Factors Influencing Development of Down Syndrome Children in The First Three Years of Life: Siriraj Experience

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Objective: *To analyze factors influencing development of Down syndrome children in the first three years of life.*
Material and Method: *A cross-sectional study was conducted in 100 Down syndrome (DS) children attending at the Genetics clinic, Department of Pediatrics, Siriraj Hospital between January 2002 and December 2005. All individuals were three to six years of age. The data was collected from January to December 2006, including general information and factors on the child and their families. The child developmental quotient (DQ) was evaluated by Capute Scales Cognitive Adaptive Test/Clinical Linguistic & Auditory Milestones Scale (CAT/CLAMS) at three years of age. Data were analyzed by descriptive statistic and multiple linear regression with the significant level at p-value < 0.05.*
Results: *The mean development quotient (DQ) was 63.78 $\pm$ 11.25 (range 32-91) with the majority being mild developmental delay. The child and family factors contributing to developmental quotient (DQ) outcome were birthplace, congenital heart disease, age at the first genetic counseling, regular follow-up in the Genetics clinic, age at the first early stimulation program/speech training program, parental education/occupation, and family income. Only family income and age at the first speech-training program were found to be independently associated with developmental quotient (DQ) at the age of three years (p-value < 0.05).*
Conclusion: *Down syndrome is the most common genetic cause of mental retardation. Various factors contribute to developmental quotient (DQ) outcome but the most important factors are family income and age at the first speech-training program. Therefore, Down syndrome children with the above factors should be followed-up and monitored closely for the optimal long-term outcome.*

Keywords: *Down syndrome, Development, Factors*

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Down syndrome (DS) is the most common chromosomal abnormality with an incidence of 1:600-800 live births and also the most common genetic cause of mental retardation and multiple congenital anomalies[1-3]. Although many congenital anomalies are commonly found in these children such as congenital heart diseases (40-50%)[1-4], gastrointestinal disorders (10-15%)[1-3], congenital and/or compensated hypothyroidism (2-25%)[1-3,5], ophthalmic problems (50%)[1-3,6,7], and hearing loss (75%)[1-3,6,8], developmental delay or mental retardation is the problem of the most concern.

The development of children during the first three years is very important, as it is fundamental for child development outcome. Particularly for DS children, this period can be called "Preparatory phase" for them[9]. To promote the proper development for the

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children, family factors are important because they are the first environment for child growth and development. Good childcare and rearing will enable children to have good physical, intellectual, and psychosocial developments. Other factors such as parental education, socioeconomic status of a family are important and influence the children's development[10-12]. Regarding developmental delay or mental retardation, intervention with an early stimulation program and speech-training program starting in the first years of life has been proved beneficial on development[13]. The authors performed a cross-sectional study to analyze the factors including both child and family factors that influence development in the first three years of DS children.

Material and Method

A cross-sectional study was conducted on 100 children with Down syndrome who were followed-up at Siriraj Hospital between January 2002 and December 2005. All individuals were three to six years of age. The data was collected from January to December 2006, including general information and factors on the child and their families. The child developmental quotient (DQ) was evaluated by Capute Scales Cognitive Adaptive Test/Clinical Linguistic & Auditory Milestones Scale (CAT/CLAMS) at three years of age. CAT/CLAMS are a highly recommended tool for developmental assessment of 1-36-month-old children. The Capute Scales are designed to assess the two streams of cognitive development, longitudinal language pathway based on sequential milestones language (CLAMS) and visual motor solving tasks (CAT). Scoring of the Capute CAT/CLAMS is based on the child's performance on test items corresponding to developmental milestones. The scores are divided by the child's chronological age to determine the DQ[14]. All developmental tests of Down syndrome children were conducted by the same developmental pediatrician (S.T.).

The study factors were (i) child factors including gender, birthplace, age at the first genetic counseling, associated congenital anomalies, attending the early stimulation program, and speech-training program, and (ii) family factors including parental age, education, occupation, family income, major caregiver, number of siblings, and other family members.

Concerning associated congenital anomalies, all DS children were evaluated for congenital heart diseases, gastrointestinal anomalies, and hypothyroidism by pediatricians within the first two months. Children with suspected congenital heart disease were referred to pediatric cardiologists and those with suspected gastrointestinal anomalies were referred to pediatric gastroenterologists and pediatric surgeons. Thyroid function tests were routinely performed in all DS children and all individuals were referred to pediatric endocrinologists if the results were abnormal. Vision and hearing assessments were also done in all DS children before 18 months of age.

