Developmental Outcome of Nicu Graduate Weighing Less than 2500 Grams in A Tertiary Care Hospital

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Abstract

Background and objective: The early intervention programmes designed for low birth weight babies can be beneficial to improve the prognosis in terms of physical growth and neurodevelopmental outcome. The purpose of this study was to determine the factors influencing these, so that the low birth infants can be screened early for better outcome.

Methodology: 50 NICU graduates weighing less than 2500 grams were enrolled into the study. The various antenatal, perinatal and postnatal factor influencing growth and neurodevelopmental outcome were recorded in a predesigned performa. The outcome was measured at one year of age in terms of hearing by BERA at 6-8 weeks, physical growth by anthropometric measurements, neurodevelopment status by DASII, vision by ophthalmologist as per predesigned protocol.

Results: 26% of all NICU graduates were ELBW. Smallest one in present data was 750 grams and 26 weeks of gestation. The babies at a gestational age between 28-32 weeks were at increased risk for neonatal problems. Maternal disease was more consistently associated with ELBW babies though it was also common with VLBW babies. Respiratory Distress Syndrome was the most common problem faced in 44% of all babies. In ELBW population Necrotizing Enterocolitis also formed important risk. The developmental outcome measured showed delay in attainment of milestones especially in ELBW babies.

Interpretations and Conclusion: ELBW babies require much more intervention than VLBW babies. 92% of ELBW babies were given partial parentral nutrition, antibiotics and oxygen therapy as compared to 55.8% in VLBW group. Overall ELBW babies had delayed achievement of gross motor milestones than VLBW babies. In our study both the physical and neurological growth was satisfactory.

Key words: ELBW, NICU Graduate, Neurodevelopment, Physical, VLBW.

Introduction

With better understanding of physiology and pathology of low birth weight newborns and with the advent of fine technology people looking after such low birth weight newborns became more concerned about the long term outcome. Now tons of stationery is being used for the sole purpose of neurodevelopmental follow up of low birth weight babies. The neonatology has improved by leaps and bounds in last century and it is now becoming synonymous with the care of low birth weight babies. With early intervention programmes, problems of premature and low birth weight babies can be predicted early and natural history can be improved. Also, better understanding of neurophysiology has made physiotherapy a boon for such babies. LASER surgery for Retinopathy of prematurity and modern hearing aid and cochlear implants have limited sensory disabilities. However, the centre of gravity is now shifting towards intellectual outcome, judgment problems and learning disabilities. Thus with more and more efforts we are close to the dream of a "Smiling low birth weights".

The present study was undertaken to evaluate the antenatal, and perinatal factors and their correlation with physical and neurodevelopmental outcome at 1 year of age in low birth weight babies so that early screening of high risk infants is possible.

Material and Methods

Study Design: Prospective cohort study

Subjects: Inborn Low birth weight infants admitted to NICU of a tertiary care hospital.

Inclusion Criteria: All neonates weighing less than 2500 grams.

Exclusion criteria: Infants with major congenital anomalies

Sample size: 50 Low birth weight infants (< 2500grams)

Method of follow up: The neonate who were discharged from NICU were enrolled into the study after the verbal consent from the parents. The baseline data were recorded from the case sheets and maternal history was taken from the mother. These neonates were followed up as per predesigned proforma.

Follow up schedule:

Frequency of follow up;
<2000gms - Weekly x 1 month
2000 - 2500gms - Fortnightly x 1 month

Later – Monthly into 3 months, thereafter once in 3 months till 1 year**.**

At each visit, a comprehensive medical/ neurodevelopmental assessment was performed to detect physical and neurological deficit. This included anthropometric measures; general physical examination with assessment of overall age; neurological examination along with neuromotor and neurodevelopmental assessment. The gross/fine motor/ language/ social development screening was done as per Denver Development Screening test and Trivandrum Development Screening test. Amiel Tieson score was used to evaluate tone abnormalities. The infants were subjected to DQ assessment by DASII at one year of age.

