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The Spectrum of β-Thalassemia Mutations in the Population Migration in Lebanon: A 6-Year Retrospective Study

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ABSTRACT

β-Thalassemia (β-thal) is highly prevalent among the Mediterranean populations. In Lebanon, the carrier rate of the disease is estimated to be around 2.0–3.0%. In this retrospective study, we determined the spectrum of β-thal mutations in a total of 170 individuals from a sample of 140 Lebanese, Iraqi and Syrian refugee families in Lebanon, over a period from 2012 to 2018. Twenty-eight different β-globin gene mutations were identified. The most prevalent mutations were IVS-I-110 (G>A) (*HBB*: c.93-21G>A), IVS-II-1 (G>A) (*HBB*: c.315+1G>A), IVS-I-6 (T>C) (*HBB*: c.92+6T>C) and IVS-I-1 (G>A) (*HBB*: c.92+1G>A), accounting for the majority of mutations found in *HBB* mutations analysed in 250 alleles. Ten different β-globin gene mutations that were not previously described in Lebanon were identified in our study. These mutations include the IVS-II-848 (C>A) (*HBB*: c.316–3C>A), codons 9/10 (+T) (*HBB*: c.30_31insT), codon 15 (–T) (*HBB*: c.46delT), −86 (C>G) (*HBB*: c.-136C>G), Cap +22 (G>A) (*HBB*: c.-29G>A), −28 (A>C) (*HBB*: c.−78A>C), codon 7 (*GAG>TAG*) (*HBB*: c.22G>T), codon 26 (*GAG>TAG*) (*HBB*: c.79G>T), codons 41/42 (–TTCT) (*HBB*: c.126_129delCTTT), and codons 82/83 (–G) (*HBB*: c.250delG). Of these, six mutations [codons 9/10, codon 15 (–T), −86, codon 7, codon 26, codons 82/83) were identified in Lebanese samples only; one mutation (IVS-II-848) was identified in both Lebanese and Iraqis; and three mutations (Cap +22, −28, codons 41/42) were identified in Iraqi samples only. Further studies will help better delineate the spectrum of β-thal mutations among different ethnic groups, and provide crucial prevention strategies.

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Introduction

β-Thalassemia (β-thal) is caused by mutations or more rarely large deletions in the β-globin gene on chromosome 11 [1], resulting in an imbalance between α and β chains and consequent ineffective erythropoiesis and peripheral hemolysis [2,3]. The highest prevalence of β-thal in the Mediterranean countries is reported in Cyprus, initially as high as 17.2%, with a decrease to 12.1% in the last two decades following the implementation of prenatal diagnosis (PND) and premarital screening [4]. In Arab countries, β-thal has been described with variable prevalence, with heterogeneous genotypes and carrier rates ranging from 1.0 to 11.0% [5]. β-Thalassemia poses a major public health problem in Lebanon where the carrier rate of the disease (2.0–3.0%) is one of the highest with respect to the country's small population size [6].

To date, more than 350 different β-thal mutations have been reported worldwide [7], the vast majority being point mutations, while deletions of the β-globin gene are rare [8]. The most common and widespread mutation among Arabs is the IVS-I-110 (G>A) (*HBB*: c.93-21G>A), most frequently reported in Lebanon, Egypt, Syria, Jordan and parts of Saudi Arabia. Other mutations reported in the Arab countries include the IVS-I-1 (G>A) (*HBB*: c.92+1G>A) and IVS-I-6 (T>C) (*HBB*: c.92+6T>C) mutations, with the highest rates described in the Palestinian territories, Syria and Egypt [5]. Mutations reportedly originating in Arab countries include IVS-II-745 (C>G) (*HBB*: c.316–106C>G) with the highest frequency in Jordan [9], and codon 29 (C>T) (*HBB*: c.90C>T) with the highest frequency in Lebanon [10]. Twenty different β-globin gene mutations have been previously described in Lebanon. The most common reported mutations following IVS-I-110 were IVS-I-1 (G>A), IVS-I-6 and codon 29 [10].

