Clinical Abnormalities, Intervention Program, and School Attendance of Down Syndrome Children in Southern Thailand

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Background : *Down syndrome is the most common chromosomal abnormality with an incidence of 1:700 livebirths. In southern Thailand, most Down syndrome patients are referred to Songklanagarind Hospital for surgical, medical treatment and/or stimulation intervention.*
Objective : *To study the clinical features and school attendance of Down syndrome children.*
Material and Method : *A total of 295 Down syndrome children attended Songklanagarind Hospital. The clinical features of Down syndrome, percentage of children receiving the stimulation intervention program, and attending school were studied.*
Results : *Congenital heart disease was found in 38.6%, gastrointestinal anomalies 16.9%, hematologic malignancy 6.1%, and thyroid disorders 11.4%. The mortality rate of Down syndrome children was 13.2%. Most children (65.6%) received the early stimulation, but only 38.9% attended the speech intervention program within the first 2 years of life. Of the total 109 Down syndrome children aged over 5 years that are still being followed, only 74 (67.9%) attended school. The school attendance was correlated with the family income, but not correlated with the level of maternal or paternal education.*
Conclusion : *Congenital heart disease and gastrointestinal anomalies are commonly found in Down syndrome children. Most children received an early intervention program, but only 38.9% received speech intervention. In children aged > 5 years, only 68% attended school, and school attendance was correlated with the family income.*

Keywords : *Down syndrome*

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Down syndrome is the most common chromosomal abnormality with an incidence of 1:700-800 livebirths[1-3]. All individuals with Down syndrome have distinctive facial appearances, hypotonia, and some degrees of mental retardation. Major congenital anomalies are also commonly found in these children, such as congenital heart diseases (30-40%)[2-4], gastrointestinal defects (10-15%)[2-4], and congenital hypothyroidism (2-15%)[5-7]. The mortality rate has been reported to be greater and life expectancy is shorter than the general population[8-10]. Regarding

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developmental delay and mental retardation, intervention with psychomotor and speech stimulation starting early in the first year of life has been described as having a beneficial effect on development.

In Thailand, despite the basic medical care that has been completely provided nationwide, the intervention program for special groups of children is limited only to specific institutions, medical schools, and some provincial hospitals. Songklanagarind Hospital is the medical school in southern Thailand, in which early stimulation intervention programs have been provided since 1988. The authors have had the opportunity to provide medical care and stimulation intervention in children with Down syndrome living in this area. The authors performed a retrospective review of the children with Down syndrome for the purpose of studying the clinical features, the mortality rate, the percentage of children receiving stimulation intervention as well as the speech training, and lastly, the percentage of school attendance.

Patients and Method

A retrospective study was conducted in 295 children diagnosed as Down syndrome who attended Songklanagarind Hospital from January 1992 to December 2002. All patients had characteristic features of Down syndrome: flat nasal bridge, small eyes, upward slant palpebral fissures, epicanthal folds, small ears, and loose skin fold at the nape. Chromosome study was done in all patients, with 274 children done in this hospital and 21 patients done in other hospitals. The chromosome study of 274 children revealed trisomy 21 in 263 (96.0%), 14/21 translocation in 5 (1.8%), 21/21 translocation in 5 (1.8%), and mosaicism in 1 (0.4%). For 21 children who had chromosome studies done in other hospitals, the parents were informed that their children had Down syndrome, however, the authors did not have the official report of the chromosome study. Of the total 295 children, 160 were boys and 135 were girls giving the ratio of male to female of 1.2:1. The median age at first visit was 0.9 ± 2.0 years (range 1 day - 14 years). The mean maternal age at the time of the children's birth was 33.1 ± 6.6 years (range 17-50 years) with maternal age over 35 years of 46.1%. The mean paternal age at the time of the children's birth was 35.4 ± 7.5 years (range 17-62). The affected children were the first child of the mother in 85 (28.8%), the second child in 97 (32.9%), the third child in 60 (20.3%), and ranged from the fourth to fifteenth in 53 (18.0%). The average birth weight was $2,845 \pm 474$ grams (range 1,220-4.100) with average gestational age of 39.1 ± 1.7 weeks (range 30-42). At the time of the present study, 238 (81%) families decided to have no further children, 55 (18.7%) had 1-2 normal children (prenatal diagnosis was done in 40 cases), and 1 family (0.3%) had the next child affected with Down syndrome (the parents refused to do the prenatal diagnosis and both children were trisomy 21, chromosome studies of the parents were normal). All Down syndrome children were screened for cardiological and gastrointestinal anomalies by pediatricians. Children suspected to have congenital heart disease were then referred to pediatric cardiologists, and those suspected of gastrointestinal defects were referred to pediatric surgeons. Hematologic disorders were screened in children who developed anemia, bleeding disorders, and/or organomegaly. Thyroid function tests (free T_4, TSH) were routinely performed in all individuals, except for those whose parents refused to have the blood tests done on their children.

