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ORIGINAL ARTICLE

Neuropsychological Assessment of Children with Transfusion Dependent Thalassemia Major

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Background Thalassemia is considered a serious public health problem due to the high prevalence which extent from the Mediterranean basin and part of Africa, throughout the Middle East. Young children may express psychological distress in the form of conduct problems and somatization while older children have a growing insight into the nature of the illness which might account for the increase in depressive symptoms.

Aim The aim of this study is to assess behavioral and emotional problems in children with thalassemia major.

Subjects and Methods This is a case control study which was conducted on 150 transfusion dependent βeta–thalassemia major patients and equal number of healthy controls with matched age and sex. Psychological assessment was done by Childhood Behavioral Check List.

Results Among all the studied cases, (56.7%) of cases had clinical total behavioral problems, internalizing disorders in (67.3%) -withdrawn/depressed in (36.7%), somatic complaint in (28.7%), anxious depressed in (21.3%), externalizing disorders in (36%), aggressive behaviors in (29.3%), rule breaking behavior in (6.7%), social problems in (19.4%), attention problems in (4.7%), thought problems in (3.3%).

Conclusions The study revealed that, ~ half of the patients with thalassemia major had a clinical psychological problem.

Keywords Behavioral, Depression, Thalassemia major.

INTRODUCTION

β-Thalassemia major, also known as Cooley's anemia, is a chronic, genetic hematologic disorder characterized by defect in erythropoiesis, peripheral hemolysis, and severe anemia (Galanello *et al*., 2010). Thalassemia is considers a serious public health problem due to the high prevalence which extent from the Mediterranean basin and part of Africa, throughout the Middle East. Its prevalence globally is about 2/1000 newborns and 50 000 to 100 000 children died from thalassemia major in low and middle income countries, and about 7% of the world's population is a carrier of a hemoglobin disorder (Baghianimoghadam *et al*., 2011).

Thalassemia is a major healthcare problem which make a great psychological and financial stress on the affected families and make a huge burden on the healthcare system (Ahmed Kiani *et al*., 2016). Chronicity of disease, burden of treatment, morbidities and expectation of early death resulting from complications, all these causes may lead to many psychosocial problems in thalassemia patients (Khairkar *et al*., 2010). Children with thalassemia have been described to show impaired abstract reasoning, deficits of, memory, visual spatial skills, language, attention and executive functions, all of these impairments are more prominent in patient with hemosiderosis (Adam *et al*., 2017).

In this study we aim to assess behavioral and emotional problems in children with thalassemia major, to compares rate of behavioral and emotional problems between patients and normal children, and to detect predictors for behavioral and emotional problems.

SUBJECTS AND METHODS

This is a case control study which was conducted on 150 transfusion-dependent βeta–thalassemia major patients and equal number of healthy controls with matched age and sex. Patients were collected from hematology outpatient clinic in Mansoura University Children's Hospital. While the control group was collected from general outpatient clinic in Mansoura University Children Hospital and Al Sinbellawin General Hospital during the period from March 2019 to September 2019.

Inclusion criteria

(1) Patients already diagnosed as *β*-thalassemia major by:

(a) Clinical symptom and signs of chronic hemolytic anemia: (pallor, dark urine, jaundice, abdominal enlargement, and failure to thrive).

(b) Examination: (pallor, jaundice, mongoloid facies, and organomegaly).

(c) Investigations:

(i) Microcytic hypochromic anemia.

(ii) Increase Reticulocyte count.

(iii) Increase Serum iron and serum ferritin.

(iv) Decrease Total iron binding capacity.

(v) Hemoglobin electrophoresis show (NHLBI, 2016).

(2) Aged from 5 to 15 years.

(3) Duration of disease more than 6 months.

Exclusion criteria

(1) Patients previously diagnosed with any psychological, or neurological disorders.

(2) Mentally retarded patients.

Controls selection

(1) Children between 5 and 15 years.

(2) No past history of chronic illness.

