A Study of Follow up of Preterm Infants from Six to Twelve Months Corrected Age at Alexandria University Children’s Hospital

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Abstract
To perform clinical and developmental follow up for the preterm neonatal intensive care unit graduates from six months till one year corrected age.

For all preterm graduates <37 weeks and reached six months corrected age. Measurement of the growth parameters was done and the results was plotted on gestation adjusted CDC 2000 growth charts, The associated co morbidities was detected, Neurodevelopment was assessed by Hammersmith Infant Neurological Examination and Ages and Stages Questionnaires third edition at six, nine, and twelve months corrected age.

In our population of 71 preterm graduates, the mean weight was (7.31±0.76, 8.29±1.1, 9.3±1.11), the mean length was (66.09±2.46, 69.54±2.63, 72.93±2.58), the mean head circumference was (42.26±0.90, 43.79±1.40, 45.30±1.39) at corrected age of six, nine, and twelve months respectively. 6 (8.5%) cases was diagnosed with cerebral palsy and developmental delay. Different morbidities was detected as iron deficiency anemia in 35.2%, rickets in 31% cases, wheezy chest in 15.5%, gastroenteritis in 12.7%, epileptic attack in 4.2% of cases. Also 12.7% cases readmitted due to respiratory morbidities, 1.4% for gastroenteritis and severe dehydration, and 1.4% due to meningitis. Ophthalmological complications as strabismus was detected in 5.6% of cases, myopia in 1.4%, developmental cataract in 1.4%, and blindness in 1.4%. Hearing impairment was detected in 5.6% of cases.

Premature birth is a significant cause of infant and child morbidity. Long term complications include delayed growth and development, ophthalmological complications, impairment of hearing, iron deficiency anemia. The most frequent cause of hospital readmission was respiratory morbidities.
Introduction
Preterm birth is any birth before 37 completed weeks of gestation.\(^1\)

In recent years, with the advances in medical technology, the survival rate of premature infants has increased significantly.\(^2\) However, infants who survived might suffer from severe disabilities, intellectual disability, cerebral palsy, hearing and visual impairments.\(^3\)

The first year of an infant’s life is a critical period especially for brain development.\(^4\) Follow-up of development should be a continuous and flexible process.\(^5\) For diagnosing normal or abnormal development and evaluating the degree of abnormality, there are a number of different development screening tests. The American Academy of Pediatrics (AAP) recommends that the Ages and Stages Questionnaires (ASQ) third edition is advisable to be included in follow-up programs preterm children. The ASQ is a brief measure in which parents rate their child’s current skills and development, from 1 to 66 months of age. Twenty-one questionnaires are available within this age range. Parents answer 30 questions covering 5 domains of development, including communication, gross motor, fine motor, problem-solving, and adaptive skills.\(^6\)

During the first year of life, special attention should be given to preterm motor progress, The Hammersmith Infant Neurological Examination (HINE),\(^7\) has recently been proposed as one of the early neurological examination tools for the diagnosis of CP.\(^8\) It is a simple and scorable method designed for evaluating infants between 2 months and 24 months of age. It includes 26 items that assess different aspects of neurological examinations such as cranial nerves, posture, movements, tone, reflexes and reactions.\(^8\)

Early detection of developmental delay and early intervention can minimize the lifelong disabilities.

It is very important to monitor the growth rate of the preterm infant by means of periodic anthropometric measurements assessed for progress along standard, age and sex specific, curves that are generally expressed in percentiles. The growth curves that are most used currently are the CDC/NCHS-2000 curves.\(^13\) Premature children whose growth curves do not approach the curves for minimum normal limits, exhibit flattening or even go into reverse need to be investigated.\(^14,15\)

The purpose of this work is clinical and developmental follow up for the NICU graduates from six months till one year corrected age, in order to make applicable strategy to follow up preterm infants and identify their problems.

Material and Methods

Study design:
Prospective cohort study.

Study setting:
This study was conducted in the outpatient clinic at Alexandria university children hospital to all the study population reaching six months corrected age.
The following examination tools were performed for all infants at six, nine, twelve months corrected age:

Growth monitoring by measurement of the weight, length, and head circumference and plotting the results on gestation adjusted CDC 2000 growth charts.\(^9\)

Physical examination and appropriate investigations were done for the associated co morbidities.

