

Received: 17 January 2015 • Accepted: 22 March 2015

Research

doi:10.15412/J.JBTW. 01040304

Prevalence and Socio-Demographic Characteristics Related to Stress, Anxiety, and Depression among Patients with Major Thalassemia in the Kermanshah County

Firoozeh Khamoushi¹, Seyed Mojtaba Ahmadi², Behzad Karami-Matin³, Touraj Ahmadi-Jouybari⁴, Mehdi Mirzaei-Alavijeh⁵, Mari Ataee^{4*}, Mohammad Mahboubi⁶

¹ Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

² Department of Psychiatry, Faculty of Medicine, Kermanshah University of Medical Science, Kermanshah, Iran

³ Department of Public Health, School of Health, Kermanshah University of Medical Sciences, Kermanshah, Iran

⁴ Clinical Research Development Center, Imam Khomeini Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran

⁵ Social Determinants of Health Research Center, Yasuj University of Medical Sciences

⁶ Abadan School of Medical Sciences, Abadan, Iran

*correspondence should be addressed to Mari Ataee, Clinical Research Development Center, Imam Khomeini Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran; Tell: +988337272049; Fax: +988337272049; Email: mariaataee@yahoo.com.

ABSTRACT

Thalassemia is one of the most common chronic and genetic blood disorders in the world that can followed by several complications, such as mental disorders. The aim of this study was to determine the prevalence and socio-demographic characteristics associated with stress, anxiety and depression among patients with thalassemia major in Kermanshah during 2014. This cross-sectional study done among 64 patients with thalassemia major during 2014; in the participants were randomly selected among patients who referred to Mohammad Kermanshahi hospital in the Kermanshah County to take part in this study. A standard questionnaire (DASS-21) which analyzed stress, anxiety and depression was applied for collecting data and data were analyzed by SPSS version 20 using chi-square statistical tests. The mean age of respondents was 22.31 years [95% CI: 20.42, 24.21], ranged from 14 to 58 years. Findings showed the 60.9%, 59.4 % and 18.8 % of the respondents were suffering from extremely severe anxiety, depression, and stress, respectively. Furthermore, our findings showed marital status and job have significant relationship with anxiety ($P<0.05$); education level has significant relationship with depression ($P<0.05$). Our findings indicated high level of prevalence of mental disorder among patients with thalassemia major. These results can be warning to health policy makers in Iran; and should be the focus of special attention.

Key words: Thalassemia Major, Mental Disorder, Anxiety, Depression, Stress

Copyright © 2015 Firoozeh Khamoushi et al. This is an open access article distributed under the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/).

1. INTRODUCTION

Thalassemia is one of the most common chronic and genetic blood disorders in the world (1) and each year about 60000 infants are born with this disorder (2). Iran is located on the thalassemia belt in the world and thalassemia carriers are evaluated from 1 to 10 percent [average % 4.5] transitively (3). Thalassemia is a major sanitary problem not only for the patients and their families but also for each country's public health systems with regard to treatment expenses including regular injections,

iron chelating agents, frequent hospitalizations and other medical consistencies (1). Beta thalassemia is the most common case which occurs as Thalassemia minor, thalassemia intermediate and major thalassemia (4). Beta Thalassemia major symptoms include severe and chronic anemia, slow growth, hepatoplenomegaly and bone disorders which severely affect individual's life (5). However, using of regular transfusion, treatment with iron chelating agents, proper management on consequences and good supportive cares, makes a normal life length possible to patients with

