

NEUROLOGIC SEQUELAE IN HIGH RISK INFANTS- A THREE YEAR FOLLOW UP

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Objective: To determine the neurologic sequelae in high risk infants. **Design:** A three year longitudinal follow up. **Setting:** Inborn and outborn infants discharged from the Neonatal Special Care Unit (NSCU) of a referral hospital. **Methods:** High risk infants were identified for follow up using predetermined risk criteria. A detailed neurodevelopmental examination was done 3 monthly in the first year and 6 monthly subsequently. The Amiel-Tison Method, Bayley Scales of Infant Development and Raval's Scale for social maturity were used. EEG was done in children with seizures. Hearing and ophthalmic assessments were done at 6 months. **Results:** Three hundred and thirty six high risk infants and 70 normal control infants came for regular follow up. Out of these, 16 (4.8%) had cerebral palsy and 11 had associated mental retardation. Six other children had mental retardation without motor problems. None of the children in the control group had any neurological problems. Sensorineural hearing loss was present in 5 (1.5%) children while 1 subject had cortical blindness. Three children with cerebral palsy had infantile myoclonus, nine had generalized seizures and one child had a focal seizure. The incidence of seizure disorders was 3.9%. **Conclusions:** The incidence of major handicap in our study was low. Many of the risk factors which caused adverse outcome could have been prevented by good antenatal and perinatal care.

Key words: Neurologic sequelae, High risk infant, Cerebral palsy, Neurodevelopmental follow up.

THERE has been a marked improvement in the survival of "high risk" infants in the past two decades(1). In fact, neonates are surviving after insults which were previously thought to be fatal(2). However, it would be of interest to document if mortality is being converted into morbidity. There are many studies in the Western literature on long term neurodevelopmental follow up of high risk infants(3-5) who are considerably different from those in our setup. They are basically extremely premature with very low birth weights, but appropriate for gestational age, and have survived due to hi-tech intensive care (6).

We are still battling with problems like birth asphyxia, hyper-bilirubinemia, septicemia and a large group of our low birth weight babies are small for gestational age. This longitudinal study was undertaken to determine the neurologic sequelae in the so called "graduates" of the Neonatal Special Care Unit (NSCU).

Subjects and Methods

This prospective study started in October 1987 and ended in April 1992. The enrollment of the study sample was done in the initial 18 month period. Infants

charged from the Neonatal Special Care Unit (NSCU) of KEM Hospital, Pune, were identified for follow up using predetermined selection criteria. Ours is a referral unit and admits both inborn and out born neonates. The following risk criteria were used for selection: (i) Gestation less than 37 weeks(7); (ii) Birth weight less than 2000 g. The low birth weight babies were further classified into AGA and SGA(8); (iii) Birth asphyxia, namely, Apgar less than 5 at 5 minutes. Hypoxic ischemic encephalopathy was classified according to Sarnat staging(9); (iv) Septicemia or meningitis; (v) Hyperbilirubinemia, namely, serum bilirubin level more than 12 mg/dl in preterms and more than 15 mg/dl in full terms; (vi) Apnea; (vii) Seizures; (viii) Intraventricular hemorrhage on ultrasonography of the brain; and (ix) Respiratory distress due to underlying lung problems like hyaline membrane disease, meconium aspiration syndrome, *etc.* The infants were identified for follow up if they had one or more of these risk factors. Infants with congenital anomalies were excluded. At the time of discharge, they were given a special High Risk (HR) card. The importance of a regular follow up was explained to the parents and especially to the paternal grandmother who is an important decision maker in many families. Since many infants lived in far off places, financial assistance for transport was given if the family was poor.

High Risk Clinic (HRC)

This special clinic was held twice a week. It was run by a multidisciplinary team of neonatologist, social worker, psychologist and occupational therapist, with the neonatologist acting as the chief coordinator. The clinic fulfilled the following functions: (i) Primary Care; (ii) Immunizations; (iii) Neurodevelopmental assessments; and (iv) Referrals to other

departments like ENT (for BERA), and Ophthalmology. All these assessments were made to coincide with the HRC visit. All these facilities were available under one roof in our TDH Rehabilitation Centre. The parents were given a special sheet for recording intercurrent illnesses which was to be filled by the doctor, if the child took treatment elsewhere.

A. Neurodevelopmental Assessments

Since this was an "in depth study", neurodevelopment was assessed using 3 different methods (*Table I*). Corrected age was used in preterm infants.

I. Combined, Amiel-Tison Method and Occupational Therapists' (AT OT) Method.

A combined neurological assessment was done by the neonatologist and occupational therapist (OT). The neonatologist used the method described by Amiel-Tison(10), while the therapist acted as the second observer. The OT tested several additional features based on the Ayres Bobath method(11), which are important for giving therapy. The combined assessment did away with duplication of effort, saved time and early intervention could be started immediately, whenever necessary. The presence of a second observer increased the reliability of the assessment.