Neurodevelopmental assessment:

Hammersmith Infant Neurological Examination (HINE) was performed while the child is calm. The results were recorded at the printable form of the HINE sheet and the overall score was calculated.\(^10\)

Ages and Stages Questionnaires (ASQ) third edition was fulfilled by the parents with the help of the clinician in translating and clearing the items to the parents.\(^11\)

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0.

Qualitative data were described using number and percent. Quantitative data were described using minimum and maximum, mean, and standard deviation.

Chi-square test was used in the comparison between two groups with qualitative data and Fisher exact test was used instead of the Chi-square test when the expected count in any cell found less than 5.

The comparison between more than two groups with quantitative data and parametric distribution were done by using One Way Analysis of Variance (ANOVA) test and Kruskall-Wallis test was used in the comparison between more than two groups with quantitative data and non-parametric distribution.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

- P > 0.05: Non significant
- P < 0.05: Significant
- P < 0.01: Highly significant

Results

71 preterm infants were studied with mean gestational age of 33.51±1.71 weeks, and mean birth weight of 1.54±0.49 kg,

<table>
<thead>
<tr>
<th>Table (1): Anthropometric measurements of the studied infants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean weight</td>
</tr>
<tr>
<td>6 m corrected age</td>
</tr>
<tr>
<td>9 m corrected age</td>
</tr>
<tr>
<td>12 m corrected age</td>
</tr>
</tbody>
</table>

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Table (2): Incidence of cases with suspected developmental delay using Age and stage questionnaire third edition (ASQ3) at the end of the study.

<table>
<thead>
<tr>
<th>Developmental delay</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>6</td>
<td>8.5</td>
</tr>
<tr>
<td>No</td>
<td>65</td>
<td>91.5</td>
</tr>
</tbody>
</table>

Table (3): The incidence of suspected cases of cerebral palsy using Hammersmith infant neurological examination (HINE) at the end of the study.

<table>
<thead>
<tr>
<th>Suspected CP</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>6</td>
<td>8.5</td>
</tr>
<tr>
<td>No</td>
<td>65</td>
<td>91.5</td>
</tr>
</tbody>
</table>

Table (4): Morbidities didn’t require hospital admission in the studied infants during the study.

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron deficiency anemia</td>
<td>25</td>
<td>35.2</td>
</tr>
<tr>
<td>Rickets</td>
<td>22</td>
<td>31</td>
</tr>
<tr>
<td>Wheezy chest</td>
<td>11</td>
<td>15.5</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>9</td>
<td>12.7</td>
</tr>
<tr>
<td>Epileptic attack</td>
<td>3</td>
<td>4.2</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Table (5): Eye complications in the studied infants.

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>%</th>
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</thead>
<tbody>
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<td></td>
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</table>

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Discussion

Preterm infants have a broad spectrum of medical and developmental problems after NICU discharge that require comprehensive care involving many specialties. Intense medical management may improve long-term medical outcomes.\(^\text{(12)}\)

The study was conducted a prospective descriptive study of our unit outcomes and readmissions for the surviving infants born at 28 to <37 wks gestational age from six to twelve months corrected age.

During the study period, 279 preterm were discharged from our NICU. 199 of them attended to our outpatient clinic from their discharge date till they reach 6 months chronological age. Among these infants 128 of them (64.3%) didn’t attend to our outpatient clinic from the age of six months till twelve months corrected age as 8 of them died and the other 120 didn’t attend to outpatient clinic even once. 71 cases attended to our outpatient clinic during this period. So out of 279 discharged infants, 71 cases (25.4%) attended from the age of six months till twelve months corrected age.
previous retrospective cohort study was conducted by D’Agostino et al in the primary care network at the Children’s Hospital of Philadelphia for preterm infants (defined by a gestational age of ≥22 and ≤35 weeks) to assess the adherence of premature infants till 18 months. It was found that 43% infants attended all the expected health supervision visits.\(^{13}\) The low percentage of adherence in the present study (25.4%) is attributed to many reasons, the most important of them is the far distance to our hospital as most of the cases settle in faraway cities and villages. Other factors include poor family education, poverty so they couldn’t pay for transportation. Moreover most parents only attend to the clinic when they feel that their babies are unwell.