1. Growth assessment for the corrected post-conceptual age was based on the national centre for health Statistics (NCHS) standards
2. The following terms are used to define the outcome parameters.
   a. Microcephaly i.e. head circumference more than 3 SD below the mean.
   b. ROP screening was done for babies less than 35 weeks/ <1700gms/ prolonged oxygen therapy and were followed up every month.
   c. Hearing impairment assessed by a specialist and BERA examination at 6-8 weeks.
3. Screening for Intraventricular hemorrhage was done for babies less than 32 weeks at day 3,7 and 30 of life. Ultrasonography and computerized tomography was used as diagnostic modality.
4. Hypoxic ischemic encephalopathy was defined according to the Sarnat staging and CT/ MRI scan.
5. Necrotizing enterocolitis was diagnosed by clinical, hematological and radiological findings.
6. Respiratory distress as respiratory rate of more than 60 with recession or grunting lasting for more than 4 hours duration.
7. Apnoea as a cessation of respiration for more than 20 sec or bradycardia or cyanosis.
8. Hypothermia as less than 35 degree centigrade of axillary temperature.
9. Hyperbilirubinimia as serum bilirubin of more than 15 mg/dl
10. Polycythemia as capillary hematocrit of more than 70%
11. Hypoglycemia as whole blood glucose of less than 40mg/dl during NICU stay
12. Septicemia was diagnosed based on the clinical presentation and course confirmed by positive blood culture.
13. Hypocalcemia by the estimation of serum calcium level < 7mg/dl or ionic calcium <3.5mg/dl
14. Persistent pulmonary Hypertension was diagnosed on the basis of clinical, arterial blood and 2-dimensional Echo
15. Chronic lung disease (CLD) was diagnosed by Oxygen dependency at least for 4 weeks or till 36 weeks of gestational age and radiological features.

Statistical Analysis: Data was analyzed using SPSS 16. Chi square test was used to analyze the association between various risk factors and neurodevelopmental outcome.

Results

A total of 800 deliveries took place during this period out of which 200 babies were low birth weight. 50 neonates admitted to NICU were enrolled in the study. All the subjects attended follow up clinic at tertiary care hospital.

Table 1: Base line variables (n=50)

Variable	n (%)
Sex (male)	23(46%)
Birth weight (mean+ 2SD)	1448 + 437 grams
Birth weight group	
<1000gms	13(26)
1000-1500gms	18(36)
1500-2500 gms	19(38)
Gestational age	
<28weeks	6(12)
28-32 weeks	18(36)
32-36 weeks	22(44)
Birth weight for gestational age group	
SGA	32(64)
AGA	18(36)

Table 2: Maternal risk factors

Variable	n (%)
Maternal education	
Graduate	34(68)
High school	15(30)
Senior secondary	1(2)
PIH	22(44)
Gestational DM	4(8)
Recurrent abortion	0
Antenatal steroid	2(4)
PPROM	2(4)
Febrile illness	1(2)
Oligohydraminos	2(4)
Polyhydraminos	2(4)
Others	2(4)

Table 3: Intrapartum/postpartum risk factors

Variable	n (%)
Fetal heart rate	
Bradycardia	15(30)
Tachycardia	20(40)
Normal	15(30)
APGAR 5 min	
3-6	13(26)
>6	37(74)

Table 4: Postnatal risk factor

Variable	n (%)
HIE	13(26)
RDS	22(44)
IVH	2(4)
Metabolic	6(12)
Sepsis	7(14)
NEC	1(2)

Table 5: Intervention done

Intervention	n (%)
Partial parenteral nutrition	36(72)
Antibiotics	37(74)
Oxygen therapy Fio2>30%	35(70)
CPAP	2(4)
Ventilation	15(30)
Phototherapy	3(6)
Exchange transfusion	0

Table 6: Growth parameters

Variable	n (%)
Weight (percentiles)	
$<5^{th}$ p	17(34)
5-25p	26(52)
25-50p	7(14)
Length(percentiles)	
$<5^{th}$ p	15(30)
5-25p	33(66)
25-50p	2(4)
Head circumference(percentile)	

