Review Article

J Babol Univ Med Sci
Vol 18, Issu 9; Sep 2016. P:39-48

Prevalence of Hypoparathyroidism in Patients with Thalassemia Major in Iran

M. Azami (MD)[1], Sh. Rahmati (BSc)[1], K. Sayehmiri (PhD)*[2]

1.Student ResearchCommittee, Ilam University of Medical Sciences, Ilam, I.R.Iran

2.Psychosocial Injuries Research Center, Ilam University of Medical Sciences، Ilam, I.R.Iran

J Babol Univ Med Sci; 18(9); Sep 2016; PP: 39-48

Received: Mar 10th 2016, Revised: Jun 1st 2016, Accepted: Jul 27th 2016.

ABSTRACT

BACKGROUND AND OBJECTIVE: Hypoparathyroidism is one the common complications of endocrine in patients with thalassemia major. Several studies have been conducted to report the prevalence of Hypoparathyroidism in patients with thalassemia major in Iran. However, there is no comprehensive assessment of it. Therefore, the present study was conducted to investigate the prevalence of Hypoparathyroidism in patients with thalassemia major in Iran through systematic review and meta-analysis.

METHOD: The present study was conducted based on PRISMA checklist for systematic review and meta-analysis studies. We searched national and international online databases such as Magiran, Iranmedex, SID, Medlib, Scopus, PubMed, Science Direct, Cochrane, Web of Science, Springer, Online library Wiley and Google Scholar for certain standard keywords without time limit until 2016.

FINDING: In 19 studies, 3219 patients with thalassemia major were examined. Prevalence of Hypoparathyroidism in patients with thalassemia major in Iran was calculated to be 10% (CI-95%: 7-10). Moreover, the percentage for various regions of Iran was different; 14% in the west, 18% in the east, 10% in the north, 12% in the south and 7% in the center of Iran. Prevalence of Hypoparathyroidism in men and women was estimated to be 9 and 14, respectively.

CONCLUSIONS: Prevalence of Hypoparathyroidism in patients with thalassemia major in Iran is high. Therefore, new policy and planning are necessary to minimize the complications of endocrine glands including Hypoparathyroidism in patients with thalassemia major in Iran.

KEYWORDS:*Hypoparathyroidism, Thalassemia major, Iran, systematic review, Meta-analysis.*

Please cite this article as follows:

Azami M, Rahmati Sh, Sayehmiri Sh. Prevalence of Hypoparathyroidism in Patients with Thalassemia Major in Iran. J Babol Univ Med Sci. 2016;18(9):39-48.

***Corresponding author: K. Sayehmiri (PhD)**

Address: Department of Social Medicine & Biostatistics, Ilam University of Medical Sciences, Ilam, I.R.Iran

Tel: +98 841 2227126

E-mail: sayehmiri@razi.tums.ac.ir

[DOR: 20.1001.1.15614107.1395.18.9.6.6]

[DOI: 10.22088/jbums.18.9.39]

Introduction

Thalassemia syndrome is a hereditary hemoglobinopathy which istransferred to individuals through mutation of genes in alpha or beta globin chains. In the case of beta thalassemia, there is disorder in beta chain genes. If both beta genes are impaired, then the person will suffer from thalassemia major or severe anemia (1, 2).

Life of these patients depends on frequent blood transfusions (3). This disease is common in the Mediterranean region, parts of North and West Africa, Middle East, Indian Peninsula, Far East and Southeast Asia. These regions are known as "the thalassemia belt". Hemoglobinopathy is a common beta-thalassemia in Iran. Some estimates suggest that 20000 people in Iran suffer from thalassemia and about 2 to 3 million people (4% of the population) are disease carriers. That being said, the distribution of disease is not equal nationwide. Thalassemia is more common in coastal areas near the Caspian Sea in the north and Persian Gulf and Sea of Oman in the south. Estimates show that in coastal provinces such as Khuzestan, Bushehr, Hormozgan, Sistan and Baluchestan, Kerman, Mazandaran and even central provinces such as Isfahan and Fars, up to 10% of the population carry thalassemia gene (4, 5).

The initial sign of thalassemia is paleness which is observed within the first 6 months of life and thereafter, symptoms include inadequate growth, inability to recover from infectious diseases, psychological stress, muscle pain and general weakness (6). In these patients, red blood cells have a short life and are destroyed at a faster rate (7). Thalassemia is accompanied with mild or severe anemia, bone disorders, weakness and growth delay (8). Patients with thalassemia regularly receive monthly blood transfusion sessions, which decreases the acute symptoms of the disease.

