Clinical Analysis of 1048 Children with Developmental Delay

I-Chun Chen, MD; Chia-Ling Chen, MD, PhD; May-Kuen Wong, MD; Chia-Ying Chung, MD; Chia-Hui Chen; Chia-Ho Sun

**Background:** Children with developmental delay (DD) have a variety of problems in developmental functions. The purposes of this study were to analyze the underlying diseases and risk factors in children with different functional delays.

**Methods:** We collected data on 1048 children who underwent assessments of developmental function, related diseases, and risk factors. All children were classified into 6 functional delay groups: cognitive, speech, motor, pervasive, global, and non-specific DDs. Differences in related diseases and risk factors of the 6 functional delay groups were determined.

**Results:** Most children had global (51.2%), speech (21.9%), and motor (13.9%) delays. Approximately 62.8% of children were associated with biological factors (19% with genetic defects or congenital anomalies, 16.5% with central nervous system lesions, 13.9% with prematurity/low birth body weight, and 13.4% with neonatal insult). We could not identify the risk factors in 36.6% of the children. Most children with motor delay had brain/neuromuscular diseases and were associated with risks of prematurity or low birth body weight; while most children with global delay had brain neuromuscular diseases or psychological/mental disorders and were associated with risks of genetic defects or congenital anomalies.

**Conclusion:** Our findings suggest that there are heterogeneous risk factors and related diseases in children with different kinds of functional delay. (Chang Gung Med J 2002;25:743-50)

**Key words:** developmental delay, developmental function, risk factor, related disease.

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important to survey the risk factors to be able to identify children who are suspected of having DD at an early stage and subsequently monitor their developmental function. It would be advantageous if it could be determined at an early time whether children suspected of having DD really do have developmental problems and to clarify the range of associated deficits; then clinicians could offer a complete service system for early intervention. A series of steps are included: a thorough evaluation such as medical assessment and psychological testing, a rehabilitation program with physical, occupational, and speech therapy for positioning, handling, feeding, language, and cognitive stimulation, and an educational plan to instruct families in proper functioning. Tirosh et al. suggested that children with fine motor deficits possessed risk factors associated with early antepartum, possibly of genetic origins, while there were few clinical studies to follow up the developmental functions for children with different risk factors.

The purposes of this study were to investigate the underlying diseases according to the developmental function and early detection of children with risk factors. We attempted to classify children with DD into functional delay groups based on their developmental dysfunction. Then, we analyzed the related underlying diseases and risk factors in children of different functional delay groups.

METHODS

From October 1998 to September 2000, infants or young children with DD, who were either referred from the Pediatric Department or sent to our clinics for first aid, were recruited into this study. In total, data on 1048 patients were collected in this study. The children underwent an assessment of functional development, related diseases, and risk factors. To assess the functional development, we used the Chinese Children Developmental Inventory (CCDI) to assess 8 functional domains: gross motor, fine motor, expressive language, concept comprehension, social comprehension, self help, personal social, and general development. Based on the clinical assessment combined with the results of the CCDI and other evaluation tests including the Peabody Developmental Motor Scale, Peabody Picture Vocabulary Test, Gross Motor Functional Measure, Wechsler Preschool and Primary Scale of Intelligence, etc, all children were classified into 6 functional delay groups: cognitive, speech, motor, pervasive, global, and non-specific DD. "Significant" was defined as 2 or more standard deviations below the mean of normal references of developmental screening or assessment tests.

Cognition involves the high-integrated processes of attention, perception, memory, and functional task performance. Neuropsychological and intelligence tests are helpful in identifying children with cognitive DD. Speech DD indicates a deficit in articulation function, verbal expression, comprehension, or mixtures of the above conditions. Motor DD was defined as a delay in gross motor or fine motor skills with presentation of age-appropriate performances in other developmental domains. Children with core features of observed qualitative deficits in social skills, communication, and repetitive/restrictive patterns of behavior were placed in the pervasive DD group, and those children with visual, hearing, or sensory integration (SI) dysfunction were placed in the non-specific DD group. SI dysfunction results from a disturbance in the integrating process of the subcortical multisensory system. Children whose developmental quotients were less than 80% in 2 or more domains were placed in the global DD group.