As regarding growth parameters of the studied preterm neonates during the follow up period we found the following: the mean weights of the studied cases were (7.31±0.76 / 8.29±1.1 / 9.3±1.11) at corrected age of six, nine, and twelve months respectively. A previous study conducted by Mariana G, et al. found that the mean weight at 6 and 12 months corrected age for very low birth weight preterm infants were 6907.1 ±973.5 and 8916.6 ±1190.6 grams respectively which is lower than the present study as they included the very low birth weight infants.\(^{14}\) At 6 months corrected age, no cases had abnormal weight were detected, while at 9 months corrected age, 4 cases (5.6%) weight was abnormal with the weight of one of them is over the normal range and the others weight was below the normal range, and at 12 months corrected age, 5 cases (7%) weight was abnormal with the weight of 3 of them were over the normal range and the other 2 cases (2.8%) weight was below the normal range. A similar study done by Islami Z, et al. on the growth parameters of NICU admitted low birth weight preterm neonates at corrected ages of 6 and 12 months corrected age using WHO growth charts found that at 6 months corrected age 18.4% cases were underweight.\(^{15}\) The percentage of cases are more than ours, as cases of the present study were regularly checked after discharge at the outpatient and adequate intervention occurred. The mean lengths were (66.09±2.46 / 69.54±2.63 / 72.93±2.58) at corrected age of six, nine, and twelve months respectively. Mariana G, et al. study also found that the mean length at 6 and 12 months CA were 64.8±3.7 and 74.1±3 respectively which is lower at 6 months CA than the present study may be because the study is on very low birth weight infants but higher results at 12 months CA may due to different ethnicity.\(^{14}\) At 6 months corrected age, 1 case (1.4%) length was below normal range, and at 9 months corrected age, 3 cases (4.2%) length was below normal range, while at 12 months corrected age, 6 cases (8.5%) length was below normal range. The previously mentioned Islami Z, et al. study detected 34.7% cases with short stature at the age of six months CA and 6.2% at the age of 12 months CA.\(^{15}\) The present study had lower percentage at 6 months corrected age and higher percentage at 12 months corrected age may be due to the prevalence of rickets among our cases, different ethnicity, also the other study exclude small for gestational age (SGA) infants which have increased risk for short stature.\(^{16}\) The mean head circumferences were (42.26±0.90 / 43.79±1.40 / 45.30±1.39) at corrected age of six,

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nine, and twelve months respectively. At Mariana G, et al. study the mean head circumference of the cases were 42.7±1.7 , and 45.2 ±1.6 at 6 and 12 months CA respectively which is in agree with the present study.\(^{(14)}\) At 6 months corrected age, 1 case was detected, with head circumference below normal and at 9 months corrected age, 12 cases (16.9 %) head circumference was below normal range, while at 12 months corrected age, 4 cases (5.6 %) head circumference was below normal range. Islami Z, et al. study also mentioned that microcephalic cases were 8.2% at the age of six months CA and 0% at the age of 12 months CA.\(^{(15)}\) The present study had lower percentage at 6 months corrected age and higher percentage at 12 months corrected age may be due to the other study excluded infants at risk of developmental delay as cases with severe asphyxia, chromosomal abnormalities, genetic syndromes and neonates who had serious complications such as intraventricular hemorrhage, hydrocephaly during NICU admission period.

As regard the development, 6 (8.5%) cases diagnosed with developmental delay by using Age and stage questionnaire third edition (ASQ3) and were referred to the neuropsychiatry clinic in our hospital for management and early intervention. the MRI findings show that one of those cases had PVL, one had hydraencephaly, and four had atrophic changes.

