Analysis of intelligence quotient in patients with homozygous beta-thalassemia

Mehran Karimi, MD, Hooman Yarmohammadi, MD, Maria Domenica Cappellini, MD, PhD.

ABSTRACT

Objective: To compare the intelligence quotient (IQ) of patients with thalassemia major (TM) to that of normal children.

Methods: We conducted the study in April and May 2002 on 294 homozygote beta-thalassemia patients, (157 male and 137 female, mean age of 13.2 years; range, 9-18 years). These 294 patients were randomly selected from the 984 TM patients who routinely refer to Shiraz Cooley's Medical Center in Dastgheyb Hospital, Iran for blood transfusion. Another 294 subjects age and gender matched control group were studied. Intelligence quotients were computed using the Ravin test.

Results: The mean IQ score ± standard deviation (SD) in the thalassemia group was 109.83 ± 15.94. This score revealed no statistically significant difference with the control group's score ($p \leq 0.079$). A correlation existed between the thalassemia patients' IQ and their level of education ($p < 0.049$).

Conclusion: The IQ of TM patients does not differ significantly from the normal population.

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Thalassemia is among the most common hereditary disorders worldwide. Thalassemia usually leads to chronic and potentially lethal anemia. Recent progresses in early diagnosis and treatment facilities have significantly increased the life expectancy and survival rates.[1-3] However, the chronic conditions, as well as frequent infections challenge optimal physical and mental development.[1-3] Despite a large amount of information pointing to retardation in physical growth and psychosocial problems in patients with thalassemia major (TM) (homozygous beta-thalassemia or Cooley's anemia),[4-8] little has been reported regarding the intelligence and mental development. Intelligence quotient (IQ) is an important factor, affecting both the psychosocial and social aspects of the patient's life. There are different definitions for intelligence and different tests for evaluating it.[9-12] Previous study defined IQ as the result of division of mental age by the chronological age, multiplied by 100.[13] Therefore, people with an IQ of 100 were normal and those with an IQ below 100 were below normal,[13] but since it has been assumed that the maximum development of mental age is up to 16 years of age, calculation of IQ in adulthood became problematic. The Ravin test or Ravin Progressive Matrix test was developed before the 2nd World War. It has been revised many times since then and can be used for both children and adult (from 5 years old to adulthood).[14] This test has been normalized in our country and is being used for the evaluation of IQ.[14] The purpose of this study is to investigate the intelligence development in a large cohort (n=294) of thalassemia patients, 9-18 years

From the Department of Pediatric (Karimi), Hemostasis and Thrombosis Unit, Hematology Research Center, Department of Surgery (Yarmohammadi), Namazee Hospital, Shiraz University of Medical Sciences, Shiraz, *Iran* and the Hereditary Anemia Center (Cappellini), Ospedale Maggiore IRCCS, Milan, *Italy.*

Address correspondence and reprint request to: Dr. Mehran Karimi, Hematology Research Center, Pediatric Department, Namazee Hospital, Shiraz University of Medical Sciences, Shiraz, *Iran*. Tel. +98 (711) 626-5024. Fax. +98 (711) 235-9317. E-mail address: karimim@sums.ac.ir

old, and compare the results with children without any hematological diseases as controls representing the same age range.

Methods. We conducted the study in April and May 2002 on 294 homozygote beta-thalassemia patients (157 male and 137 female, mean age of 13.2 years; range, 9-18 years). These 294 patients were randomly selected from the 984 TM patients who routinely refer to Shiraz Cooley's Medical Center in Dastgheyb Hospital, Iran for blood transfusion. Randomization was carried out by a medical staff member who was not informed regarding the study, who started selecting the patients from a computer base data file and according to a random table number (randomly starting with number 4 and selecting by adding 5 to the previous number). All of the patients had established diagnosis with hemoglobin electrophoresis and alkali resistant hemoglobin estimation. Each of the patients was receiving blood transfusions every 3-4 weeks to maintain hemoglobin levels between 10.5 and 13.5 g/dl (normal range 12-14 g/dl). They were also receiving desferrioxamine subcutaneously (S.C.) as chelation therapy (25-50 mg/kg body weight infused S.C. 4-6 days a week to maintain serum ferritin level <1500 ng/ml). The IQ evaluations were performed at 7 ± 1.5 days after transfusion. At the time of IQ testing the hemodynamic parameters were normal. All clinical data of the patients are summarized in **Table 1.**

Two hundred and ninety-four healthy subjects matched for age and gender (157 male and 137 female, mean age of 13.5; range 9-18 years) with normal hematologic laboratory data and no evidence of any specific hematologic, nephrologic, urologic and cardiovascular diseases were studied. These healthy subjects were selected from schools, randomly selected by an intern uninformed regarding the study. Moreover, they were without parental history of hematologic diseases and all cases in which parent history was suspicious of having a hematological disease were excluded from the study. An informed written consent was taken from each patient and control group or from their parents.

At the beginning of the study, the authors participated in a 3-session (each session 3 hours long) workshop, training how to test subjects with the Ravin test and the scoring method. Afterwards, the authors themselves tested all the subjects (patients and control). The method of answering each questions in the Ravin test and the time limit they had (45 minutes for answering) was explained to each patient individually and thoroughly. After the patient had completed the test, several other questions presented in a prepared questionnaire was also asked and filled by them. This questionnaire contained information about age, gender, educational level of the patient, patient's mother and father, the patient's mother and father occupation, number of siblings, age of onset of transfusion dependency, the duration of transfusion among others. The same method was used for the control group. The results of each test were also reviewed with a psychiatrist, for higher accuracy.