However, blood transfusion has several complications such as infection, alloimmunization and excess iron deposition in various body organs, which may lead to hepatic and cardiac insufficiency, diabetes mellitus, hypothyroidism, hypoparathyroidism and hypogonadism (8-10). In order to prevent such complications, iron chelation therapy is prescribed to remove excess iron from the body, but endocrine disorders are still observed (10, 11). In systematic review and meta-analysis, one can present a more detailed picture of the dimensions of a problem in society by investigating all relevant documentations and providing a general estimate (12,13). Several studies have been conducted on the prevalence of Hypoparathyroidism in patients with thalassemia major in Iran and they reported various Hypoparathyroidism prevalence rates (14-17). Therefore, considering the increasing importance of the issue, the present study was conducted to estimate the prevalence of Hypoparathyroidism in patients with thalassemia major in Iran through systematic review and meta-analysis.

Methods

The present study was conducted based on PRISMA checklist for systematic review and meta-analysis studies (18). To avoid bias, search, selection of studies, quality assessment and data extraction was done by two researchers independently. We searched national and international online databases such as Magiran, Iranmedex, SID, Medlib, Scopus, PubMed, Science Direct, Cochrane, Web of Science, Springer, Online library Wiley and Google Scholar for certain standard keywords without time limit until 2016.

In order to maximize the comprehensiveness of our search, general Persian keywords such as prevalence, complications, endocrine, Hypoparathyroidism, endocrine disorders, ferritin, hemosiderosis, iron overload, iron chelation therapy and thalassemia major were used in national databases. The English equivalent of these key words as well as combinations of these words using "and" and "or" were also searched in international online databases. To obtain further information, we also referred to the list of references.In the present study, the main criterion for inclusion was Hypoparathyroidism in patients with thalassemia major in Iran. Exclusion criterions were: non-random sample size, irrelevance, insufficient data and lack of clinical and laboratory diagnosis. Diagnosing Hypoparathyroidism based on clinical and laboratory findings includes low calcium, increased serum phosphate, low levels of

[DOR: 20.1001.1.15614107.1395.18.9.6.6]
[DOI: 10.22088/jbums.18.9.39]

parathyroid hormone and the mismatch between levels of parathyroid hormone and serum calcium (2). Quality assessment was done independently by two researchers using STROBE checklist (19), which is a standard and international checklist for quality assessment. The authors adopted a simple method of scoring. Two points were given to each part of the checklist and the points given to each article by the two researchers were compared in the end.

The minimum acceptable score was 16 and the articles that got minimum quality assessment score entered meta-analysis process. A pre-prepared form (containing the name of the author, year of publication, the number of participants, overall prevalence rate and gender-specific prevalence) was used to extract the required data. In case of ambiguity or a specific question, we contacted the authors by email. Since the prevalence of Hypoparathyroidism in patients with thalassemia major and the number of samples was extracted for each study, a binomial distribution was used to calculate the variance of each study in statistical analysis. To assess the heterogeneity of studies, Cochran's Q test and I^2 index were used. In this study, the heterogeneity was found to be 88%, which falls into the category of studies with high heterogeneity (if I^2 index is lower that 25%, the heterogeneity is low; if it is between 25 to 75%, the heterogeneity is medium and if it is higher than 75%, the heterogeneity is high). Due to the heterogeneity of studies and significance of I^2 index, random effects model was used in the meta-analysis (20,21). Mean weight was used to combine the prevalence in different studies and weight was given to each study according to its variance. Meta-regression model was used to determine the relationship between prevalence of Hypoparathyroidism and year of the study. The data were analyzed using Stata Ver.11.1 software and $p<0.05$ was considered significant.

Results

169 articles were identified in the systematic review, out of which 58 articles were excluded due to being duplicates. Full text of 111 articles was studied. After assessing inclusion/exclusion criteria and evaluating the quality of articles, 19 qualified studies, conducted from 1998 to 2013, entered meta-analysis (Fig 1). 3219 people with mean age of 17.44 and standard deviation of 6.5 participated in the study (table 1).