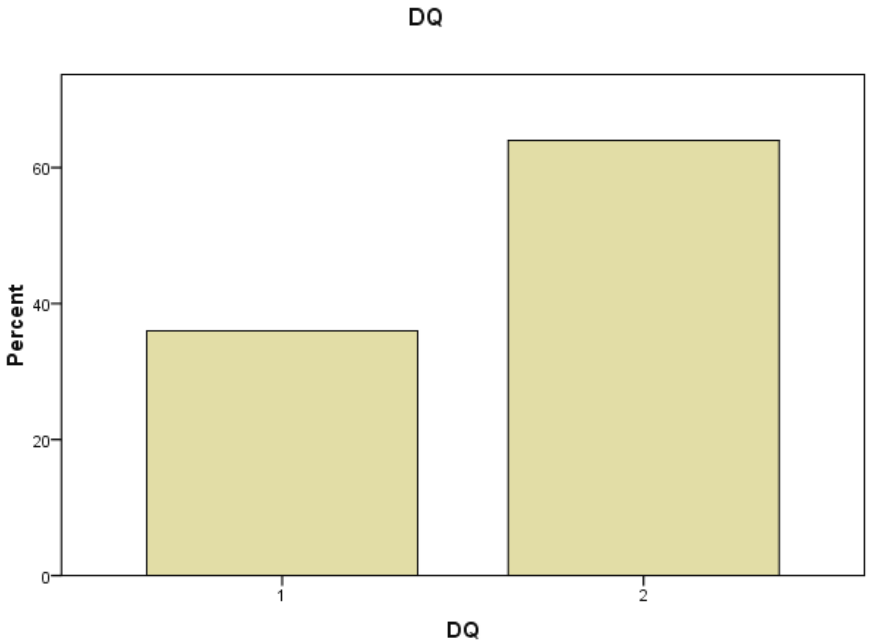
<5th p	8(16)
5-25p	42(84)
25-50p	0

Table 7: Developmental outcome at one year

Variable	n(%)
Gross motor delay	7(14)
Fine motor delay	6(12)
Language delay	12(24)
Social delay	4(8)
Vision impairment	16(32)
Hearing impairment	15(30)
Developmental Quotient(DQ)	18(36)

Table no 8: Factors affecting DQ at one year of age

Factors	n(%)	P value
Birth weight gp(SGA/AGA)	32(64)/18(36)	0.364
Maternal illness(PIH)	22(44)	0.457
HIE stage 2	13(26)	0.830
RDS	22(44)	0.522
IVH	2(4)	0.279
Metabolic	6(12)	0.885
Sepsis	7(14)	0.684
NEC	2(4)	0.674
APGAR 5min		0.664



DQ assessment at 1year
1. <2 SD
2. > 2SD

Discussion

Daily tons of papers are being written regarding low birth weight babies and their outcome. We've tried to relate few of those things with the present data. We've taken into account the immediate and late morbidities.

Maternal Disease: 74% of babies in our study group (37/50) have history of some maternal illness. ELBW population has higher incidence of maternal diseases i.e. 11/13 (84%) as compared to VLBW babies (20/43=46.5%). Of 37 mothers 22 had PIH and one had HTN + DM, so overall 50% babies had mothers with PIH. There were 34(68%) mother who were graduate and other were high school pass.

The major disability risk is increased by PIH[1]. There is an increased risk of febrile convulsions in childhood. There are number of risk factors and underlying causes of growth restriction, including pre eclampsia, infection, placental insufficiency, maternal smoking inadequate maternal nutrition, small maternal size and low maternal weight gain. However, in most cases, decreased rates of fetal growth as evidenced by an SGA outcome seem to be an adaptation to an inadequate nutrient supply during gestation. Growth restricted infants are characterized by fetal hypoglycemia, which acts to maintain the maternal fetal glucose concentration gradient and transport of glucose across placenta to fetus. Hypoglycemia also limits insulin secretion, initially potentiating fetal glucose production but subsequently resulting in increased protein breakdown, decreased protein accretion and thus slower growth.