Since the onset of the Syrian crisis in 2011, Lebanon has witnessed a massive influx of the Syrian population seeking refuge from the war [11]. Recent data show that around 1.5 million Syrians reside in Lebanon [12]. Added to these, nearly 18,000 Iraqis among others, live in Lebanon [12]. Therefore, the following retrospective observational study aims to update the spectrum of β-thal mutations in Lebanon, and to assess whether the genetic demography was impacted by the migrational flux dynamics that followed the political turmoil in the Middle East.

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Methods

Study design and subjects

The American University of Beirut Medical Center (AUBMC), Beirut, Lebanon is a leading tertiary referral center in the Middle East. Conflict-related massive migration resulted in a growing number of Syrian and to a lesser extent Iraqi individuals seeking care at our institution. This is a retrospective observational study that was carried out at the Medical Genetics Unit at AUBMC. The study was approved by the Institutional Review Board (IRB) at the American University of Beirut (AUB), Beirut, Lebanon.

Archived genetic results of patients who were referred for molecular analysis of the *HBB* gene as an evaluation of anemia between the years 2012 and 2018 at the Medical Genetics Unit, AUBMC, were reviewed. A total of 170 patients from a sample of 140 Lebanese, Iraqi and Syrian refugee families in Lebanon were included in this study. The vast majority of our patients were Lebanese (126 individuals) representing 74.0% of the whole population studied. The remaininder were divided into 26 (15.0%) and 18 (11.0%) Iraqi and Syrian individuals, respectively.

DNA extraction and HBB mutation analysis

Genomic DNA was extracted from 200 µL of whole blood collected in EDTA-containing vacutainers using QIAamp DNA mini Kit (Qiagen GmbH, Hilden, Germany). DNA amplification was performed and amplified DNA sequences were analyzed by direct nucleotide sequencing of all *HBB* coding exons and their immediately flanking intron regions using BigDye terminator cycle sequencing ready reaction kit v3.1 (Applied Biosystems, Waltham, MA, USA). Sequence analysis was performed on an ABI PRISM® 3500 DNA sequencer (Applied Biosystems). The *HBB* mutations (HbVar database: https://globin.bx.psu.edu/hbvar/menu.html) [13] were analyzed in a total of 250 alleles, and allelic frequencies were calculated in percentages and compared to previously reported data in Lebanon and in some neighboring Mediterranean and Arab countries.

Results

Our analyses revealed that 60 out of 126 (47.6%) Lebanese individuals were found to be affected with β-thal, of which 47 (78.3%) individuals (adults: 65.9%; children: 34.0%) were found to be homozygotes and 13 (21.7%) individuals (adults: 38.5%; children: 61.5%) were found to be compound heterozygotes, while 66 (52.4%) Lebanese individuals (adults: 92.4%; children: 7.6%) were found to be carriers (heterozygotes) of β-thal mutations. In the Iraqi samples, 10 out of 26 (38.5%) individuals were found to be affected with β-thal, of which eight (80.0%) (adults: 12.5%; children: 87.5%) were found to be homozygotes and two (20.0%) individuals (adults: 0.0%; children: 100.0%) were found to be compound heterozygotes, while 16 (61.5%) Iraqi individuals (adults: 75.0%; children: 25.0%) were found to be carriers of β-thal (heterozygous). In the Syrian samples, 10 out of 18 (55.6%) individuals were found to be affected with β-thal, of which five (50.0%) were homozygotes (adults: 0.0%; children: 100.0%) and five (50.0%) were compound heterozygotes (adults: 0.0%; children: 100%), while eight (44.4%) Syrian individuals (adults: 50.0%; children: 50.0%) were found to be carriers of heterozygous β-thal mutations (Table 1).