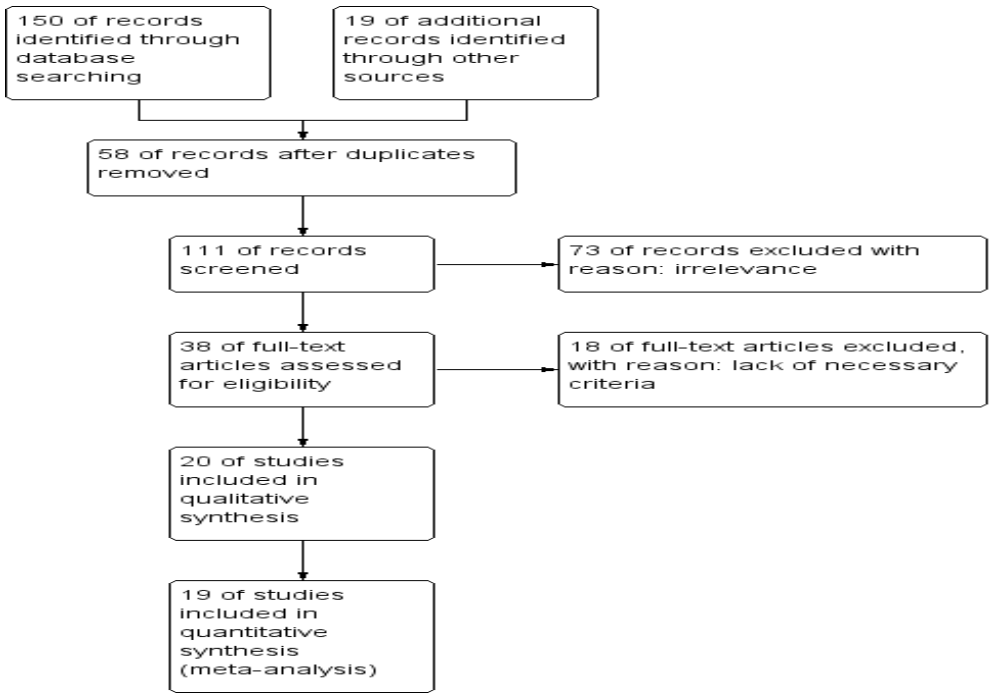


Figure 1. Process of selecting studies included in systematic review and meta-analysis

[DOR: 20.1001.1.15614107.1395.18.9.6.6]
[DOI: 10.22088/jbums.18.9.39]

Table 1. A summary of articles included in the study

Reference	Author	Region	Year	Sample volume	Male	Female	Mean Age (Mean±S)	Hypoparathyroidism(%)	Hypoparathyroidism in men (%)	Hypoparathyroidism in women (%)
14	Zandian	Ahwaz	2003	96	49	47	17.1±7	27.1	32.7	21.3
15	Rostami	Bushehr	2009	60	26	34	20.9±2.3	21.7	26.9	17.64
16	Vahidi	Kerman	2008	340	155	185	14.7±7.6	8.5	9	1.8
17	Saffari	Qazvin	2006	63	35	28	20.8±5	6.3	11.4	0
22	Chehkandi	Birjand	2003	31	17	14		12.9		
23	Razavi	Hamedan	2002	56				14.2		
24	Ansari	Shiraz	2005	806	406	400	15.34±7.6	6.9	4.9	9
25	Rabani	Tehran	2000	315	188	127		2.2		
26	Soheilkhah	Yazd	1998	53			10.7	24.5		
27	Mahdavi Anari	Tehran	1999	60	28	32		5		
28	Yazdi	Yazd	2005	65			10.3	6		
29	Shiva	Tabriz	2006	71	54	26	12.9±5.7	16.9		
30	Saffari	Qazvin	2012	77			21.2±4.5	7.8		
31	Arjmandi Rafsanjani	Tehran	2004	245	137	136	14±6.5	1.2		
32	Moaieri	Tehran	2006	158	76	82	15.1±4.8	7.6		
33	Karamifar	Shiraz	2003	150				7.3		0
34	Shamshirsaz	Tehran	1999	220	113	106	15.2±3.1	7.6	12.1	3
35	Miri	Zahedan	2013	223			23±4	18.4		
36	Hamidie	Qom	2007	130	60	70	16±10	14.6	18.3	11.4

