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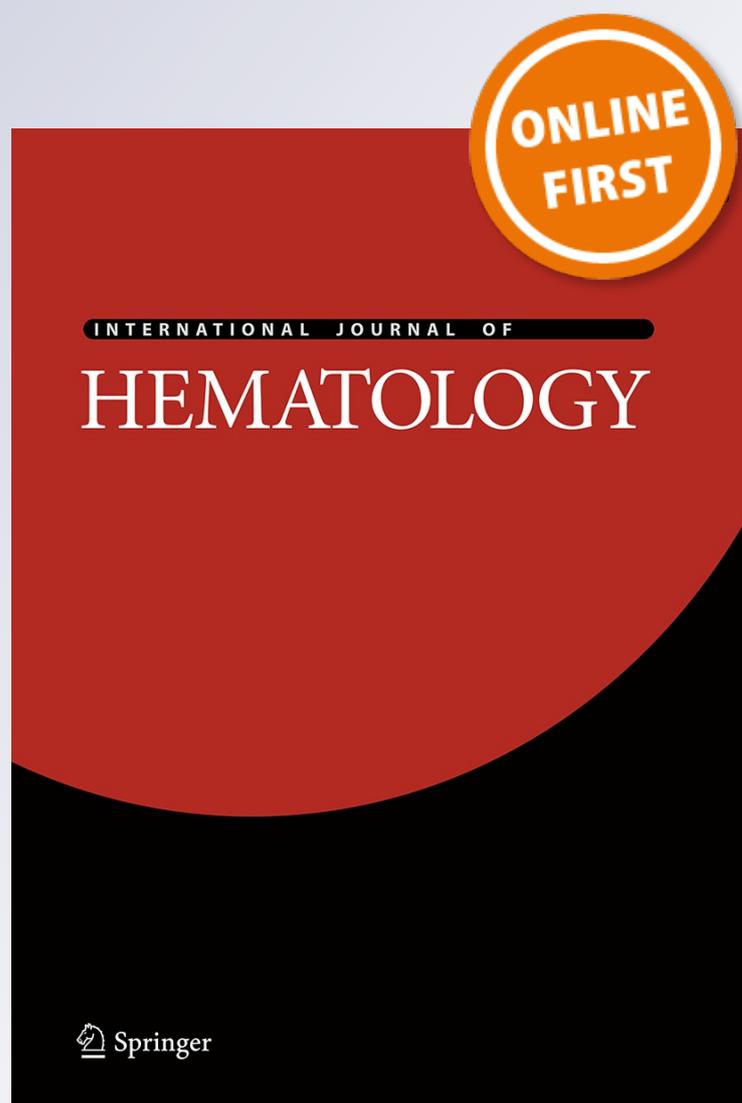
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Predictors of anxiety and depression in Egyptian thalassemic patients: A single center study

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Abstract Thalassemic patients are vulnerable to emotional and behavioral problems. Each patient age group exhibits problems unique to that stage of development, and although up to 80 % of thalassemic patients are likely to have psychological disorders, e.g., anxiety and depression, predictors of these disorders remain poorly understood. The present study was designed to assess the prevalence of anxiety and depression in a sample of Egyptian thalassemic patients and to identify predictors of these psychiatric disorders. A case–control study was conducted in 218 thalassemic patients, with 244 healthy subjects as a control. All patients and control subjects were subjected to thorough evaluation of medical history and clinical examination, and examined by a psychiatrist using the clinician version of the structured clinical interview for DSM-IV (SCID-CV), hospital anxiety and depression scale and Coopersmith self-esteem inventory. Abnormal and borderline anxieties were reported by 36.7 and 20.6 % of thalassemic patients, respectively, while abnormal and borderline depressions were reported by 32.1 and 16.1 %

of patients, respectively. Hospitalization, low self-esteem, diabetes mellitus and heart failure were independent predictors of anxiety. The independent predictors of depression were heart failure, hospitalization, diabetes mellitus, short stature and delayed puberty. Thalassemic patients were more vulnerable to anxiety and depression, indicating that screening and management for such psychiatric disorders should be considered in treating all such patients.

Keywords Anxiety · Depression · Thalassemia · Prevalence · Predictors · Egypt

Introduction

Chronic diseases have assumed an increasingly important role in public health research and intervention. They have a common psychological threat, the uncertainty about the progression and unpredictability of illness provokes anxiety in the patients as well as therapist. Understanding the relationship between chronic diseases and depressive disorders appears vital to public health assessment as without treatment depressive disorders characteristically assume a chronic course [1].