thalassemia and there has been a significant increase in their life expectancy (6, 7); there is a permanent long life which need to follow a complicated and unpleasant medical diet, which could have an undesirable effect on patients' mental and emotional functioning (8). In this regard, studies showed that chronic, physically limiting diseases such as thalassemia could have undesirable effects on mental health of patients and their families and lead to mental and emotional problems among them (9-11). Nevertheless, there has been little discussion on social-mental aspects of Thalassemia major; studies showed that the patients suffer from mental problems such as anxiety and depression and are easily hurt by mental problems (8). Some studies reported that up to 80 % of patents with Thalassemia major suffered experienced severe mental disorders (10). The other point to be considered is the significant effect of thalassemia major on physical wellbeing which results in physical disorders, lag of growth and late maturation (12); it has a severe undesirable effect on patient's self-concept due to its chronic nature and its consequences, which could increase anxiety and depression among patients and negatively affect their future lives (13). On the other hand, previous researches suggested that individuals with thalassemia had the feelings such as shame, lack of confidence on the disease outcomes and fear of stigma or sudden death. also, in developing countries, adults with thalassemia avoid their treatment due to lack of general information on the field, high expenses of treatment or no access to drugs, therefore, experience severe emotional problems such as despairing, sadness, animosity, depression, anxiety, fear of death, lack of self-confidence, insularity and anger (1). Thalassemia is a public sanitary problem around the world which is developing (14, 15). With regard to medical developments to cure thalassemia, there has been a significant increase in patients' lifetime and life expectancy (6, 7). On the other hand, chronic diseases and their undesirable and lifelong treatments could lead to metal disorder among patients (8). A study reported 28 to 80% of psychological maladjustment among patients with thalassemia major (16). Naderi et al. showed that 50.8 % of patients with thalassemia major suffered from mental disorders (17). These findings indicate designing mental disorders preventive program among patients with thalassemia is necessary (18, 19). On the other hand, studies introduced epidemiologic inves-

tigation as the basic necessary activities needed to design preventive interventions (20). Considering the importance of the issue, present study aims to determine the prevalence and socio-demographic characteristics associated with stress, anxiety, and depression among patients with Thalassemia major in the Kermanshah County.

2. MATERIALS AND METHODS

It is a cross sectional study which studied 64 patients with thalassemia major (the sample size was according to the results of a pilot study) during 2014. The participants randomly selected among patients who referred to Mohammad Kermanshah hospital in the Kermanshah province city for participation in this study. Data selected based on standard questionnaire (DASS-21) which analyzed stress, anxiety and depression. All samples were justified on goals and information security of study. Measurement included two parts and information was gathered by self-reports and interviewing participants. Part one: demographic questioner; it included eight questions investigating age, gender (male or female) marital status (single or married), education level (high school, diploma, under graduate), age at diagnosis, parental consanguinity (yes, no), occupation (student, jobless, employed), having heart disease (yes, no). Part two: The mental disorder among participants evaluated by DASS-21 standard scale. Each item was measured on an ordinal four-point Likert-type scaling (1 = never, 4 = very much). DASS-21 scale, including 3 scopes (anxiety, stress, and depression). Reliability of the questionnaire has been confirmed and its alpha coefficient was reported to be 0.97, 0.92 and 0.95 for depression, anxiety and stress, respectively (21). Each subscale of DASS-21 includes 7 questions where final score of each results from the sum of the scores of the relative questions; as DASS-21 is a short form of the original scale (including 42 questions), scores from each subscale should be 2 times to gain the severity of the symptoms (21). Table 1 shows the severity of the symptoms according to the test and also questions in each subscale; the higher the score, the more the stress, anxiety and depression.

Table 1 . The short form of DASS-21

Field name	Depression	Anxiety	Stress
Item NO	3, 5, 10, 13, 16, 17, 21	2, 4, 7, 9, 15, 19, 20	1, 6, 8, 11, 12, 14, 18
Normal	0- 0-9	0-7	0-14
Mild	10-13	8-9	15-18
Moderate	14-20	10-14	19-25
Severe	21-27	15-19	26-33
Extremely Severe	+ 28	+ 20	+ 33

Data were analyzed by SPSS version 20 using chi-square test, at 95% significant level.

demographic characteristics of the participants are shown in Table 2.