All patients in the study were subjected to:

(1) History taking including: name, age, sex, residence and years of education. Family history and socioeconomic status: history of consanguinity and similar condition in family. Socioeconomic status by Fahmy and Elsherbiny scale. This scale is used to assess the socio-economic level of the family (Fahmy, 1983). Age of diagnosis depending on suggestive clinical symptom and signs of chronic hemolytic anemia (pallor, dark urine, jaundice, abdominal enlargement, and failure to thrive). Age at which patients started to receive blood transfusion. Frequency of blood transfusion and numbers of hospital admission. Mean serum ferritin from a documented data with patients.

Clinical examination: a) General examination for pallor, jaundice, and mongoloid facies. b) Abdominal examination for organomegaly. c) Neurological examination.

Psychological assessment: By Child Behavioral Check List (CBCL). The Child Behavior Checklist (CBCL) is a parent-report questionnaire on which the child is rated on various behavioral and emotional problems. It was first developed by Thomas M. Achenbach and has been one of the most widely-used standardized measures in child psychology for evaluating maladaptive behavioral and emotional problems in preschool patients aged 2 to 3 or in patients between the ages of 4 and 18. CBCL assesses internalizing (i.e., anxious, depressive, and overcontrolled) and externalizing (i.e., aggressive, hyperactive, noncompliant, and uncontrolled behaviors). Several subareas are measured including social withdrawal, somatic complaints thought problems, attention problems, aggressive behavior, and delinquent behaviors (Achenbach, 1991). We used the Arabic version (Koura, 1991).

Statistical analysis was performed using SPSS statistical software (version 22; IBM Corporation, Armonk, NY, USA). Student-*t* test was used to compare continuous parametric variables; Mann–Whitney U test was used for continuous nonparametric variables; χ^2 test or Fisher´s Exact test, Monte Carlo tests were used for categorical variables when appropriate. Kolmogrov-Smirnov test was done to examine the distribution of data. Linear regression was done to detect predictors of the outcome. *p* value was considered significant when= 0.05.

RESULTS

Table 1 shows socio-demographic characteristics of the studied groups, there were statistically significant differences between two groups regarding education (p=0.03) and socio-economic status (p<0.01).

Regarding anxious depressed domain, there were statistically significant differences between both groups (p<0.001) where 21.3% of cases group showed clinical level in this domain. For somatic complaints domain, there were statistically significant differences between both groups (p<0.001) where (28.7%) of cases group showed clinical level in this domain. On assessing social problems domain, there were statistically significant differences between both groups (p<0.001) where (19.4%) of cases group showed clinical level in this domain (Table 2).

And for thought problems domain, there were statistically significant differences between both groups (p<0.012) where (3.3%) of cases group showed clinical level in this domain. For attention problems, there were statistically significant differences between both groups (p<0.001) where (4.7%) of cases group showed clinical level in this domain. regarding rule breaking behavior domain, there were statistically significant differences between both groups (p<0.001) where (6.7%) of cases group showed clinical level in this domain. On assessing aggressive behavior domain, there were statistically significant differences between both groups (p<0.001) where (29.3%) of cases group showed clinical level in this domain (Table 2).

Internalizing problems assessment revealed that there were statistically significant differences between both groups (p<0.001) where (67.3%) of cases group showed clinical level in this domain. Externalizing problems assessment of the studied groups showed that there were statistically significant differences between both groups (p<0.001) where (36%) of cases group showed clinical level in this domain. Total problems assessment of the studied groups, showed statistically significant differences between both groups (p<0.001) where (56.7%) of cases group showed clinical level in total score (Table 2).

Table 3 shows association between sex and behavioral domains among cases group, no statistically significant differences between them as a total score, but there were statistically significant differences between them in somatic problems (p<0.001), social problems (p<0.001) and rule breaking behavior problems (p<0.001). Also, (Table 3) shows the association between residence and behavioral domains among cases group, no statistically significant differences between them as a total score, but there was statistically significant difference in withdrawn/depressed domain (p=0.046).

