J Current Biomed Report
ISSN: 2717-1906
2024, Volume 5, Number 2
Research Paper

Demographic and clinical characteristics, and prevalence of *Helicobacter pylori* infection in individuals with major beta-thalassemia in Guilan province, Iran

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Article info:
Received: 02 Apr 2024
Accepted: 21 June 2024

Keywords:
Beta-thalassemia
Helicobacter pylori
Splenectomy
Iron chelator

ABSTRACT

Beta-thalassemia major is a severe genetic blood disorder requiring complex management, with patients facing multiple chronic health challenges related to iron metabolism and treatment strategies. The current study investigated the prevalence of *Helicobacter pylori* antigen and related clinical characteristics in beta-thalassemia major patients. This cross-sectional study involved 66 beta-thalassemia major patients and 36 of their non-cohabiting family. *H. pylori* infection was assessed using the stool antigen test via ELISA, and clinical and demographical data of patients was recorded. The mean age of patients was 36.72±9.46 years and for their family members was 41.54±12.46 (P <0.05). Twenty-eight (42.4%) of patients and 11 (30.6%) of their family members were males (P >0.05). The mean levels of hemoglobin and ferritin were 8.36±0.84 g/dL and 2108.63±1741.93 ng/mL, respectively. Splenectomy was performed in 59.1% of patients (mean age at procedure 15.59±9.50 years). Deferiprone was the most common iron chelator (45.5%), and O^+ was the predominant blood group (33.3%). Statistically significant differences were observed in iron chelator and blood group distributions (P <0.001). The findings illustrated no *H. pylori* antigen was detected in participants. The analysis of *H. pylori* antigen revealed no positive results in any of the participants, indicating an absence of *H. pylori* infection in major beta-thalassemia patients.

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1. Introduction

Beta-thalassemia, a common autosomal recessive hereditary anemia affecting 1.5% of the global population, is characterized by reduced or absent synthesis of β-globin chains, leads to ineffective erythropoiesis, chronic anemia, and dependence on regular blood transfusions for survival in major type [1,2]. Following chronic blood transfusions, excess iron is deposited in various organs and these patients often suffer from complications, which can damage the heart, liver, and endocrine organs, as well as increased susceptibility to infections due to immune dysfunction [3,4]. The chronic medical burden and repeated hospitalizations not only impact the quality of life for individuals with beta-thalassemia major but may also place them at greater risk for acquiring infections like *Helicobacter pylori*. Patients with beta-thalassemia major may be particularly susceptible to *H. pylori* infection due to frequent blood transfusions, impaired immune function, and potential disruptions in gastric mucosal integrity caused by iron chelation therapy [5,6]. *H. pylori*, a Gram-negative microaerophilic bacterium, is a major global health concern due to its association with a variety of gastrointestinal and extra-gastrointestinal disorders [7–9]. It is considered one of the most prevalent human pathogens, infecting over 50% of the world's population, with higher prevalence rates observed in developing countries. Transmission primarily occurs via oral-fecal and oral-oral routes, facilitated by inadequate sanitation and close living conditions [10–12]. The bacterium is strongly associated with chronic gastritis, peptic ulcers, and gastric cancer, and has also been implicated in conditions such as iron deficiency anemia and thrombocytopenia, highlighting its systemic impact [13,14].

Several studies have demonstrated an increased prevalence of *H. pylori* infection in patients with beta-thalassemia (minor and major), raising concerns about its role in exacerbating gastrointestinal symptoms and contributing to iron metabolism dysregulation in this population [5,15,16]. In Iran, the prevalence of *H. pylori* infection is notably high [17], particularly this infection is highly prevalent among the population of Guilan province, reflecting both regional and global public health concerns associated with this pathogen [17,18]. Evidence indicated that socioeconomic factors and dietary habits are significantly associated with exacerbating *H. pylori* infection prevalence and its related complications [19,20]. Given the notable coexistence of beta-thalassemia minor and *H. pylori* infection in northern Iran [21,22], along with the high prevalence of gastric disorders in thalassemia patients in this region, and also reported a high prevalence of *H. pylori* infection among minor beta-thalassemia individuals in northern Iran [5], we examined *H. pylori* infection among individuals with major beta-thalassemia in Guilan Province, northern Iran.