II. Bayley Scales of Infant Development (BSID)

The infants were tested by using the Baroda Norms(12) and a mental or motor quotient below 70 was considered as retardation. Only those high risk children who had at least 2 testings in the first year and two subsequently are included in this analysis.

III. Raval's Scale of Social Maturity(13)

The social maturity of the child was estimated by interviewing the mother or

TABLE I—Methods of Assessment

Assessment tool	Tester	Area assessed	Age of Testing (months)	Setting
1. Combined Amiel Tison and Ayres & Bobath	Neonatologist and Occupational Therapist	Neurological assessment and Therapy oriented assessment	3, 6, 9, & 12	High Risk Clinic
2. Bayley Scales of infant development	Two Psychologists	Psychomotor development	3, 6, 9, 12, 18, 24 & 30	Sound proof room with one way mirror
3. Raval's Scales of social maturity	Interview of caretaker by psychologist	Social maturity Important for CP & MR infants	3, 6, 9, 12, 18, 24 & 30	Development clinic
4. Hearing assessment				
(a) Audiometry	Audiologist	Screening test for hearing	6	Free field audiometry room
(b) BERA	Audiologist	Confirmation of hearing loss	6	ENT Department
5. Ophthalmological assessment	Ophthalmologist	Examination of anterior chamber retina & fundus	6	Ophthalmology Department

caretaker. The interview was different for rural and urban mothers. This interview was done after the BSID testing and was particularly useful in children with cerebral palsy whose mental development could not be assessed accurately on BSID due to their motor handicap.

A simple stimulation programme was explained to all mothers at the end of each visit.

B. Neurosensory Assessment

1. Hearing Assessment

An audiometry was done at 6 months using a 700 MK II audiometer with a free field system in a sound proof room. The testing was carried out at three levels using gross sounds, pure tones and verbal sounds

Turning towards the sound was the expected reaction, which was observed by two observers. Since we did not have facilities for brainstem evoked response audiometry (BERA) at that time, infants were referred elsewhere. Only those children who did not give a satisfactory response on free field audiometry or those who were considered high risk for deafness, were referred for BERA.

2. Ophthalmological Assessment

An ophthalmic check up was done at 6 months by the Consultant Ophthalmologist. This consisted of examination of the anterior chamber, retina and fundus.

If the 6 months appointment was missed, the examination was done at a later convenient date.

C. Information About Family, Parents and Environment

The home environment in which the child was growing up, the socio-economic status⁽¹⁴⁾ and the educational level of the parents and other family members was estimated by interviewing the parents using a standard protocol. This was confirmed by the social worker by making a home visit.

The whole team interacted with the family right from the time the neonate was admitted in the NSCU. This established a close rapport which was very important for this long follow up. If the children needed hospitalization, they were admitted under the care of the same consultants in the children's ward. The social workers were the key figure for ensuring regular attendance for so many assessments. A letter was sent 7 days prior to the appointment and a home visit was made if the appointment was missed.

Full term normal neonates with a normal antenatal, natal and postnatal history, weighing more than 2500 g were enrolled as controls. They were followed with the same protocol as HR infants.

Records

All records were entered into a specially prepared HRC file. Data was processed and analysed on IBM compatible PC/XT using Epi-Info.

Results

Four hundred and twenty five infants were enrolled in the study. When the infants did not come on the day of appointment, a home visit was made. Twenty one babies could not be traced as their parents belonged to a migrant population. Nineteen children lived in far off places and

could not come for regular visits. However, they kept in touch and visited us whenever they were in the city. The drop out rate was 9%. Ten mothers from the high socio-economic group opted to go to private pediatricians, but we insisted that they visit us at least once a year. One child developed tubercular meningitis at one year and was excluded from the study. Thirty eight babies died during the study period. This drop out is not likely to introduce any bias in the results because their profiles with respect to birth weight, gestation, sex ratio and other risk factors did not differ significantly from the rest of the sample. This analysis is restricted to 336 infants who had at least two assessments six months apart, in the first year and two more subsequently. Out of 86 controls that were enrolled, 70 had regular attendance. The frequency distribution of the HR infants according to their birth weight and gestational age is shown in *Table II*. Two hundred and one infants were males and one hundred and thirty five were females. Two hundred and fifty eight infants (74%) weighed less than 2000 g, whereas 109 (32.4%) weighed less than 1500 g. Sixty two per cent of the cohort was preterm. Out of the 128 full term infants, 70 (54.6%) were SGA. Out of the 208 preterm, 121 (57.6%) were SGA and 42% were AGA.