All families were routinely advised to attend the early stimulation program in the first visit, and attend the speech training at age about 10-18 months. The early stimulation program was provided by occupational therapists and physiatrist (WL) at Songklanagarind Hospital. The stimulation program involved facilitating the development of gross motor and fine motor skills, assisting with oral-motor feeding problems, facilitating self-help skills (feeding, dressing, grooming, etc), and facilitating play and leisure skills. The children who did not attend the program at all or attended only once were classified as "no intervention" and those who attended the intervention program more than once, either at our hospital or other hospitals were classified as "receiving intervention". At each visit, the patients were evaluated for developmental milestones by pediatrician (SJ) and physiatrist (WL), using Denver Developmental Screening Test (DDST). The parents of children aged over 5 years were asked for school attendance of their children and were asked for the level of education, occupation, and income of the mother and the father.

Frequency table and percentage were shown to describe the prevalence and types of disorder.

Description statistics and 95% confidence interval, chi-square test, unpaired t test and/or Mann-Whiteney U-test were applied to test the significance different. P value of < 0.05 was considered statistically significant.

This study was approved by the Ethics committee of Songklanagarind Hospital.

Results

Of the total 295 Down syndrome children, 182 (61.2%) were evaluated by pediatric cardiologists. The children who were examined by pediatricians and had no signs or symptoms of heart diseases were assumed to have no cardiac abnormality. Using these criteria, congenital heart diseases were found in 114 children (38.6%). The definite diagnoses were confirmed by 2D-echocardiogram. The most frequent congenital heart disease was ventricular septal defect, followed by endocardial cushion defect and patent ductus arteriosus. Congenital gastrointestinal anomalies were found in 50 patients (16.9%) in which imperforate anus was the most common defect, followed by duodenal atresia. Hematologic disorders were found in 18 patients (6.1%). The signs/symptoms leading to hematologic investigations were anemia and purpura/petechia. Thyroid function tests were evaluated in 263 children which were found to be abnormal in 30 children (11.4%): 23 (8.8%) with congenital hypothyroidism, 4 (1.5%) with acquired hypothyroidism and 3 (1.1%) with thyrotoxicosis (Table 1).

During the period of study, 39 children died resulting in the mortality rate of 13.2%. The median age at death was 2.5 $\pm$ 2.0 years. The major cause of death was bacterial infection, followed by congenital heart diseases and hematologic malignancies. Of the 21 patients who died from bacterial infection, 15 (71%) had underlying diseases, either congenital heart diseases, congenital gastrointestinal anomalies or hematologic malignancies (Table 2).

Of the 256 patients who survived, 168 (65.6%) received the early stimulation intervention and only 103 (38.9%) attended speech training programs. For the data of developmental milestones, only 160 and 126 children had the records of time of appearance of gross motor and language development, respectively. The mean ages of time of appearance of developmental landmarks in children with Down syndrome receiving early intervention and speech training compared to those without intervention are shown in Table 3. Of the total 109 children aged over 5 years who are still being followed-up in the hospital, only 74 (67.9%) attended school : 21 (19.3%) regular public school, 23 (21.1%) regular private school, 24 (22.0%) special public school, and 6 (5.5%) special private school.

Table 1. Prevalence and types of disorders found in Down syndrome children

Type of disorders	Patients N=295	%
Congenital heart diseases	114	38.6
Ventricular septal defect	35	11.9
Endocardial cushion defect	26	8.8
Patent ductus arteriosus	22	7.4
Atrial septal defect	15	5.1
Tetralogy of Fallot	8	2.7
Complex heart disease	8	2.7
Congenital gastrointestinal anomalies	50	16.9
Imperforate anus	21	7.1
Duodenal atresia	16	5.4
Hirschsprung disease	8	2.7
Others	5	1.7
Hematologic disorders	18	6.1
Acute myelomonoblastic leukemia	12	4.1
Myeloproliferative disorders	6	2.0
Thyroid disorders (n = 263)	30	11.4
Congenital hypothyroidism	23	8.8
Acquired hypothyroidism	4	1.5
Thyrotoxicosis	3	1.1