Nonparametric statistics were performed using Mann-Whitney, and Chi-square tests where appropriate. Spearman's rank correlation test was performed to measure the strength of the relationship between 2 variables. A value of $p<0.05$ was taken as the level of statistical significance. The data were entered using the Statistical Package for Social Sciences (Chicago, IL) software, version 10.0 and Microsoft EXCEL (Microsoft, Redmond, WA) software.

Results. No apparent difference was observed between the means and distributions of the 2 groups

Table 1 - Clinical and hematological profile of patients with beta-thalassemia major.

Characteristics	Values	Range
Gender (M/F)	157/137	
Age (years)	13.2	9 - 18
Body mass index (kg/m^2)	16	14.3 - 19.1
Hemoglobin (g/dL)	12.4	10.9 - 13.1
Mean Serum ferritin (ng/ml)	1469	901 - 2251
Chelating therapy (year)	12.5	3.5 - 16.9
Dose of desferrioxamine (mg/kg)	42	35 - 54
Transfusion (years)	12.1	2.5 - 17
Age of onset of transfusion (year)	1.5	0.25 - 7
Intelligence quotient	109.83	63 - 155

Table 2 - Intelligence quotient distribution of thalassemia patients according to Ravin's clinical classification compared to the control group.

Intelligence quotient	Number of patients (%)	Number of control group (%)	*P*-value
125 < IQ < 148	51 (17.3)	60 (17.5)	>0.05
113 < IQ < 124	98 (33.3)	84 (28.6)	>0.05
89 < IQ < 112	114 (38.8)	133 (45.4)	>0.05
77 < IQ < 88	22 (7.5)	17 (5.8)	<0.05
65 < IQ < 76	4 (1.4)	0	-
IQ ≤ 64	5 (1.7)	0	-
Total	**294**	**294**	-

(p>0.05). The IQ distributions of the thalassemia patients and control group are presented in **Table 2**. The mean IQ score (± SD) in the thalassemia patients was 109.83 ± 15.94 and the IQ score for the control group was 115 ± 12.23. The IQ of patients (p=0.351) and control group (p=0.922) did not show any correlation with age. The mean IQ score in female patients was 110.85 ± 11.43, and in male, 108.93 ± 12.33. In the control group, the mean IQ score in female was 109.06 ± 13.45 and in male was 106.0 ± 10.33, and there was no correlation between gender and IQ (p=0.161). There was no significant difference between the father's job (p≥0.053) or onset and duration of transfusion of patient (p=0.24) and IQ. The mean educational level of the patients was 7.2 years while the control group was 8.5 years, (p>0.05). Most of the patients were in the elementary schools (42.9%) and guidance schools (41.5%). In the control group most of them were in the guidance schools (51.6%). A comparison between the patients and control group educational levels showed no statistically significant difference (p>0.05). The mean years of formal education of the patient's father was 15.6 years, whereas for the mother was 6.4 years. For the control group, the mean years of formal education of the father was 9.5 years, while for the mother was 15.6 years. The parents with a higher educational level had children with a higher IQ; this was especially more significant when the educational level exceeded Master of Science (MS) or Associates of Art (AA). The onsets of blood transfusion and the duration of blood transfusion in TM patients are shown in **Table 1**. All the patients had more than 2 years duration of blood transfusion.

Discussion. Our study suggests that patients with Cooley's anemia (homozygous beta-thalassemia) show an intellectual development within the expected normal range. This finding was observed in patients who were on regular transfusions and had low to moderate hemoglobin levels. Patients with lower hemoglobin levels, mostly due to more severe type of disease or less accurate treatment, also showed lower levels of IQ. The lack of patients without treatment makes it impossible for us to establish whether adequate treatment plays an essential role in normal IQ development. Similar results were also observed in previous studies carried out on IQ and thalassemia.[15,16] Previous studies in thalassemia patients and other chronic diseases show that thalassemia has significant effects on emotional factors.[4-6] However, contrary to expectation, thalassemia by itself and chronic blood transfusions did not cause mental retardations. An interesting finding in our study was that no significant correlation was found between gender and IQ. In Iran, educational facilities are more reachable for boys rather than girls. However, this almost equal range of IQ may be related to the equality in the treatment that both gender had received and also the educational facilities, which have been expanded and more reachable for the girls than in the past.

Iran is one of the most endemic populations of TM in the world. More than 20,000 TM patients live in Iran and the prevalence of ß-thalassemia minor gene is 10%.[17] Therefore, from psychosocial and economical aspects, it is very important to show whether or not TM patients can live, work, marry, and others similar to other normal people.

From the results achieved in our study, we can conclude that IQ in thalassemic patients is not related to the educational level of their parents nor is it related to the gender, age, or job of their parents and even the patients' educational level. The present study indicates that, although abnormalities in affective state, behavior, and character are common in this condition, the intellectual functions remain generally within the expected normal range and these patients can participate in normal activities of the society. In fact, their chronic disease does not interfere with their mental and IQ scoring.

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