

Prognostic Indicators of Developmental Outcome in Preterm Infants

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Background: Long term follow up studies had revealed a high frequency of developmental disturbances in preterm survivors of neonatal intensive care.

Objective: To determine risk factors associated with adverse developmental outcome at 2-5 years in preterm infants.

Design: Retrospective Study.

Setting: Pediatric Department, Salmaniya Medical Complex.

Method: One hundred and fourteen children, aged 2-5 years, born prematurely at the gestational age of less than 37 weeks were included in the study. The children were grouped into three categories: 1. Normal development. 2. Mild to moderate impairment (ambulant cerebral palsy, or hearing loss 30 to 89 dB). 3. Severe impairment (hearing loss more than or equal to 90 dB or severe non ambulant cerebral palsy).

Result: Sixty-seven (58.8%) patients had normal development, 35 (30.7%) had mild to moderate impairment and 12 (10.5%) had severe impairment. Factors associated with developmental impairment were high grade intraventricular hemorrhage, serum bilirubin requiring exchange transfusion and retinopathy of prematurity (ROP).

Conclusion: An abnormal cranial ultrasound, high serum bilirubin and presence of necrotizing enterocolitis and retinopathy of prematurity are postnatal risk factors associated with an adverse developmental outcome in infants born prematurely.

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The survival rate of preterm and low birth weight children has steadily improved over recent decades, but information on the long-term developmental consequences of preterm babies is scarce. Assessments of the long-term follow-up of preterm infants are essential for the continuous improvement of perinatal and neonatal care. The developmental outcome of these children is of paramount importance. Many studies have been published, which show the

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outcomes at the first year of life, while less information is available about the developmental consequences of preterm infants of preschool age¹⁻⁸.

It is important to determine the factors which are associated with a poorer outcome. Follow up studies have shown that preterm infants are at risk of neurological dysfunctioning such as cerebral palsy⁹⁻¹². Many preterm children experience difficulties in speech and language skills as well as clumsiness, and attention and behavioral problems, all of which can affect school performance and attainment¹³⁻¹⁹.

Mild developmental disturbances usually pose no problem for the child until greater demands have to be met at school or when more detailed evaluations are made.

It is important to understand the potential factors predisposing to developmental disturbances, in order to facilitate an adequate and timely signaling of children who need special help to meet their developmental capacities.

The aim of this study is to identify the perinatal and neonatal factors associated with adverse developmental outcomes.

METHOD

One hundred and fourteen children between 2-5 years seen at the child developmental unit between January and December 2008 with the following criterion: gestational age less than 37 weeks, were included in the study.

Patients with chromosomal abnormalities were excluded. The following data were documented: multiplicity of birth, gestational age (completed weeks), birth weight (grams), method of delivery (caesarean or vaginal delivery), hydrocephalus, peak serum bilirubin level (SBR), Apgar scores at 1 minute, grade of retinopathy of prematurity (ROP), postnatal sepsis (blood culture proven) and the presence of necrotizing enterocolitis.

Infants were classified according to their birth weight: less than 1000 gm, 1000 to less than 1500 gm, and 1500 to less than 2500 gm which would indicate whether weight had any detrimental effect on the prognosis of the child's development. Intracranial hemorrhages were classified as follows: grade I-II, III-IV and those who did not have. All the above variables were tested, to determine any association with poor developmental outcome.

Children were considered to have mild or moderate cerebral palsy (CP) if they were ambulant but had abnormal neurological signs and impairment in motor function. They were considered to have severe CP if they were unable to walk even with support.

Classification of Impairment

1. Normal.
2. Mild/moderate developmental impairment (Ambulant cerebral palsy, or hearing loss 30 to 89 dB).
3. Severe developmental impairment (hearing loss 90 dB or more and severe non ambulant CP).

RESULT

One hundred and fourteen children, at an age of 2-5 years, born prematurely at the gestational age of less than 37 weeks were included in the study.

Thirty-eight children were delivered by Caesarean section. Intraventricular hemorrhages (IVH) grades I-IV occurred in 33, I-II in 20 (17.5%) grade III-IV in 13 (11.4%). All the children with cerebral hemorrhages were less than 1500 gm. Grade III/IV bleedings occurred in a larger proportion; eleven out of thirteen patients (84.6%) in infants with birth weight less than 1000 gm.