To determine the related diseases, children with DD received detailed clinical and laboratory investigations across specialized departments such as neurological (echography, magnetic resonance imaging, computed tomography, electroencephalography, brain auditory evoked potential, etc.), genetic (chromosome, DNA, etc.), metabolic, hearing, or visual studies depending on individual indications. Based on the related diseases ultimately determined by various experts (neurologists, psychiatrists, geneticist, otologists, ophthalmologists, etc), the children with DD were classified into 5 major categories: brain/neuromuscular, psychological/mental, genetic or congenital, visual, hearing, and other diseases. Children with brain lesions (cerebral palsy (CP), hypoxic encephalopathy, microcephaly, central nervous system (CNS) infection, traumatic brain injury, epilepsy, hydrocephalus, tumor, etc.), and neuromuscular diseases (motor neuron disease, peripheral neuropathy, myopathy, etc.) were categorized as having
brain/neuromuscular diseases. Children with mental retardation (MR), speech delay, articulation disorder, attention-deficit/hyperactive disorder, SI dysfunction, autism, and non-specific psychomotor retardation were categorized as having psychological/mental disorders. Children with chromosomal or genetic abnormalities, congenital syndromes, metabolic or endocrine diseases, and inborn-error metabolic diseases were categorized as having genetic/congenital diseases. Children with other systemic diseases, such as orthopedic, cardiovascular, digestive, or urinary pathologies, were categorized as having other diseases.

To survey the related risk factors in children with DD, all children underwent detailed birth history taking, chart review, and prospective clinical investigations. The risk factors contributing to DD were categorized into 6 factors: prematurity or low birth body weight (BBW), genetic defects or congenital anomalies, neonatal insult, CNS lesions caused by disease or trauma, environmentally related factors, and unknown causes. A gestational age (GA) below 32 weeks was defined as prematurity, and a BBW of < 2000 g was defined as low BBW. Those who had chromosome or genetic abnormalities, craniofacial anomalies, spinal bifida, congenital heart disease, and limb deformities/deficiencies were categorized into the genetic defect or congenital anomaly group. Neonatal insults included the related factors which had occurred before, during, or after pregnancy, such as low Apgar scores (a score of < 5 at 5 min), infantile spasms, and severe hyperbilirubinemia post-exchange transfusion. CNS lesions consisted of hydrocephalus, intracranial hemorrhage, hypoxic encephalopathy, infection, and seizure disorders. However, we only included parent’s mental and psychological disorders as categorized as environmentally related factors in this study. Risk factors not clearly determined were categorized as unknown factors. In addition, the age, body weight (BW), body height (BH), gender, GA, BBW, and delivery modes for the pregnancy were also recorded.

Differences in the continuous data (age, BH, BW, BBW, and GA) among the 6 functional delay groups were determined using ANOVA with Tukey’s HSD multiple comparison. Differences in the categorical data (gender, delivery mode, risk factors, and related diseases) among the 6 functional delay groups were determined using Chi-square test. A value of $p < 0.05$ was considered statistically significant.

**RESULTS**

Based on the geographic distribution, approximately 87% of children came from the Taoyuan area (35.7%) and Taipei area (Taipei County: 29.9%, Taipei City: 21%). The other 13% of children came from other areas (Hsinchu area: 7.4%, Miaoli area: 2.6%, Taichung: 2.1%, and eastern Taiwan: 1.3% including the Keelung, Ilan, and Taitung areas).

According to the assessment of functional development, most children had global (51.2%), speech (21.9%), and motor (13.9%) delays (Fig. 1). The average age of all children with DD at the first visit was 37.8 months, with males dominant (60% vs. 40%) (Table 1). The age range of children with speech, pervasive, and non-specific DDs was 45-57 months, while that of children with cognitive, motor, and global delay was approximately 32-33 months. Male dominance (71%-83%) was observed in children with speech, pervasive, and non-specific DDs, but a female dominance (62%) was observed in those with cognitive DD. Tracing the birth history, the average GA of all subjects was 37 weeks, and the BBW was 2834 g. However, the average GA and BBW were lower in children with motor and global delays (motor: 35 weeks, 2546 g; global: 37 weeks, 2701 g). There were no significant differences in the delivery modes (natural spontaneous delivery: 55%, cesarean section: 45%) (Table 1).

