or the dominant cause of death regardless of birth weight or other causes.
2) Birth weight $\leq$ 750 gm without congenital anomalies, regardless of other causes.
3) Respiratory distress syndrome (RDS), when onset of respiratory distress was within 1 hour of life, required assisted ventilation and had roentgenograms compatible with diagnosis of RDS.
4) Birth asphyxia, when Apgar scores were $\leq$ 5 at one and 5 minutes without stabilization.
5) Infection, when the clinical course was compatible with diagnosis and in most cases cultures or autopsy findings documented infection. Infection in our study was expanded to include viral and fungal infections as well as bacterial.
6) Intraventricular (IVH) and intracerebral hemorrhage (ICH), when diagnosed by ultrasonography and/or autopsy and when no other dominant disease such as RDS was present.
7) Others included myocardial infarction, airway obstruction, meconium ileus.

Autopsy cause of death did not include asphyxia as this was most often a clinical diagnosis.

3 Results

During the period of the study there were 31 234 live births of whom 398 had BW 500–1500 g. These VLBW infants represented 1.3% of all live births.

Survival (i. e. discharge from nursery) evaluated by BW categories of BW 500–750 g (group 1), 751–1000 g (group 2), 1001–1250 g (group 3) and 1251–1500 g (group 4) is shown on figure 1. Neonatal survival for the group as a whole was 58% and when anomalies were excluded 61%. After excluding anomalies, significant differences in survival were found between groups 1 and 2 ($p < 0.001$), between 2 and 3 ($p < 0.001$), and between groups 3 and 4 ($p < 0.001$).

Survival by gestational age category is shown in figure 2. Survival was significantly different between infants born < 26 weeks and 26–27 weeks ($p < 0.001$), between 26–27 and 28–29 weeks ($p < 0.01$) and between 30–31 and 32–33 weeks ($p < 0.05$). After 33 weeks gestation there were no differences in survival when successive GA categories were compared.

When GA and BW were combined, survival increased progressively with increase in BW and GA categories (table I). When successive BW/GA categories were compared, survival for infants with BW > 1000 g was not significantly affected by GA. For the group with BW 500–750 g survival was increased if GA was $\geq$ 28 weeks ($p < 0.01$). For the 751–1000 g BW group, survival was increased if GA was $\geq$ 26 weeks ($p < 0.05$).

3.1 Age at death

Seventy-nine percent of infants with BW 500–750 g died within the first 24 hours, while 51% of the 751–1000 g group and only 30% of the > 1000 g group died during the same period. Although the majority of infants died in the neonatal period, eleven or 6.6% died after the neonatal period. The 6 post neonatal deaths (PND) with BW $\leq$ 1000 g accounted for 5% of all nursery deaths in this BW category. However, the 5 PND with BW > 1000 g represented 17% of the deaths within this BW group.

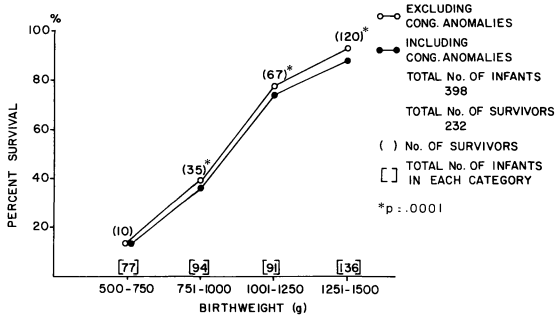

Figure 1. Survival of very low birth weight infants by birth weight categories with and without anomalies. Differences were found in all successive birth weight categories.

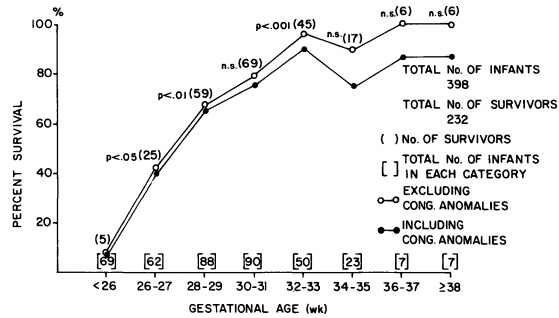

Figure 2. Survival of very low birth weight infants by gestational age categories with and without anomalies. When deaths due to anomalies were removed no differences were found in survival in successive GA categories after 31 weeks gestation.

Table I. Survival by birthweight/gestational age.