Neonatal sepsis with a positive blood culture occurred in 21(14.5%) and patent ductus arteriosus (PDA) was observed in 46 (40.35%).

Other medical complications were necrotizing enterocolitis in seventeen (14.9%) and retinopathy of prematurity in fourteen (12.3%) children, see table 1.

Table 1: Clinical Characteristics of Patients

Patient characteristics	Number of patients	Percentage of the total patients
Small for gestational age	29	25.4%
Necrotizing enterocolitis	17	14.9%
Intraventricular hemorrhage Grade I-II	20	17.5%
Intraventricular hemorrhage Grade III-IV	13	11.4%
High bilirubin requiring exchange transfusion	25	21.9%
First one minute Apgar score less than 5	30	26.3%
Neonatal sepsis	21	18.4%
Retinopathy of Prematurity	14	12.3%

Anthropometry at the Date of Delivery

At the date of delivery, twenty-nine (25.4%) infants had a body weight below the 3rd percentile for sex and age. Length was considerably low; twenty (17.5%) infants had a length below the 3rd percentile. The head circumference was within the normal range in 101 (88.6%).

Thirty-seven children (32.4%) were less than 1000 gm at birth, forty-one weighed between 1000 gm and less than 1500 gm, and thirty-six were equal or more than 1500 at birth, see table 2.

Preschool Assessments Age

Minor impairment was diagnosed in thirty-five children (30.7%) and major impairment in twelve (10.5%).

Children with major impairment (n=12) showed the following deficiencies: 7 quadriplegia, 4 triplegia and one diplegic, all children with major impairment required special assistance and education.

Table 2: Classification of Patients according to Birthweight

Birth weight	Number of patients	Percentage of the total patient group
1500 to less than 2500 gm	36	31.6%
1000 to less than 1500 gm	41	36%
Less than 1000 gm	37	32.4%

Association between Risk Factors and Outcomes

Twelve (92.3%) out of thirteen of the children with major cerebral hemorrhages (IVH grade III-IV) had developmental impairment at pre-school age, of which 9 (69.2%) had severe developmental delay.

Female infants had better developmental outcome only 6.8% (four out of fifty-eight females) versus 14.2% (eight out of fifty-six males) had major developmental impairment at pre-school age.

Bowel perforation and/or necrotizing enterocolitis were associated with substantially increased risk for subsequent impairment, 14 (82.3%) out of seventeen with necrotizing enterocolitis showed developmental impairment and only three patients (17.6%) had normal development at the pre-school age.

Multiple birth, small for gestational age or having low one minute Apgar Score had no influence on the outcomes of major impairment, see table 3.

Thirty-two children out of thirty-six (88.8%) of birth weight more than 1500 gm had normal development by 2-5 years of age compared to 6 out of thirty-seven (16.2%) below 1000 gm subgroup.

Thirty-six patients out of 114 weighed more than 1500 gm, forty-one patients were between 1000-1500, and thirty-seven patients were less than 1000 gm, see table 4.

Fourteen (37.8%) patients of the thirty-seven with a birth-weight of less than 1000 gm had intraventricular hemorrhage grade I-II, and eleven (29.7%) out of thirty-seven patients developed intraventricular hemorrhage grade III-IV, while none of the thirty-six patients with birthweight of more than 1500 gm developed intraventricular hemorrhage of any grade, see table 5.