Thalassemic patients are vulnerable to emotional and behavioral problems, each age group of patients has problems unique to that stage of development; up to 80 % of thalassemia children are likely to have psychological disorders, e.g., anxiety and depression [2, 3], as they attend hospital regularly for blood transfusion and frequent absence from school [4]. Thalassemia is a chronic illness that badly affects self-esteem in children [5]. This low self-esteem is expected to increase the prevalence of anxiety and depression, and could affect badly children future life.

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Many authors have assessed psychiatric disorders in thalassemic patients [2, 6–9], but relatively little is known about predictors of these disorders, thus the aims of this study were to assess the prevalence of anxiety and depression and to identify the predictors of these psychiatric disorders in a sample of Egyptian thalassemic patients.

Patients and methods

This is a case–control study conducted during the period from January 2012 till August 2012. The cases 218 are all thalassemic patients: 116 males and 102 females; with ages above 12 years old (16.9 ± 2.99) registered in Mansoura University Children's Hospital. The control group included 244 healthy subjects; 128 males and 116 females randomly chosen from the nearby clubs, schools and university. Controls were apparently healthy and were free from any chronic diseases.

Data collected from patients' sheets included socio-demographics, e.g., age, sex, residence, education, socioeconomic standard (according to Fahmy and Sherbini [10]); birth order; treatment modalities (blood transfusion rate and number; iron chelating agents) frequency of cannulation and blood sampling; presence or absence of blood-borne infection; history of hospitalization (number and duration); history of splenectomy and lastly the cost of blood and treatment. All patients were examined by clinicians for Mongoloid facies; presence of diabetes, heart failure, bronzed skin, short stature, delayed puberty and liver cell failure.

All patients and controls were examined by a psychiatrist using clinician version of structured clinical interview for DSM-IV (SCID-CV) [11] with the help of information given by their parents and psychiatric morbidities were categorized into major depressive disorder and anxiety disorders (generalized anxiety disorder, panic disorder, phobic disorder, obsessive compulsive disorder) according to DSM-IV-TR [12]. Children with immature cognitive linguistic development may not be able to describe inner mood states and therefore may present with vague physical complaints, sad facial expression or poor eye contact. Irritable mood may appear as “acting out”; reckless behavior; or hostile, angry interactions [12]. Furthermore, the severity of anxiety and depression were measured using hospital anxiety and depression scale (HAD) [13]. The Arabic version of the HAD scale was validated by El-Rufaie and Absood [14]. The scale was validated in children from age 12 years and above [15, 16]. Self-esteem was examined using Coopersmith Self-Esteem Inventory-Arabic version, this test was validated in children [17, 18].

Exclusion criteria for both patients and control group were positive family history of mood disorders; substance use disorders; less than 12 years old and mental retardation (IQ below 70; using the Arabic version of Stanford Binet Intelligence Scale fifth edition [19]). Thirty-six cases and 22 controls were excluded from the study.

This study was approved by the Research Ethics Committee of Mansoura University, Egypt. All parents of patients and control group have to give fully informed consent before the start in the study.

Statistical methods

Data were analyzed using SPSS (Statistical Package for Social Sciences) version 16. Qualitative variables were presented as number and percent. Chi-square was used for comparison between groups. Quantitative variables were tested for normality distribution by Kolomogorov–Smirnov test. Normally distributed variables were presented as mean \pm SD and unpaired *t* test was used for group comparison. Non-parametric variables were presented as median (minimum–maximum). Mann–Whitney test was used for comparison between groups. Significant predictors in bivariate analysis were entered into a logistic regression analysis using forward Wald methods. Odds ratios (ORs) and their 95 % confidence intervals (CIs) were calculated. A $P \leq 0.05$ was considered statistically significant.

Results

Table 1 shows that cases and controls were matched in their age, sex, residence and social class of their families. However, thalassemic patients are more likely to be less educated ($P \leq 0.001$), with high percent of parental consanguinity ($P = 0.001$) and of higher birth order ($P \leq 0.001$) than the controls. More than half of affected children have another affected family member, compared to none of the control group.

Table 2 reveals that abnormal and borderline anxieties were reported by 36.7 and 20.6 % of cases compared to 0 and 15.6 % of the controls; respectively ($P \leq 0.001$). Also, abnormal and borderline depressions were significantly higher in cases than controls (32.1 and 16.1 % vs. 0 and 0 %; respectively). Current age and age at diagnosis show no significant differences with the anxiety status and depression status (Table 3)

Table 4 reveals that both anxiety and depression are associated with delayed puberty, mongoloid facies, presence of diabetes mellitus, heart failure, bronzed skin, short stature, use of chelating agents, previous hospitalization, splenectomy and low self-esteem.