Birth Asphyxia: The incidence of asphyxia reported from the developed countries varies from 1.8-6.7 per 1000 live births, whereas death or severe neurological impairment following asphyxia occurs in 0.5-1 per 1000 live births[2,3]. In developing countries, the incidence is much higher varying from 9.4-22 per 1000 live births As per NNPD report of 2000, perinatal asphyxia was present in 1.4% of all intra mural deaths and it was primary cause in 20% of all deaths. A study on 1000 cases of cerebral palsy from Northern India recorded asphyxia as underlying cause for CP in 45.3% of cases. In national collaborative perinatal project (NCPP) 21% of children with CP had significant markers of intrapartum asphyxia and CP had a significant association with APGAR scores of 0-3 at 10 minutes. Follow up study by Misra et al till 12 months of age in babies with low. APGAR score noted adverse neurodevelopmental outcome with 5 minute APGAR of less than 6. Children with low APGAR scores and cerebral depression who did not develop CP had an increased risk of developing a variety of neurodevelopmental impairments. The 10.7% incidence in the present data of low APGAR scores well correlates with the developing countries.

Birth weight and gestation: In our study 13 out of 50 babies were less than 1000gm i.e. ELBW. 18(36%) patients were appropriate for gestation (AGA) and rest 32 (64%) were small for gestation (SGA). This is in contrast with western countries where AGA comprises major part of VLBW and ELBW babies[4,5].

In Indian context 30% of all babies born are low birth weight, two third of them are growth retarded i.e. SGA. The western studies show significantly more subtle neurological dysfunction in form of lower intelligence scores, motor incompetence and behavioral difficulties. The longitudinal study done at Pune by Pandit & Chaudhary revealed poor visuomotor skills, reading and writing difficulties in 21.5% similar to observations of Saigal et al from Canada where 15-20 percent had these problems. In the present data 3 children had these problems (5.4%). The lower incidence might be due to small number of patients in data. The preterm SGA fared worst because of double jeopardy of prematurity and growth retardation.

Neonatal Problems

Respiratory distress syndrome (RDS): In present study, ELBW had increased risk of development of RDS. Of all the 50 babies 22(44%) had RDS. The antenatal steroid was given to 9 mothers. In other words 60% babies who developed RDS had not received antenatal steroids. This indicates antenatal steroids had a protective role against development of RDS[6,7]. In US 50% of babies between 26-28 weeks and 20-30% between 30-32 weeks developed RDS. In India overall incidence is 10-15%. The overall incidence in our study 44% is slightly higher than general Indian standard.

In present data 4% babies were put to CPAP, while 30% babies were ventilated. RDS was the commonest indication for ventilation in present study as reported by Reynolds et al. 2 babies (13%) were ventilated in view of deterioration after suspected sepsis. This is quite less compared to higher incidence noted by Krishnan et al (30%) and Shukla et al (29%).

Intra ventricular Hemorrhage (IVH): We had only two case of IVH (Stage II) (4%) in our study. This was the smallest baby in our study with birth weight 750 grams and 29 week gestational age. Mother had PIH & antenatal steroids given. Baby was ventilated for RDS, received brufen for PDA. Probably these multiple factors contributed to development of IVH[8]. In this case protective role of antenatal steroids was not seen.

Incidence of IVH is 35-40% in newborns with birth weight less than 1500 grams or gestational age less than 35 weeks. IVH increases inversely with GA and 50% babies<1500 grams have IVH. By gestational age, it is 75% in 24-25 week, 67% in 26-27 weeks, 52% in 28-29 weeks, 41% in 30-31 weeks and 26% in 32 weeks. We had only two babies with IVH 29 week GA i.e. out of 4 babies between 28-30 weeks. This was probably a result of ventilation, antenatal steroids, minimal handling of babies and better nursing care.

Metabolic Problems: The overall incidence of metabolic problem was 6(12%) in our study. Only one ELBW baby suffered hypoglycemia (1.9% of study

group, 7.7% of ELBW group). This was the same baby discussed in IVH section. Thus this baby had risk factors of being born to mother with PIH, ELBW extreme prematurity and stressful interventions like ventilations.

The incidence of hypoglycemia in SGA babies is 14.7% and in preterm SGA babies it is as high as 67%[9]. In our study it was 2.6% in preterm SGA (1/38). This low incidence can be related to meticulous screening and maintenance of proper glucose infusion rate (GIR). Maternal factors play important role in hypoglycemia as discussed earlier.