Table 2. Causes of death of 39 patients with Down syndrome and underlying diseases

Causes of death	N	Underlying diseases
Bacterial pneumonia	12	Congenital heart disease (8 patients)
Septicemia	9	Gastrointestinal anomalies (5) Hematologic malignancy (2)
Heart diseases	9	
Leukemia	6	
Prematurity	1	-
Drowning	1	-
Car accident	1	

Table 3. Mean age (months) $\pm$ SD of time of appearance of developmental milestones in children with Down syndrome receiving early intervention compared to those without early intervention

Developmental milestones	Early intervention (n = 113)	No intervention (n = 47)	P value
Roll over	5.0 $\pm$ 1.2	6.4 $\pm$ 1.6	0.001
Sit unsupported	10.3 $\pm$ 3.3	13.3 $\pm$ 3.5	0.01
Stand up	19.3 $\pm$ 5.3	22.2 $\pm$ 6.3	0.01
Walk unassisted	24.2 $\pm$ 6.2	27.7 $\pm$ 8.3	0.015
	Speech training (n = 56)	No training (n = 70)	
First word	29.3 $\pm$ 13.0	36.1 $\pm$ 15.8	0.016
First sentence	44.5 $\pm$ 14.6	78.7 $\pm$ 13.2	0.002

The mean age of school entering was 6.2 ± 1.8 years. The school attendance was correlated with family income, but not correlated with maternal nor paternal education (Table 4).

Discussion

The results of the present study revealed that the mean maternal age of children with Down syndrome was relatively advanced with a high percentage of maternal age ≥ 35 years (46.1%) at the time of pregnancy, and more than 50% were either the first or the second child in the family. After having the affected individuals, most of the parents (81%) decided to have no further children. The mothers who had their first child affected with Down syndrome and were younger than 30 years decided to have the second pregnancy which mostly resulted in a normal child, except in one family that resulted in trisomy 21, giving the recurrence risk of 1.8%. This evidence strongly confirmed the importance of prenatal diagnosis in the next pregnancy regardless of the age of the mother.

The incidence of associated diseases/defects in Down syndrome children in the present study is about the same percentage as previously reported in western countries[1-3] as well as in Thai children[11]. Congenital heart disease is the most frequent congenital anomaly with the incidence of 38.6%. The common heart disease in the present study is ventricular septal defect, which is different from the reports from western countries in which the most common heart disease is endocardial cushion defect. The incidence of congenital gastrointestinal anomalies is 16.9% with the most common defect being imperforate anus, followed by duodenal atresia. The incidence of hematologic malignancy is 6.1%. The mortality rate of Down syndrome from the present study was high up to 13.2%. As expected, congenital heart diseases and respiratory infections were the major causes of death of children with Down syndrome. Underlying diseases, either heart, gastrointestinal, or hematologic malignancies were the leading factors that made these children more susceptible to superimposed bacterial infection. Another factor that can explain the increased susceptibility to bacterial infection in children with Down syndrome is abnormalities of the immune system, particularly the reduction number of T lymphocytes[12,13].

Thyroid disorders have been recognised to occur more frequently in children with Down syndrome. The incidence of congenital hypothyroidism has been reported to be 28 times that of the general population[7]. Acquired hypothyroidism and hyperthyroidism caused by autoimmunity have been reported with a high prevalence in individuals during the childhood period[13-17]. Therefore, thyroid function tests are recommended as a yearly routine evaluation in these children.

All individuals with Down syndrome have developmental delay and mental retardation and their problems are one of the major concerns of the parents. The specific causes of developmental delay and mental retardation have not been clearly documented, although a decreased number of cortical neurons, malformed dendritic trees and spines, defective lamination of the cortex, down-regulation of neuron-restrictive silencing factor, and lower thyroxine concentrations have been demonstrated[18-21]. Up to the present, no pharmacological therapy has been shown to have a beneficial effect. Early stimulation intervention starting in the first year of life has been proven to have a positive effect on development[22-25]. As shown in the present study, children receiving early intervention significantly attained their developmental milestones 2-4 months earlier than those not receiving intervention. In Down syndrome children, language development is often more delayed than the motor skills, and functional language may appear at age 4-5 years. In the present study, children receiving speech training had their first meaningful word 7 months and their first sentence 3 years earlier than those without intervention. The results of the present study verify the importance of early intervention and the influence of environmental factors in attainment of developmental milestones. The results of the present study also demonstrated that only 60% of children with Down syndrome attended the early stimulation intervention, only 40% attended the speech training program, and only 68% of children aged over 5 years attended school. the present results reflect the current situation that the basic non-medical support system in Thailand is insufficient. Most of the intenvention programs are limited only to the medical centers and some provin-