Number of hospital admission is a statistically significant predictor of total score of behavioral problems (p=0.047). Lower education and frequency of hospital admission are statistically significant predictors of aggressive behavior score (p=0.031), (p=0.006), respectively. Low SES is a statistically significant predictor of anxious/depressed score (p=0.045). Age is a statistically significant predictor of somatic problems score (p<0.001) (Table 4).

Years of education and numbers of hospital admissions are statistically significant predictors of social problems (p=0.036), (p=0.047), respectively. Serum ferritin is a statistically significant predictor of thought problems score (p=0.003). Number of hospital admission is a statistically significant predictor of attention problems score (p=0.048). Younger age, high SES, lower education and serum ferritin are statistically significant predictors of rule breaking behavior score (p=0.001), (p=0.035), (p=0.001), (0.003) (Table 4).

Table 1: Socio-demographic characteristics of the studied groups

	Cases *N*= 150 (%)	Control *N*= 150 (%)	Test of significance
Age/years Mean±SD	9.57±3.16	9.11±3.03	t=1.304, p=0.0193
Sex			
Male	67 (44.7)	71 (47.3)	χ^2=0.215
Female	83 (55.3)	79 (52.7)	p=0.643
Residence			
Urban	35 (23.3)	49 (32.7)	χ^2=3.24
Rural	115 (76.7)	101 (67.3)	p=0.072
Duration of education/years Median (Min-Max)	3.0 (0.0–9.0)	2.0 (0.0-9.0)	Z=2.15, p=0.03*
Socio-economic status			
Very low	47 (31.3)	59 (39.3)	MC p<0.001*
Low	33 (22.0)	48 (32.0)	
Middle	53 (35.3)	43 (28.7)	
High	17 (11.3)	0	

T: Student *t* test; MC: Monte Carlo test; χ^2: Chi-Square test; *Z*: Mann–Whitney *U* test; *: statistically significant; SD: standard deviation.

Table 2: Behavioral domains assessment of the studied groups

Anxious depressed	Total	Cases *N*= 150 (%)	Control *N*= 150 (%)	Test of significance
Normal	236	90 (60.0)	146 (97.3)	MC
Borderline	32	28 (18.7)	4 (2.7)	$p<0.001^*$
Clinical	32	32 (21.3)	0	
Somatic complaints				
Normal	214	76 (50.7)	138 (92.0)	$\chi^2=62.79$
Borderline	37	31 (20.7)	6 (4.0)	$p<0.001^*$
Clinical	49	43 (28.7)	6 (4.0)	
Social problems				
Normal	243	98 (65.3)	145 (96.7)	MC
Borderline	27	23 (15.3)	4 (2.7)	$p<0.001^*$
Clinical	30	29 (19.4)	1 (0.6)	
Thought problems				
Normal	280	134 (89.3)	146 (97.3)	MC
Borderline	15	11 (7.3)	4 (2.7)	$p=0.012^*$
Clinical	5	5 (3.3)	0	
Attention problems				
Normal	282	132 (88.0)	150 (100.0)	MC
Borderline	11	11 (7.3)	0	$p<0.001^*$
Clinical	7	7 (4.7)	0	
Rule breaking				
Normal	276	126 (84.0)	150 (100.0)	MC
Borderline	14	14 (9.3)	0	$p<0.001^*$
Clinical behavior	10	10 (6.7)	0	
Aggressive behavior				
Normal	216	77 (51.3)	139 (92.7)	MC
Borderline	39	29 (19.3)	10 (6.7)	$p<0.001^*$
Clinical	45	44 (29.3)	1 (0.7)	
Internalizing				
Normal	143	24 (16.0)	119 (79.3)	MC
Borderline	45	25 (16.7)	20 (13.3)	$p<0.001^*$
Clinical	112	101 (67.3)	11 (7.3)	
Externalizing				
Normal	197	62 (41.3)	135 (90.0)	MC
Borderline	48	34 (22.7)	14 (9.3)	$p<0.001^*$
Clinical	55	54 (36.0)	1 (0.7)	
Total				
Normal	173	36 (24.0)	137 (91.3)	MC
Borderline	42	29 (19.3)	13 (8.7)	$p<0.001^*$
Clinical	85	85 (56.7)	0	

T: Student *t* test; MC: Monte Carlo test; χ^2: Chi-Square test; *Z*: Mann–Whitney *U* test; *statistically significant; SD: standard deviation.