2. Materials and Methods

2.1 Study design and participants

The study population consisted of 66 patients with major beta-thalassemia and aged >18 years who were referred to Razi Hospital and Besat Clinic, Guilan University of Medical Sciences, Rasht, Iran as a case group and also their family members who were not affected by beta-thalassemia major and did not share meals with the patients as the control group (36 in each group). Participants were selected through a census-based and convenient sampling method and the sample size was calculated by 80% power of study with α of 0.5%. Individuals who were unwilling to participate, those who had used *H. pylori* eradication medications or proton pump inhibitors within the past month, were excluded from the study. All individuals consented to participate in the study and the study was confirmed by the ethical committee of the Guilan University of Medical Sciences, Rasht, Iran [IR.GUMS.REC.1401.230].

2.2 Data Collection and Procedures

Data of age, gender, history of splenectomy, mean ferritin levels over the past six months, hemoglobin level, type of iron chelation therapy, blood group, and duration of iron chelation therapy were collected. To assess the *H. pylori* infection, stool samples were collected from participants and *H. pylori* Ag was analyzed via Tecan Sunrise RC4 ELISA (Tecan Austria GmbH, Austria).

2.3 Statistical analysis

Statistical data was reported as number, percentage, and mean ± standard deviation (SD). The assumptions for parametric tests were assessed using the Kolmogorov-Smirnov test for normality and Levene's test for homogeneity of variances. For data analysis, independent samples T-test, and Chi-Square were applied. All statistical analyses were performed using SPSS software version 28, with a significance level set at 0.05 for all tests.

3. Results

The mean age of patients and their family members were 36.72±9.46 years and 41.54±12.46 years, respectively, which showed a marginal difference between the two groups (P=0.049). Thirty-eight (57.6%) of the patients and 25 (69.4%) of the control group were females, and no statistically significant difference was observed in gender disparity among studies groups (P=0.238). *H. pylori* Ag analysis demonstrated negative results in all participants. About 39 patients (59.1%) had splenectomy (P=0.140) and the mean age of splenectomy was 15.59±9.50 years. The mean hemoglobin level was 8.36 ± 0.84 g/dL, and

ferritin averaged 2108.63 ± 1741.93 ng/mL (Table 1). Deferiprone was the most commonly used iron chelator (45.5%), while the combination of deferasirox and deferoxamine was the least frequent (3.0%). Among blood groups, O^+ was the most prevalent (33.3%), and AB^- was absent. Statistically significant differences were observed in the distributions of iron chelators and blood groups (P<0.001) (Table 2).

4. Discussion

Beta-thalassemia remains a significant public health challenge, particularly in regions with high prevalence rates, such as northern Iran. The current study addressed a critical gap in medical knowledge by investigating the prevalence of *H. pylori* infection among beta-thalassemia patients in Guilan province, Iran. The study provided valuable insights that could potentially improve clinical strategies, early detection methods, and overall healthcare outcomes for individuals with major beta thalassemia, who are already managing complex medical conditions and potential long-term health complications. The findings of the current study showed the majority of female gender among patients with beta-thalassemia, though we did not find a statistically significant gender disparity. Findings from Mediterranean and Middle Eastern countries have reported a gender distribution with a male-to-female ratio of 1.26, indicating potential genetic or environmental factors contributing to this pattern [23]. The evidence revealed significant gender-based variations in beta-thalassemia, with notable differences observed in clinical manifestations and disease progression [24]. Females demonstrated higher hemoglobin F levels, better survival rates, and fewer cardiac complications, while males showed increased susceptibility to diabetes, iron overload sensitivity, and more severe osteoporosis. These gender-specific differences are related to multiple biological pathways, including oxidative stress defense, lipid metabolism, and erythropoietin activity [24–27]. More than half of the patients in our study had a history of splenectomy. The hematological parameters revealed critical aspects of patient management, with low mean hemoglobin and an exceptionally high mean ferritin level, which underscored the significant iron overload challenges faced by beta-thalassemia patients. Previous studies have consistently emphasized the importance of iron chelation therapy in managing these parameters, with ferritin levels serving as a crucial indicator of iron burden [28,29]. The current research found that patients had been receiving iron chelation therapy for almost 15 years, which is particularly noteworthy and reflects the long-term therapeutic interventions required for this chronic condition. The iron chelation therapy approach in this study demonstrated interesting variations in treatment strategies. Deferiprone was the most commonly used iron chelator, while combination therapies were less frequent. This finding diverges from some international guidelines that recommend combination or alternate chelation strategies [30]. Deferiprone, as an orally active iron chelator commonly used to manage iron overload in patients with thalassemia major, offers comparable efficacy to desferoxamine in removing body iron and superior effectiveness in treating myocardial siderosis. It can be used in cases of severe iron overload or poor compliance with desferoxamine infusions and has a well-established long-term safety profile despite rare but serious side effects like agranulocytosis [31]. Recent studies have increasingly advocated for personalized approaches to iron chelation, considering individual patient factors such as liver iron concentration, cardiac iron loading, and individual tolerance to different chelators [32,33].