Hammersmith infant neurological examination (HINE) was used in the present study to detect the cases with suspected cerebral palsy. Out of 71 cases, 6 cases (8.5%) were detected to have suspected cerebral palsy. The mean score of HINE was \((68.19±4.52 / 67.49±8.8 / 69.16±8.18)\) at corrected age of six, nine, and twelve months respectively. A previous study done by Domenico R, et al. on very premature infants (less than 32 wks) found that the mean score of HINE was 59.5± 10.2 at 6 months CA, 63.1± 10.1 at 9 months CA, and 64.9± 10.4 at 12 months CA. This results are lower than ours as that study was on the very preterm infants.\(^{(17)}\)

During follow up of the studied infants different morbidities were diagnosed, some of them need hospital admissions and others didn’t. The most frequent morbidities didn’t require hospital admission were in descending order, Iron deficiency anemia was the main morbidity, 25 cases (35.2%) diagnose by iron deficiency anemia, 22 cases (31%) had rickets. 11 cases (15.5%) had wheezy chest, 9 cases (12.7%) had gastroenteritis, 3 cases (4.2%) experience epileptic attack one of them diagnosed as west syndrome based on that he had triad of mental retardation, and infantile spasms, electroencephalogram (EEG) showed Generalized epileptiform activities picture of hypsarhythmia, the other 2 cases experience single epileptic attack but they had normal development, irrelevant family history and no other associated manifestations and 2 cases (2.8%) had pneumonia not need admission.

The studied infants were readmitted for different morbidities. The most frequent cause for readmission was respiratory morbidities, 9 cases (12.7%) were admitted due to respiratory morbidities as 6 cases (8.5%) were admitted for pneumonia and 3 cases (4.2%) admitted for wheezy chest. 1 case (1.4%) admitted for gastroenteritis and severe dehydration and another case (1.4%) for

\(^1\)Mohamed Hazem Gouda, \(^2\)Mona Khalil Mohamed, \(^3\)Adham Ahmed Badieb, \(^4\)Manal Moustafa
meningitis. A previous study done by MA Underwood, et al. revealed that the incidence of hospital readmissions for the preterm infants during the first year were 9.1 % for respiratory causes either acute or chronic, 3% due to infectious causes, 2.9 % due to gastrointestinal causes, 1.5% due to hematological causes, 0.28% due to neurological causes.(18) There is agreement that respiratory morbidities is the main cause of readmission.

During the present study numerous ophthalmological complications were detected. The most frequent was strabismus detected in 4 cases (5.6%), 2 cases of them previously had ROP that spontaneously improved in one and the other infant need injection, one case was delayed so the cause here may be central, the other case didn’t had a relevant cause. Also one case had myopia, one case had developmental cataract and one case had blindness. A previous study done by Gerd H, et al. on 198 prematurely born children found that at 2.5 years there was 26% of cases had astigmatism, 10% had myopia, 8.4% had anisometropia, and 4% had metroapia.(19),(20) There is agreement that the strabismus was the main complication.

Hearing loss was evaluated by auditory brain stem response (ABR) during the present study as a follow up for previously done screening or because it wasn’t done before. The overall incidence of cases who failed the test was (5.6%). Out of the 4 cases one case had bilateral mild hearing loss because of middle ear effusion because of adenoids hypertrophy not respond to medical treatment so planned for surgery this infant had previously passed the test, one case had bilateral moderately severe hearing loss improved with follow up, other case had bilateral profound hearing loss and needed hearing aids, the last case had unilateral mild hearing loss improved with follow up. All those infants who had failed ABR were referred for further medical examination and subsequent therapy. Among the 6 infants who passed the test, 2 of them were previously failed. In study conducted by Rechia, et al in otorhinolaryngology department in Universidade Federal de Santa Maria (UFSM) in Brazil in which 140 infants with mean gestational age 34.76 weeks and mean birth weight of 2299 g underwent hearing loss screening. 16 of 140 (11.42 %) failed ABR and 124 passed it.(21) The incidence in our study is lower than that in the reported study in Brazil. This could be explained by the wider range of gestational age in their study.

Conclusions

- Premature birth is a significant cause of infant and child morbidity and mortality.
- The first year of an infant’s life is a critical period especially for brain development.
- Respiratory morbidities are the most frequent cause of hospital readmission of preterm infants after discharge from NICU.
- Iron deficiency anemia is common among premature infants followed by rickets.
- Preterm infants are a high risk group. They have increased susceptibility to growth problem, developmental delay, cerebral palsy, ophthalmological complications, and hearing impairment.

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Early detection and early intervention is very crucial to minimize the long term disabilities in this fragile group and to ensure better life for the child and the parents.

References