There were several additional risk factors in these neonates, in fact some had two or three other risk factors. Birth asphyxia was present in 32 (9.5%) neonates while 47 (13.9%) had hyperbilirubinemia. Septicemia/meningitis with positive cultures was diagnosed in 61 (18%) neonates. Forty two infants (12.5%) had seizures in the neonatal period whereas 40 had apneic spells. Intraventricular hemorrhage was diagnosed in eighteen neonates. Twenty six neonates had respiratory distress due to lung diseases.

TABLE II—Birth Weight and Gestation of High Risk Infants

Birth weight (g)	n	%	Gestation (weeks)	n	%
≥ 2500	58	17.3	≥ 37	128	38.0
2001 – 2499	29	8.6	35 – 36	84	25.2
1751 – 2000	44	13.0	33 – 34	81	24.2
1501 – 1750	93	27.6	31 – 32	36	10.7
1251 – 1500	73	21.6	29 – 30	6	1.7
1001 – 1250	33	9.8	≤ 28	1	0.2
≥ 1000	6	1.7			
Total	336			336	

Full term SGA = 70 (54.6%); Preterm SGA = 121 (57.6%)

Cerebral Palsy and Mental Retardation (CP/MR)

The diagnosis of cerebral palsy was made in 16 children, out of which 15 were out born and one was inborn. All these children had motor quotients well below 70 on the Bayley Scales. Eleven of these children had associated mental retardation with mental quotients below 60. One child with birth asphyxia (Sarnat Stage IIB) had profound mental retardation. The Raval's Social maturity score was particularly useful in assessing the mental development of these children with motor handicaps.

Spastic quadriplegia was the commonest type of CP and was present in 8 children. The incidence of CP in our study was 4.8%. A detailed analysis of the risk factors and associated sequelae in these children is shown in Table III. Hyperbilirubinemia with serum bilirubins above 20 mg/dl were present in 5 newborns, four of these had blood group incompatibility. All these infants were out born and were referred late to us. Birth asphyxia with consequent hypoxic ischemic encephalopathy (Sarnat stages II and III) was present in 4 children. Two infants had septicemia with positive

blood cultures, whereas 4 had probable sepsis.

Mental retardation without associated motor handicap was present in 6 children. Three of these children were preterm and three were full term. Five were small for gestational age. Three had septicemia (2 *klebsiella* and 1 *pseudomonas*), one had hyperbilirubinemia with ABO incompatibility and one had birth asphyxia (Sarnat IIB). Only one preterm SGA infant had no additional risk factors. In all, 17 infants had mental retardation, giving an incidence of 5% in our cohort. Out of the 191 SGA babies, 13 (6.8%) had major neurologic sequelae in the form of CP and/or MR whereas the incidence was 6.2% in the AGA group. The incidence was 6.7%, 5.0% and 7.3% in our preterm, LBW and VLBW groups, respectively. None of the 70 control children had any neurological problems.

Seizure Disorders

Seizures were present in 22 children. Nine children had febrile seizures with normal EEGs. Ten children had unprovoked seizures, 9 had generalized tonic-clonic seizures and one had focal seizures.

TABLE III—Neonatal Problems and Other Sequelae in CP Children

S.No.	Type of CP	Gestation	Wt. for gestation	Other neonatal problems	Other Sequelae
1.	Athetoid	FT	AGA	Hyperbilirubinemia Rh incompatibility Max. serum bil. 22 mg/dl	Deafness Mental retardation
2.	Athetoid	FT	AGA	Hyperbilirubinemia AO incompatibility Max. serum bil. 32 mg/dl	Mental retardation
3.	Athetoid	FT	SGA	Hyperbilirubinemia BO incompatibility Max. serum bil. 31 mg/dl	Mental retardation
4.	Athetoid	PT	SGA VLBW	Probable sepsis Hyperbilirubinemia Max. serum bil. 20 mg/dl	Mental retardation
5.	Spastic Quadriplegia	FT	AGA	Birth asphyxia Sarnat stage IIB	—
6.	Spastic quadriplegia	FT	AGA	Birth asphyxia Sarnat stage III	—
7.	Spastic quadriplegia	FT	AGA	Birth asphyxia Sarnat stage III	Mental retardation Myoclonus, blindness
8.	Spastic quadriplegia	FT	SGA VLBW	Birth asphyxia Sarnat stage II B	Profound mental retardation
9.	Spastic quadriplegia	PT	AGA	Septicemia (<i>pseudo-</i> <i>monas</i>), apnea, seizures, HMD, IVH, hydrocephalus	Mental retardation Myoclonus
10.	Spastic quadriplegia	PT	AGA VLBW	Probable sepsis	Mental retardation Myoclonus
11.	Spastic quadriplegia	PT	SGA	—	Mental retardation Generalized seizures
12.	Spastic quadriplegia	PT	SGA VLBW	Probable sepsis	Mental retardation Generalized seizures
13.	Right hemiplegia	PT	SGA VLBW	Seizures Probable sepsis	Mental retardation Microcephaly
14.	Right hemiplegia	PT	AGA	Septicemia (<i>Salmonella</i>), apnea	Generalized seizures
15.	Spastic diplegia	FT	AGA	Hyperbilirubinemia Max. serum bil. 27, apnea	Generalized seizures
16.	Spastic diplegia	PT	SGA VLBW	—	—