3. RESULTS AND DISCUSSION

The mean age of respondents was 22.31 years [95% CI: 20.42, 24.21], ranged from 14 to 58 years. More details of

Table 2. Distribution of the demographic characteristics among the participants

Variables		Number	Percent
Age group	Under 20	26	40.6
	20-30	30	46.9
	Upper 30	4	6.3
	Unanswered	4	6.3
Sex	Male	31	48.4
	Female	32	50
	Unanswered	1	1.6
Marital Status	Single	59	92.2
	Married	5	7.8
	Unanswered	1	1.6
Education	Under Diploma	29	45.3
	Diploma	20	31.3
	Academic	13	20.3
	Unanswered	2	3.1
Job	Student	28	43.8
	Unemployed	24	37.5
	Employed	11	17.2
	Unanswered	1	1.6
Heart Disease	Yes	7	10.9
	No	57	89.1

Almost the 57.8 % of participants were reported their parents have a consanguineous marriage. In addition Table 3 , Table 4 & Table 5 showed the relation between independent variable (such as; age, sex, education, marital status, job and heart disease) and anxiety, depression and

stress of the participants. However, there was no significant difference between anxiety, depression and stress with age (P> 0.05).

Table 3 . Relation between demographic characteristics and anxiety

Variables		Anxiety			P
		Moderate	Severe	Extremely Severe	
Sex	Male	4 (12.9 %)	10 (32.3 %)	17 (54.8 %)	0.680
	Female	3 (9.4 %)	8 (25 %)	21 (65.6 %)	
Marital Status	Single	4 (6.8 %)	17 (28.8 %)	38 (64.4 %)	0.001*
	Married	3 (60 %)	1 (20 %)	1 (20 %)	
Education	Under Diploma	2 (6.9 %)	9 (31 %)	18 (62.1 %)	0.792
	Diploma	3 (15 %)	4 (20 %)	13 (65 %)	
	Academic	2 (15.4 %)	4 (30.8 %)	7 (53.8 %)	
Job	Student	3 (10.7 %)	6 (21.4 %)	19 (67.9 %)	0.024*
	Unemployed	0 (0 %)	9 (37.5 %)	15 (62.5 %)	
	Employed	4 (36.4 %)	2 (18.2 %)	5 (45.5 %)	
Heart Disease	Yes	0 (0 %)	2 (28.6 %)	5 (71.4 %)	0.606
	No	7 (12.3 %)	16 (28.1 %)	34 (59.6 %)	

Table 4 . Relation between demographic characteristics and depression

Variables		Depression			P
		Moderate	Severe	Extremely Severe	
Sex	Male	7 (22.6 %)	5 (16.1 %)	19 (61.3 %)	0.842
	Female	7 (21.9 %)	7 (21.9 %)	18 (56.3 %)	
Marital Status	Single	11 (18.6 %)	11 (18.6 %)	37 (62.7 %)	0.081
	Married	3 (60 %)	1 (20 %)	1 (20 %)	
Education	Under Diploma	7 (24.1 %)	3 (10.3 %)	19 (65.5 %)	0.009*
	Diploma	3 (15 %)	2 (10 %)	15 (75 %)	
	Academic	2 (15.4 %)	7 (53.8 %)	4 (30.8 %)	
Job	Student	7 (25 %)	6 (21.4 %)	15 (53.6 %)	0.0672
	Unemployed	3 (12.5 %)	5 (20.8 %)	16 (66.7 %)	
	Employed	3 (27.3 %)	1 (9.1 %)	7 (63.6 %)	
Heart Disease	Yes	1 (14.3 %)	1 (14.3 %)	5 (71.4 %)	0.786
	No	13 (22.8 %)	11 (19.3 %)	33 (57.9 %)	