Suspected Sepsis: Stoll and colleagues showed that up to 25% VLBW babies showed positive blood culture. St Geme and colleagues showed four fold increase in sepsis with PROM> 24 hrs. 4 of our babies with suspected sepsis had PROM>24 hr. Thus incidence of suspected sepsis was increased to 20% in mothers with PROM> 24 hr (3/15) compared to 2.4%(1/41) in mothers without PROM in our study. The overall incidence was 14% in our study. This is comparable to 15.2% incidence found world wide[10,11]. The slight increase can be explained by the other risk factors like prematurity, birth asphyxia & interventions[12,13] required in these babies and also the small number of patients in present data.

Necrotising Enterocolitis: Currently the incidence of NEC has increased in most centers and has emerged as most common gastrointestinal emergency in neonatolology affecting 2000- 4000 babies in USA each year.[14] Of these 10% -50% die resulting in 1000 deaths per year. Overall incidence of NEC ranges from 3 -7%. Glaucy et al reported 10% incidence of NEC in < 1500 gram birth weight group. Our study had one baby with NEC. This baby had risk factors like prematurity, SGA, PIH mother, Umbilical catheterization and Birth asphyxia. NEC was suspected in babies with increase resistance to umbilical blood flow, adverse S/D ratio on umbilical Doppler study and reversal of diastolic flow. Odds ratio for NEC is increased with APH, PROM > 36 hr and 5 minutes APGAR scores below 7.

Developmental Outcomes

Growth: In our study growth of all the babies was equated as percentile of NCHS charts. Both weight and height were affected in 1st year of life. About 34% of babies had weight and height < 5th percentile. Head circumference was the 1st parameter to be achieved.

Ross and colleagues had shown that although as group VLBW babies were smaller than their peers at age 3 yrs, but by age 7 yrs they achieved between 46.9% and 48.5% of mean growth percentile. The collaborative infant health development programme performed longitudinal growth measurements; this states that there was little catch up growth in 1st yr of life in any parameters. Kitchen& colleagues followed VLBW infants to age 8yrs with similar findings. This correlates well with our study. In the present data 60% of pre term / AGA babies less than 1 year (3/5) achieved 5-25 percentile of both height and weight compared to only one (11%) of preterm / SGA group. 78% of preterm / SGA in less than one year group were below 5th percentile of NCHS charts for weight and height as compared to 40% of pre term / AGA. In contrast 60% of preterm/ SGA remained below 5th percentile for head circumference, whereas 30% of pre term / AGA had achieved head circumference of 5-25 percentile below 1 year. Thus with increase in age both groups achieved similar head circumference but lagged behind their peers.

Studies of the body composition of SGA infants at birth have shown that lean body mass and bone mineral content are reduced compared to their AGA counterparts. However much like young children after an episode of starvation or illness that cause growth falter, SGA infants should have potential to catch up in growth outside the restrictive intrauterine environment depending on extent of retardation. For example, the growth restriction associated with maternal smoking during pregnancy seems to be largely overcome within 1st year of life.

Unlike SGA infants born at term, preterm/SGA infants show limited or no catch up growth at least through 1st 12 months of life. This correlates well with our data.

Visual System: This includes ROP and myopia of prematurity[15]. In our study ROP and refractive error was noted in 16 babies (32%) during NICU course. After discharge 6 of 7 (86%) ROP were grade I and one (14%) was grade II ROP. All these six cases of grade I ROP resolved without any active treatment. All six cases were noted in ELBW babies i.e. Incidence of ROP in ELBW was 46.2% and in VLBW, it was 2.3%.

The only baby with grade II ROP in both eyes was 26 week / AGA with birth weight 1.1 kg. Mother had placenta parevia, baby had not received antenatal steroids. He had RDS, for which he was ventilated. Later due to apnea of prematurity he had prolonged course of CPAP and ventilation till day 28 of life. He required laser therapy for ROP, which regressed after that.

Multicentre NIH trial found the incidence of ROP as 66% in high risk population. Study done in St. John Medical College and Hospital, Bangalore showed 46% as overall incidence of ROP, while Maheshwari with Kumar et al reported incidence of 21% in study done in Delhi The incidence of ROP in India varies from 20-57% is < 1500 grams In developed nations it is 38-52%. Our incidence of 13.5% is still lower. The incidence of is <1000 gm is 73.3-90%, which is also higher than incidence in present study (46.2% in< 1000gm)

Regression occurred in 6 of 7 i.e. 85.7% patients in our study. This finding correlated with the natural history of ROP. 3 out of 7 babies with ROP had developer refractive error i.e. 42.9%. Philips and Robinson et al reported late sequalae like refractory errors & blindness seen in 30-50% of babies who had ROP. This is well correlated in our study.