When risk factors were analyzed, it was found 62.8% of all children had associated biological factors (20% with genetic defects or congenital anomalies, 16.3% with CNS lesions, 14.2% with prematurity or low BBW, and 13.5% with neonatal insults), and 0.8% of all children were associated with environmental factors (Table 2). However, we could not identify the related risk factors in 35.2% of the children, especially in 48%-72% of children with speech, pervasive, and non-specific DDs. Children with cognitive and global delays were associated with 28%-48% of risks of genetic defects or congenital anomalies, while those with motor delay were associated with 32.4% of risks of prematurity or low BBW (Table 2).

Based on the related diseases in the 6 major cat-
Fig. 1 Percentage of Cases among the 6 Functional Delay Groups.

Table 1. Demographic Data of the 6 Functional Delay Groups

<table>
<thead>
<tr>
<th>Data</th>
<th>Group</th>
<th>A (N = 21)</th>
<th>B (N = 230)</th>
<th>C (N = 145)</th>
<th>D (N = 29)</th>
<th>E (N = 537)</th>
<th>F (N = 86)</th>
<th>Total (N = 1048)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td></td>
<td>33.3±16.2</td>
<td>46.1±17.5</td>
<td>33.0±21.4</td>
<td>44.7±15.9</td>
<td>32.1±22.7</td>
<td>57.0±17.4</td>
<td>37.8±22.4</td>
</tr>
<tr>
<td>BH (cm)</td>
<td></td>
<td>81.0±9.8</td>
<td>99.6±12.3</td>
<td>88.6±17.0</td>
<td>102.1±10.2</td>
<td>87.1±16.4</td>
<td>107.7±12.0</td>
<td>92.7±16.9</td>
</tr>
<tr>
<td>BW (kg)</td>
<td></td>
<td>10.8±2.8</td>
<td>16.5±4.3</td>
<td>12.5±4.6</td>
<td>17.3±4.5</td>
<td>11.9±6.0</td>
<td>19.5±5.1</td>
<td>19.5±5.1</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>31.8%</td>
<td>70.7%</td>
<td>47.9%</td>
<td>82.8%</td>
<td>54.9%</td>
<td>75.6%</td>
<td>59.5%</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>61.9%</td>
<td>29.3%</td>
<td>52.1%</td>
<td>17.2%</td>
<td>45.1%</td>
<td>24.4%</td>
<td>40.5%</td>
</tr>
<tr>
<td>Delivery mode</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSD</td>
<td></td>
<td>68.4%</td>
<td>52.5%</td>
<td>50.0%</td>
<td>75.0%</td>
<td>54.5%</td>
<td>61.4%</td>
<td>54.8%</td>
</tr>
<tr>
<td>C/S</td>
<td></td>
<td>31.6%</td>
<td>47.5%</td>
<td>50.0%</td>
<td>25.0%</td>
<td>45.5%</td>
<td>38.6%</td>
<td>45.2%</td>
</tr>
<tr>
<td>GA (weeks)</td>
<td></td>
<td>39.0±2.1</td>
<td>38.6±2.3</td>
<td>35.3±4.9</td>
<td>39.0±1.7</td>
<td>36.8±4.1</td>
<td>39.0±2.0</td>
<td>37.3±3.95</td>
</tr>
<tr>
<td>BBW (g)</td>
<td></td>
<td>3136±740</td>
<td>3118±624</td>
<td>2546±963</td>
<td>3283±596</td>
<td>2701±784</td>
<td>3218±523</td>
<td>2834±797</td>
</tr>
</tbody>
</table>