Table 3: Developmental Outcome according to Patients' Characteristics

Risk factor	Number of patients	Normal development	Mild to moderate developmental delay	Severe developmental delay
Small for gestational age	29	12 (41.4%)	10 (34.5%)	7 (24%)
First one minute Apgar score less than 5	30	11 (36.7%)	12 (40%)	7 (23.3%)
High bilirubin requiring exchange transfusion	25	2 (8%)	14 (56%)	9 (36%)
Necrotizing enterocolitis	17	3 (17.6%)	9 (53%)	5 (29.4%)
Intraventricular hemorrhage grade I-II	20	4 (20%)	10 (50%)	6 (30%)
Intraventricular hemorrhage grade III-IV	13	1 (7.7%)	3 (23%)	9 (69.2%)
Neonatal sepsis	21	9 (42.9%)	7 (33.3%)	5 (23.8%)
Retinopathy of prematurity	14	2 (14.3%)	4 (28.6%)	8 (57.14%)
Multiple births	19	8 (42%)	6 (31.6%)	5 (26.3%)

Table 4: Developmental Outcome according to Birth Weight

Birth weight	Number of patients	Normal development (n=67)	Mild to moderate developmental impairment (n=35)	Severe developmental impairment (n=12)
1500 to less than 2500 gm	36	32 (88.9%)	4 (11.1%)	0
1000 to less than 1500 gm	41	29 (70.73%)	8 (19.5%)	4 (9.8%)
Less than 1000 gm	37	6 (16.2%)	23 (62.2%)	8 (21.6%)

Table 5: Relationship between Patients' Characteristics and Birthweight

Patient characteristics	Birth weight less than 1000 gm (n=37)	Birth weight 1000 -< 1500 gm (n=41)	Birth weight 1500 -< 2.5 kg (n=36)
Small for gestational age	9 (24.3%)	13 (31.7%)	7 (19.4%)
Multiple birth	6 (16.2%)	7 (17.6%)	6 (16.6%)
Necrotizing enterocolitis	13 (35.1%)	4 (9.75%)	0
Intraventricular hemorrhage grade I-II	14 (37.8%)	6 (14.6%)	0
Intraventricular hemorrhage grade III-IV	11 (29.7%)	2 (4.8%)	0
High bilirubin requiring exchange transfusion	17 (45.9%)	5 (12.2%)	3 (8.3%)
First one minute Apgar score less than 5	8 (21.6%)	12 (29.26%)	10 (27.7%)
Neonatal sepsis	10 (27%)	6 (14.6%)	5 (13.8%)
Retinopathy of prematurity	12 (32.4%)	2 (4.87%)	0

DISCUSSION

The proportion of children with impairment was inversely related to birth weight and gestational age. Twenty-one percent of infants with a birth weight of less than 1000 gm had major impairment compared to 9.7% with a birth weight between 1000-1500 gm, and none of the children with birth-weight in excess of 1500 gm had major impairment.

A number of neonatal complications proved to be important for developmental outcome at preschool age. Previous studies have shown necrotizing enterocolitis (NEC) and/or bowel perforation had detrimental effects in the majority of children, which was in agreement with the present study²⁰⁻²².

A study found that in 124 surgically treated infants with necrotizing enterocolitis (NEC) were associated with significant growth delay and adverse neurodevelopment outcomes at 18 to 22 months corrected age²⁰. Despite modern medical and surgical treatment, NEC remains a serious disorder in premature infants and could have considerable impact on later child development.

We found that an abnormal cranial ultrasound, a very high bilirubin level and the presence of ROP are important postnatal risk factors associated with an adverse developmental outcome in infants. Oh et al reported that high serum bilirubin concentrations in extreme low birth weight infants are directly correlated with hearing impairment and a Psychomotor Developmental Index of less than 70²³. Our data are consistent with these reports.

In this study, retinopathy of prematurity was associated with developmental delay. Retinopathy of prematurity was associated with poor developmental outcome at the preschool age²⁴. Hungerford et al reported that retinopathy of prematurity in infants with gestational age less than 33 weeks was strongly associated with evidence of brain damage, often consistent with hypoxic ischemic injury²⁵. The factors that contribute to development of ROP, for example prematurity, hypoxia-hyperoxia,.. etc might adversely affect other areas in the developing brain. Retinopathy of prematurity acts as a marker for neonatal morbidity and its presence in severe grades should alert the physician towards the possibility of adverse developmental outcome in later years.

CONCLUSION

This study showed that the presence of intraventricular hemorrhage and high serum bilirubin had negative correlation on developmental outcomes.

Further research is needed to evaluate aggressive treatment of hyperbilirubinemia, which could modify the long-term outcome.

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