Table 3: Association between sex and residence to the behavioral domains among cases group

	Residence			Sex		
	Residence			Sex		
	Urban *n*= 35 (%)	**Rural *n*= 115 (%)**	**Test of significance**	**Male *n*= 67 (%)**	**Female *n*= 83 (%)**	**Test of significance**
Anxious depressed						
Normal	18 (51.4)	72 (62.6)	χ^2=1.72	37 (55.2)	53 (63.9)	χ^2=1.42
Borderline	7 (20.0)	21 (18.3)	*p*=0.422	3 (19.4)	15 (18.1)	*p*=0.491
Clinical	10 (28.6)	22 (19.1)		17 (25.4)	15 (18.1)	
Withdrawn/depressed						
Normal	20 (57.1)	46 (40.0)	MC	27 (40.3)	39 (47.0)	χ^2=3.77
Borderline	2 (5.7)	27 (23.5)	*p*=0.046*	10 (14.9)	19 (22.9)	*p*=0.152
Clinical	13 (37.1)	42 (36.5)		30 (44.8)	25 (30.1)	
Somatic complaints						
Normal	18 (51.4)	58 (50.4)	χ^2=0.015	39(58.2)	37 (44.6)	χ^2=16.17
Borderline	7 (20.0)	24 (20.9)	*p*=0.992	4 (6.0)	27 (32.5)	*p*<0.001*
Clinical	10 (28.6)	33 (28.7)		24 (35.8)	19 (22.9)	
Social problems						
Normal	21 (60.0)	77 (67.0)	χ^2=2.67	36 (53.7)	62 (74.7)	χ^2 = 16.02
Borderline	4 (11.4)	19 (16.5)	*p*=0.263	19 (28.4)	4 (4.8)	*p*<0.001*
Clinical	10 (28.6)	19 (16.5)		12 (17.9)	17 (20.5)	
Thought problems						
Normal	31 (88.6)	103 (89.6)	MC	59 (88.1)	75 (90.4)	MC
Borderline	2 (5.7)	9 (7.8)	*p*=0.624	6 (9.0)	5 (6.0)	*p*=0.779
Clinical	2 (5.7)	3 (2.6)		2 (3.0)	3 (3.6)	
Attention problems						
Normal	29 (82.9)	103 (89.6)	MC	62 (92.5)	70 (84.3)	χ^2=5.94
Borderline	4 (11.4)	7 (6.1)	*p*=0.525	5 (7.5)	6 (7.2)	*p*=0.051
Clinical	2 (5.7)	5 (4.3)		0 (0.0)	7 (8.4)	
Rule breaking						
Normal	31 (88.6)	95 (82.6)	MC	63 (94.0)	63 (75.9)	MC
Borderline	2 (5.7)	12 (10.4)	*p*=0.665	1 (1.5)	13 (15.7)	*p*=0.006*
Clinical behavior	2 (5.7)	8 (7.0)		3 (4.5)	7 (8.4)	
Aggressive behavior						
Normal	17 (48.6)	60 (52.2)	MC	38 (56.7)	39 (47.0)	MC
Borderline	6 (17.1)	23 (20.0)	*p*=0.755	10 (14.9)	19 (22.9)	*p*=0.379
Clinical	12 (34.3)	32 (27.8)		19 (28.4)	25 (30.1)	
Internalizing						
Normal	4 (11.4)	20 (17.4)	MC	8 (11.9)	16 (19.3)	MC
Borderline	4 (11.4)	21 (18.3)	*p*=0.368	9 (13.4)	16 (19.3)	*p*=0.227
Clinical	27 (77.1)	74 (64.3)		50 (74.6)	51 (61.4)	
Externalizing						
Normal	14 (40.0)	48 (41.7)	MC	30 (44.8)	32 (38.6)	χ^2=0.609
Borderline	5 (14.3)	29 (25.2)	*p*=0.268	14 (20.9)	20 (24.1)	*p*=0.738
Clinical	16 (45.7)	38 (33.0)		23 (34.3)	31 (37.3)	
Total						
Normal	7 (20.0)	29 (25.2)	χ^2=0.404	16 (23.9)	20 (24.1)	χ^2=0.008
Borderline	7 (20.0)	22 (19.1)	*p*=0.817	13 (19.4)	16 (19.3)	*p*=0.929
Clinical	21 (60.0)	64 (55.7)		38 (56.7)	47 (56.6)	