Gestational age (weeks)	Birthweight (grams)			
	500–750 n = 75 %	751–1000 n = 89 %	1000–1250 n = 87 %	1251–1500 n = 129 %
<26	7	7		
26–27	8	38**	77	67
28–29	71*	44	67	100
30–31	0	54	81	89
32–33		67	100	97
34–35		100	100	90
36–37				100
38–39				100

* Survival of 26–27 week GA compared with 28–29 week GA significant at $p < 0.01$
** Survival of < 26 week GA compared with 26–27 week GA significant at $p < 0.05$

In the infants who expired beyond the neonatal period, age of death ranged from 29 to 305 days with a median of 57 days. There were no differences in sex or racial distribution or in incidence of SGA when compared to the group as a whole. All of these PND infants had severe cardiopulmonary problems with hypo- and hypertension and/or symptomatic patent ductus arteriosus. They required ventilatory assistance for prolonged periods. Their nursery courses were very complicated. 45% and necrotizing enterocolitis, 55% had infection, 64% had seizures and 82% required one or more surgical procedures. Autopsy findings showed multiple organ system pathology.

3.2 Cause of death

Clinical causes of death were immaturity (BW < 750 g) 39%, RDS 17%, asphyxia 15%, anomalies 11%, IVH/ICH 9%, infection 5% and other 4%.

Major causes of death by birth weight category are shown in figure 3. Congenital anomalies causing death were found in 18 infants or 4.5% of the VLBW population. The incidence of lethal anomalies was similar throughout the four BW categories, however as would be expected the anomalies accounted for proportionately fewer deaths among the very tiny infants but were the major causes of death in infants

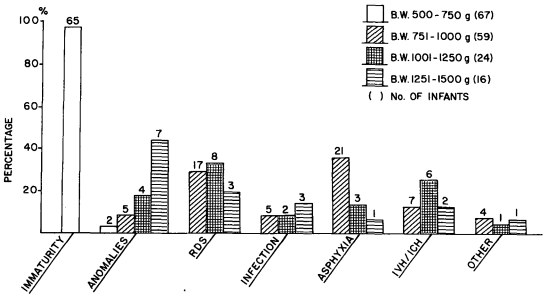

Figure 3. Cause of death by birthweight category. Anomalies were the major cause of death in infants with BW > 1250 g. Asphyxia and respiratory distress syndrome were the major cause of death in infants with BW 751 – 1000 g.

with BW > 1250 g, accounting for 44% of all deaths in this weight group. Eleven (61%) anomalies affected the central nervous system: 7 infants with anencephaly, 3 with encephalocele, and 1 with hydrocephaly. Three infants had dwarf syndrome [3, 13] with asphyxiation, 3 had trisomy 18, and 1 infant had severe gastroschesis. RDS was a major cause of death in all categories of birth weight > 750 g. In infants with BW 751 – 1000 g, RDS and asphyxia were major causes of death while in the 1001 – 1250 g weight group, RDS and IVH were major causes. The proportion of deaths due to infection was similar in all BW categories > 750 g.

Clinical cause of death was evaluated by gestational age category (table II). As expected, immaturity was found to be a major cause of death in infants < 28 weeks gestation. Congenital anomalies were a major cause of death after 31 weeks gestation. RDS and IVH were among major causes of death between 26 – 33 weeks gestation. Infection was a major cause of death > 33 weeks.

3.3 Autopsy cause of death

The overall autopsy rate was 68%. The predominant causes of death remained the same (with the exclusion of asphyxia) but incidence varied. In 45% of infants immaturity was found as cause of death, in 15% anomalies, in 14% RDS, in 8% infection, in 12% IVH/ICH and in 6% other. Immaturity was found to be a cause of death in 49% of infants with BW 751 – 1000 g. IVH/ICH was found with greatest frequency in infants 1001 – 1250 g. Under 30 weeks gestation immaturity was a major contributor. RDS, infection and congenital anomalies were major causes after 30 weeks.

3.4 Factors relating to outcome

The relationship of maternal demographic, medical and pregnancy problems, perinatal and nursery factors to outcome were studies.

Table II. Cause of death by gestational age.

