CHROMOSOMAL ANALYSIS OF MENTALLY RETARDED CHILDREN WITH MICROCEPHALY

ANALISIS KROMOSOM PADA ANAK RETARDASI MENTAL DENGAN MIKROSEFALI

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CHROMOSOMAL ANALYSIS OF MENTALLY RETARDED CHILDREN WITH MICROCEPHALY

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ABSTRACT

Background: Mental retardation is a common condition with the incidence of 1-3% of the entire population; about 25% - 50% of them are genetic causes. Chromosomal causes account for up to 28%. Microcephaly and mental retardation may occur together as a syndrome. Cytogenetic and molecular analysis has been approved to definitively diagnose those syndromes. This research is aimed to know the chromosomal characteristic of children with mental retardation and microcephaly.
Method: This research is observational descriptive study with retrospective data taken start from 2007-2009. The data of head circumference and chromosome analysis from 39 children were processed. The data are then presented as a descriptive statistic after being analyzed using Microsoft Excel 2007.
Results: Chromosomal analysis results shows 18 (46.15%) children with 46,XX karyotype, 11 (28.21%) children with 46, XY karyotype, 5 (12.82%) children with 47,XX+21 karyotype, and 4 (10.26%) children with 47,XY+21 karyotype. There is also one Robertsonian translocation with 46,XX,+21, t(14;21) karyotype.
Conclusion: Normal karyotype (46,XX and 46,XY) were found in 29 (74.36%) children. Visible chromosomal abnormalities detected includes 9 cases of Down syndrome trisomy 21 and one case of Robertsonian translocation with t(14;21) karyotype.

Keyword: Mental retardation, microcephaly, chromosomal analysis

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ABSTRAK

Latar Belakang: *Retardasi mental adalah kondisi yang sering terjadi dengan insidensi sebesar 1-3% dari populasi umum, dan sekitar 25% - 50% nya disebabkan oleh kelainan genetik. Kelainan kromosom memiliki peran pada sekitar 28% kasus. Mikrosefali dan retardasi mental dapat muncul bersamaan sebagai sindrom. Analisis sitogenetik dan molekular telah banyak digunakan untuk menegakkan diagnosis definitif untuk sindrom tersebut. Penelitian ini bertujuan untuk mengetahui gambaran kromosom dari anak dengan retardasi mental dan mikrosefali.*

Metode: *Penelitian ini merupakan penelitian deskriptif observasional dengan pengambilan data secara retrospektif mulai tahun 2007 – 2009. Data lingkar kepala dan analisis kromosom dari 39 anak diproses. Data kemudian disajikan dalam bentuk statistik deskriptif setelah dianalisis dengan Microsoft Excel 2007.*

Hasil: *Hasil analisis kromosom menunjukan 18 (46.15%) anak dengan kariotipe 46,XX; 11 (28.21%) anak dengan kariotipe 46, XY; 5 (12.82%) anak dengan kariotipe 47,XX+21, dan 4 (10.26%) anak dengan kariotipe 47,XY+21. Ditemukan pula satu translokasi Robertsonian dengan kariotipe 46,XX, +21,t(14;21).*

Simpulan: *Kariotipe normal (46,XX and 46,XY) ditemukan pada* 29 (74.36%) *anak. Kelainan kromosom yang terlihat terdiri dari 9 kasus Down syndrome dengan trisomi 21 dan satu kasus translokasi Robertsonian dengan kariotipe t(14;21).*

Kata kunci: *Retardasi mental, mikrosefali, analisis kromosom*

PREFACE

Mental retardation (MR), nowaday called ntellectual disability, is not only a disability condition of intellectual functioning, but also adaptive behavior. This condition can be shown in the patients conceptual skill, as well as social and practical adaptive skill.1 This is a very common human disorder.[2,3]

It was estimated that 1-3 % of the entire population is defined as having mental retardation by the characteristic of having IQ below 70, and suffers from learning and adaptive disabilities.2 Another research said that this condition happens on average at 2,3 % of the total population.4 Many mentally retarded individual still be able to maintain part-time or full-time employment, according to the severity of their disability.[5]

There are many heterogeneous causes of mental retardation. Mostly unknown, but about 25% - 50% of them are genetic causes.[5] Chromosomal causes account for up to 28%, including numerical or partial chromosomal abnormalities, and also cytogenetically invisible microdeletions.[2] Hence, accurate testing for genomic imbalance is essential in terms of diagnosis.[6] Chromosomal analysis is also a key to provide better prevention and management of mental retardation, including accurate genetic counseling services.[7]

Microcephaly, which defined as a small head circumference more than two standard deviation below the mean population, is a common physical sign of mental retardation. Children with microcephaly may carry high risk of low IQ. Despite the fact that this characteristic is not a good indicator of a mental

retardation, the presence of microcephaly may suggests the attending physician to test for existing mental retardation.[9]

Microcephaly and MR may occur together usually as a syndrome, such as Down syndrome, Rett syndrome, and other well known condition.[4,8] These syndrome should be recognized easily because their characteristic in multiple congenital abnormalities, behavioral problems, and certain dysmorphism, but the definitive diagnosis for syndromes of mental retardation with microcephaly should be confirmed by cytogenetic analysis and molecular technique.[8]

This research is aimed to to describe the chromosomal characteristic of children with mental retardation and microcephaly, and to provide information and reference for further research. Thus the better diagnostics method and counseling can be carried out.