15 babies of study group i.e. 28.8% had error of refraction. Of these 6 babies were ELBW and 9 were VLBW. Thus 46.2% of ELBW babies and 20% of VLBW babies had some error of refraction error. Thus in our study ELBW babies were at increased risk of developing both ROP and errors of refraction.

Also severe disease developed in extremely pre mature baby with prolonged ventilatory requirement. Thus this baby had both major risk factors.

ROP has become amongst the most important cause of blindness in developed world and forth-important cause in developing countries after eye injuries, infections and Vitamin A deficiency. Retinal causes of visual loss present during infancy including retinal dystrophies & ROP account for 20 -30% of the childhood blindness in South Asia, Latin America & Europe. 1% of ELBW in USA are blind.

Hearing Impairment: In our study incidence of hearing impairment was 30% (ie 15/50). The incidence in VLBW and ELBW was 4.7% and 7.7%. This incidence was more than those found in USA[16] especially in VLBW. The ELBW baby with hearing impairment was 31 week/ SGA with birth weight 940grams and presented with suspected NEC and birth asphyxia.

Of VLBW babies one was 31 week/SGA , second 28 week/ AGA and last one was one of twin 32 week/ SGA. Last One had birth asphyxia, RDS suspected sepsis.

Neurodevelopment outcome: Gross motor delay was common problem noted with frequency of 14% overall. It is more common in ELBW (15.40%) than VLBW (9.3%). The fine motor skill delay was 15.4% in ELBW while 9.3% in VLBW. This data correlates well with developed countries. Mc Cormice et al reported neurodevelopmental sequelae in17% VLBW babies. 14% rate was reported by Scottish study. In the longitudinal study done at Kalawati Saran hospital Delhi 7% had developmental delay. Similar findings were noted by Bhargava et al[17].

Verbal skills were achieved late, more commonly in ELBW group where incidence was 30.8% as compared to VLBW group (18.9%). Of all 12 cases of speech delay (21.1%) only 3 were associated with hearing impairment. Thus 25% of patients with speech delay had hearing impairment .Thus in our study ELBW babies presented with hearing impairment and speech disorders. The similar findings were noted by Saigal et al. However, most children picked up with their peers due to early interventions. This signifies role of early intervention. Only one baby had hearing impairment but was not using hearing aid. Studies carried out by Laura et al showed that a change in cognitive functions occurred over time in those born preterm[18]. Singer et al showed that 20-40% of VLBW infants had receptive language delay at toddlers and young children.

The incidence of cerebral palsy was 1.8% in our study. This can be explained by a small size of the data, less ex-utero transfer, proper & timely resuscitation, low incidence of complications in neonatal period like hypoglycemia & IVH. Also early intervention has played the key role in improving outcome. Globally incidence of CP is between 6-10%. Praveen et al showed incidence of 5% at <33 weeks gestation & 6 % at 33-36 weeks gestation. Lorenze et al showed CP in 12% of <26 weeks and 85 of < 800 grams survivor[19]. The most common disability in that study was mental retardation, found in 14% of < 26 weeks & <800 grams survivors. In Pune low birth weight study by Chaudhary & Pandit founded mental retardation in 5% and CP in 4.8%, however their subjects were low risk than many of the western studies[53].

In the present study Chi Square test was used as an analytical test to study various factors (antenatal/perinatal) which influence the developmental outcome but due to small sample size the definitive correlation was not established. However, it is clear that proper neonatal care and early intervention in these low birth weight neonate has changed the outcome.

Conclusion

The following conclusions were drawn from study:

1. The various antenatal and perinatal risk factors had not shown significant correlation with developmental outcome at one year of age.
2. This could be due to the small sample size and short term follow up of low birth weight babies. Perhaps a larger sample size and long term follow up will yield more conclusive data.

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