The prevalence of Hypoparathyroidism in patients with thalassemia major in Iran with a significance level of p=0.000 and I^2 index of 88% was calculated to be 10% (CI-95%: 7-10). High level of I^2 index indicated high heterogeneity of studies. The lowest level was found in the study of Arjmandi et al. (31) in Tehran (1.2%), while the highest level was found in the study of Zandian et al. (14) in Ahwaz (27.1%) (Fig 2). Due to high heterogeneity of studies, we studied the prevalence of Hypoparathyroidism in patients with thalassemia major in various regions of Iran; lowest and highest prevalence rate was found in the center (7%) and east (18%) of Iran, respectively (Fig 3). In the process of investigating the gender-specific prevalence of Hypoparathyroidism in patients with thalassemia major, we did not find a significant relationship and prevalence among men and women was 9% (CI-95%: 5-13) and 14% (CI-95%: 8-20), respectively (table 2). The Meta-regression year-specific figure of studies demonstrated an increasing trend in prevalence of Hypoparathyroidism in patients with thalassemia major in Iran from 1998 to 2013, but the relationship was not statistically significant (Fig 4). Four studies investigated the relationship between level of serum ferritin and Hypoparathyroidism in patients with thalassemia major and our estimate of the standardized difference in mean serum ferritin in case group and control group was 0.01 ng/ml (CI-95%: 0.24-0.27). Since confidence interval crossed 0, the difference is not statistically significant (Fig 5).

Table 2. Gender-specific assessment of the prevalence of Hypoparathyroidism in patients with thalassemia major in Iran(N=6)

Variable	Sample volume	I^2	CI-95%	Overall assessment (%)
Man	844	70.2	5-13	9
Woman	870	81.1	8-20	14

[DOR: 20.1001.1.15614107.1395.18.9.6.6]
[DOI: 10.22088/jbums.18.9.39]

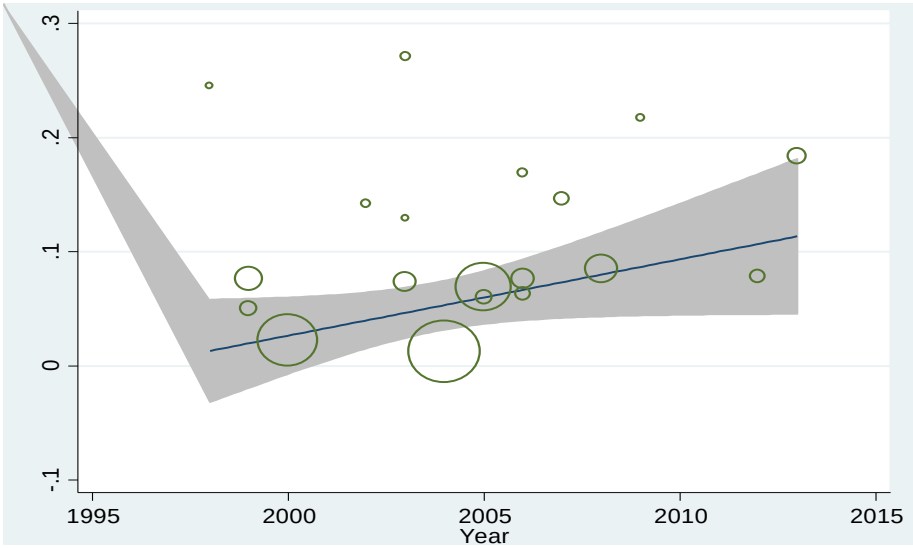


Figure 4. Meta-regression model of the prevalence of Hypoparathyroidism in patients with thalassemia major based on year of study. Circles indicate the weight of the study. Bigger circles indicate a higher number of samples (p=0.433)

