RESEARCH PAPER

Cognitive Functions and Psychological Problems in Children with Sickle Cell Anemia

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Objective: To study the cognitive functions and psychological problems in children with Sickle cell anemia (SCA).

Methods: Children with SCA were compared with an age-, sex- and community- matched control group of children with no SCA. Malin's Intelligence Scale for Indian children, modified PGI memory scale, and Childhood Psychopathology Measurement Schedule were used to assess cognitive functions and psychological problems.

Results: Verbal quotient, performance quotient and intelligence quotient in SCA group were 77, 81, 78, respectively versus 92, 95, 93, respectively in non-SCA group (P <0.001). Borderline intellectual functioning and mild mental retardation were more common in SCA (70% and 16%, respectively). Children with SCA had impaired attention, concentration and working memory and more behavior problems compared to children without SCA.

Conclusions: Cognitive functions are impaired in children with SCA and they have more psychological problems. Facilities for early identification and remediation of psychological and intellectual problems should be incorporated with health care services for children with sickle cell anemia.

Keywords: *Behavioral problems, Intellectual disability, Memory, Psychopathology.*

Sickle cell anaemia (SCA) is the most common inherited hematological disorder world-wide. It is estimated that about 18 to 34 % of the tribal population in the Wayanad district of Kerala, India suffer from SCA [1,2].

Studies from abroad have reported neurocognitive and developmental problems associated with SCA [3,4]. Very few authors have studied the cognitive functions and psychological problems in children with SCA in India [5].

The Government of Kerala provides comprehensive care to children with SCA through monthly sickle cell anemia clinics conducted in primary health centers in the district. The present study aimed to assess the cognitive functions and psychological problems of children with SCA attending the monthly clinics.

Methods

The study period was from February 2011 to July 2012 and the study protocol was approved by the Institutional ethics committee of Government. Medical College, Kozhikode. Fifteen monthly SCA clinics conducted in Wayanad, provide comprehensive healthcare to 276 children with SCA in the age group of 0-15 years. The study was conducted in 8 of these SCA clinics. A total of 18 visits were required. Children in the 6-15 year age group attending the SCA clinics, who were already diagnosed to have SCA by hemoglobin electrophoresis or high performance liquid chromatography were included in the study after obtaining informed consent from their parents. Children with sickle cell crisis, history of stroke, other chronic illnesses, and neurological disorders were excluded.

Children with no SCA who were attending the same primary health center for minor illnesses were included in the control group. The children in the control group were screened negative for SCA by clinical examination and solubility test. Children in the study group and control group were matched for age, sex and community.

All children were evaluated using Malin's Intelligence Scale for Indian Children (MISIC), Childhood Psychopathology Measurement Schedule (CPMS), and modified PGI Memory Scale. The evaluation was done by a pediatric resident trained in the use of the scales. Every child was allotted one hour, 25 minutes and 15 minutes for MISIC, PGI memory scale and CPMS tests, respectively and all tests were done in a single sitting.

MISIC is the Indian adaptation of Wechsler's intelligence scale for children. It gives a verbal quotient (VQ), performance quotient (PQ) and total quotient (IQ) [6]. CPMS is a parent-reported rating scale for children of age 4 to 14 years [7]. CPMS scale translated to the local language for the purpose of the study by the investigators was given to the parent and each item in the scale was explained to them to get the response.

The PGI memory scale contains 10 subtests and is standardised for adults [8]. A modified version of PGI memory scale was found to be applicable in Indian children [9]. In the present study, three questions in remote memory subtest were modified to be applicable to children and the modified questionnaire was tested in ten normal children to check for their ability to answer the questions.

The data was entered in excel data sheet and analyzed using the SPSS 10.0 software. Two-tailed paired t test was used to assess the statistical significance and a *P* value of less than 0.05 was taken as statistically significant. Correlation of age with the deterioration of cognitive functions of both cases and controls were done using scatter plots of IQ.

RESULTS

Fifty eight children with SCA in the age group of 6 -15 years attended the SCA clinics during the visits. Out of them, three had seizure disorder, two had bronchial asthma, five refused to participate in the study, and four opted out of the study because of the time consuming intelligence tests. Thus, study and the control group finally consisted of 44 children (25 boys and 19 girls) in the 6-15 year age group. The mean age was 9.9 (2.67) years. All of them were receiving comprehensive care for the last four years. Thirty two children (72.7%) in each group belonged to Paniya community while 10 children (22.7%) were from Kuruma community.