Table 5 . Relation between demographic characteristics and stress

Variables		Stress			P
		Normal	Mild	Moderate	
Sex	Male	18 (58.1 %)	9 (29 %)	4 (12.9 %)	0.229
	Female	12 (37.5 %)	12 (37.5 %)	8 (25 %)	
Marital Status	Single	28 (47.5 %)	20 (33.9 %)	11 (18.6 %)	0.947
	Married	2 (40 %)	2 (40 %)	1 (20 %)	
Education	Under Diploma	13 (44.8 %)	9 (31 %)	7 (24.1 %)	0.157
	Diploma	6 (30 %)	9 (45 %)	5 (25 %)	
	Academic	9 (69.2 %)	4 (30.8 %)	0 (0 %)	
Job	Student	16 (57.1 %)	8 (28.6 %)	4 (14.3 %)	0.402
	Unemployed	10 (41.7 %)	8 (33.3 %)	6 (25 %)	
	Employed	3 (27.3 %)	6 (54.5 %)	2 (18.2 %)	
Heart Disease	Yes	3 (42.9 %)	1 (14.3 %)	3 (42.9 %)	0.184
	No	27 (47.4 %)	21 (36.8 %)	9 (15.8 %)	

Furthermore, our findings showed the 60.9 %, 59.4 % and 18.8 % of the respondents were suffering from extremely severe anxiety, depression, and stress, respectively (Diagram 1).