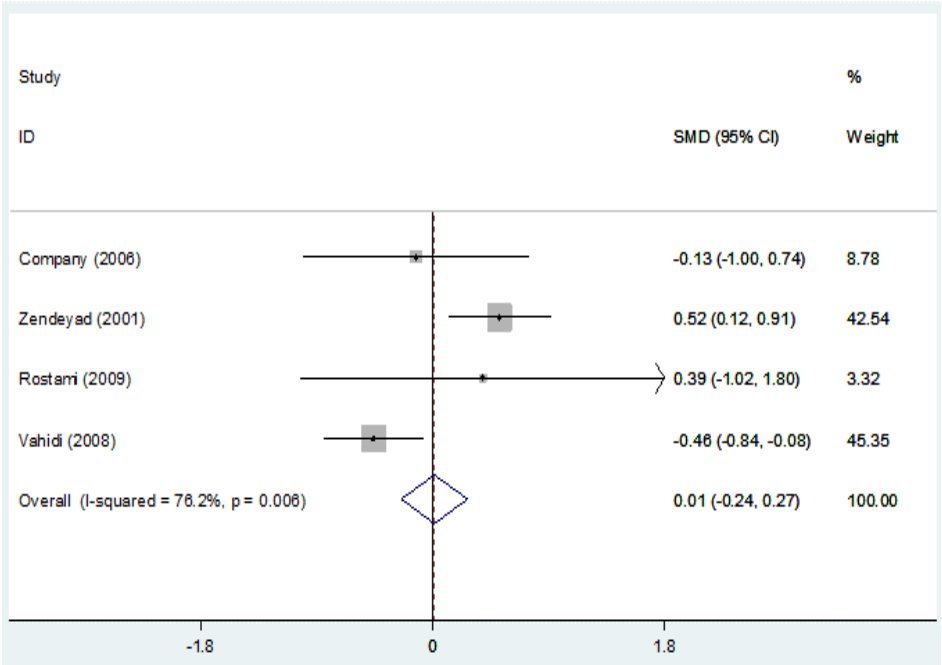


Figure 5. Relationship between level of serum ferritin and Hypoparathyroidism based on random effects model. Point estimate shows the percentage and length of segments show CI-95% in each study

Discussion

This is the first systematic review and meta-analysis study regarding the prevalence of Hypoparathyroidism in patients with thalassemia major in Iran. In this study, the prevalence of Hypoparathyroidism in patients with thalassemia major was investigated in terms of geographic region, gender and year of study. The overall prevalence of Hypoparathyroidism in these patients was calculated to be 10%. Several researches have been conducted to study endocrine disorders in patients with thalassemia major in Iran, reporting the prevalence of Hypoparathyroidism to be 5.7% (37), diabetes to be 9.4% (38) and impaired glucose tolerance to be 9.6% (39). The pathogenesis of endocrine disorders in patients with thalassemia major was

[DOR: 20.1001.1.15614107.1395.18.9.6.6]
[DOI: 10.22088/jbums.18.9.39]

recognized to be iron overload due to frequent blood transfusions. Therefore, extensive iron chelation therapy has been suggested (40, 41).

In a systematic review of patients with thalassemia major in Iran, the prevalence of regular iron chelation therapy was reported to be 54%. Therefore, it is necessary to note that iron chelation therapy in many patients with thalassemia major is done unsystematically (42).

Toxicity of iron may cause obvious Hypoparathyroidism in 3 to 4% of patients with thalassemia, whereas recent reports demonstrated that preclinical Hypoparathyroidism occurs in about 100% of thalassemia patients with iron toxicity (43). It seems that the best way to reduce glandular complications in patients with thalassemia major is receiving regular deferoxamine as well as coordinating the age to receive iron chelation therapy with the age to receive a blood transfusion (39, 40).

Prevalence of Hypoparathyroidism in other countries such as Saudi Arabia (11.1-20%) (44, 45), United Arabic Emirates (10.5%) (46), Turkey (2.8%) (47), Oman (10.1%) (48) and Italy (3.6%) (49) was reported to be varied.

The difference in prevalence of Hypoparathyroidism in various countries may be due to a genetic talent related to the toxic effects of iron overload in endocrine tissue or level of serum ferritin. It may also be due to the difference in follow-up and treatment in terms of blood transfusion, deferoxamine therapy method (regular or irregular), start time and dosage of deferoxamine.

In studying the region-specific prevalence of Hypoparathyroidism in patients with thalassemia major, the highest and lowest prevalence rate was found in east (18%) and center (7%) of Iran. The most probable reason for the high prevalence of Hypoparathyroidism in the east may be a low volume of samples in this region. Endocrine complications in patients with thalassemia major usually occur in the second decade of life (2-4).

In this study, the mean age was found to be 17.5 and most patients were over 10 years old. Hypoparathyroidism can be asymptomatic (9). Therefore, due to high prevalence of this disease, it is necessary to examine patients with thalassemia major in terms of Hypoparathyroidism every six months from age 10. The most comprehensive study in terms of volume of samples and regions in Iran belongs to Ansari (19) with a sample volume of 806 patients.

This study found the prevalence of Hypoparathyroidism to be about 7%, which was in accord with our study. Prevalence of Hypoparathyroidism in men and women with thalassemia major was calculated to be 9% (CI-95%: 5-13) and 14% (CI-95%: 8-20), respectively. Although prevalence rate was higher in men, the relationship was not statistically significant, because confidence intervals overlapped. In other studies, the prevalence of Hypoparathyroidism in men was also reported to be higher than women; maybe 2 or 4 times higher in some studies (47-50).

To study the relationship between mean serum ferritin and Hypoparathyroidism in patients with thalassemia major, random effects model was used and the relationship was not statistically significant. Other studies revealed different results in this regard. This relationship was not found to be significant in the study of Mula-Abed (48), but it was reported to be significant in the study of Gamberini (40).