Table 1 Sociodemographics of control vs. cases

	Control (244) [N (%)]	Cases (218) [N (%)]	Sign. test
Sex			
Male	128 (52.5)	116 (53.2)	$\chi^2 = 0.03,$ $P = 0.9$
Female	116 (47.5)	102 (46.8)	
Age (X ± SD)	16.6 ± 2.99	16.9 ± 2.99	$t = 1.1,$ $P = 0.3$
Residence			
Rural	172 (70.5)	165 (75.7)	$\chi^2 = 1.6,$ $P = 0.2$
Urban	72 (29.5)	53 (24.3)	
Social class			
High	42 (17.2)	23 (10.6)	$\chi^2 = 6.0,$ $P = 0.049$
Middle	114 (46.7)	97 (44.5)	
Low	88 (36.1)	98 (45.0)	
Education			
Illiterate/primary	124 (50.8)	136 (62.4)	$\chi^2 = 21.8,$ $P \leq 0.001$
Preparatory	44 (17.5)	33 (15.1)	
Secondary	48 (19.0)	46 (21.1)	
University	28 (11.1)	3 (1.4)	
Consanguinity	23 (9.4)	96 (44.0)	$\chi^2 = 72.1,$ $P \leq 0.001$
Birth order			
First	96 (39.3)	49 (22.5)	$\chi^2 = 29.7,$ $P \leq 0.001$
Second	56 (23.0)	82 (37.6)	
Third	40 (16.4)	48 (22.0)	
Fourth	36 (14.8)	15 (6.9)	
Fifth and more	16 (6.6)	24 (11.0)	
Other affected family members	0 (0)	57 (26.1)	$\chi^2 = 72.8,$ $P \leq 0.001$

The logistic regression analysis revealed that independent predictors of anxiety are hospitalization (OR = 10.2), presence of heart failure (OR = 6.8), presence of diabetes mellitus (OR = 6.3) and self-esteem (OR = 5.7); in order. The independent predictors of depression are heart failure (OR = 8.4), hospitalization (OR = 7.4), diabetes mellitus (OR = 5.4), short stature (OR = 4.3) and delayed puberty (OR = 4.2) (Table 5).

Discussion

Egyptian thalassemic patients are special population who suffer much in facing illness which exposes them to much stress, anxiety and depression.

The present study shows that the most significant sociodemographic difference between children with and without thalassemia was lower educational level. This may be explained by the frequent absence from school for regular blood transfusion or for weakness associated with this

Table 2 Anxiety and depression in control vs. cases

	Control (244) [N (%)]	Cases (218) [N (%)]	Sign. test
Anxiety			
Normal	206 (84.4)	93 (47.7)	$\chi^2 = 108.7,$ $P \leq 0.001$
Borderline	38 (15.6)	45 (20.6)	
Abnormal	0 (0)	80 (36.7)	
Median (min–max)	7 (3–8)	9 (0–20)	M.W.: $z = 6.2,$ $P \leq 0.001$
Depression			
Normal	244 (100.0)	114 (51.8)	$\chi^2 = 152.1,$ $P \leq 0.001$
Borderline	0 (0)	35 (16.1)	
Abnormal	0 (0)	70 (32.1)	
Median (min–max)	5 (1–7)	7 (0–19)	M.W.: $z = 6.3,$ $P \leq 0.001$

M.W. Mann–Whitney test

chronic illness, beside the negative effect of chronic anemia and disease complications to the learning ability of the patients. Moreover, in Egypt parents are emotionally charged and so when they have ill child they very commonly develop over protective parenting style; this style may hinder the child to go school when they actually could. This finding is in agreement with the results noted by other researchers on thalassemic patients [20]. In Indian study, 90 % of students with thalassemia have multiple days off from school which affects more than 70 % of their academic achievement [21]. Anxiety disorder and border line anxiety were significantly higher than controls and nearly similar to the percentage reported by Mednick et al. [22] in USA. Saraviet al. [23] cited that patients with thalassemia are exposed to many severe stresses which play important role in causation of anxiety including frequent blood samplings for laboratory tests, multiple transfusions and frequent subcutaneous injections of iron chelator drugs. Moreover, these patients are more anxious about the treatment modalities, effectiveness of iron chelation and complications related to the iron chelation [24]. In the present study, previously mentioned painful interventions like frequent hospitalization, cannulation, use of chelating agents and splenectomy significantly associated with anxiety and depressive disorders.

