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Original Article

Factors associated with intelligence in young children with Down syndrome

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Abstract

Introduction Despite the considerable number of children with Down syndrome in Indonesia, there is little data available on the success of intervention programs. This study was performed to define factors affecting the intelligence of young children with Down syndrome.

Objective To determine factors associated with lower intelligence in children with Down syndrome, including growth parameters and participation in intervention programs.

Methods This cross-sectional study was undertaken from December 2010 to March 2011. Subjects were 60 children with Down syndrome aged 2-6 years who were enrolled in an intervention program at both the Medical Rehabilitation Department, Cipto Mangunkusumo Hospital, and the Growth and Development Clinic, Harapan Kita Women's and Children's Hospital. Parents' data was obtained through self history-taking and perusal of medical records. Subjects' anthropometric data (body weight, body height, and head circumference) was obtained through measurements using calibrated instruments. A psychologist administered IQ tests on the subjects. Results of the anthropometric and IQ tests were given to parents one week following the examinations.

Results From the 111 children with Down syndrome registered in the intervention programs, 60 children (36 boys and 24 girls) met the inclusion criteria. The mean age of subjects was 4 years 6 months. Most subjects were well-nourished. Fifty-five subjects had microcephaly. Eighty-two percent of subjects participated in the program regularly and 70% of subjects had started in the program at less than 1 year of age. Subjects' mean IQ was 52.8. Analysis showed that girls, subjects who were overweight and obese, subjects with microcephaly, those with irregular attendance in the program, and those living under the poverty line were at highest risk for severe mental retardation.

Conclusion Factors associated with the intelligence in children with Down syndrome were female gender, overweight/obesity, severe microcephaly, below-poverty line economic status, and irregular participation in the program. **[Paediatr Indones. 2012;52:194-9]**.

Keywords: *Down syndrome, intelligence, factors*

Children with Down syndrome (DS) have multiple congenital anomalies and mental impairment due to the presence of extra genetic material from chromosome 21. Medical management, home environment, education, and vocational training can significantly affect their level of functioning and facilitate transition into adulthood. Several factors require continual assessment throughout childhood and periodic reviews at the appropriate ages. These factors include personal support from the family, available financial and medical support programs for the child and family, injury and abuse prevention, as well as special consideration for developmental skills, diet and

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exercise to maintain appropriate weight.[1-3]

Data provided by the University of Indonesia Faculty of Medicine, Biology Department, from 1992 to 2004 showed there were 1,987 individuals with DS based on chromosomal analysis evaluation.[4] Although definitive data is unavailable, if we extrapolate from the 2010 population census, there are approximately 235,000 children with DS living in Indonesia.[5]

Several congenital anomalies are commonly found in children with DS, such as congenital heart diseases (40-50%), gastrointestinal disorders (10-15%), congenital and/or compensated hypothyroidism (2-25%), ophthalmic problems (50%), and hearing loss (75%).[1-3,6] However, the main problems are developmental delay or mental retardation. In order to overcome these problems, intervention with early stimulation and speech training programs starting in the first years of life are highly recommended and have been proven beneficial for the development of DS children. The first three years of life are fundamental in children's developmental outcome, particularly for those with DS. Family factors such as maternal age, parental education, and socioeconomic status, also play an important role in determining the results of participating in an intervention program.[8]

Despite the considerable number of children with DS in Indonesia, there is little data available on the success of intervention programs. To our knowledge, outcomes of such programs have never been studied in Jakarta. We aimed to observe factors affecting the intelligence of children with DS who participated in an early intervention program.

Methods

This cross-sectional study was held from December 2010 to March 2011 in 60 children with DS who were enrolled in the early intervention program in both the Medical Rehabilitation Department, Cipto Mangunkusumo Hospital, and the Growth and Development Clinic, Harapan Kita Women's and Children's Hospital. We included subjects aged 2 to 6 years with extra material, translocation, or mosaicism in chromosome 21 (proven by chromosomal analyses). Subjects also attended the intervention program regularly in the six months prior to the study, and had neither bone deformities (based on clinical assessment) nor hydrocephalus (based on head circumference measurement and clinical assessment). Subjects with illness, lack of parental consent, or incomplete examinations were excluded. Subjects were sampled consecutively. Sample size estimation was determined using the consensus the rule of thumb (total of independent variables multiplied by ten).[9] The dependent variable was intelligence quotient (IQ), and independent variables were maternal age, gender, nutritional status, degree of microcephaly, family income, and regularity in attending the intervention program.