χ^2=Chi-Square test; MC: Monte Carlo test; *: statistically significant (*p*<0.05).

Table 4: Linear regression for prediction of behavioral changes among studied cases

Predictors	Beta	*T*	*P*
(Constant)	70.864	51.642	<0.001*
Serum ferritin	–0.397	–1.860	0.160
Frequency	–0.087	–0.339	0.757
Number of hospital admission	0.809	3.268	0.047*
log total psychological score= 70.86-0.809* number of hospital admission R2= 0.881			
Constant)	9.06	9.445	<0.001*
SES	–0.164	–2.021	0.045*
log total anxious depressed= 9.06-0.1* SES, R2= 0.027			
(Constant)	1.239	1.838	0.068
Age/years	0.366	5.380	<0.001*
Number of hospital admissions	0.204	1.322	0.188
log somatic= 1.24+0.366* age/years, R2= 0.191			
(Constant)	4.93	10.828	<0.001*
Education/years	0.172	2.112	0.036*
Numbers of hospital admission	0.162	2.001	0.047*
Log social= 4.93+0.172* education duration +0.162* number of hospitalizations, R2= 0.067			
(Constant)	1.394	4.654	<0.001*
Serum ferritin	0.241	3.022	0.003*
LOG thought problems= 1.39+0.241* serum ferritin			
(Constant)	8.41	5.813	0.004*
Frequency of blood transfusion	0.202	0.609	0.575
Number of hospital admission	–6.92	–2.809	0.048*
log attention problem= 8.41-6.92* number of hospital admission, R2= 0.697			
(Constant)	55.147	3.794	<.001*
Age/years	–8.62	–3.544	<0.001*
SES	0.0.071	2.134	0.035*
Education duration/years	–8.498	–3.501	<0.001*
Serum ferritin	0.243	2.980	0.003*
log rule breaking behavior= 55.15–8.62* age-0.071* SES+8.498* education duration+0.243* serum ferritin, R2= 0.147			
(Constant)	18.405	15.914	<0.001*
Education/years	–1.429	–3.857	0.031*
Frequency	0.494	1.948	0.147
Number of hospital admission	13.244	6.918	0.006*
log aggressive behavior= 18.41-1.429* education-13.24* number of hospitalization, R2= 0.964			

DISCUSSION

We found higher level of behavioral problems in cases group compared with healthy group. 56.7% of cases had clinical total behavioral disorders, internalizing problems in 67.3%, externalizing problems in 36%, this was nearly similar to a study in Germany, where meta-analysis was computed to integrate the results of 569 studies that used the Child Behavior Check List. The study showed that young people with a chronic physical illness had higher levels of internalizing, externalizing and total behavior problems than healthy peers (Pinquart and Shen, 2011).

Also, in India, a cross-sectional study involving 100 transfusion dependent thalassemic children of age 6-18 years, were assessed by Child Behavior Check, revealed 39% of patients had clinical total score, abnormal internalizing problems scores were seen in 41% children, abnormal externalization problems score were seen in 37% of them (Kumar *et al*., 2018).

In Iraq, a cross sectional study conducted in the thalassemia Center in Al-Batool (Kareem, 2014) revealed abnormal total scores were high in 32% patients. Also in India, 39 children (8–16 years) with transfusion dependent

thalassemia attending day care services for blood transfusion, were assessed for psychological problems revealed that 44% of the children had psychological problems, anxiety and related problems, 67% of them had depression, 62% had somatization and 56% had conduct problems (Shaligram *et al*., 2007). Similar findings were reported in a Greek study (Tsiantis *et al*., 1982) where 42.9% had psychological problems.