METHOD

This research is observational descriptive study with retrospective data taken start from 2007-2009. The target population of this research is all mentally retarded children with microcephaly. The accessible population is mentally retarded children in SLB Widya Bhakti. Physical examination to determine microcephaly condition has been done in SLB Widya Bhakti, while the cytogenetic examination has been done in parallel at CEBIOR Faculty of Medicine Diponegoro University. The data of head circumference and chromosome analysis from 39 children were processed. The data are then

presented as a descriptive statistic after being analyzed using Microsoft Excel 2007.

RESULTS

From the result obtained, there are 29 (74.36%) samples with normal karyotype, and 10 (25.64%) cases of Down syndrome. The table shows the chromosomal analysis results.

Karyotype	Number	Percentage
Normal Karyotypes		
46,XX	18	46.15%
46,XY	11	28.21%
Down Syndromes		
47,XX,+21	5	12.82%
47,XY,+21	4	10.26%
46,XX,t(14;21)+21	1	2.56%
Total	**39**	**100%**

DISCUSSION

A total of 10 (25.64%) children are obtained having chromosomal abnormalities, while 29 (74.36%) children have normal karyotype. But in spite of that fact, the diagnosis of chromosomal disorders still cannot be eliminated from these samples because there is still probability of submicroscopic abnormalities and they are cytogenetically invisible.[4,5] Previous studies shows that there are submicroscopic aberrations in 5-17% of mentally retarded patient with normal result in cytogenetic examination.[42,43]

The number of male children with mental retardation is 56 (52.83%) children, larger than the number of female children (47.17%). This finding is consistent with previous research result which shows that among those with IQ >70, in the range of mild deficiency, boys exceeded girls by a ratio of 2.2:1.[44] Another research also shows a male-female ratio between 2.1 to 2.6:1.[45] But this finding contradict the result found in mentally retarded children with microcephaly of this research. It was found that among mentally retarded children with microcephaly, female number exceeds those of male. It was found that 24 (61.54%) of them are female, and 15 (38.46%) of them are male. The same finding was found in mentally retarded children with microcephaly whose have normal karyotypes, with 18 (46.15%) female children and 11 (28.21%) male children identified.

Down syndrome is the responsible cause for 25%-30% mental retardation all around the world. The overall incidence is aroung 0.3%-3.4% in entire population.[46,47] The same result was found in this research, where ten cases (25.64%) of Down Syndrome was found in this research.

Among all ten Down syndrome cases found, nine (23.08%) children are identified with trisomy of chromosome 21, a condition that suggest a classic type of Down Syndrome.[31,32] This result is consistent with the previous research, which shows that about 94% of Down Syndrome cases were caused by this trisomy.[36,37]

Four male children and six female children were identified from all cases of Down syndrome, giving the male-to-female ratio of 1:1.5. This result is

in contrast with previous research which shown higher number of male with Down syndrome than female with one. It says that the male-to-female ratio in newborn with Down syndrome is 1.15:1. This lower ratio is maybe due to the lower sample number used in this research. Another research also shown almost same result, in which the male-to-female ratio in Down syndrome is 1.36:1. This ratio is also said to be higher in the case of trisomy 21, which is appeared to be 1.73:1.[48,49]

Down syndrome is characterized by some physical feature, such as flat occiput, flat facial profile, small simply formed arms, simian crease, and sandal gap.[31,32] All Down syndrome children from this research show sandal gap, simian crease, and upslanting palpebral fissure. There are also some children with brachycephaly, flat occiput, low set ear, and flat nasal bridge.

One case of Robertsonian translocation are also found among Down syndrome children of this research. The karyotipe is identified as 46,XX,t(14;21), +21. This type is known to be the commonest translocation casuse of Down syndrome. A previous study said that translocation causes are responsible for 3.5% of Down syndrome cases, and t(14;21) is described to be the cause of 1.7% Down syndrome cases.[36,37,38]

Genetic counseling and screening programs for children with mental retardation and microcephaly should be encouraged,and information from this research needs to be delivered to other genetic experts for medical and academic interests, so better diagnosis and counseling for children with mental retardation and microcephaly can be carried out.

Also, Futher research with larger number and more advanced techniques is also needed to detect sub-microscopic chromosomal abnormalities which cannot be seen with conventional technique, in order to provide better diagnostic method for children with mental retardation and microcephaly.

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