A total of 28 different β-globin gene mutations were identified in all patients, corresponding to a total of 250 alleles; 160 alleles correspond to 80 patients affected with β-thal (homozygotes and compound heterozygotes) and 90 alleles correspond to 90 patients who were heterozygous carriers of β-thal mutations. These mutations in decreasing order of frequency were IVS-I-110, IVS-II-1 (G>A) (*HBB*: c.315+1G>A), IVS-I-6, IVS-I-1 (G>A), codon 6 (or Hb S) (A>T) (*HBB*: c.20A>T), codon 29 or IVS-I (–3) (GG*C*>GG*T*) (Gly→Gly) (*HBB*: c.90C>T), codon 8 (–AA) (*HBB*: c.25_26delAA), IVS-I (–25 bp) (*HBB*: c.93-21_96del), codon 39 (CAG>*T*AG) (*HBB*: c.118C>T), codon 5 (–CT) (*HBB*: c.17_18delCT), codon 44 (–C) (*HBB*: c.135delC), codon 30 (G>C) (*HBB*: c.92G>C), IVS-I-5 (G>C) (*HBB*: c.92+5G>C), IVS-II-848 (C>A) (*HBB*: c.316-3C>A), codons 8/9 (+G) (*HBB*: c.27_28insG), codons 9/10 (+T) (*HBB*: c.30_31insT), codon 15 (–T) (*HBB*: c.46delT), codons 36/37 (–T) (*HBB*: c.112delT), −86 (C>G) (*HBB*: c.−136?C>G), Hb Lepore-Boston-Washington (or Hb LBW) ($\delta^{87};\beta^{116}$) (NG_000007.3: g.63632-71046del, −88 (C>T) (*HBB*: c.-138C>T), Cap +22 (G>A) (*HBB*: c._29G>A), −28 (A>C) (*HBB*: c.−78A>C), −30 (T>A) (*HBB*: c.-80T>A), codon 7 (GAG>*T*AG) (*HBB*: c.22G>T), codon 26 (GAG>*T*AG) (*HBB*: c.79G>T), codons 41/42 (–TTCT) (*HBB*: c.126-129delCTTT) and codons 82/83 (–G) (*HBB*: c.250delG). The different β-globin gene mutations detected among the Lebanese, Iraqi and Syrian individuals and their frequencies are shown in Table 2. The most prevalent β-globin gene mutations detected among the Lebanese individuals in our study were IVS-I-110 followed by IVS-I-6 accounting for 44.0% of the total 186 alleles analysed. Likewise, the

Table 1. Lebanese, Iraqi and Syrian β-thalassemic patients and carriers in Lebanon.

	Lebanese		Iraqi		Syrian	
Patients/carriers	Adults	Children	Adults	Children	Adults	Children
Homozygous β-thal patients, *n* (%)	31 (65.9)	16 (34.0)	1 (12.5)	7 (87.5)	0 (0.0)	5 (100.0)
Subtotal, *n* (%)	47 (78.3)		8 (80.0)		5 (100.0)	
Compound heterozygotes, *n* (%)	5 (38.5)	8 (61.5)	0 (0.0)	2 (100.0)	0 (0.0)	5 (100.0)
Subtotal, *n* (%)	13 (21.7)		2 (20.0)		5 (50.0)	
Total, *n* = 80 (%)	60 (47.6)		10 (38.5)		10 (55.6)	
Heterozygous β-thal carriers, *n* (%)	61 (92.4)	5 (7.6)	12 (75.0)	4 (25.0)	4 (50.0)	4 (50.0)
Total, *n* = 90 (%)	66 (52.4)		16 (61.5)		8 (44.4)	
Total individuals, *n* = 170 (%)	126 (74.1)		26 (15.3)		18 (10.6)	

Table 2. Types and frequencies (%) of β-thalassemia mutations detected in the Lebanese, Iraqi and Syrian populations in Lebanon.