Table 1. Hematological parameters and iron chelation therapy duration in 66 beta-thalassemia patients.

Variables	Mean ± SD	Min-Max
Hb levels over the past six months (g/dL)	8.36±0.84	6.50-10.20
Ferritin level over the past six months	2108.63±1741.93	29-7120
Duration of iron chelator therapy (year)	14.9314.22	1-46

Table 2. Frequency of iron chelators and blood groups among 66 individuals with beta-thalassemia.

Variables		Frequency n (%)	P value*
Types of iron chelators	Deferoxamine	14 (21.2)	<0.001
	Deferiprone	30 (45.5)	
	Deferasirox	7 (10.7)	
	Deferasirox-Deferoxamine	2 (3.0)	
	Deferoxamine-Deferiprone	9 (13.6)	
	Deferiprone-Deferasirox	4 (6.0)	
Blood group	A+	18 (27.3)	<0.001
	A-	3 (4.5)	
	B+	15 (22.7)	
	B-	1 (1.5)	
	AB+	1 (1.5)	
	AB-	0 (0.0)	
	O+	22 (33.3)	
	O-	6 (9.2)	

*Chi-Square; Significant level <0.05

A study by Mohamed et al. demonstrated that iron chelation therapy among adolescents with transfusion-dependent thalassemia was influenced by socioeconomic status and linked to clinical indicators like serum ferritin levels [32].

Blood group distribution in the current study presented that O^+ was most prevalent. A study by Waheed et al. reported that the blood group distribution showed O>B>A>AB, with O and A more common in females and B and AB more common in males, though the differences were non-significant. AB blood group predominates in beta-thalassemia major and B in the other types. Overall, O^+ was the most frequent, and AB^- was the least frequent blood group among beta-thalassemia patients [34]. Sinha et al. found that beta thalassemia was most common in individuals with O^+ blood group, who also have a higher likelihood of a family history of the same disease, while severity varies by blood group, being highest in B^- and lowest in O^+ [35]. Findings from the present study revealed *H. pylori* infection was not detected in either the patient or control groups. A study by Zamani et al. found that *H. pylori* infection was significantly more prevalent in minor beta-thalassemia patients compared to controls, with age being the only factor positively correlated with the infection [5]. Imran Khan et al. reported a significant prevalence of iron deficiency among *H. pylori*-infected patients, particularly in older adults, males, and those with longer infection duration [36]. Some studies have suggested that reduced hemoglobin in thalassemia patients with *H. pylori* infection might result from iron deficiency induced by the bacterial infection [37,38]. A key mechanism potentially underlying the increased *H. pylori* susceptibility in thalassemia patients might be the role of iron as a critical growth factor for bacterial proliferation [5]. In the current study, the absence of positive *H. pylori* results in the beta-thalassemia population could be due to factors such as study population, different diagnostic methods, or variations in immune responses in thalassemia patients that may affect bacterial colonization or detection. Furthermore, we assessed *H. pylori* infection using a stool antigen test, whereas most previous studies evaluated *H. pylori* using serum antibody tests, which can remain positive even after the infection has been cleared. Moreover, the prevalence of *H. pylori* may vary between minor and major beta-thalassemia due to differences in iron metabolism, immune function, and treatment-related factors. In minor beta-thalassemia, altered iron dynamics could promote *H. pylori* colonization, whereas in major thalassemia, factors like iron chelation therapy, blood transfusions, and chronic inflammation might create an environment less favorable for the bacteria. Differences in lifestyle and medical care might further contribute to this variability. The limitations of this study include a relatively small sample size, the cross-sectional study design, and the absence of serum-based diagnostic analyses, which have been suggested to be considered in future investigations.