A: cognitive developmental delay group, B: speech developmental delay group, C: motor developmental delay group, D: pervasive developmental delay group, E: global developmental delay group, F: non-specific developmental delay group, BW: body weight; BH: body height; cm: centimeter; kg: kilogram; NSD: natural spontaneous delivery; C/S: cesarean section, BBW: birth body weight, GA: gestational age. The categorical data (gender and delivery mode) are expressed as percent (%) of cases and were tested with Pearson's Chi-square test among the 6 functional delay groups. The continuous data (Age, BH, BW, BBW, and GA) are expressed as the mean ± SD and were tested with ANOVA with Tukey's HSD multiple comparison among 6 functional delay groups. *p < 0.01; + p < 0.05.
categories, our results show that 53.8% of all cases were diagnosed with psychological/mental disorders, 34.4% were diagnosed with brain/neuromuscular diseases, and 7.7% were diagnosed with genetic diseases (Table 3). Approximately 83% of children with motor delay were associated with brain/neuromuscular diseases, while 80% of children with global delay were associated with brain/neuromuscular or psychological/mental disorders (Table 3).

**DISCUSSION**

Some studies have suggested that the categories of cerebral dysgenesis, hypoxic-ischemic encephalopathy (HIE), antenatal toxin exposure, and chromosomal disorders provided 77% of the diagnoses of children with global DD; 69% of children with motor DD had HIE, cerebral dysgenesis, or benign congenital hypotonia. We found that most children (83%) with motor delay were associated with brain/neuromuscular diseases, while most children (80%) with global delay were associated with brain/neuromuscular diseases or psychological/mental disorders. These findings could provide clinicians with clues to investigate the related underlying diseases according to the developmental functions of children. For example, when approaching a child presenting delays in many functional domains, brain or psychological/mental disorders should be considered and evaluated.

We found that children with motor delay were associated with 32.4% of the risks of prematurity or low BBW, even if prematurity or low BBW contributed only 14.2% of the risk to all children with DD. Although prematurity or low BBW is a commonly mentioned risk factor related to DD, the pre-
vious literature indicated that it by itself is a relative-
ly weak factor. Approximately 80%-95% of preterm
infants are free of severe disabilities.\textsuperscript{13-17} The causes
and complications of prematurity have been found to
be more predictive of developmental outcome than
only prematurity.\textsuperscript{18} Lindahl et al.\textsuperscript{9} found that a
small GA, low BBW, and signs of cerebral depres-
sion all increased the risk of poor motor performance
by about 2-3 fold. Prematurity is well known as a
strong risk factor for CP with spastic diplegia.\textsuperscript{19,20}
Thus, clinicians should closely monitor functional
outcomes, especially the motor domain for children
with a history of prematurity and low BBW.

In this study, children with cognitive and global
delays were associated with 28%-43% of the risks of
genetic defects or congenital anomalies, although all
children with DD were only associated with 19% of
those risks. Previous studies also pointed out that
infants with major congenital anomalies had an
increased incidence of developmental problems
whether there were any associated chromosomal dis-
orders or dysmorphic syndrome.\textsuperscript{21,22} Thus, further
surveys such as chromosomal, genetic, and metaboli-
ic studies are indicated with this clinical approach for
infants or children with DD, especially those with
cognitive and global delays.

We found the neonatal insults and CNS lesions
contributed about 30% of the risk factors in all chil-
dren with DD. Thus, we should longitudinally fol-
low-up developmental outcomes of children with a
history of pre-, peri-, and postnatal insults and inves-
tigate CNS dysfunction. Prenatal maternal factors
such as drug abuse during pregnancy have been stud-
ied and were proven to be associated with intra-
terine growth retardation, neonatal withdrawal syn-
drome, subtle neurological abnormalities, fetal dis-
tress, congenital anomalies, and developmental
sequelae.\textsuperscript{23-25} It is also well known that perinatal
asphyxia results in marked symptoms like seizures,
coma, lethargy, or muscle tone abnormalities. In
studies of severely asphyxiated full-term newborns,
30%-50% died; of those who survived, 12%-30% de-
veloped CP or MR.\textsuperscript{26-28} Kernicterus appeared
to be a low risk factor for DD; our data showed only
a 0.5% incidence, but it is still suggested that moni-
toring be carried out on the developmental outcome
of infants whose bilirubin rises to 20-25 or those
who have received an exchange transfusion.\textsuperscript{7} The
data imply that CNS lesions like diffuse encephalo-
malacia, intraventricular hemorrhage, and intra-
parenchymal hemorrhage all carry a high risk (70%-90%)
of a major handicap in full-term infants.\textsuperscript{29}
Sepsis complicated with meningitis increased the
risk of DD including hearing impairment and con-
genital infections resulting in CNS injury and long-
term developmental sequelae.\textsuperscript{30}