Cause of death	Gestational age (weeks)					
	< 26 (n = 64) %	26 – 27 (n = 37) %	28 – 29 (n = 31) %	30 – 31 (n = 21) %	32 – 33 (n = 5) %	> 33 (n = 8) %
Immaturity	78	27	9	9		
Anomalies	3	5	7	14	60	75
RDS*	3	30	26	29	20	
Infection	2	8	7	9		25
Asphyxia	14	14	29	9		
IVH/ICH**		16	19	9	20	
Other			3	20		

* Respiratory distress syndrome
** Intraventricular/intracerebral hemorrhage

Medical problems of maternal substance abuse and cigarette smoking were evaluated. Pregnancy history factors evaluated included: lack of prenatal care, obstetrical history of prior stillbirths, neonatal deaths, low birth weight infants or two or more spontaneous abortions. Pregnancy problems evaluated included toxemia, eclampsia, bleeding, placenta previa, abruptio and anemia, ruptured membranes greater than 24 hours. Pregnancy illness evaluated included infections (including amnionitis), hypertension, diabetes, cardiac condition, treated psychiatric problems. Of the listed factors, only one was found to differ in that mothers of non-surviving infants had greater incidence of total lack of prenatal care than mothers of survivors ($p < 0.025$). No other icidence differences were found between survivors and non-survivors (table III).

Differences were found in mean BW and GA (table IV) but not in sex, incidence of small for gestational age (SGA) and multiple birth. More non-surviving infants had low 1 and 5 minute Apgars, required intubation at birth, had an initial nursery pH < 7.2, and had RDS than did survivors (table IV).

Since so few infants < 750 g survived, further comparisons were made on the two weight groups above 750 g, i.e. 751 – 1000 and 1001 – 1500 g. The incidence of pregnancy factors was similar in BW groups and showed no impact on survival in either BW categories (table V). Although the incidence of no prenatal care was higher in non-surviving infants of both BW categories, differences were not satistically significant. Sixty-five or 21% of the infants with BW ≥ 750 g were SGA. Demographic factors by BW category are shown in table VI. The incidence of SGA was higher in survivors of both BW categories but differences were not statistically significant. Differences in BW and GA were found in both BW categories with surviving infants being heavier and more mature.

The effect of the method of delivery on outcome was evaluated by comparing outcome of vaginal vertex with non-emergency C-section and with emergency C-section. Since it is the policy in our hospital to deliver VLBW breech infants by C-section, vaginal breech deliveries were excluded from analysis. Non-emergency C-section is defined as a C-Section done for inevitable

Table III. Relation of maternal demographic, health and pregnancy factors to outcome.

	Survivors (n = 232) %	Non-survivors (n = 148) %	p
Maternal age (years) < 18	12	11	ns
< 35	13	9	ns
Primigravida	25	22	ns
Gravidity > 4	21	18	ns
Race:			
Hispanic	76	76	ns
Black	16	14	ns
Pregnancy history**	27	18	ns
Medical problems***	9	12	ns
Pregnancy problems****	44	33	ns
Pregnancy illness*****	49	34	ns
ROM* > 24 hours	21	16	ns
No prenatal care	15	25	< 0.025

* Rupture of membranes
** No prenatal care, prior stillbirths and neonatal deaths, ≥ prior abortions, < BW infants
*** Substance abuse, excess smoking
**** Toxemia, eclampsia, bleeding, anemia, placenta previa
***** Infections, hypertension, diabetes, cardiac conditions

Table IV. Relation of infant demographic factors status at birth to outcome.

	Survivors (n = 232) %	Non-survivors (n = 148) %	p
Mean BW (grams)	1211 ± 222	823 ± 231	< 0.001
Mean GA (weeks)	30.4 ± 2.8	26.3 ± 2.9	< 0.001
Sex:			
Female	50	40	ns
Male	50	60	ns
SGA	24	18	ns
Multiple birth	12	16	ns
Apgar 1′ ≤ 4	39	85	< 0.01
Apgar 5′ ≤ 4	9	56	< 0.001
Intubation at birth	52	75	< 0.05
Initial pH < 7.2*	13	42	< 0.01
Asst. ventilation	67	73	ns
RDS**	47	77	< 0.01

* Blood gases done on 208 survivors, 104 non-survivors.
** 33 infants excluded who died shortly after birth.

Table V. Relation of maternal health and pregnancy factors to outcome by birthweight categories.

	Birthweight (grams)			
	751 – 1000		1001 – 1500	
	Survivors (n = 35) %	Non-survivors (n = 54) %	Survivors (n = 187) %	Non-survivors (n = 29) %
Pregnancy history	24	14	28	17
Medical problems	3	9	10	18
Pregnancy problems	56	33	40	38
Pregnancy illness	47	35	36	28
ROM > 24 hr	15	8	22	14
No prenatal care	18	26	14	25

Differences were not significant

delivery but prior to evidence of fetal distress. No differences in outcome were found by method of delivery in the larger weight group. In the infants with BW 751 – 1000 g non-emergency C-section had more favorable outcome than vaginal delivery ($p < 0.05$) (figure 4).