Our findings provided valuable insights into the prevalence of *H. pylori* in patients with beta-thalassemia major, demonstrating the absence of bacterial detection. Results also highlighted significant variations in iron chelation therapy and blood group distribution, underscoring the complexities of managing this chronic genetic disorder. Consequently, there appears to be no substantial concern regarding infection with this organism in thalassemia patients, as the likelihood of *H. pylori* infection in individuals with beta-thalassemia major is comparable to that of the general population.

Acknowledgments

The current study is derived from the MD thesis of Samaneh Toloui (Registry Code: 4280).

Authors' contributions

ASh and BD participated in the research design. ST, AB, and ME participated in writing the first draft. ST, AB, and ME participated in the performance of the research and analytic tools. ASh and BD participated in data analysis. All authors reviewed and confirmed the final manuscript.

Conflict of interest

No potential conflict of interest was reported by the authors.

Ethical declarations

Written informed consent was obtained from all particioants. The study design was approved by the ethical committee of the Guilan University of Medical Sciences, Rasht, Iran [IR.GUMS.REC. 1401.230].

Financial support

Self-funded.

References

1. Sadiq IZ, Abubakar FS, Usman HS, Abdullahi AD, Ibrahim B, Kastayal BS, Ibrahim M, Hassan HA. Thalassemia: Pathophysiology, diagnosis, and advances in treatment. Thalassemia Reports. 2024;14(4):81-102. DOI: 10.3390/thalassrep14040010
2. Ali S, Mumtaz S, Shakir HA, Khan M, Tahir HM, Mumtaz S, et al. Current status of beta-thalassemia and its treatment strategies. Molecular genetics & genomic medicine. 2021;9(12):e1788. DOI: 10.1002/mgg3.1788 PMID: 34738740
3. Gluba-Brzózka A, Franczyk B, Rysz-Górzyńska M, Rokicki R, Koziarska-Rościszewska M, Rysz J. Pathomechanisms of Immunological Disturbances in β-Thalassemia. Int J Mol Sci. 2021;22(18):9677. DOI: 10.3390/ijms22189677 PMID: 34575839
4. Mishra AK, Tiwari A. Iron overload in Beta thalassaemia major and intermedia patients. Maedica (Bucur). 2013;8(4):328-32. PMID: 24790662
5. Zamani M, Vahedi A, Tamaddoni A, Bijani A, Bagherzade M, Shokri-Shirvani J. Relationship between β-Thalassemia minor