Another study in India revealed that 46.7% of children with thalassemia had psychological disorders (Gupta *et al*., 2011). The observations are similar to the findings of a study carried out on Indian children at different centers, where 54% had psychological disorders by Childhood Psychopathology Measurement Schedule (CPMS) (Saini *et al*., 2007).

Studies from developed countries had also reported high incidence of psychopathology in these children. A multi centers European study reported psychological problems in 47% of children (Clemente *et al*., 2002). With a high rate of psychopathology being reported from developed countries also, it can be argued that the nature of the illness causes severe distress in the child and family even when the resources are not scarce.

In a study of 20 thalassemic and 34 healthy children, it was observed that children with thalassemia were at increased risk of psychopathology (Cakaloz *et al*., 2009). The frequency of psychiatric problems was significantly higher in children with thalassemia 55% as compared with the control group (14.7%).

Recent study in Sri Lanka, 288 transfusion dependent *β*-thalassemia patients and equal number of controls were recruited. Prevalence of abnormal psychological symptom scores in all domains were significantly higher among patients compared with controls (Mettananda *et al*., 2020). This confirms findings of a previous study done among 60 Iranian children with thalassemia major who reported higher rates of behavioral problems in all domains compared with healthy children (Behdani *et al*., 2015).

In Turkey, a study on 38 patients, CBCL scores of them remained within the normal range. However, it was observed that behavioral problems scores such as anxiety, depression, aggression, internalizing and total problem were surprisingly higher among children whose compliance with the treatment was good than among those with poor compliance to treatment. A possible explanation is that the children who were more conscious of their illness were found to be more worried and anxious children. Although, these feelings seem to positively influence compliance with the treatment (Aydinok *et al*., 2005).

We detected higher prevalence of internalizing problems in 56% of cases group, this is similar to the study by (Shaligram *et al*., 2007; Pradhan *et al*., 2003).

Clinical anxiety and borderline anxieties were reported by 21.3%, 18.7% in cases group compared with 0%, 2.7% in control group, respectively. Similarly, an Egyptian case control study done on 218 cases and 244 control, revealed that abnormal and borderline anxieties were reported by 36.7 and 20.6% of cases compared with 0 and 15.6% of the controls, respectively (Yahia *et al*., 2013). Also, this is similar to the percentage reported by (Mednick *et al*., 2010; Saravi *et al*., 2007).

Also, clinical depression and borderline depression were significantly higher in cases than control 36.7%, 19.3% versus 2.7%, 12.0%, respectively, this is similar to the result in (Yahia *et al*., 2013) in which they reported abnormal and borderline depressions were significantly higher in cases than controls 32.1 and 16.1% versus 0 and 0%, respectively. Also similar results were found in an Egyptian study by (Sabry and Salama, 2009) in which they reported that there were no patients with thalassemia found to be free of depressive symptoms. Also, in an Iranian study, depression rate was three times more in thalassemia patients than control group (Saravi *et al*., 2007). A nearly similar rate was reported by (Aydinok *et al*., 2005 *et al*., Shaligram *et al*., 2007).

Iron overload in thalassemic patients often leads to bone expansion (mongoloid facies), short stature and delayed puberty. These features increase the child's feeling of oddness which by its turn, leads to reduced self-esteem, feelings of difference, poor self-image, being dependent which make them more socially isolated and depressed. Limited daily life activity was also noted by (Huurre and Aro, 2002) in those patients.

In addition, the complications of iron over load, as diabetes mellitus, delayed puberty, heart failure and liver cell failure, this makes them feel that the illness has no effect on their present life only, but frequently overthrew their plans for the future and their ability to enjoy themselves (Moussa *et al*., 2005).