Genetic counseling was given to the families by a geneticist in the first visit in the Genetics clinic. All families were routinely advised to attend the early stimulation program in the first visit and attend the speech-training program at the age about 12-18 months. The children who attended the Genetics clinic less than 7 times in the first three years of age, or attended the early stimulation program less than 8 times annually were classified as "irregular".

Means $\pm$ standard deviations, ranges, numbers, and percentages were used for descriptive statistics. Developmental quotients (DQ) by various factors were compared using the independent samples t-test and ANOVA with statistically significance at p-value < 0.05. Stepwise multiple linear regression analysis was used for analyzing factors influencing development of DS children with significance at p-value < 0.05.

Results

Demographic and clinical data of Down syndrome children (Child factors)

Of the 100 DS children, 59 (59%) were males and 41 (41%) were females. Regarding birthplaces of these children, 69 (69%) were born in hospitals in Bangkok including Siriraj Hospital and 31 (31%) were born in provincial hospitals. Genetic counseling by a geneticist was provided to all families in the first Genetics clinic visit with mean age at the first genetic counseling being 5.28 ± 6.98 months (range 1 day-37 months). In these 100 DS children, 85 (85%) were regularly followed-up in the Genetics clinic, 96 (96%) received the early stimulation program with regular follow-up in 79 (82.29%) and only 75 (75%) regularly attended the speech-training program. Mean ages at the first early stimulation program and the first hearing assessment (speech training program) were 3.64 ± 2.89 months (range 1-18) and 23.67 ± 10.34 months (range 7-60), respectively (Table 1).

All DS children who had signs or symptoms of congenital heart diseases were evaluated by pediatric cardiologists and confirmed by echocardiogram.

Table 1. Number, percentage and developmental quotient (DQ) of Down syndrome children by child factors

Characteristics	n (%)	DQ (Mean ± SD)	p-value
Gender	100		
Male	59 (59)	62.42 ± 11.88	0.149*
Female	41 (41)	65.73 ± 10.10	
Birthplace	100		
Siriraj hospital & Bangkok	69 (69)	66.00 ± 10.91	0.003*
Provincial	31 (31)	58.84 ± 10.56	
Age at the 1st genetic counseling	100		
< 3 month	54 (54)	67.24 ± 10.80	0.001*
≥ 3 month	46 (46)	59.72 ± 10.48	
Follow-up (genetic clinic)	100		
Regular	85 (85)	65.04 ± 10.78	0.007*
Irregular	15 (15)	56.67 ± 11.58	
Early Stimulation Program & Speech Training Program			
Age at the 1st early stimulation program	93		
< 3 month	44 (47.31)	67.52 ± 11.58	0.009*
≥ 3 month	49 (52.69)	61.43 ± 10.52	
Follow-up (early stimulation program)	96		
Regular	79 (82.29)	65.67 ± 10.70	0.003*
Irregular	17 (17.71)	56.82 ± 11.74	
Age at the 1st speech training program	95		
< 18 months	27 (28.42)	70.89 ± 9.60	<0.001*
≥ 18 months	68 (71.58)	61.53 ± 10.93	
Follow-up (speech training program)	100		
Yes	75 (75)	66.13 ± 10.67	<0.001*
No or irregular	25 (25)	56.72 ± 10.09	
Associated Congenital Anomalies			
Congenital heart diseases	100		
Yes	49 (49)	61.51 ± 11.89	0.047*
No	51 (51)	65.96 ± 10.25	
Hypothyroidism	100		
Yes	23 (23)	64.74 ± 14.44	0.702*
No	77 (77)	63.49 ± 10.20	
Isolated hyperthyrotropinemia	100		
Yes	35 (35)	64.60 ± 9.37	0.595*
No	65 (65)	63.34 ± 12.19	
GI disorder	100		
Yes	8 (8)	63.63 ± 8.63	0.968*
No	92 (92)	63.79 ± 11.49	
Visual problem	94		
Yes	26 (27.66)	66.77 ± 12.52	0.070*
No	68 (72.34)	62.07 ± 10.51	
Age at the 1st visual assessment	94		
< 18 months	16 (17.02)	66.69 ± 8.06	0.196*
≥ 18 months	78 (82.98)	62.69 ± 11.70	

* Independent sample t-test

Congenital heart diseases were found in 49 (49%) children, 31 (63.27%) and 24 (48.98%) were treated with medications and surgical corrections respectively. Congenital gastrointestinal disorders were found in eight (8%) children. Thyroid function tests were evaluated in all DS children and found to be abnormal in 58 children, 23 (23%), and 35 (35%) were diagnosed with hypothyroidism and isolated hyperthyrotropinemia and mean age at diagnosis of both conditions were 10.46 ± 11.47 months (range 1-39), and 11.90 ± 13.99 months (range 0-61), respectively. In hypothyroidism, all 23 (100%) children were treated immediately

after diagnosis was established whereas in isolated hyperthyrotropinemia, 31 of 35 (88.57%) children were treated. Ninety four (94%) and 95 (95%) of 100 DS children were assessed for ophthalmic problems and hearing loss, and found to be abnormal in 26 (27.66%) children for ophthalmic problems, and 2 (2.1%) children for hearing loss at 50 dB and 70 dB. Mean age at the first visual assessment was 32.39 $\pm$ 16.94 months (range 4-78).