This study was approved by the Medical Research Ethics Committee of the University of Indonesia Faculty of Medicine. Informed consent was obtained from subjects' parents. Subjects' weight, height, and head circumference were measured using calibrated instruments. A psychologist performed IQ tests using the Stanford-Binet scale, form L-M. Anthropometric measurements and IQ test results were given to the parents, with explanations.

Economic status was categorized as below or above the poverty line of IDR 211,726 per capita per month.[10] Mental retardation was classified into mild (IQ score 50 - 69), moderate (IQ score 35 - 49), or severe (IQ score 20 - 34). Subjects' intelligence levels were otherwise classified into borderline (IQ score 60 - 69) or low average (IQ score 80 - 89).[11] Regular intervention program attendance was defined as attending the program at least once a week for the six months prior to the study. Microcephaly was classified into mild (head circumference 2 - 3 SD below normal average) or severe (head circumference exceeding 3 SD below normal).

Results

From December 2010 to March 2011, 111 children with DS attended intervention programs in the Medical Rehabilitation Department, Cipto Mangunkusumo Hospital (25 children) and the Growth and Development Clinic, Harapan Kita Women's and Children's Hospital (86 children). From the 86 children at Harapan Kita Women's and Children's Hospital, 62 children met the inclusion criteria. Sixty of these children's parents agreed to participate, but eventually 5 of these children were

excluded (2 children with illness and 3 children with behavioral disorders that prevented them from being examined). From the 25 children at Cipto Mangunkusumo Hospital, 15 children met the inclusion criteria. Eleven children were successfully contacted, but only 5 children's parents consented. The total number of subjects was 60 children.

Mean weight, height, and head circumference were 14.7 kg (SD 3.8), 93.3 cm (SD 8.4), and 46.5 cm (SD 1.6), respectively. Short stature was observed in 90% of subjects (aged 3 years 1 month to 5 years 9 months). The mean IQ was 52.8 (SD 14.1). Other characteristics of subjects are listed in **Table 1**.

Subjects who tended to have moderate or severe mental retardation were female, overweight/obese, had severe microcephaly, irregularly attended the intervention program, came from families with below-poverty line incomes, and began the intervention program at greater than 1 year of age (**Table 2**).Some factors that were less significant, but still eligible for multivariate analysis (P<0.25) were duration of intervention program attendance (P<0.25) and nutritional status (P<0.071) **(Table 3).**

Logistic regression analysis revealed that risk factors associated with severe mental retardation were female gender, being overweight/obese, irregularly attending the intervention program, and family income below the poverty line. We found that girls with DS were 46.3 times more likely to have moderate/severe mental retardation than boys with DS. Overweight and obesity increased the risk of moderate/severe mental retardation as much as 85.5 times compared to well- and undernourished children. Subjects who did not regularly follow the intervention program were at risk of having moderate/severe mental retardation approximately 77 times higher than those who regularly attended the program. Children who came from families with incomes below the poverty line were at risk of moderate/severe mental retardation approximately 37.8 times more than those who came from families with incomes above the poverty line. Discrimination by logistic regression analysis was assessed by the area under the curve (AUC) by receiver-operating curve (ROC) method. The AUC value was 92.5% (P <0.001, 95% CI 0.860 to 0.990) and showed a strong correlation. Calibration with test P value of 0.905 with Hosmer -Lemeshow test indicated good calibration[12] **(Table 4).**