When perinatal factors were evaluated by the two weight groups, only the 5 minute low Apgar and low initial pH were significant in the infants with BW 751 – 1000 g. In the larger BW infants, low 1 and 5 minute Apgar, immediate intubation for resuscitation, low initial pH and RDS were found more often in non-surviving infants.

4 Discussion

The contribution of the VLBW infant to neonatal mortality is dependent upon the incidence of these births and on the incidence of survival of these infants. The significant impact of social, economic, racial and maternal factors on the incidence of birth of the VLBW infant is well accepted [5, 14, 16]. Less well accepted is the impact of these factors upon the survival of these infants. We have evaluated these factors in our hospital VLBW population to determine their impact on incidence and outcome. The racial background of women delivering at

Table VI. Relationship between infant demographic and perinatal factors with outcome by birthweight categories.

	Birthweight (grams)					
	751–1000			1001–1500		
	Survivors (n = 35) %	Non-survivors (n = 54) %	p	Survivors (n = 187) %	Non-survivors (n = 29) %	p
BW	987 ± 76	862 ± 76	< 0.05	1297 ± 141	1193 ± 145	< 0.01
GA	28.6 ± 2.6	27.1 ± 2.0	< 0.01	31.0 ± 2.6	29.4 ± 2.1	< 0.01
Female	54	35	ns	49	41	ns
Male	46	65	ns	51	59	ns
SGA	43	22	ns	20	7	ns
Apgar 1′ < 4	57	86	ns	34	69	< 0.05
Apgar 5′ < 4	6	49	< 0.01	8	24	< 0.05
Intubation at birth	89	89	ns	43	90	< 0.05
Initial ph < 7.2	11	42	< 0.05	12	31	< 0.05
Assist. ventilation	89	91	ns	61	97	ns
RDS	66	84*	ns	40	79	< 0.05

* Excluding 5 infants who died shortly after birth.

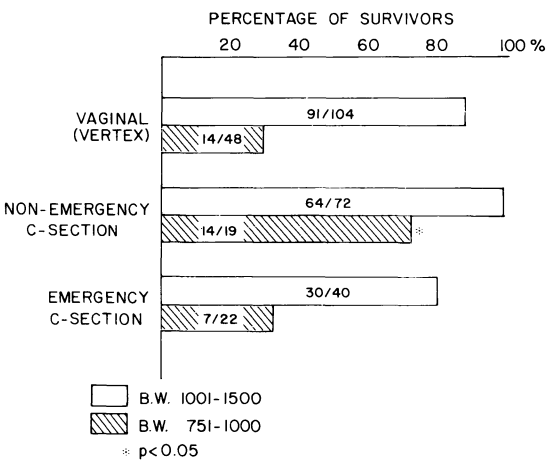

Figure 4. Relation of method of delivery to outcome. Infants with birth weight ≤ 1000 g delivered by non-emergency C-section survived more often than those delivered vaginally.

LAC/USC Medical Center has changed dramatically over the past 20 years from a low socioeconomic, predominantly black population to a low socioeconomic, predominantly Hispanic population. In addition to low socioeconomic status the hispanic population is largely Spanish speaking and immigrant with few or no community supports. Despite these population differences the incidence of VLBW infants has remained below 1.5% of all births during the period of population change. Although the VLBW infants constitute a small percentage of total births, they accounted for 72% of all neonatal deaths during the two year study period.

Nursery survival was not found to be related to socioeconomic, racial, maternal or prenatal factors studied. This is in agreement with the findings of Yu and Hollingsworth in their analysis of data from 55 infants weighing ≤ 1000 g [22]. Survival of infants with BW 500–1500 g was directly related to BW and GA. Maturity as measured by GA was more reliable than BW in determining outcome in those infants with BW ≤ 1000 g. The prenatal prediction of BW in the infant ≤ 1000 g has been accurate and useful in our center, while the prenatal prediction of maturity is often more difficult and less accurate. In infants with BW ≤ 1000 g, in addition to maturity, survival was determined by their condition at birth as measured by Apgar score. When these infants were delivered by elective C-section without evidence of acidosis or depression they had better survival in our nursery.

Whereas survival was influenced by weight in all BW categories, a BW of 1000 g seemed to be a critical weight above which survival was not dependent upon method of delivery. However, gestation continued to influence survival until > 31 weeks. Infants at or less than 26 weeks gestation had a much higher mortality than those above 26 weeks. From the morphological and functional developmental point of view this is to be expected e. g. the lung will not be functional in the human of less than 26 weeks [18]. Condition at birth and need for vigorous ventilatory support were determinants of outcome.