Meta-regression model was used to determine the relationship between prevalence of Hypoparathyroidism and year of the study which demonstrated an increasing trend from 1998 to 2013, though the relationship was not statistically significant.

High overall prevalence of Hypoparathyroidism necessitates screening for early diagnosis of endocrine disorders in these patients. Deficiencies of national databases to offer combined search options for keywords and failure to mention deferoxamine dosage, blood transfusion intervals and the amount of blood transfused in most studies were some the limitations of this study.

Results showed that prevalence of Hypoparathyroidism in patients with thalassemia major is high. Hence, we need new policy and planning to minimize endocrine complications due to Hypoparathyroidism in patients with thalassemia major in Iran such as improved blood transfusion protocols, chelation therapy and informing parents and patients of

[DOR: 20.1001.1.15614107.1395.18.9.6.6]
[DOI: 10.22088/jbums.18.9.39]

endocrine complications due to iron overload. As advised by the World Federation of Thalassemia, these patients need to be examined every six months regarding Hypoparathyroidism.

Acknowledgments

Hereby, we express our deepest sense of gratitude and indebtedness toStudent Research Committeeof Ilam University of Medical Sciences for their support.

[DOR: 20.1001.1.15614107.1395.18.9.6.6]
[DOI: 10.22088/jbums.18.9.39]

References

1. Rund D. Thalassemia: Modern medicine battles an ancient disease. Am J Hematol. 2016; 91(1):15-21.

2.Al-Akhras A, Badr M, El-Safy U, Kohne E, Hassan T, Abdelrahman H, et al. Impact of genotype on endocrinal complications in β-thalassemia patients. Biom Rep. 2016;4(6):728-36.

3.Chirico V, Rigoli L, Lacquaniti A, Salpietro V, Piraino B, Amorini M, et al Endocrinopathies, metabolic disorders, and iron overload in major and intermedia thalassemia: serum ferritin as diagnostic and predictive marker associated with liver and cardiac T2* MRI assessment. Eur J Haematol. 2015; 94(5): 404-12.

4.Najafipour F, Sarisorkhabi R, Bahrami A, Zareizadeh M, Ghoddousi K, Aghamohamazadeh N, et al. Evaluation of endocrine disorders in patients with thalassemia major. Iran J Endocrin Metab. 2008; 10(1): 35-43. [In Persian]

5.Saki N, DehghaniFard A, Kaviani S, Jalali Far M, Mousavi S, AL- Ali K. et al. Beta thalasemia; Epidemiology, diagnostic and treatment approach in iran. Gen 3 M. 2012; 10(1): 2675-83.

6.Lanzkowsky P. Manual of pediatric hematology and oncology; 4th ed., Philadelphia:Elsevier. 2005; p. 181-90.

7.Kurtoglu AU, Kurtoglu E, Temizkan AK. Effect of iron overload on endocrinopathies in patients with beta-thalassaemia major and intermedia. Endokrynol Pol. 2012; 63(4): 260-3.

8.Galanello R, Origa R. Beta-thalassemia. Orphanet J Rare Dis. 2010;5:11.

9.Borgna-Pignatti C, Gamberini MR. Complications of thalassemia major and their treatment. Expert Rev Hematol. 2011;4(3):353-66.

10.Saliba AN, El Rassi F, Taher AT. Clinical monitoring and management of complications related to chelation therapy in patients with β-thalassemia. Expert Rev Hematol. 2016; 9(2):151-68.

11.Borgna-Pignatti C, Marsella M. Iron Chelation in Thalassemia Major. Clin Ther. 2015; 37(12): 2866-77.

12. Azami M, Khataee M, Bigdeli-shamloo M, Abasalizadeh F, Rahmati Sh, Abasalizadeh Sh, et al. Prevalence and Risk Factors of Hepatitis B Infection in Pregnant Women of Iran: A Systematic Review and Meta-Analysis. Iran J Obstet Gynecol Infertil. 2016; 19(18):17-30. [In Persian]

13.Sayehmiri K, Azami M, Nikpey S, Borji M, Sayehmiri F. Hepatitis B vaccination coverage in health personnel of iran: a systematic review and meta-analysis study. Iran J Epidemiol. 2015;11(3):1-10. [In Persian]

14.Zandian KM, Mohammadian Nasab AM, Riahy K, Shahbazian H, Khoshhal Dehder F, Ashrafi MR, Salajaghah N. The prevalence of hypoparathyroidism among Patients with major thalassemia aged above 10 years. Iran J Pediatr. 2005;15(2):158-64.[In Persian]

15.Rostami P, Hatami G, Shirkani A. Endocrine complications in patients with major β-thalassemia. ISMJ. 2011; 14(4): 240-45.