Table 4. Factors influencing school attendance

Factors	P value	95% confidence interval
Maternal education < primary school	0.85	0.41-2.95
Paternal education < primary school	0.53	0.70-2.02
Family income < 10,000 Baht/month	0.004	1.91-30.1

cial hospitals, not throughout the country. There is only a partial public system available for the families of this special group of children to reach the non-medical health and education supports. A significant number of these children, particularly those from families with low socioeconomic status, were reared at home without receiving any intervention, were underserved by health and educational services, and some were neglected by the community. At school, these children need more attention by specially trained educational professionals to teach and help them in learning the life skills. Government as well as the non-government organizations should have more concern in supporting these children and their families to reach the basic requirements for better health and education in the future.

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ลักษณะทางคลินิก การกระตุ้นพัฒนาการ และการเข้าโรงเรียนของเด็กกลุ่มดาวน์ในภาคใต้ของประเทศไทย

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กลุ่มอาการดาวน์เป็นความผิดปกติของโครโมโซมที่พบบ่อยที่สุด มีอุบัติการณ์ 1:700 ของทารกแรกเกิดมีชีวิตในภาคใต้ ผู้ป่วยกลุ่มอาการดาวน์จะถูกส่งต่อมายังโรงพยาบาลสงขลานครินทร์เพื่อการรักษาและการกระตุ้นพัฒนาการ

วัตถุประสงค์ *: เพื่อศึกษาลักษณะทางคลินิก ร้อยละของการได้รับการกระตุ้นพัฒนาการ และร้อยละของการเข้าโรงเรียนของเด็กกลุ่มอาการดาวน์ที่มารับการรักษาที่โรงพยาบาลสงขลานครินทร์*

ผู้ป่วยและวิธีการ *: เด็กกลุ่มอาการดาวน์ที่มารับการรักษาที่โรงพยาบาลสงขลานครินทร์ จำนวน 295 คน ทำการศึกษาย้อนหลังถึงลักษณะทางคลินิก ร้อยละของการได้รับการกระตุ้นพัฒนาการ และร้อยละของการเข้าโรงเรียน*

ผลการศึกษา *: พบโรคหัวใจพิการแต่กำเนิด ร้อยละ 38.6 ความผิดปกติของระบบทางเดินอาหาร ร้อยละ 16.9 มะเร็งระบบโลหิตวิทยา ร้อยละ 6.1 และความผิดปกติของต่อมไทรอยด์ ร้อยละ 11.4 อัตราการเสียชีวิตในเด็กกลุ่มอาการดาวน์พบร้อยละ 13.2 ผู้ป่วยกลุ่มดาวน์ส่วนใหญ่ (ร้อยละ 65.6) ได้รับการกระตุ้นพัฒนาการ แต่มีผู้ป่วยเพียงร้อยละ 40.2 ของผู้ป่วยทั้งหมดที่ได้รับการฝึกพูดภายในอายุ 2 ปี มีเด็กกลุ่มอาการดาวน์ที่อายุมากกว่า 6 ปี จำนวน 109 ราย ที่ยังได้รับการติดตามอย่างต่อเนื่อง ซึ่งพบว่ามีเด็กเพียง 74 ราย (ร้อยละ 67.9) ที่ได้เข้าโรงเรียน การเข้าโรงเรียนมีความสัมพันธ์กับรายได้ของครอบครัว แต่ไม่สัมพันธ์กับระดับการศึกษาของบิดาหรือมารดา*

สรุป *: โรคหัวใจพิการแต่กำเนิดและความผิดปกติของระบบทางเดินอาหารเป็นความผิดปกติแต่กำเนิดที่พบได้บ่อยในกลุ่มอาการดาวน์ ผู้ป่วยส่วนมากได้รับการกระตุ้นพัฒนาการ แต่มีเพียงร้อยละ 40.2 เท่านั้นที่ได้รับการฝึกพูด ในเด็กอายุมากกว่า 5 ปี ได้เข้าโรงเรียนเพียงร้อยละ 68 และการเข้าโรงเรียนมีความสัมพันธ์กับรายได้ของครอบครัว*