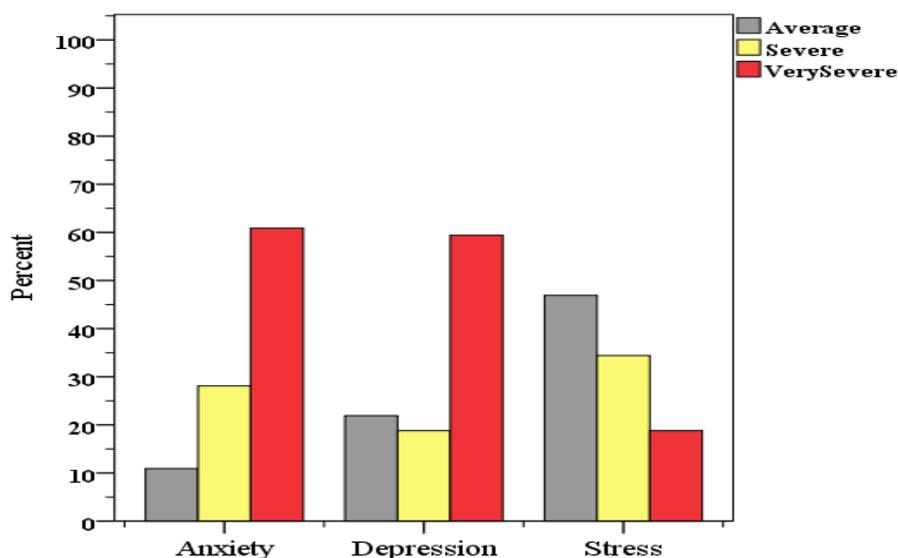


Diagram 1. Status of Anxiety, and Depression, and Stress among Participants

The main aim of our study was to determine prevalence and socio-demographic characteristics associated with stress, anxiety, and depression among thalassemia major patients in the Kermanshah County. Our results showed severe stress, anxiety and depression among patients with thalassemia major were %18.8, %60.9 and %59.4, respectively. In this regard, Yengel et al. also introduced depression (%49) and anxiety (%43) as the main disorders among patients with thalassemia major (11). In a study on psychopathology, Ghanizadeh et al. expressed depression and anxiety as the most common disorders among patients with thalassemia major (22). Case studies by Hashemi et al. and Yahia et al reported higher rates of depression and anxiety among patients with thalassemia major in comparison to control group (13, 23). Based on the results from the present study, mental disorders were dominant among the patients who suffer from high levels of anxiety and depression, which have negative effect on their physical, mental and social lives. It could be understand that the chronic nature of the disease, clinical protests and unpleasant side effects of treatments would result in anxiety and depression disorders in patients' lives. Hajibeigi et al. reported treatment method iron chelating agents and its side effects, and also consequences of the disease to be the reasons of anxiety among patients with thalassemia; they emphasized that if the side effects were not controlled, there would be emotional outbursts among the patients, where ignoring them led to anxiety disorders (24). Also, anxiety patients with thalassemia could result from physical disorders and anxiety about pain and death (19). Oliveros et al. also represented a relationship between pain and increase of anxiety and depression among patients having thalassemia (25). Another study suggested that patients with thalassemia experienced high rates of stress due to frequent blood sampling and continuous subcutaneous injections of iron chelating agents which played an important role to create anxiety among the patients (26). Pradhan et al. suggested depression as the most common mental disorder among patients with thalassemia (27). In this regard, it could be find that thalassemia is a chronic and enervative disease creating feelings such as being different that decreases self-esteem. On the other hand, due to the physical side effects of the disease on bones and creating chronic anemia, it leads to a short stature and a delayed puberty among patients; the sum of the side effects creates depression and social isolation of the patients, while there is a relationship between delayed puberty and higher levels of depression (19, 28). These results indicated high levels of anxiety and depression disorders among the patients with thalassemia in the west of Iran; and should be the focus of special attention. Based on our findings, 57.8 % of the patients had a parent with history of consanguineous marriage. In this regard, Ghazanfari et al. reported this rate to be 58.3 percent (29). Marriage among relatives has been reported to be an important factor in congenital anomalies, which is common in Iran. Studies showed that the chance of giving birth to children with disabilities was twice or three times

more than normal marriages (30). It could be said that the acceptable and effective ways to avoid cases of thalassemia are carrier screening and genetics counseling among people at high risk (31). In this regard, it is suggested to make use of genetic counseling strategies before marriage and pregnancy, and also to screen carrier couples and thalassemia gene carriers in health system. Along with the results from the present study, there has been no meaningful relationship reported between stress, anxiety, depression and patient's age which corresponds to the studies by Hashemi et al., Yahia et al. and Messina et al. (13, 17, 23, 32, 33). However, some studies reported higher levels of mental disorders among young adults (8, 34, 35). Also, there was no significant relationship between patients' gender and their mental disorders which corresponded to studies by Shafiee et al., Hashemi et al. and Naderi et al. (17, 23, 33). Though, results of our study on age and gender were in contradiction with Mednick et al. reporting higher levels of depression among women and elder people in comparison to men and children (8). A main side effect to thalassemia major is heart diseases and heart failures. Yahia et al. introduced heart disease as an independent factor to thalassemia which increases anxiety and depression among the patients (13). In our study, 89.1 percent of the patients were free of heart diseases, which suggested no meaningful relationship between heart disease and higher levels of mental disorders. Another finding in the present study reported a significant relationship between education and depression among the patients where the higher the education level, the lower the depression; in this regard, it could be concluded that higher levels of education and knowledge could be influential to accepting environmental difficulties, improving individual life quality and having a positive attitude to life. On the other hand, higher educational levels of the patients help to better adaptation to the disease and accepting it and continuing their treatments (7). Also, according to our results, single and unemployed patients showed meaningful higher levels of anxiety, which contrasted the results from the study by Naderi et al. that suggested no significant relationship among patients' marital status, their occupation and their mental conditions (17). Along with our results, in a case study Mikelli et al. reported lower rate of marriage among patients with thalassemia major in comparison with control group (36); it could be a reason to high levels of anxiety among patients, though it needs more investigations.

4. CONCLUSION

Based on our result, it seems that design and the implementation of mental health promotion intervention among the patients with thalassemia major is necessary. We recommend the designing of intervention programs to reduce mental disorder among thalassemia major patients.

ACKNOWLEDGMENT

This study was funded by the Deputy of Research of Kermanshah University of Medical Sciences. We would like to thank Deputy of Research of Kermanshah University of Medical Sciences for financial support of this study. Furthermore, the authors would like to thank Dr. Mohammad Reza Golpayegani, Shirin Fallah-Pakdel and Babak Soltani for cooperation with researchers during the process of research project.