16.Vahidi AA, Parvaresh S, Torabinegad MH, Ahmad Ai, Mohammadi R. The Frequency of β-thalasemia Major Complications in Patients Referred to Kerman Center for Special Diseases during 6 Months. J Kerman Univ Med Sci2011; 18(4): 179-86. [In Persian]

17.Saffari F, Abolfazl M. Bone mineral density in patients with Beta- Thalassemia Major in Qazvin. J Isfahan Med Sch. 2008; 26(89):179-86.

18.Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009; 62(10):1006-12.

19.Von Elm E, Altman DG, Egger M, et al. TheStrengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement:guidelines for reporting observational studies.Lancet 2007; 370(9596):1453-7.

20.Azami M, Darvishi Z, Sayehmiri K. Systematic Review and Meta-Analysis of the Prevalence of Anemia among Pregnant Iranian Women (2005 - 2015). Shiraz E-Med J 2016; 17: e38462.

21.McKenzie JE, Beller EM, Forbes AB. Introduction to systematic reviews and meta-analysis. Respirology. 2016; 21(4): 626-37.

[DOR: 20.1001.1.15614107.1395.18.9.6.6]
[DOI: 10.22088/jbums.18.9.39]

22.Chahkandi T, Kazemi T, Jalili A, Ghaderi F. Evaluation of cardiac function in patients with major beta thalassemia in Birjand. Scientific Journal of Iran Blood Transfus Organ 2013; 10(1): 86-92.
23.Razavi Z, Bazmamoun B, Sadegh Saba M. The frequency of hypoparathyroidism in patients with Beta-thalassemia in Hamadan - Iran. J Gorgan Uni Med Sci 2009; 10:29-33.
24.Ansari H, Tabatabai, H. Study of factors in major beta thalassemia complications in patients admitted to shahid dastghaib hospital in shiraz, iran (2004-5). J Sabzevar Univ Med Sci.2007; 14(1):62-72. [In Persian]
25.Rabbani A, Azar Keiwan A, Farhadi Langeroudi M, Korosdari GH. Clinical evaluation of 413 Thalassemic patients. Tehran Univ Med J. 2000; 58: 35-41. [In Persian]
26.Soheili Khah S, Eslami S. Endocrine disorders in Thalassemia major in Yazd. J Shahid Sadoughi Univ Med Sci Health Serv. 2000;8(1):7-11. [In Persian]
27.Mahdavi Anari F, Ahmadian A, Haghshenas Z, Alawi Yazdi Z. Comparison of the frequency of four endocrine disorders in patients with thalassemia major referred to thalassemia clinic of Tehran Imam Khomeini Hospital in 2000. [Dissertation]. Tehran: Tehran University of Medical Sciences; 2000.
28.Amanat Yazdi M, Hashemi A, Afkhami G, PourShamsi F. Evaluation relationship between endocrine disorders in B-thalassemic patients with serum ferritin levels. [Dissertation]. Yazd: Shahid Sadoughi Univ Med Sci; 2004.
29. Shiva S, SariSorkhabi R. Short stature in patients with beta-thalassemia. Urmia Med J. 2008; 19:125-31. [In Persian]
30.Saffari F, Mahyar A, Jalilolgadr Sh. Endocrine and metabolic disorders in β-thalassemia major patients. Caspian J Intern Med. 2012; 3(3): 466-72.
31.Arjmandi Rafsanjani Kh, Razzaghy-Azar M, Zahedi-Shoolami L, Vossough P, Modarres A, Taheri N. Bone mineral density in β thalassemia major and intermedia, correlation with biochemical and hormonal profiles. Iran J Blood Cancer. 2009; 1(4):121-7.
32.MoayeriH, Oloomi Z. Prevalence of growth and puberty failure with respect to growth hormone and gonadotropins secretion in beta-thalassemia major. Arch Iran Med. 2006; 9(4): 329-4.
33.Karamifar H, Shahriari M, Sadjadian N. Prevalence of endocrine complications in beta-thalassaemia major in the Islamic Republic of Iran. East Mediterr Health J. 2003; 9(1-2):55-60.
34.Shamshirsaz AA, Bekheirnia M, Kamgar M, Bouzari N, Hashemi R, Larijani B, et al. Endocrinologic complications in major beta thalassemia: a multicenter study in Tehran. BMC Endocr Disord. 2003;3(1):4.
35.Miri-Aliabad Gh, Fadaee M, Khajeh A, Naderi M. Marital status and fertility in adult iranian patients with β-thalassemia major. Indian J Hematol Blood Transfus. 2016. 32(1):110-3.
36.Hamidieh AA, Moradbeag B, Pasha F, Jalili M, Hadjibabaie M, Keshavarznia M. High prevalence of hypoparathyroidism in patients with beta-thalassemia major. Int J Hematol-Oncol Stem Cell Res. 2009. 3(3):17-20.
37.Azami M, gheisoori A, Sayehmiri F,Sayehmiri K. The prevalence ofhypothyroidismin patientswith Beta thalassemia major inIran-Asystematic review andmeta-analysisstudy. J Kurdistan Univ Med Sci 2016; 21(1): 104-16.
38.Azami M, Sayemiri K. Prevalence of diabetes mellitus in iranian patients with thalassemia major: a systematic review and meta-analysis. J Mazandaran Univ Med Sci. 2016; 26(141):192-204. [In Persian]
39.Azami M, Tarde Z, Abangah G, Sayemiri K. The prevalence of impaired glucose tolerance in patients with thalassemia major in iran: a systematic review and meta-analysis. J Shahid Sadoughi Univ Med Sci. 2016; 23(10): 912-22.[In Persian]
40.Gamberini MR, De Sanctis V, Gilli G. Hypogonadism, diabetes mellitus, hypothyroidism, hypoparathyroidism: incidence and prevalence related to iron overload and chelation therapy in patients with thalassaemia major followed from 1980 to 2007 in the Ferrara Centre. Pediatr Endocrinol Rev. 2008; 6(Suppl 1): 158-69.
41. Dmochowski K, Finegood DT, Francombe W, Tyler B, Zinman B. Factors determining glucosetolerance in patients with thalassemia major. J Clin Endocrinol Metab. 1993; 77(2):478-83.