and *Helicobacter pylori* infection. Caspian J Intern Med. 2018;9(1):54-59. DOI: 10.22088/cjim.9.1.54 PMID: 29387320
6. Nairz M, Weiss G. Iron in infection and immunity. Molecular Aspects of Medicine. 2020;75:100864. DOI: 10.1016/j.mam.2020.100864
7. Ali A, AlHussaini KI. *Helicobacter pylori*: A Contemporary Perspective on Pathogenesis, Diagnosis and Treatment Strategies. Microorganisms. 2024;12(1):222. DOI: 10.3390/microorganisms12010222 PMID: 38276207
8. Malfertheiner P, Camargo MC, El-Omar E, Liou JM, Peek R, Schulz C, et al. Helicobacter pylori infection. Nat Rev Dis Prim. 2023;9(1):19. DOI: 10.1038/s41572-023-00431-8
9. Xu W, Xu L, Xu C. Relationship between Helicobacter pylori infection and gastrointestinal microecology. Frontiers in cellular and infection microbiology. 2022;12:938608. DOI: 10.3389/fcimb.2022.938608
10. Salih BA. Helicobacter pylori infection in developing countries: the burden for how long? Saudi J Gastroenterol. 2009;15(3):201-7. DOI: 10.4103/1319-3767.54743 PMID: 19636185
11. Bashir SK, Khan MB. Overview of Helicobacter pylori infection, prevalence, risk factors, and its prevention. Advanced Gut & Microbiome Research. 2023;2023(1):9747027. DOI: 10.1155/2023/9747027
12. Kayali S, Manfredi M, Gaiani F, Bianchi L, Bizzarri B, Leandro G, et al. Helicobacter pylori, transmission routes and recurrence of infection: state of the art. Acta Biomed. 2018;89(8-S):72-76. DOI: 10.23750/abm.v89i8-S.7947 PMID: 30561421
13. Al Mutawa OA, Izhari MA, Alharbi RA, Sindi AAA, Alqarni AM, Alotaibi FE, et al. *Helicobacter pylori* (*H. pylori*) Infection-Associated Anemia in the Asir Region, Saudi Arabia. Diagnostics (Basel). 2023;13(14):2404. DOI: 10.3390/diagnostics13142404 PMID: 37510148
14. Reyes VE. *Helicobacter pylori* and Its Role in Gastric Cancer. Microorganisms. 2023;11(5):1312. DOI: 10.3390/microorganisms11051312 PMID: 37317287
15. Balci YI, Aral YZ, Covut IE, Polat Y, Turk M, Acimis N. The frequency of Helicobacter Pylori infection in Beta Thalassemia major Patients with recurrent abdominal pain. Pakistan Journal of Medical Sciences. 2011;27(2). URL: https://www.researchgate.net/publication/228470010
16. Poosheshdoost P, Faraji N, Zeinali T, Baghersalimi A, Miremarati A, Darbandi B. Visual and auditory complications during deferasirox therapy in beta-thalassemia. Iranian Journal of Pediatric Hematology & Oncology. 2022. DOI: 10.18502/ijpho.v12i4.10913
17. Hosseini E, Poursina F, de Wiele TV, Safaei HG, Adibi P. Helicobacter pylori in Iran: A systematic review on the association of genotypes and gastroduodenal diseases. J Res Med Sci. 2012;17(3):280-92. PMID: 23267382
18. Mansour-Ghanaei F, Taefeh N, Joukar F, Besharati S, Naghipour M, Nassiri R. Recurrence of Helicobacter pylori infection 1 year after successful eradication: a prospective study in Northern Iran. Med Sci Monit. 2010;16(3):CR144-148. PMID: 20190685
19. Monno R, De Laurentiis V, Trerotoli P, Roselli AM, Ierardi E, Portincasa P. Helicobacter pylori infection: association with dietary habits and socioeconomic conditions. Clinics and research in hepatology and gastroenterology. 2019;43(5):603-7. DOI: 10.1016/j.clinre.2018.10.002
20. , He X, Duan Y, Luo Y, Li Y, Li J, et al. The impact of diet, exercise, and sleep on Helicobacter pylori infection with different occupations: a cross-sectional study. BMC Infect Dis. 2024;24(1):692. DOI: 10.1186/s12879-024-09505-8
21. Zeinalian M, Nobari RF, Moafi A, Salehi M, Hashemzadeh-Chaleshtori M. Two decades of pre-marital screening for beta-thalassemia in central Iran. J Community Genet. 2013;4(4):517-22. DOI: 10.1007/s12687-013-0142-4 PMID: 23467976