Depression and borderline depression were significantly higher in thalassemic patients than control group. Similar results were found in an Egyptian study by Sabry and Salama [25] in which they reported that there were no patients with thalassemia found to be free of depressive symptoms. Also in another study in India, most of patients with thalassemia complained of dysphoric moods and low self-esteem [26]. Also, in an Iranian study depression rate was three times more in thalassemia patients than control

Table 3 Age and age at diagnosis in anxious and depressed thalassaemic patients compared to the non-affected patients

	Current age (Mean ± SD)	Age at diagnosis [Median (min–max)]
Anxiety		
No	16.98 ± 2.9	1.5 (1–8)
Yes	16.9 ± 3.1	1.5 (1–5)
Significance test	$t = 0.2, P = 0.8$	$Z = 0.2, P = 0.9$
Depression		
No	17.0 ± 2.9	1.5 (1–8)
Yes	16.8 ± 3.1	1.4 (1–5)
Significance test	$t = 0.4, P = 0.7$	$Z = 0.4, P = 0.7$

Z of Mann–Whitney test

group [23]. A nearly similar rate was reported by Aydinok et al. [20] and Shaligram et al. [4]. Also, Khurana et al. [26] tried to explain the increased rate of depression among thalassemia patients as follows: thalassemia is chronic disabling illness which is usually associated with feelings of being different and inferior, leading to decreased self-esteem.

Also, as a result of bone expansion, a characteristic mongoloid facies occurs. This bone affection with anemia and iron overload in thalassaemic patients often leads to 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 [27] in those patients. One more factor is that, delayed puberty is usually associated with other endocrine disturbances, which participate in the development of depression.

In developing countries, as in Egypt, we cannot offer chelation therapy freely to thalassaemic patients in a regular way as needed for economic purposes. Therefore, a considerable percentage of our patients have iron overload and secondary complications related to iatrogenic hemosiderosis. In the current study, we find a significant association between anxiety and depressive disorders with diabetes mellitus, bronzed skin, delayed puberty, short stature, heart failure and liver cell failure, this owing to the cumulative psychological burden of the mentioned complications especially diabetes mellitus and heart failure added to the psychological burden of the original thalassaemic disease.

The researches conducted in the general psychiatric literature as well as in thalassaemic patients indicate that psychiatric disorders are more prevalent in adults than adolescents [22, 28, 29]; contrary to this finding, we did not find any significant differences in anxiety status and depression status with the current age and age at diagnosis.

Table 4 Bivariate analysis of significant predictors of anxiety and depression in thalassaemic patients

	Total	Anxiety		Depression	
		N (%)	Sign. test	N (%)	Sign. test
Overall	218	125 (57.8)		105 (48.2)	
Delayed puberty					
No	130	63 (48.5)	$\chi^2 = 10.4, P = 0.001$	46 (35.4)	$\chi^2 = 20.1, P \leq 0.001$
Yes	88	62 (70.5)		59 (67.0)	
Mongoloid facies					
No	151	75 (49.7)	$\chi^2 = 11.8, P = 0.001$	57 (37.7)	$\chi^2 = 21.4, P \leq 0.001$
Yes	67	50 (74.6)		48 (71.6)	
Diabetes mellitus					
No	105	38 (36.2)	$\chi^2 = 37.0, P \leq 0.001$	33 (31.4)	$\chi^2 = 22.7, P \leq 0.001$
Yes	113	87 (77.0)		72 (63.7)	
Heart failure					
No	1630	79 (48.5)	$\chi^2 = 20.8, P \leq 0.001$	61 (37.4)	$\chi^2 = 29.9, P \leq 0.001$
Yes	55	46 (83.6)		44 (80.0)	
Bronzed skin					
No	172	90 (52.3)	$\chi^2 = 8.4, P = 0.004$	72 (41.9)	$\chi^2 = 12.89, P \leq 0.001$
Yes	46	35 (76.1)		33 (71.7)	
Short stature					
No	148	74 (50.0)	$\chi^2 = 10.2, P = 0.001$	54 (36.5)	$\chi^2 = 25.2, P \leq 0.001$
Yes	70	51 (72.9)		51 (72.9)	
Chelation therapy					
No	184	96 (52.2)	$\chi^2 = 12.9, P \leq 0.001$	79 (42.9)	$\chi^2 = 12.9, P \leq 0.001$
Yes	34	29 (85.3)		26 (76.5)	
Hospitalization					
No	135	52 (38.2)	$\chi^2 = 51.3, P \leq 0.001$	39 (28.9)	$\chi^2 = 52.8, P \leq 0.001$
Yes	83	73 (88.0)		66 (79.5)	
Splenectomy					
No	121	57 (47.1)	$\chi^2 = 11.6, P = 0.001$	42 (34.4)	$\chi^2 = 19.7, P \leq 0.001$
Yes	97	68 (70.1)		63 (64.9)	
Self-esteem					
High	92	32 (34.8)	$\chi^2 = 33.1, P \leq 0.001$	32 (34.8)	$\chi^2 = 11.4, P = 0.001$
Low	126	95 (73.8)		73 (57.9)	

Other non-significant predictors for anxiety and depression are sex, residence, social class, education, consanguinity, affected family, birth order, cannulation, blood sampling and blood infections

This may be because our patients were less educated with less awareness and less insight about the nature of their illness, its morbidity and early mortality.