Hb Name	HGVS Nomenclature	Lebanese	Iraqi	Syrian	Alleles, *n* (%)
IVS-I-110 (G>A)	*HBB*: c.93-21G>A	60 (32.0)	6 (17.0)	7 (25.0)	73 (29.20)
IVS-II-1 (G>A)	*HBB*: c.315+1G>A	20 (11.0)	11 (31.0	2 (7.0)	33 (13.20)
IVS-I-6 (T>C)	*HBB*: c.92+6T>C	22 (12.0)	1 (3.0)	1 (4.0)	24 (9.60)
IVS-I-1 (G>A)	*HBB*: C.92+1G>A	13 (7.0)	4 (11.0)	2 (7.0)	19 (7.60)
codon 6 (G*A*G>G*T*G) (Hb S)	*HBB*: c.20A>T	16 (9.0)	0 (0.0)	0 (0.0)	16 (6.40)
codon 29 (C>T) or IVS-I (–3) (GG*C*>GG*T*)	*HBB*: C.90C>T	13 (7.0)	1 (3.0)	0 (0.0)	14 (5.60)
codon 8 (–AA)	*HBB*: c.25_26delAA	4 (2.0)	3 (8.0)	1 (4.0)	8 (3.20)
IVS-I (–25 bp del) (3′ end)	*HBB*: c.93-21_96del	5 (3.0)	2 (6.0)	1 (4.0)	8 (3.20)
codon 39 (CAG>*T*AG)	*HBB*: c.118C>T	2 (1.0)	0 (0.0)	5 (18.0)	7 (2.80)
codon 5 (–CT)	*HBB*: c.17_18delCT	4 (2.0)	0 (0.0)	3 (11.0)	7 (2.80)
codon 44 (–C)	*HBB*: c.135delC	2 (1.0)	0 (3.0)	3 (11.0)	6 (2.40)
codon 30 (G>C)	*HBB*: c.92G>C)	6 (3.0)	0 (0.0)	0 (0.0)	6 (2.40)
IVS-I-5 (G>C)	*HBB*: c.92+5G>C	4 (2.0)	0 (0.0)	0 (0.0)	4 (1.60)
IVS-II-848 (C>A)	*HBB*: c.316-3C>A	1 (1.0)	3 (8.0)	0 (0.0)	4 (1.60)
codons 8/9 (+G)	*HBB*: c.27_28insG	0 (0.0)	1 (3.0)	4 (4.0)	2 (0.80)
codons 9/10 (+T)	*HBB*: c.30_31insT	2 (1.0)	0 (0.0)	0 (0.0)	2 (0.80)
codon 15 (–T)	*HBB*: c.46delT	2 (1.0)	0 (0.0)	0 (0.0)	2 (0.80)
codons 36/37 (–T)	*HBB*: c.112delT	2 (1.0)	0 (0.0)	0 (0.0)	2 (0.80)
–86 (C>G)	*HBB*: c.-136C>G	2 (1.0)	0 (0.0)	0 (0.0)	2 (0.80)
Hb LBW[a] ($\delta^{87};\beta^{116}$)	NG_000007.3: g.63632-71046del	0 (0.0)	0 (0.0)	2 (7.0)	2 (0.80)
–88 (C>T)	*HBB*: c.−138C>T	2 (1.0)	0 (0.0)	0 (0.0)	2 (0.80)
+22 (G>A)	*HBB*: c.−29G>A	0 (0.0)	1 (3.0)	0 (0.0)	1 (0.40)
–28 (A>C)	*HBB*: c.−78A>C	0 (0.0)	1 (3.0)	0 (0.0)	1 (0.40)
–30 (T>A)	*HBB*: c.−80T>A	1 (1.0)	0 (0.0)	0 (0.0)	1 (0.40)
codon 7 (G*A*G>*T*AG)	*HBB*: c.22G>T	1 (1.0)	0 (0.0)	0 (0.0)	1 (0.40)
codon 26 (G*A*G>*T*AG)	*HBB*: c.79G>T	1 (1.0)	0 (0.0)	0 (0.0)	1 (0.40)
codons 41/42 (–TTCT)	*HBB*: c.126_129delCTTT	0 (0.0)	1 (3.0)	0 (0.0)	1 (0.40)
codons 82/83 (–G)	*HBB*: c.250delG	1 (1.0)	0 (0.0)	0 (0.0)	1 (0.40)

[a]Hb LBW: Hb Lepore-Boston-Washington (a δ-β hybrid).

most frequent β-globin gene mutation detected among the Syrian individuals was IVS-I-110; however, the second most prevalent mutation in this population was codon 39 accounting for 43.0% of the total 28 alleles analysed. In the Iraqi sample, IVS-II-1 (G>A) was the most common followed by IVS-I-110 accounting for 48.0% of the total 36 alleles analysed (Table 2). The different β-globin gene mutations detected in our study were compared to previously reported mutations in Lebanon (Table 3) and in some neighboring Mediterranean and Arab countries (Table 4).