Also, we found that somatic complaints were significant in 28.7% of cases, this is similar to (Gupta *et al*., 2011) in which children with thalassemia had higher scores in factors of conduct problems, special symptoms and somatization. Somatic complaint may either be related to the nature of the disease or be a sign of anxiety.

Regarding social problems, we found it in 19.4% only. In (Elzaree *et al*., 2018) also, only 8% had below average social skills. A possible explanation for this could be

that children with *β*-thalassemia receive more attention, making them feel better socially. Similarly, socialization was affected in 18% of *β*-thalassemic children in a Syrian study, they explained their mild deficit in social interactions to be attributed to well-built family relations in the Arabic community (Gharaibeh *et al*., 2009). However, these findings were not similar to another study (Naderi *et al*., 2012).

Percentage of the cases with externalizing behavior in our study were 36%, mainly aggressive behavior 29.3% and rule breaking behavior 6.7%. This is similar with cases in the study in India described as being more aggressive, not obeying rules, irritable and difficult to control (Gupta *et al*., 2011). Also, clinically significant abnormal CBCL externalization score was seen in 37% of the patients in (Kumar *et al*., 2018).

Children with chronic illness tend to underreport their symptoms, because they want to present themselves as healthy functioning individuals. So, they may express this feeling by aggressive manners (Huberty *et al*., 2000).

Attention problems were reported in our study in 12%, in accordance, an Indonesian study (Gamayani *et al*., 2017) investigated attention and executive function in *β*-thalassemic patients, attention impairment was found in 26% of their sample children.

In our present study, older patients more vulnerable to withdrawn/depressed, somatic problems and internalizing syndrome. Similar to other studies, older children had higher CBCL scores and thus had more behavioral problems (Kumar *et al*., 2018; Kareem, 2014).

Children in our study were largely from the lower socioeconomic communities where higher incidence of consanguineous marriage is usually found. Consanguinity is a risk factor for thalassemia; since thalassemia is an autosomal recessive disorder. Economic burden on those families associated with increase psychological burden on the children (Yahia *et al*., 2013).

Our present study reported that the increase in serum ferritin was associated with increase in the psychological problems especially thought problems. In contrary to the study in turkey (Aydinok *et al*., 2005), revealed that the psychiatric diagnosis was significantly higher in the patients who were more compliant to desferrioxamine (whose have low serum ferritin) compared with the noncompliant group (with high serum ferritin). A possible explanation is that children who were more conscious of their illness were found to be more worried and anxious children. Although, these feelings seem to positively influence compliance with the treatment.

Chronic anemia and hypoxic state, iron overload due to chronic blood transfusion, and toxicity due to chelating agents may be associated with brain dysfunction in *β*-thalassemia major patients. Thinking and attention are parts from neurocognitive functions of the brain. So, may be affected in those patients (Sinniah *et al*., 1977).

In most cases, neurological involvement in b-thalassemia major patients does not initially present relevant signs and symptoms (i.e. subclinical), they are presented only during neurophysiological and neuropsychological evaluation (Zafeiriou *et al*., 2006).

Also, body iron status measured with serum ferritin was not associated with psychological symptoms among patients with transfusion dependent *β*-thalassemia in (Mettananda *et al*., 2020). A previous study from Brazil in apparently physically healthy children also could not found a relationship between peripheral markers of iron status and psychological symptom scores (Menegassi *et al*., 2010).

Also, neither scores of adaptive behavior nor the Psychopathy Checklist (PSCL), correlated with ferritin levels in study (Elzaree *et al*., 2018). In accordance, a study carried out by (Cakaloz *et al*., 2009) the mean score of the children behavior checklist and the ferritin levels showed no correlation.

A single measurement of serum ferritin concentration may not be a reliable parameter for assessing body iron burden, serial measurements seem to be correlated with changes in total body iron (Gabutti and Piga, 1996).

Also, our patients were less educated with less awareness and less insight about the nature of their illness, its morbidity and early mortality (Yahia *et al*., 2013). This may explain high level of serum ferritin in our population study.

CONCLUSION

Our study revealed that, approximately half of the patients with thalassemia major had clinical psychological problems.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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