Demographic data of the families of Down syndrome children (Family factors)

The mean maternal age at the time of the child's birth was 32.79 $\pm$ 6.07 years (range 16-45 years) with maternal age over 35 years (44%) whereas the mean paternal age the time of the child's birth was 35.04 $\pm$ 6.66 years (range 22-56 years) with paternal age over 35 years (54%). Regarding paternal education of these DS children, 32 (32.99%) were at primary level, 16 (16.49%) were at secondary level, 16 (16.49%) had received a diploma and 33 (34.02%) were college graduates or higher. Regarding the maternal education 33 (33.33%) were primary level, 7 (7.08%) secondary level, 22 (22.22%) diploma and 37 (37.37%) were college graduate or higher. The majority (31.63%) of father were employed, while the majority (35%) of mothers were unemployed (Table 2).

In the 100 DS families, about half (51%) had family income greater than 20,000 Baht per month, 64 (64.65%) had more than three family members, and 60 (60.61%) had more than three caregivers. Regarding the number of siblings, 42 (42%) had only one sibling, 41 (41%) had two siblings and 17 (17%) had three or more siblings. The mean family income was 30,914 $\pm$ 37,595.64 Baht per month (range 2,400-300,000), whereas the mean number of siblings and mean number of family members were 1.81 $\pm$ 0.86 (range 1-4) and 3.98 $\pm$ 1.02 (range 2-8), respectively. The majority (77%) of DS children had mothers as the major caregivers.

The relation of the child factors and the family factors to their development quotient (DQ)

Of the 100 DS children who completed developmental testing (DQ) at the age of three years, 29 (29%) were borderline (DQ 70-90), 62 (62%) were mild (DQ 50-70), seven (7%) were moderate (DQ 35-50), and two (2%) were severe (DQ 20-35) developmental delay. Mean development quotient (DQ) was 63.78 $\pm$ 11.25 (range 32-91). For the child factors, the results showed that birthplace, congenital heart diseases, age at the first genetic counseling, regular follow-up in Genetics clinic, age at the first early stimulation program and speech training program, and regular attendance had a significant relation to developmental quotient (DQ) of these children (p-value < 0.05). The family factors that demonstrated significant effect on the development of these children were paternal and maternal education, paternal occupation, and family income (p-value < 0.05) (Table 1, 2).

The result of stepwise multiple linear regression analyses assessing the relation between developmental quotient (DQ) and various child and family factors revealed that only the family income of more than 20,000 Baht per month, and the age at the first speech-training program < 18 months of age were found to be independently associated with greater developmental quotient (DQ) at the age of three years (Table 3).

Discussion

The results of the present study revealed that all Down syndrome individuals had developmental delay with the majority (62%) of these children having mild developmental delay. The child factors contributing to child developmental quotient (DQ) were birthplace, congenital heart disease, age at the first genetic counseling, regular follow-up in the Genetics clinic, age at the first early stimulation program, speech training program, and Genetics clinic attendance on regular basis. In Thailand, although basic medical care has been provided nationwide, early intervention program for children with special needs is limited to medical schools and some provincial hospitals. This can explain why DS children born in the provincial hospitals had lower developmental quotient (DQ) than those born in Siriraj Hospital and other hospitals in Bangkok.

"Genetic counseling" is recommended in Siriraj Hospital to be provided within the first 1-2 months of life to facilitate bonding between parents and DS children. As for well-educated or previously informed parents, the authors provided genetic counseling as soon as families were ready[9]. More importantly, it should be done after parents have established infant-parent bonding during the first 1-2 months of life. Parents of children with DS should be advised to enroll their babies into an "Early stimulation program" on a regular basis within the first months of life because it has been proven beneficial to their development as in previous reports in Thailand and other countries[9,13,15-19]. As shown in the present study, DS children receiving the first genetic counseling and early stimulation program within the first 3 months of life

Table 2. Number, percentage and developmental quotient (DQ) of Down syndrome children by family factors