Table 1. Characteristics of the subjects

Characteristics	n= 60
Gender, n (%)	
Male	36 (60)
Female	24 (40)
Age, n (%)	
2 - 4 years	38 (63)
4 years 1 month - 6 years	22 (37)
Nutritional status, n (%)	
Undernourished	8 (13)
Well-nourished	36 (60)
Overweight	7 (12)
Obese	9 (15)
Stature, n (%)	
Normal	6 (10)
Short	54 (90)
Head circumference, n (%)	
Normal	9 (15)
Mild microcephaly	37 (62)
Severe microcephaly	14 (23)
Classification based on IQ score, n (%)	
Low average	3 (4)
Borderline	4 (7)
Mild retardation	27 (56)
Moderate retardation	16 (27)
Severe retardation	10 (17)
Congenital anomaly, n (%)	
Heart	35 (58)
Eye	5 (8)
Endocrine (hypothyroidism)	2 (3)
Digestive tract	1 (2)
Heart and Eye	1 (2)
None/unknown	16 (27)
Age at onset of intervention program attendance, n (%)	
≤ 1 year	42 (70)
> 1 year	18 (30)
Regularity of intervention program attendance, n (%)	
Regular	49 (82)
Irregular	11 (18)
Duration of intervention program attendance, n (%)	
≤ 2 years	24 (40)
> 2 years	36 (60)
Maternal age, n (%)	
<35 years	34 (57)
≥35 years	26 (43)
Family income, n (%)	
Below poverty line	15 (25)
Above poverty line	45 (75)

Table 2. Risk factors associated with mental retardation classification

Risk factors		Mental retardation classification		P
		Mild n (%)	Moderate & severe n (%)	
Gender	Male	25 (69.4)	11 (30.6)	0.018
	Female	9 (37.5)	15 (62.5)	
Nutritional status	Undernourished	5 (62.5)	3 (37.5)	0.071
	Well-nourished	23 (63.9)	13 (36.1)	
	Overweight/obese	6 (37.5)	10 (62.5)	
Head circumference	Normal	8 (88.9)	1 (11.1)	<0.001
	Mild microcephaly	26 (70.3)	11 (29.7)	
	Severe microcephaly	0 (0)	14 (100)	
Regularity of intervention program attendance	Regular	33 (67.3)	16 (32.7)	<0.001
	Irregular	1 (9.1)	10 (90.9)	
Duration of program attendance	≤2 years	18 (75)	6 (25)	0.202
	>2 years	21 (58)	15 (42)	
Age at intial intervention	≤1 years	27 (45)	8 (13.3)	0.017
	>1 years	7 (11.7)	18 (30)	
Family income	Below poverty line	3 (20)	12 (80)	0.001
	Above poverty line	31 (68.9)	14 (31.1)	

Table 3. Factors associated with mental retardation classification

	Mental retardation classification	n	Mean, years	SD	P
Age at onset of intervention program attendance	Mild	34	0.87	0.68	0.017
	Moderate & severe	26	1.53	1.63	
Maternal age	Mild	34	33.03	5.56	0.050
	Moderate & severe	26	33.78	6.30	

Table 4. Results of multivariate analysis with logistic regression method

Variables	Coefficient	P	OR	95% CI
Female gender	3.84	0.006	46.3	3.0 to 704.9
Overweight/obesity	4.45	0.003	85.5	4.7 to 1565.7
Regular attendance of intervention program	4.35	0.008	77.6	3.2 to 1886.7
Family income below poverty line	3.63	0.006	37.8	2.8 to 506.5
Age at first complying the intervention program	0.95	0.309	2.6	0.41 to 16.2
Maternal age	0.03	0.973	1.0	0.18 to 6.04
Duration of intervention program attendance	0.45	0.114	1.6	0.9 to 2.7

Discussion

This study was cross-sectional in design. Since there was no preliminary IQ score data available, we were unable to compare subjects' IQ score before and after intervention. A prospective study is needed to ascertain the advantages of intervention programs. Children with DS are also known to have specific behavioral disorders, such as poor concentration (70%), requiring more nurturing (61%), acting repulsively (51%), and secluding themselves (28%).[13,14] These disorders may also affect test results, given that the examiner has limited time to get acquainted with subjects.