We found a relatively low incidence of environ-
ment factors in our children, although cognitive
delay was associated with 14.3% of environmental
factors. While previous studies conducted before
1989 reported that cognitive and speech/language

disorders were prevalent among children of parents
with a low educational level or low social class,\textsuperscript{9,10,11,31}
this discrepancy may possibly have been caused by
the patient classification, definitions of environment
factors, Chinese culture, risk factor categorization,
and genetic technology improvements among stud-
ies. In this study, all children with pervasive delays
were autistic, and most children with speech delays
had articulation disorders. Environmental factors
only included the parental MR or psychological dis-
orders and child abuse, and did not include low edu-
cational level or low social class. In Chinese culture,
people usually do not mention any family history of
MR, psychological disorders, or child abuse. Thus,
it is possible that the environmental factors were
underestimated in this study. Only 1 major risk fac-
tor was selected for statistical analysis, and there
may have been several risk factors coexisting simul-
taneously. The risk factors were categorized into
biological factors such as genetic defects, congenital
anomalies, neonatal insults, and CNS lesions if com-
bined with environmental factors. Environment fac-
tors categorized before 1990 might have been re-cat-
erized into genetic defects or congenital anomalies
due to rapid improvements in molecular biology and
genetic technology in recent years. Thus, the deter-
ned risk of genetic defects or congenital anomalies
was relatively increased, and that of environmental
factor was relatively decreased in this study.

This study shows there are heterogeneous risk
factors and related diseases in children with different
functional delays. These findings provide clues from
which to investigate underlying diseases according to
developmental function and a comprehensive assess-
ment and to follow up the specific functional out-
comes in children with different risk factors. It is
worthwhile and beneficial to identify and provide
therapeutic intervention as early as possible to decrease disabilities and family stress in children with DD. Further efforts should stress the development of a referral organization which integrate aspects of medical, educational, and social affairs units.

REFERENCES

1048例發展遲緩兒童之臨床分析

陳怡君 陳嘉玲 黃美涓 鍾佳英 陳嘉惠 孫家禾

背景: 發展遲緩兒童在發展功能表現上各有不同，本篇研究主要的目的為根據這些不同發展功能作分類，分析相關疾病及危險因子。

方法: 本篇研究共收集了1,048例發展遲緩兒童，分別接受發展功能評估、相關疾病診斷、及危險因子之分析後分為六組發展功能遲緩群，包括：認知類、語言類、動作類、廣泛性、全面性以及非特異性發展遲緩，並以此六組為根據，分析各組不同之相關疾病診斷及危險因子。

結果: 研究中顯示多數發展遲緩兒童為全面性發展遲緩(51.2%)，語言類發展遲緩(21.9%)及動作類發展遲緩(13.9%)。大約62.8%的兒童經分析為有生物學危險因子(其中19%為基因缺陷或先天異常，16.5%為有中樞神經系統病變，13.9%為早產或低體重兒，13.4%為有新生兒傷害因子)，但仍有36.6%的兒童找不到相關危險因子。動作發展遲緩的兒童其主要合併的疾病為腦部或神經肌肉病變，且伴有多產及低體重之相關危險因子；然而全面性發展遲緩的患兒則較常合併腦部、神經肌肉病變或精神心智疾患，並以基因缺陷或先天異常為最多見之相關危險因子。

結論: 以上的結果顯示各類發展功能遲緩兒童有其主要相關疾病及危險因子，此結果可提供臨床醫師作爲發展遲緩兒童診斷及追蹤之根據。

(長庚醫誌 2002;25:743-50)

關鍵字: 發展遲緩，發展功能，危險因子，相關疾病診斷。