Characteristics (N)	n (%)	DQ (Mean ± SD)	p-value
Paternal age	100		
≥ 35	54 (54)	63.00 ± 12.18	0.455*
< 35	46 (46)	64.70 ± 10.12	
Maternal age	100		
≥ 35	44 (44)	62.02 ± 12.86	0.167*
< 35	56 (56)	65.16 ± 9.70	
Paternal education	97		
Primary	32 (32.99)	59.78 ± 9.21	0.008*
Secondary	16 (16.49)	61.31 ± 9.89	
Highschool diploma	16 (16.49)	64.06 ± 8.66	
College degree or higher	33 (34.02)	68.82 ± 13.10	
Maternal education	99		
Primary	33 (33.33)	60.30 ± 8.86	<0.001**
Secondary	7 (7.08)	56.14 ± 9.58	
Highschool diploma	22 (22.22)	62.05 ± 11.17	
College degree or higher	37 (37.37)	69.73 ± 11.15	
Paternal occupation	98		
Governmental	18 (18.37)	61.44 ± 10.39	0.008**
Self-employed	26 (26.53)	66.08 ± 12.37	
Employee	31 (31.63)	59.39 ± 10.20	
Business	23 (23.47)	68.87 ± 9.54	
Maternal occupation	100		
Governmental	13 (13)	61.38 ± 10.80	0.071**
Self-employed	19 (19)	66.68 ± 12.26	
Employee	13 (13)	59.38 ± 6.836	
Business	20 (20)	8.65 ± 11.23	
Unemployed	35 (35)	61.94 ± 11.37	
Family income	100		
< 20,000	49 (49)	60.04 ± 8.79	0.001*
≥ 20,000	51 (51)	67.37 ± 12.23	
No. of siblings (including patient)	100		
1	42 (42)	63.95 ± 11.88	0.768**
2	41 (41)	64.34 ± 10.08	
≥ 3	17 (17)	62.00 ± 12.79	
No. of family member	99		
≤ 3	35 (35.35)	64.71 ± 12.19	0.562*
> 3	64 (64.65)	63.33 ± 10.86	
No. of caregivers (including major caregiver)	99		
2	39 (39.39)	65.79 ± 10.60	0.209*
≥ 3	60 (60.61)	62.97 ± 11.03	
Major caregiver	100		
Mother	77 (77)	64.39 ± 11.31	0.324*
Non-mother	23 (23)	61.74 ± 11.04	

* Independent sample t-test
** ANOVA

Table 3. Stepwise multiple linear regression model for independent predictors developmental quotient (DQ) at the age of three years

Predictor variables	β	Standard error (SE)	p-value
Family income (100)	60.43	1.50	<0.001
Age at the 1st speech training program (95)	0.122	0.028	0.003

and attending the Genetics clinic on regular basis significantly attained their developmental quotient (DQ) better than those who did not receive the same. The results were similar for DS children who received the first speech-training program within the first 18 months of life. The results indicate that genetic counseling, an early stimulation program, speech-training program starting at the appropriate time, and regular follow-up in the Genetics clinic or by general pediatrician are the most important for attainment of optimal developmental outcome.

The prevalence of associated congenital anomalies in DS children in the present study is similar to the previous studies in Western countries except for hearing loss that has a lower incidence in the present report[1-6,9,13,15]. Congenital heart disease is the most common congenital anomaly with the incidence of 49%, whereas the incidence of hypothyroidism, isolated hyperthyrotropinemia, and congenital gastrointestinal anomalies are 23%, 35%, and 8%, respectively. Regarding associated congenital anomalies, only congenital heart diseases were found to be associated with worse developmental quotient (DQ). This could be explained by frequent hospitalizations in these children corresponding to the results of previous studies that found that congenital heart diseases and pulmonary diseases are the major cause of hospitalization in young infants with DS[15,20]. Hypothyroidism and isolated hyperthyrotropinemia are also common in DS children but they did not contribute to low developmental quotient (DQ) because all DS cases with hypothyroidism or significant hyperthyrotropinemia were treated by thyroxine hormone as soon as diagnosis was made. Therefore, thyroid screening test in the neonatal period and annual thyroid function test are the standard recommendation in Down syndrome[3,5,13,15,20,21] children. An echocardiogram is also standard recommendation in many reports because abnormal findings of serious heart diseases may be absent due to early pulmonary vascular resistance[3,6].

The family factors affecting child development are parental education, occupation and family income of which family income is the most important determining factor. The paternal age, the number of siblings, family members and caregivers do not contribute to developmental outcome as in the previous study[22,23]. Although the majority (77%) of DS families had mothers as the major caregiver, education levels of both parents were associated with developmental quotient (DQ) of DS children because parents with higher education would be more knowledgeable to raise and care for children with DS. Regarding paternal occupation, children who lived with full-time employee fathers had a higher chance of delayed development than those who lived with fathers who were businessmen. This might be because employee-fathers may have less time to take care of their children. This also explains why children from low socioeconomic status or poor income will have greater developmental delay[10-13,15].