Ten different β-globin gene mutations that were not previously reported in Lebanon were identified in the present study. These mutations were IVS-II-848, codons 9/10, codon 15 (–T), −86, Cap +22, −28, codon 7, codon 26, codons 41/42 and codons 82/83. Six of these mutations including, codons 9/10, codon 15 (–T), −86, codon 7, codon 26 and codons 82/83 were detected among the Lebanese individuals only; one mutation, namely, IVS-II-848, was detected among both the Lebanese and Iraqi individuals, and three mutations including Cap +22, −28 and codons 41/42, were detected among the Iraqi individuals only (Table 2).

Discussion

Previous studies conducted on the Lebanese population have reported a total of 20 different β-thal mutations [10,14–16]. Our study contributed to updating the spectrum of β-thal mutations, whereby a total of 28 different β-globin gene mutations were detected, the most prevalent include the mutations IVS-I-110, IVS-II-1 (G>A), IVS-I-6 and IVS-I-1 (G>A), accounting for the majority of mutations found in the 250 alleles studied. These were also the most commonly reported mutations in the neighboring Mediterranean and Arab countries with an incidence of more than 50.0%.

The most common mutation in Lebanon and in the neighboring Mediterranean and Arab countries is IVS-I-110, with the highest frequency (72.72%) being reported in Cyprus. It is believed that it originated in Turkey and was introduced to other countries through the migration flow [17]. Additionally, it has been suggested that the codon 29 mutation originated in Lebanon [10]; however, it was also reported in Syria [18] and Greece [19]. In our study, one codon 29 mutation was detected among the Iraqis, yet it was absent among the Syrians (Table 2).

The codon 15 (–T), Cap +22 and codon 26 mutations identified in our study, were not previously reported in Lebanon (Table 3) and in any neighboring Mediterranean and Arab countries (Table 4). Other mutations were not identified in the present study; however, they were reported in previous studies, such as −87 previously reported in Lebanon, Jordan, Egypt, Greece and Cyprus; IVS-II-745 was previously reported in Lebanon, Jordan, Egypt, Turkey, Palestine, Greece and Cyprus, and the 290 bp deletion (*HBB*: c.−176_92+25del) was previously reported in Lebanon (Table 3) and Syria (Table 4). Other β-globin gene mutations that were absent in our study and in previous Lebanese studies, were reported in neighboring Mediterranean and Arab countries, such as codon 27 (G>T) (Hb Knossos) (*HBB*: c.82G>T) identified in Jordan, Egypt, Turkey, Palestine and Cyprus [9,20–23], IVS-I-130 (G>C) (*HBB*: c.93-1G>C) identified in Syria, Iraq, Turkey and Greece [18,19,21,24], and the two mutations, codon 37 (G>A) (*HBB*: c.114G>A) and codon 15 (G>A) (*HBB*: c.48G>A) identified in Syria, Jordan, Palestine and Greece [9,18,19,22].

Table 3. The frequency (%) of β-thalassemia mutations detected in Lebanon.