[DOR: 20.1001.1.15614107.1395.18.9.6.6]
[DOI: 10.22088/jbums.18.9.39]

42.Azami M, Nikpay S, Abangah G, Sayehmiri K. Evaluation of the incidence of splenectomy and frequency of regular iron chelation therapy in patients with thalassemia Major in Iran: a meta-analysis. Scientific Journal of Iran Blood Transfus Organ. 2016; 13(2):122-31.

43.Even L, Bader T, Hochberg T. Nocturnal calcium, phosphorus and parathyroid hormone in the diagnosis of concealed and subclinical hypoparathyroidism.Eur J Endocrinol. 2007;156(1):113-6.

44.Habeb AM, Al-Hawsawi ZM, Morsy MM, Al-Harbi AM, Osilan AS, Al-Magamsi MS, et al. Endocrinopathies in beta-thalassemia major. Prevalence, risk factors, and age at diagnosis in Northwest Saudi Arabia. Saudi Med J. 2013; 34(1): 67-73.

45.Aleem A, Momen AK, Al-Harakai MS, Hassan A, Al-Fawaz I. Hypocalcemia due to hypoparathyroidism in s-thalassemia major patients. Ann Saudi Med. 2000;20(5-6):364-6.

46.Belhoul KM, Bakir ML, Kadhim AM, Dewedar HE, Eldin MS, Alkhaja FA. Prevalence of iron overload complications among patients with b-thalassemia major treated at Dubai Thalassemia Centre. Ann Saudi Med. 2013; 33(1):18-21.

47.Kurtoglu AU, Kurtoglu E, Temizkan AK.Effect of iron overload on endocrinopathies in patients with beta-thalassaemia major and intermedia. Endokrynol Pol. 2012; 63(4): 260-3.

48.Mula-Abed WA, Al Hashmi H,Al Muslahi M, Al Muslahi H, Al LamkiM. Prevalence of Endocrinopathies in Patients with Beta-Thalassaemia Major – A Cross-Sectional Study in Oman. Oman Medical Journal 2008; 23(4): 23(4):257-262.

49.Italian Working Group on Endocrine Complications in Non-Endocrine Disease, "Multicentre Study on Prevalence of Endocrine Complications in Thalassemia Major," Clinical Endocrinology (Oxf), 42(6); 1995: 581-586.

50.Chern JP, Lin KH, Lu MY, Lin DT, Lin KS, Chen JD,et al. Abnormal glucose tolerance in transfusion dependent beta thalassemic patients. Diab Care 2001; 24(5): 850-4.

[DOR: 20.1001.1.15614107.1395.18.9.6.6]

[DOI: 10.22088/jbums.18.9.39]