22. Khedmat H, Karbasi-Afshar R, Agah S, Taheri S. Helicobacter pylori Infection in the general population: A Middle Eastern perspective. Caspian J Intern Med. 2013;4(4):745-53. PMID: 24294467
23. Hossain MS, Raheem E, Sultana TA, Ferdous S, Nahar N, Islam S, et al. Thalassemias in South Asia: clinical lessons learnt from Bangladesh. Orphanet J Rare Dis. 2017;12:1–9. DOI: 10.1186/s13023-017-0643-z PMID: 28521805
24. Nanou A, Toumpeki C, Fanis P, Bianchi N, Cosenza LC, Zuccato C, et al. Sex-specific transcriptional profiles identified in β-thalassemia patients. Haematologica. 2021;106(4):1207-1211. DOI: 10.3324/haematol.2020.248013 PMID: 32817281
25. Pes GM, Tolu F, Dore MP. Anti-Thyroid Peroxidase Antibodies and Male Gender Are Associated with Diabetes Occurrence in Patients with Beta-Thalassemia Major. J Diabetes Res. 2016;2016:1401829. DOI: 10.1155/2016/1401829 PMID: 27123460
26. Kander MC, Cui Y, Liu Z. Gender difference in oxidative stress: a new look at the mechanisms for cardiovascular diseases. J Cell Mol Med. 2017;21(5):1024-1032. DOI: 10.1111/jcmm.13038 PMID: 27957792
27. Bhatnagar P, Keefer JR, Casella JF, Barron-Casella EA, Bean CJ, Hooper CW, et al. Association between baseline fetal hemoglobin levels and incidence of severe vaso-occlusive pain episodes in children with sickle cell anemia. Pediatr Blood Cancer. 2013;60(10):E125-7. DOI: 10.1002/pbc.24588 PMID: 23677903
28. Shah F, Huey K, Deshpande S, Turner M, Chitnis M, Schiller E, et al. Relationship between Serum Ferritin and Outcomes in β-Thalassemia: A Systematic Literature Review. J Clin Med. 2022;11(15). DOI: 10.3390/jcm11154448 PMID: 35956067
29. Taher AT, Saliba AN. Iron overload in thalassemia: different organs at different rates. Hematology Am Soc Hematol Educ Program. 2017;2017(1):265-271. DOI: 10.1182/asheducation-2017.1.265 PMID: 29222265
30. Poggiali E, Cassinerio E, Zanaboni L, Cappellini MD. An update on iron chelation therapy. Blood Transfus. 2012;10(4):411-22. DOI: 10.2450/2012.0008-12 PMID: 22790257
31. Galanello R, Campus S. Deferiprone chelation therapy for thalassemia major. Acta Haematol. 2009;122(2-3):155-64. DOI: 10.1159/000243800 PMID: 19907153
32. Mohamed R, Abdul Rahman AH, Masra F, Abdul Latiff Z. Barriers to adherence to iron chelation therapy among adolescent with transfusion dependent thalassemia. Frontiers in Pediatrics. 2022;10:951947. DOI: 10.3389/fped.2022.951947
33. Mobarra N, Shanaki M, Ehteram H, Nasiri H, Sahmani M, Saeidi M, et al. A Review on Iron Chelators in Treatment of Iron Overload Syndromes. Int J Hematol stem cell Res. 2016;10(4):239–47. PMID: 27928480
34. Waheed K, Rizvi SM, Mubarak B. Association of β-Thalassemia and its types with ABO and Rh blood groups in Lahore, Pakistan. BioScientific Review. 2023;5(2):10-7. DOI: 10.32350/BSR.52.02
35. Sinha PA, Mulkutkar SH, Bhavani JB. Study of distribution of ABO blood groups in ß-thalassemia patients. Int J Res Med Sci. 2017;5(8):3479–83. DOI: 10.18203/2320-6012.ijrms20173545
36. Khan MI, Shah J, Ullah M, Rasheed H, Khan S, Yousaf MS, et al. Prevalence of Iron Deficiency Among Patients With Helicobacter pylori Infection at a Tertiary Care Hospital. Cureus. 2024;16(8):e68168. DOI: 10.7759/cureus.68168 PMID: 39347179
37. Monzón H, Forné M, Esteve M, Rosinach M, Loras C, Espinós JC, et al. Helicobacter pylori infection as a cause of iron deficiency anaemia of unknown origin. World J Gastroenterol. 2013;19(26):4166–71. DOI: 10.3748/wjg.v19.i26.4166 PMID: 23864779
38. Motupalli SK, Oroszi TL. The nexus between Helicobacter pylori infection and anemia—a systematic review. Frontiers in Hematology. 2024;3:1423494. URL: 10.3389/frhem.2024.1423494