Mutations, Year [references]	2018 (this study)	2005 [10]	2000 [14]	1997 [15]	1987 [16]
IVS-I-110 (G > A)	29.20	34.20	33.00	40.00	62.00
IVS-II-1 (G > A)	13.20	8.60	9.90	8.20	4.00
IVS-I-6 (T > C)	9.60	14.40	15.00	5.50	8.00
IVS-I-1 (G > A)	7.60	15.00	14.90	17.30	–
codon 6 (A > T) (or Hb S)	6.40	1.00	–	–	–
codon 29 (C > T) or IVS-I (–3) (C > T)	5.60	9.60	6.90	3.60	8.00
codon 8 (–AA)	3.20	2.50	2.50	3.60	6.00
IVS-I (–25 bp) (3′ end)	3.20	0.40	1.00	0.90	–
codon 39 (C > T)	2.80	0.20	–	–	4.00
codon 5 (–CT)	2.80	5.00	4.00	4.50	–
codon 44 (–C)	2.40	1.50	1.00	1.80	–
codon 30 (G > C)	2.40	2.70	3.00	–	–
IVS-I-5 (G > C)	1.60	0.80	1.00	2.70	4.0
IVS-II-848 (C > A)	1.60	–	–	–	–
codons 8/9 (+G)	0.80	0.20	0.50	–	–
codons 9/10 (+T)	0.80	–	–	–	–
codon 15 (–T)	0.80	–	–	–	–
codons 36/37 (–T)	0.80	0.20	–	–	–
–86 (C > G)	0.80	–	–	–	–
Hb Lepore-Boston-Washington[a] ($\delta^{87};\beta^{116}$)	0.80	0.40	0.50	–	–
–88 (C > T)	0.80	0.60	1.50	0.90	–
+22 (G > A)	0.40	–	–	–	–
–28 (A > C)	0.40	–	–	–	–
–30 (T > A)	0.40	–	0.50	0.90	–
codon 7 (G > T)	0.40	–	–	–	–
codon 26 (G > T)	0.40	–	–	–	–
codons 41/42 (–TTCT)	0.40	–	–	–	–
codons 82/83 (–G	0.40	–	–	–	–
–87 (C > G)	–	0.80	1.50	0.90	–
IVS-II-745 (C > G)	–	1.10	1.00	3.60	4.00
290 bp deletion[a]	–	0.60	2.00	2.70	–
codon 30 (G > A)	–	–	–	1.80	–
Others	–	–	–	–	–
Total number of alleles	250	520	202	110	51

[a]290 bp deletion: *HBB*: c.−176_92+25del.

While consanguineous marriages have been decreasing in Lebanon [25], as a result of higher educational levels and improved economic status, it is still prevalent with an overall rate of 12.8% in Beirut, the capital city, to 42.0% in rural regions [26]. In Iraq and Syria, consanguinity rates of 47.0–60.0 and 30.3–39.8%, respectively, have been reported [27,28]. Most of the β-thal mutations detected in our study among the Lebanese and Iraqi individuals were homozygous: 78.3% homozygous *vs.* 21.7% compound heterozygous among Lebanese affected individuals, and 80.0% homozygous *vs.* 20.0% compound heterozygous among Iraqi affected individuals, reflecting a high prevalence of consanguineous marriages in these populations. However, an equal rate of affected homozygous (50.0%) carriers compared to affected compound heterozygous (50.0%) carriers was observed among the Syrian individuals (Table 1).

The Iraqi and Syrian populations, in our study, represent one-quarter (25.9%) of the referred individuals, which reflect the current demographic composition of the country due to the influx of migrants, mainly from Syria with around 1.5 million refugees [12] and 43,000 registered births per year [29], and around 18,000 Iraqi refugees [12]. These populations contributed to the addition of five mutations that have not been identified before in the Lebanese population. These mutations include: codons 8/9, Hb LBW, Cap +22, −28 and codons 41/42 (Table 2). The codons 8/9 mutation was detected among the Iraqi and Syrian populations in our study with frequencies of 3.0 and 4.0%, respectively (Table 2). It was also previously reported in Lebanon with comparable frequencies, 0.20% and 0.50% (Table 3), and in Iraq (6.80%) and Syria (0.30%) (Table 4). The Hb LBW δ-β hybrid mutation was detected in one (7.0%) Syrian individual (Table 2), and was encountered in previous Lebanese studies with comparable frequencies (0.40%) [10] and 0.50% [14] (Table 3). The Cap +22 mutation was reported for the first time in our study in one Iraqi (3.0%) individual (Table 2), and has not been previously reported in Lebanon (Table 3) and elsewhere in the neighboring Mediterranean and Arab countries (Table 4). Two mutations, −28 detected in one Iraqi (3.0%) individual, and codons 41/42, detected in another Iraqi (3.0%) individual (Table 2), were previously reported in Iraq (Table 4). The codons 41/42 mutation was also previously reported in Malaysia [30], Spain [31] and Korea [32].

Iraqi migration contributed to the addition of three β-thal mutations (Cap +22, −28 and codons 41/42), while Syrian migration had little impact on the thalassemia genotypes in our population, probably due to the higher sample size of the Iraqi population in our study sample compared to the Syrian population. The codons 8/9 and Hb LBW mutations were detected among the Syrian population in our study but not in the Lebanese; however, these were encountered in previous Lebanese studies [10,14,15]. While Iraqis seem to have a higher impact, contributing to the addition of three non Lebanese mutations (Cap +22, −28, codons 41/42), that were not previously detected in Lebanon, one of which (Cap +22) was also not detected in neighboring Arab and Mediterranean countries.