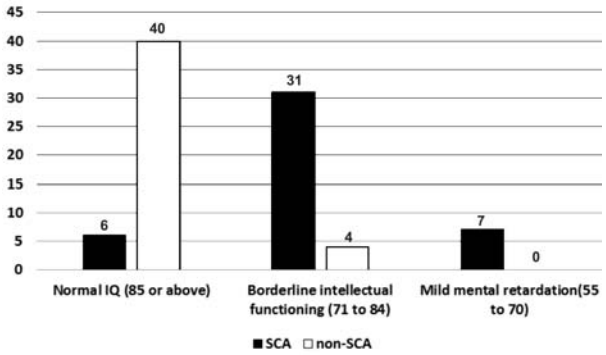

FIG. 1 *Prevalence of intellectual disability in children with and without Sickle-cell anemia.*

TABLE I MISIC SCORES IN CHILDREN WITH AND WITHOUT SICKLE CELL ANEMIA

Quotient	*Score (SD)*		*Difference (SD)*
	SCA Group	*Control Group*	
Verbal Quotient	77(6.7)	92 (7.2)	15 (6.7)
Performance Quotient	81 (7.5)	95 (7.2)	14 (7)
Intelligence Quotient	78 (7.5)	93 (7.1)	15 (6.4)

P<0.001 for all comparisons; SCA: Sickle cell anemia.

Children with SCA had lower IQ scores across all subgroups in both verbal and performance domains (***Table* I**). Children with both mild mental retardation and border intellectual function were higher in the SCA group than non-SCA group (P<0.001) (***Fig.* 1**). None of the children had moderate or severe mental retardation. There was no statistical evidence to suggest deterioration of IQ with advancing age in children with SCA.

Mean raw scores of all the eight subtests in the PGI memory scale, showed statistically significant difference ($P < 0.05$) between children with SCA and children in the control group (***Table* II**). The children in the study groups could not perform the delayed recall and retention of dissimilar pair subtests of the PGI memory scale and hence not included in the study.

Children in the study group and control group had scores below the cut-off value of 10 on the CPMS scale, but there was statistically significant difference between the mean score 4.09 (2.23) *vs.* 2.43 (1.58), respectively. On analysis of the subscales of CPMS, children in the SCA group scored significantly more on the behavior problem subscale ($P=0.002$) and the difference was not statistically significant on other items.

TABLE II PGI MEMORY SCALE SCORES IN CHILDREN WITH AND WITHOUT SICKLE CELL ANEMIA

Parameter	*Score (SD)*	
	SCA Group	*Control Group*
Remote memory	3 (1.3)	4 (1.4)
Recent memory	1 (0.6)	2 (1)
Mental balance	1 (0.4)	2 (0.5)
Attention and concentration	6 (2.1)	8 (1.6)
Immediate recall	1 (0.2)	2 (0.5)
retention of similar pairs	2 (0.9)	3 (0.8)
Visual retention	2 (0.8)	3 (0.9)
Recognition	2 (0.9)	3 (0.9)

P<0.001 for all comparisons; SCA: Sickle cell anemia.

WHAT THIS STUDY ADDS?

- Children with sickle cell anemia have impaired cognitive functions and more psychological problems compared to children without sickle cell anemia.

Even after applying ANCOVA (Analysis of co-variance) there was statistically significant difference in the cognitive functions (VQ, PQ and IQ) and CPMS score ($P<0.05$).

DISCUSSION

The present study compared cognitive functions and psychological problems in children with SCA with an age-, sex- and community-matched control group of children with no SCA. It was found that children with SCA had impaired cognitive functions and more psychological problems compared to children in the control group. Borderline intellectual functioning and mild mental retardation were more commonly seen in children with SCA.

Our findings on cognitive functions in children with SCA are comparable to the results of previous studies which have reported lower IQ scores in children with SCA [10-12]. The causes of cognitive impairment in SCA include brain infarction and chronic brain hypoxia due to low hematocrit and thrombocytosis [11,12]. Since children with history of stroke were excluded, silent infarcts and chronic brain hypoxia may be the causes for cognitive impairment in the children in the present sample.

Age related decline in cognitive functions has been reported by several studies in the past [10]. In the present study no correlation was observed between advancing age and cognitive decline. This may be due to the fact that majority of children in our sample were below 12 years, and also due to the small sample size.

A previous study from India found that children with SCA have poor quality of life and all domains *viz*. physical, psychological and cognitive domains are affected [5]. In the present sample even though all children had scores below the cut-off value on the CPMS, the scores were significantly higher compared to those of the children in the control group indicating that children with SCA have more psychological problems. Other studies have reported that psychological disorders like anxiety and depression are more frequent in children with SCA [13,14]. Gold, *et al*. [15] have reported that even though children with SCA have no more behavior problems compared to their siblings, they have more behavior problems compared to the general population. In the present sample children with SCA differed significantly on the behavior problem subscale of the CPMS. The reason for this may be that psychological disorders commonly occur when the children reach adolescence, and psychological distress in young children most often present with externalizing behaviors.

The strengths of the present study include the fact that study was conducted in a community-setting, the control group was recruited from the same tribal community, and one-to-one matching was done. Since the sample of children with SCA belonged to a tribal population with unique social and cultural characteristics, generalization of the result should be with caution. Small sample size and lack of blinding while doing the tests are also limitations of the study.

The present study emphasizes the importance of assessment of cognitive functions and psychological well-being in children with sickle cell anemia. Facility for early identification and remediation of cognitive impairments and psychological problems should be considered while planning health care services for children with sickle cell anemia.

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