Of particular interest are those infants who expired in the nursery after the neonatal period. With increased capability of ventilatory support, infants who previously died soon after birth from cardiopulmonary problems now survive beyond 28 days of life. Neonatal mortality does not address this group which made up 6.6% of all the VLBW deaths in our center. HACK et al. [8] also found 14% of their VLBW infant died in the postneonatal period. Clearly this group of infants needs to be incorporated into the overall evaluated of VLBW infant outcome. The nursery course of these infants tends to be very complicated with multiple organ system involvement. This group, although small, represents a disproportionately high utilization of hospital resources. The severe protracted course with fetal outcome results in immeasurable anxiety, grief and disappointment for families and hospital staff. A decision to discontinue support for an infant where there is no reasonable hope for survival is very difficult for staff and family to make.

In summary, factors other than those in the perinatal and postnatal period do not significantly influence survival of VLBW infants. Gestational age more than birthweight appears to be the limiting factor. Although infants with BW below 1000 g delivered by elective C-section were found to have better survival in our study; nevertheless, their survival is more dependent on maturity than on birthweight. Condition of the infant at birth, prevention of asphyxia and acidosis, as well as rapid resuscitation and stabilization after birth would reduce mortality in these VLBW infants.

And finally, despite improved survival for smaller and smaller infants only the prevention of early delivery will greatly reduce the excessive morbidity and mortality and the enormous usage of hospital resources represented by this small but significant group of infants.

Summary

398 infants with birthweight (BW) 500–1500 g born from January 2 1982 to December 1983 were studied to determine incidence and survival rate by BW and gestational age (GA) categories and to determine causes of death and factors influencing mortality. 58% of the group survived. Factors other than those in the perinatal and postnatal period did not significantly influence survival. Infants with BW below 1000 g delivered by elective C-section had better survival than those delivered vaginally. Surival increased progressively with increasing BW and GA categories with GA more than BW being the limiting factor. Eleven (6.6%) of the deaths in the very low birth weight infants occurred during the nursery period after 28 days of age. These deaths would not have been addressed in the neonatal mortality.

Keywords: Gestational age, nursery survival, very low birth weight.

Zusammenfassung

Überlebensrate von Neugeborenen mit extrem niedrigem Geburtsgewicht

Unsere Studie umfaßt 398 Kinder mit einem Geburtsgewicht von 500–1500 g, die im Zeitraum Januar 1982 bis Dezember 1983 geboren wurden. Wir wollten bestimmen, wie das Geburtsgewicht und das Gestationsalter bzw. andere Faktoren die neonatale Mortalität beeinflussen. 58% des Kollektivs überlebten. Es zeigte sich, daß in der Neonatalphase die gleichen Risikofaktoren wie in der Perinatal- und Postnatalperiode die Überlebensrate beeinflußten. Kinder mit einem Geburtsgewicht unter 1000 g, die durch primäre Sectio entbunden

wurden, hatten eine größere Chance als vaginal entbundene Kinder. Mit zunehmendem Geburtsgewicht und Gestationsalter stieg die Überlebensrate, wobei dem Gestationsalter die größere Bedeutung zukam. 11 Todesfälle (6.6%) traten erst nach dem 28. Lebenstag auf, so daß sie eigentlich nicht mehr mit der neonatalen Mortalität erfaßt würden.

Schlüsselwörter: Extrem niedriges Geburtsgewicht, Gestationsalter, Überlebensrate.

Résumé

Facteurs affectant la survie en nursérie des enfants de très faible poids de naissance

On a étudié 398 enfants de poids de naissance (P. N.) compris entre 500 et 1500 g, nés entre janvier 1982 et décembre 1983, afin de déterminer, l'incidence et le taux de survie par P. N., les tranches d'âge gestationnel (A. G.), pour déterminer également les causes de mortalité et les facteurs influencant la mortalité.

58% du groupe ont survécu. Les autres facteurs que ceux des périodes périnatales et postnatales n'influencent pas significativement la survie. Les enfants de P. N. inférieur à 1000 g nés par césarienne ont une survie meilleure que ceux nés par voie basse. La survie s'élève progressivement avec l'augmentation du P. N. et des tranches d'A. G., l'A. G. étant le facteur limitant plus que le P. N. Onze (6,6%) des morts d'enfants de très faible poids de naissance sont survenues pendant la période de nursing après 28 jours de vie. Ces morts ne devraient pas faire partie de la mortalité néonatale.

Mots-clés: Age gestationnel, enfants de très faible poids de naissance, survie en nurserie.

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