Conclusion

Down syndrome is the most common genetic cause of mental retardation. Developmental delay or mental retardation is one of the major concerns in these children. There are many child and family factors correlating with lower developmental quotient (DQ) in these children including birthplace, congenital heart disease, age at the first genetic counseling, regular follow-up in Genetics clinic, age at the first early stimulation program and speech-training program, regular follow-up in the Genetics clinic, parental education, paternal occupation, and family income. According to these factors, only family income and the age at the first speech-training program have been independently associated with developmental outcome when analyzed by multiple linear regression. Therefore, Down syndrome having the above-mentioned factors should be followed-up and assisted closely for the long-term benefit of these children.

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ปัจจัยที่มีผลต่อพัฒนาการของเด็กกลุ่มอาการดาวน์ช่วงอายุ 3 ปีแรกในโรงพยาบาลศิริราช

พรสวรรค์ วสันต์, บุญชัย บุญวัฒน์, สำรวย ไตรติลานันท์, นิธิวัชร์ วัฒนวิจารณ์, อัจฉรา เสถียรกิจการชัย, พิษณุ รัตนรักษ์, อรอนงค์ มะลิลำ, สมพร เหลี่ยมมงคลกุล

วัตถุประสงค์: *เพื่อศึกษาปัจจัยที่มีผลต่อพัฒนาการของเด็กกลุ่มอาการดาวน์ในช่วงอายุ 3 ปีแรก*

วัสดุและวิธีการ: *การศึกษาภาคตัดขวางในเด็กกลุ่มอาการดาวน์ 100 คน ช่วงอายุ 3 ถึง 6 ปีที่เข้ารับการรักษาในโรงพยาบาลศิริราช ตั้งแต่ มกราคม พ.ศ. 2545 ถึงธันวาคม พ.ศ. 2548 เก็บข้อมูลระหว่าง มกราคม ถึง ธันวาคม พ.ศ. 2549 ประกอบด้วยข้อมูลทั่วไป ปัจจัยของเด็ก และปัจจัยของครอบครัว ประเมินพัฒนาการด้วย CAT/CLAMS เมื่ออายุ 3 ปี และวิเคราะห์ข้อมูลด้วยสถิติเชิงพรรณนาและ multiple linear regression*

ผลการศึกษา: *ค่าเฉลี่ยของ developmental quotient (DQ) 63.78 ± 11.25 โดยส่วนใหญ่อยู่ในกลุ่มพัฒนาการช้าเล็กน้อย (mild developmental delay) ปัจจัยที่มีความสัมพันธ์กับค่า developmental quotient (DQ) ได้แก่ สถานที่เกิด, โรคหัวใจพิการแต่กำเนิด, อายุที่ได้รับคำปรึกษาทางพันธุศาสตร์ การกระตุ้นพัฒนาการ และการฝึกพูดเป็นครั้งแรก รวมถึงความสม่ำเสมอในการมาตรวจติดตามที่คลินิกพันธุกรรม การกระตุ้นพัฒนาการ และการฝึกพูด, การศึกษาของบิดาและมารดา, อาชีพของบิดา และรายได้ของครอบครัว และมีเพียงรายได้ของครอบครัว และอายุที่ได้รับการฝึกพูดเป็นครั้งแรก ที่มีผลต่อพัฒนาการโดยไม่ขึ้นกับปัจจัยอื่น ในเด็กกลุ่มอาการดาวน์เมื่ออายุได้ 3 ปี*

สรุป: *กลุ่มอาการดาวน์เป็นความผิดปกติทางพันธุกรรมที่พบได้บ่อยที่สุดที่ทำให้เกิดภาวะปัญญาอ่อน โดยปัจจัยหลายอย่างมีผลต่อค่า developmental quotient (DQ) แต่ปัจจัยที่สำคัญที่สุดได้แก่ รายได้ของครอบครัว และอายุที่เริ่มฝึกพูดเป็นครั้งแรก ดังนั้นในเด็กกลุ่มอาการดาวน์ที่มีปัจจัยดังกล่าวข้างต้น และได้รับการตรวจติดตามอย่างสม่ำเสมอมักจะมีเชาวน์ปัญญาในเกณฑ์ดีกว่าเด็กกลุ่มอาการดาวน์ที่ไม่ได้รับการสนับสนุนส่งเสริม*