FT – Full term. PT – Preterm; AGA – Appropriate for gestational age; SGA – Small for gestational age; VLBW – Very low birth weight; HMD – Hyaline membrane disease; IVH – Intraventricular hemorrhage; bil. – bilirubin

All ten children had EEG changes suggestive of epilepsy. Three children with CP had infantile myoclonus. EEG showed typical hypsarrhythmia. One child who migrated to the US was reported to have developed epilepsy by her Pediatrician.

Hearing Assessment

Free field audiometry was done as a screening test on all infants. One hundred and three infants had BERA. Hearing impairment was suspected on audiometry in four children. This was confirmed on BERA. All these 4 -children had moderate to profound hearing loss and were advised a hearing aid. One child had only high frequency hearing loss. The incidence of sensorineural hearing loss in this study was 1.5%.

Ophthalmological Examination

One child was found to have cortical blindness. This was confirmed by doing visual evoked potential (VEP) examination.

All the neurologic sequelae are summed up in *Table IV*. None of the controls had seizures during the study period. Their hearing and ophthalmic checkup was normal.

Discussion

This report of a three year follow up is part of a long term project entitled "An indepth longitudinal study of development of high risk newborns". Some aspects of this study have been published earlier(15, 16). This communication deals only with the neurologic sequelae diagnosed during a three year follow up.

Cerebral palsy and mental retardation are two major handicaps dreaded by physicians caring for high risk infants. The incidence of cerebral palsy in our study was 4.8% and that of mental retardation 5%.

In 1975, Fitzhardinge reported 6% incidence of cerebral palsy(17). The overall incidence of CP for the preterm infant population was reported to be 3 to 6% in contrast to 0.15% in the general population(18). In 1984, Michelsson reported an incidence of 6% in VLBW infants from Finland(5). The incidence of CP in our 109 VLBW infants was 5.5%. However, none of our babies were ventilated and only 6 infants weighed less than 1000 g in our cohort. The Scottish low birth weight study (weight less than 1750 g) reported an incidence of 7%(19).

Thirteen children (3.9%) were diagnosed to have a seizure disorder. The incidence of seizure disorders is comparable to that reported by Kitchen(4). The children with febrile seizures need a longer follow up to see if they outgrow them. Moderate to severe sensorineural hearing loss was present in 4 children and they have been advised hearing aids. One child with hyperbilirubinemia was otherwise normal, except for high frequency hearing loss.

TABLE IV- *Neurologic Sequelae in 336 High Risk Infants (Preterm-208, LBW-258, VLBW-109)*

Sequelae	n	%
Cerebral Palsy	16	4.8
Spastic quadriplegia	8	2.4
Athetoid	4	1.2
Spastic diplegia	2	0.6
Hemiplegia	2	0.6
Mental Retardation	17	5.0
With Cerebral Palsy	11	3.3
Without Cerebral Palsy	6	1.8
Seizure Disorders	13	3.9
Generalized	9	2.7
Focal	1	0.3
Infantile myoclonus	3	0.9
Hearing Impairment	5	1.5
Sensorineural Deafness	4	1.2
Only high frequency loss	1	0.3
Cortical blindness	1	0.3

Kitchen(4) also reports that 3.8% of their 169 VLBW infants had severe visual handicap. We had only one child with cortical blindness. Unlike his study, we had no children with visual handicap due to cicatricial retrolental fibroplasia.

It is apparent that most of the risk factors in children with major handicaps are preventable. Awareness, better monitoring during the antenatal and perinatal period could certainly prevent hyperbilirubinemia, birth asphyxia, septicemia and intrauterine growth retardation.

Hagberg and Hagberg(20) talk about the "Changing panorama of cerebral palsy in Sweden" over a 20 year period. Changing trends in incidence ran parallel with a steadily progressive decline in perinatal mortality in their study. We have made a beginning and presented baseline data for the nineteen eighties in India, the outcome may be better in years to come. It is not enough to be content with the low incidence of major handicaps. Neurologic dysfunction may only become apparent in the so called "normal" high risk infants in the form of learning problems, when they join school(21). A much longer follow up is desirable in this context.

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NOTES AND NEWS

ACUTE FLACCID PARALYSIS SURVEILLANCE

IAP members are requested to immediately report to the District Immunization Officer whenever they see a patient with acute flaccid paralysis. Further action will be undertaken through the existing governmental system.