AUTHORS CONTRIBUTION

This work was carried out in collaboration among all authors.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

REFERENCES

1. Koutelekos J, Haliasos N. Depression and Thalassemia in children, adolescents and adults. *Health Science Journal*. 2013;7(3).
2. Weatherall D, Clegg J. Inherited haemoglobin disorders: an increasing global health problem. *Bulletin of the World Health Organization*. 2001;79(8):704-12.
3. Ansari S, Baghersalimi A, Azarkeivan A, Nojomi M, Rad AH. Quality of life in patients with thalassemia major. *Iranian journal of pediatric hematology and oncology*. 2014;4(2):57.
4. Galanello R, Origa R. Review: beta-thalassemia. *Orphanet J Rare Dis*. 2010;5(11).
5. Hongally C, Benakappa AD, Reena S. Study of behavioral problems in multi-transfused thalassemic children. *Indian journal of psychiatry*. 2012;54(4):333.
6. Jain M, Bagul AS, Porwal A. Psychosocial problems in thalassemic adolescents and young adults. *Chronicles of young scientists*. 2013;4(1):21.
7. Amoudi AS, Balkhoyor AH, Abulaban AA, Azab AM, Radi SA, Ayoub MD, et al. Quality of life among adults with beta-thalassemia major in western Saudi Arabia. *Saudi medical journal*. 2014;35(8):882-5.
8. Mednick L, Yu S, Trachtenberg F, Xu Y, Kleinert DA, Giardina PJ, et al. Symptoms of depression and anxiety in patients with thalassemia: prevalence and correlates in the thalassemia longitudinal cohort. *American journal of hematology*. 2010;85(10):802-5.
9. Sadock BJ. Kaplan & Sadock's comprehensive textbook of psychiatry: lippincott Williams & wilkins Philadelphia, PA; 2005.
10. Ayoub MD, Radi SA, Azab AM, Abulaban AA, Balkhoyor AH, Bedair S-eW, et al. Quality of life among children with beta-thalassemia major treated in Western Saudi Arabia. *Saudi medical journal*. 2013;34(12):1281-6.
11. Yengil E, Acipayam C, Kokacya MH, Kurhan F, Oktay G, Ozer C. Anxiety, depression and quality of life in patients with beta thalassemia major and their caregivers. *International journal of clinical and experimental medicine*. 2014;7(8):2165.
12. Thavorncharoensap M, Torcharus K, Nuchprayoon I, Riewpaiboon A, Indaratna K, Ubol B-o. Factors affecting health-related quality of life in Thai children with thalassemia. *BMC Hematology*. 2010;10(1):1.
13. Yahia S, El-Hadidy MA, El-Gilany A-H, Anwar R, Darwish A, Mansour A. Predictors of anxiety and depression in Egyptian thalassemic patients: A single center study. *International journal of hematology*. 2013;97(5):604-9.