Our results revealed that each parameter of treatment modalities and disease complications could be considered as a predictor of psychiatric insult in thalassaemic patients. The independent predictors of anxiety in thalassaemic patients include hospitalization, diabetes mellitus, heart failure and self-esteem. Moreover, the independent predictors of depressive disorders in the current study were heart failure, hospitalization, diabetes, short stature and delayed puberty. In contrary, Mednick et al. [22] did not find a significant relationship between disease severity and

Table 5 Logistic regression analysis of independent predictors of anxiety and depression in thalassemic patients

	Anxiety		Depression	
	β	OR (95 % CI)	β	OR (95 % CI)
Delayed puberty				
No		1 (r)	–	1 (r)
Yes			1.4	4.2 (1.9–9.1)***
Diabetes mellitus				
No	–	1 (r)	–	1 (r)
Yes	1.8	6.3 (2.9–13.5)***	1.7	5.4 (2.4–12.2)***
Heart failure				
No	–	1 (r)	–	1 (r)
Yes	1.9	6.8 (2.5–18.9)***	2.1	8.4 (3.3–21.3)***
Short stature				
No		1 (r)	–	1 (r)
Yes			1.5	4.3 (1.7–10.5)**
Hospitalization				
No	–	1 (r)	–	1 (r)
Yes	2.3	10.2 (4.3–24.2)***	2.0	7.4 (3.3–11.8)***
Self-esteem				
High	–	1 (r)		
Low	1.7	5.7 (2.6–12.5)***		

OR odds ratio, CI confidence interval, r reference category

***** Significant at $P \leq 0.01$ and $P \leq 0.001$; respectively

experiencing symptoms of anxiety and depression. This could be explained by the fact that in developed countries patients with thalassemia are well managed with adequate chelation therapy that known to decrease disease morbidity, mortality and less secondary complications [30].

Present study shows that patients with thalassemia have significantly low self-esteem which is independent predictors of anxiety. Self-esteem is important to how much we like and value ourselves and is closely related to how we view our bodies. Suffering from any illness even flu makes us feel not good and disable us from doing things that we used to do. Moreover, illness is usually associated with pain and frustration which are the source of anxiety and suffering. More importantly, patients with a chronic illness over time believe that they will never be well. They are confident that they will always carry this illness with them as the illness is apart of them. Therefore, children with thalassemia were not allowed to go to school, they were not allowed to play or to be involved in all the normal activities that their same age children should be involved. So, they develop a bad self-image and low self-esteem [31–33]. They do not talk to friends about the illness, fearing that they will be rejected and treated differently. Moreover, suffering from a low self-esteem and a devalued sense makes patients to be always looked for approval and

acceptance from others, and they felt very easily hurt and rejected which make them to accept thing that they actually dislike [34]. All these factors increase anxiety and depression in such patients with decreased self-esteem.

This is a cross-sectional study, and predictors and outcome were assessed simultaneously. So it is difficult to assess the temporal relationship that needs a follow-up study. Further studies are needed to assess any causal association. Consanguinity is risk factor for thalassemia. Thalassemia is an autosomal recessive disorder. However, the difference in education may be the result of thalassemia because of the absence from school and the presence of chronic anemia that may lead to lack of concentration and poor school performance. The marginal difference between controls and cases in social classes may be a result of thalassemia because of the economic burden caused by the cost of iron chelation drugs and the cost of blood transfusion. Another explanation is the higher incidence of consanguineous marriage in low socioeconomic communities.

We can conclude that thalassemic patients are more vulnerable to psychiatric disorders like anxiety and depression. They may need psychological support going with the medical treatment. Once they develop secondary complications as diabetes mellitus, bronzed skin, heart failure, short stature and delayed puberty with frequent hospitalization which actually predict more anxiety and depression, they are definitely in need for strong lifelong psychological support primarily from their families, healthcare givers and even from the community for better adherence to therapy, wellbeing and treatment outcome.

Study limitations

This is a cross-sectional study and the temporal relationship between cause and outcome is difficult to ascertain.

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