Table 4. The frequency (%) of β-thalassemia mutations detected in some Arab and Mediterranean countries.

Mutations, Year [references]	Syria 2018 [18]	Jordan 2001 [9]	Iraq 2013 [24]	Egypt 2015 [20]	Turkey 2016 [21]	Palestine 2013 [22]	Greece 2008 [17]	Cyprus 2016 [23]
IVS-I-110 (G>A)	22.20	25.00	30.10	22.34	52.74	33.90	42.12	72.72
IVS-II-1 (G>A)	7.60	15.00	18.40	–	8.22	–	3.29	0.34
IVS-I-6 (T>C)	7.10	8.33	3.90	27.66	14.38	13.10	8.09	12.42
IVS-I-1 (G>A)	17.80	10.00	7.80	7.45	3.42	21.20	12.83	5.15
codon 6 (A>T) (or Hb S)	–	–	–	–	–	0.70	–	1.69
codon 29 (C>T) or IVS-I (–3) (C>T)	0.40	–	–	–	–	–	0.05	–
codon 8 (–AA)	6.00	0.83	0.97	1.06	2.40	1.10	0.79	–
IVS-I (–25 bp) (3′ end)	0.70	–	2.90	–	–	–	0.02	–
codon 39 (C>T)	8.20	4.58	1.90	3.19	–	9.50	18.81	2.36
codon 5 (–CT)	5.60	3.75	3.90	4.25	2.05	0.40	0.82	0.08
codon 44 (–C)	1.40	–	4.90	–	2.40	–	0.21	0.17
codon 30 (G>C)	0.10	1.25	–	–	–	–	0.26	–
IVS-I-5 (G>C)	4.10	1.25	9.70	–	–	0.70	–	–
IVS-II-848 (C>A)	0.10	1.25	2.90	8.51	0.68		0.26	–
codons 8/9 (+G)	0.30	–	6.80	–	–	–	0.11	–
codons 9/10 (+T)	0.30	–	–	–	–	–	–	–
codon 15 (–T)	–	–	–	–	–	–	–	–
codons 36/37 (–T)	–	–	0.83	0.97	–	–	–	–
–86 (C>G)	0.20	–	–	–	–	–	–	0.08
Hb LBW[a] ($\delta^{87};\beta^{116}$)[a]	–	–	–	–	–	–	–	–
–88 (C>T)	1.00	–	–	–	–	–	–	–
+22 (G>A)	–	–	–	–	–	–	–	–
–28 (A>C)	–	–	0.97	–	0.68	–	0.02	–
–30 (T>A)	2.30	–	–	–	8.22	–	0.02	–
codon 7 (G>T)	–	–	–	–	–	–	0.02	–
codon 26 (G>T)	–	–	–	–	–	–	–	–
codons 41/42 (–TTCT)	–	–	0.97	–	–	–	–	–
codons 82/83 (–G)	0.10	–	–	–	–	–	–	–
–87 (C>G)	–	1.25	–	6.38	–	–	1.05	1.01
IVS-II-745 (C>G)	–	14.17	–	6.38	2.47	0.70	6.30	3.46
290 bp deletion[a]	0.40	–	–	–	–	–	–	–
codon 30 (G>A)	–	–	–	–	–	–	–	–
Others	14.60	10.41	1.94	1.06	2.05	8.20	4.85	0.51
Total number of alleles	1460	240	103	94	292	274	3796	1184

[a]Hb LBW: Hb Lepore-Boston-Washington (a δ-β hybrid); 290 bp deletion: *HBB*: c.−176_92+25del.

Conclusions

In the present study, we determined a wide heterogeneous spectrum of β-thal mutations in the Lebanese, Iraqi and Syrian populations in Lebanon. Therefore, our study provides an updated map of the different types of β-thal mutations in Lebanon following the massive migratory flux that the country has been faced with, which in turn helps update the pre marriage and prenatal control policies to better fight this life-threatening disease.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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