Several studies reported that more boys than girls tend to have severe mental retardation, although

this finding is inconclusive.[15,16] In contrast, we found that 60% of subjects with moderate and severe mental retardation were girls, aged 5 years 1 month to 6 years 11 months.

An explanation for severe mental retardation may be decreased brain function due to the role of superoxide dismutase enzyme in premature brain aging.[17] Studies over last three decades have shown that levels of intelligence and rates of development decreased with age in individuals with DS. Evidence of premature brain aging in adults with DS is the significantly higher than normal incidence of Alzheimer's disease and dementia.[18] Superoxide dismutase, an enzyme catalyzing superoxide radicals to H_2O_2, has reportedly been the cause of premature brain aging in individuals with DS.[17] In this study, all subjects with severe mental retardation were aged 5 - 7 years. Their severe mental retardation may be due to a progressive decline in brain function. Therefore, the duration of intervention program attendance does not ensure increased IQ scores in children with DS.

We observed that approximately 60% of subjects were well-nourished, 15% of subjects were obese, 13% were undernourished, and 12% were overweight. Individuals with DS, especially in adolescence and adulthood, tend to have excess body weight.[19,20] This could be due to growth hormone (GH) deficiency, hypothyroidism, decreased basal metabolic rate, relatively low level of physical activity, or increased levels of leptin. Prepubertal children with DS have high levels of leptin, which have been positively correlated to body mass index and degree of adiposity. Further investigation is required to ascertain GH, thyroid function, and leptin levels in children with DS.[20] We found a significant correlation between nutritional status and the degree of mental retardation. The risk of severe mental retardation was 85.5 times higher in overweight and obese subjects. Children and adolescents with mental and physical disabilities tend to lead sedentary lifestyles, so there is a higher prevalence for overweight in this population. Overweight and obesity are not just risk factors for chronic conditions, such as hypertension, hyperlipidemia, and insulin resistance, but may also have secondary effects, such as fatigue, pain, limited mobility and social interaction, as well as reduced self-help skills. As a result, obese children with DS are often unable to attend schools with occupational therapy, and are frequently unable to mingle with peers.[19] Hence, mentally handicapped children with overweight and obesity may have lower IQ scores compared to well-nourished subjects.

There have been few studies on the impact of microcephaly on the degree of mental retardation in children with DS. However, in a normal population of school children in the United States, children with microcephaly had average IQ scores comparable to normocephalic children (99.5 vs 105). Nevertheless, the average academic performance in the microcephalic group was lower than that of the normocephalic group (49 vs 70).[21] We observed that all subjects with severe microcephaly had moderate to severe mental retardation. The bivariate analysis results also showed a significant relationship between the degree of microcephaly with mental retardation, but due to singularity (an extreme amount of cells in the data is zero), the degree of microcephaly could not be included in the multivariate logistic regression analysis. The extreme data would result in an infinite OR value.

Children with DS who attended the intervention program had IQ and social quotient (SQ) scores significantly higher than those who did not attend. Developmental quotient (DQ) results of 100 children with DS aged 3 to 6 years in Thailand who started speech therapy at age < 18 months were higher compared to that of the groups who initially attended speech therapy at ages > 18 months.[8] Our bivariate analysis revealed a significant correlation between the age at initial intervention and the degree of mental retardation. Subjects who began the program at an age of < 12 months had higher IQ scores compared to those who began the program after the age of 12 months. However, our multivariate analysis showed no significant correlation between the age at onset of attending the intervention program and the degree of mental retardation.

Two studies in Thailand showed that children from high income families had significantly higher DQs compared to those from low income families. Furthermore, children with DS who came from high income families had better school attendance.[8,16] Similarly, we found a significant correlation between family income and level of intelligence, as children with DS from high income families tended to have

milder mental retardation. We also found that in children with DS aged 2 to 6 years, there was not a significant relationship between maternal age and level of intelligence.

In conclusion, subjects who were female, had severe microcephaly, overweight/obesity, and below-poverty line family incomes tended to have more severe mental retardation. However, subjects who regularly attended intervention programs tended to have milder mental retardation.

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