14. Mazzone L, Battaglia L, Andreozzi F, Romeo MA, Mazzone D. Emotional impact in β -thalassaemia major children following cognitive-behavioural family therapy and quality of life of caregiving mothers. *Clinical practice and epidemiology in mental health*. 2009;5(1):5.
15. Vichinsky EP. Changing patterns of thalassemia worldwide. *Annals of the New York Academy of Sciences*. 2005;1054(1):18-24.
16. Saini A, Chandra J, Goswami U, Singh V, Dutta A. Case Control Study of Psychosocial Morbidity in β Thalassemia Major. *The Journal of pediatrics*. 2007;150(5):516-20.
17. Naderi M, reza Hormozi M, Ashrafi M, Emamdadi A. Evaluation of mental health and related factors among patients with beta-thalassemia major in south east of Iran. *Iranian journal of psychiatry*. 2012;7(1):47.
18. Shaligram D, Girimaji S, Chaturvedi S. Psychological problems and quality of life in children with thalassemia. *The Indian Journal of Pediatrics*. 2007;74(8):727-30.
19. Khurana A, Katyal S, Marwaha R. Psychosocial burden in thalassemia. *The Indian Journal of Pediatrics*. 2006;73(10):877-80.
20. Jalilian F, Karami-Matin B, Mirzaei Alavijeh M, Ataee M, Mahboubi M, Motlagh F, et al. Prevalence and Factor Related to Ritalin Abuse among Iranian Medical College Student: An Application of Theory of Planned Behavior. *Terapevticheski Arkhiv*. 2013;85(4s):22-7.
21. Antony MM, Bieling PJ, Cox BJ, Enns MW, Swinson RP. Psychometric properties of the 42-item and 21-item versions of the Depression Anxiety Stress Scales in clinical groups and a community sample. *Psychological assessment*. 1998;10(2):176.
22. Ghanizadeh A, Khajavian S, Ashkani H. Prevalence of psychiatric disorders, depression, and suicidal behavior in child and adolescent with thalassemia major. *Journal of pediatric hematology/oncology*. 2006;28(12):781-4.
23. Hashemi AS, Banaei-Boroujeni S, Kokab N. Prevalence of Major Depressive and Anxiety Disorders in Hemophilic and Major Beta Thalassemic Patients. *Iranian journal of Pediatric Hematology Oncology*. 2012;2(1):11-6.
24. Hajibeigi B, Azarkeyvan A, Alavian SM, Lankarani MM, Assari S. Anxiety and depression affects life and sleep quality in adults with beta-thalassemia. *Indian Journal of Hematology and Blood Transfusion*. 2009;25(2):59-65.
25. Oliveros O, Trachtenberg F, Haines D, Gerstenberger E, Martin M, Carson S, et al. Pain over time and its effects on life in thalassemia. *American journal of hematology*. 2013;88(11):939-43.
26. Saravi VG, Zarghami M, Tirgari A, Ebrahimi E. Relationship between thalassemia and depression. *Res J Biol Sci*. 2007;2(3):280-4.
27. Pradhan PV, Shah H, Rao P, Ashturkar D, Ghaisas P. Psychopathology and self-esteem in chronic illness. *The Indian Journal of Pediatrics*. 2003;70(2):135-8.
28. Huurre T, Aro H. Long-term psychosocial effects of persistent chronic illness. *European child & adolescent psychiatry*. 2002;11(2):85-91.
29. Ghazanfari Z, Arab M, Forouzi M, Pouraboli B. Knowledge level and education needs of thalassemic children's parents of Kerman city. *Journal of Critical Care Nursing*. 2010;3(3):3-4.
30. Sadat M A-LM, Farhud DD. . Consanguineous marriage in Iran. *Ann Hum Biol*. 2004;31(2):263-9.
31. Samavat A, Modell B. Iranian national thalassaemia screening programme. *Bmj*. 2004;329(7475):1134-7.
32. Messina G, Colombo E, Cassinero E, Ferri F, Curti R, Altamura C, et al. Psychosocial aspects and psychiatric disorders in young adult with thalassemia major. *Internal and emergency medicine*. 2008;3(4):339-43.
33. Shafiee A, Nazari S, Jorjani S, Bahraminia E, Sadeghi-Koupaei M. Prevalence of Depression in Patients with β -Thalassemia as Assessed by the Beck's Depression Inventory. *Hemoglobin*. 2014;38(4):289-91.
34. Kessler R, Ciu W, Deler O, Walters E. Prevalence, Severity, and Comorbidity of Twelve-Month DSM-IV Disorders in the National Comorbidity Survey Replication (NCS-R). *Archives of General Psychiatry*. 2005;62(6):617-27.
35. Collishaw S, Maughan B, Natarajan L, Pickles A. Trends in adolescent emotional problems in England: a comparison of two national cohorts twenty years apart. *Journal of Child Psychology and Psychiatry*. 2010;51(8):885-94.
36. Mikelli A TJ. Brief report: Depressive symptoms and quality of life in adolescents with β -Thalassemia. *J Adolesc*. 2004;27(2):213-6.