A review of the diverse genetic disorders in the Lebanese population: highlighting the urgency for community genetic services

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Abstract The review lists the genetic diseases reported in Lebanese individuals, surveys genetic programs and services, and highlights the absence of basic genetic health services at the individual and community level. The incidence of individual diseases is not determined, yet the variety of genetic diseases reported is tremendous, most of which follow autosomal recessive inheritance reflecting the social norms in the population, including high rates of consanguinity, which favor the increase in incidence of these diseases. Genetic services including all activities for the diagnosis, care, and prevention of genetic diseases at community level are extremely inadequate. Services are limited to some clinical and laboratory diagnostic services with no genetic counseling. These services are localized within the capital thus preventing their accessibility to high-risk communities. Screening programs, which are at the core of public health prevention services, are minimal and not nationally mandated. The absence of adequate genetic services is attributed to many factors undermining the importance of genetic diseases and their burden on society, the most important of which is genetic illiteracy at all levels of the population, including high-risk families, the general public, and most importantly health care providers and public health officials. Thus, a country like Lebanon, where genetic diseases are expected to be highly prevalent, is in utmost need for community genetics services. Strategies need to be developed to familiarize public health officials and medical professionals with medical genetics leading to a public health infrastructure

that delivers community genetics services for the prevention and care of genetic disorders at community level.

Keywords Genetic disorders · Lebanon · Community genetics · Genetic services · Public health

Introduction

Lebanon is a small country on the Mediterranean Sea, occupying no more than 10,500 km² (4,015 mi²). The Lebanese population residing in Lebanon is estimated at about 4 million people (WHO). However, this population consists of a wide range of ethnicities and religions because of the many occupations and major immigration events into the country since about 47,000 years ago until the beginning of the twentieth century (Zalloua et al. 2008b). The rich history of the country led to the existence of about 17 officially recognized ethno-religious communities, harboring a large array of pathogenic and polymorphic gene variations. In addition, throughout modern history, millions of Lebanese immigrants formed multiple Diaspora around the world. The Lebanese Diaspora led to the spread of genetic diseases to geographically distant locations, most of which are reported in the scientific literature of research-advanced countries.

The historic and social structure of the Lebanese population residing in Lebanon or elsewhere favors the high prevalence of a variety of rare and common genetic diseases. Perhaps, the most strongly associated reason would be the deeply rooted sociological norm of consanguinity, defined as a marriage among blood relatives, in addition to endogamous and arranged marriages within a community. Consanguinity rates in Lebanon, as estimated through a cross-sectional study, are still considered relatively high in comparison to developed countries, averaging around 35.5 % (Barbour and Salameh 2009). To assess the public health impact of genetic diseases

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reported in Lebanese individuals and to better understand the need for community genetics services including public health programs for screening and prevention, we performed a comprehensive literature search of the Catalogue of Transmission Genetics in Arabs (CTGA) database, Online Mendelian Inheritance in Man (OMIM) database, and PubMed articles, reviews, and book chapters written on genetic diseases in Lebanon and the region. Below, we present a list of any encountered heritable or inherited genetic disease reported in Lebanese residing in Lebanon or in the Lebanese Diaspora. The last time such a review was attempted was in 1980, at a time when Lebanon had planned to follow the trend in developing countries to deliver care, attention, and prevention for diseases causing chronic disablement such as genetic diseases (Der Kaloustian et al. 1980). The aim of the review is to provide physicians and researchers with a comprehensive list of reported genetic diseases in patients of Lebanese origin. In addition, the report aims at highlighting the need for community genetics services and public health genetics programs in Lebanon which are essential in decreasing the incidence and reducing the severity of congenital disorders and genetic diseases at the population level through the introduction of proper diagnosis, screening, and counseling. Community genetics is the art and science of utilizing health- and disease-related genetics knowledge to benefit individuals in human populations and communities. The goal of community genetics is the prevention and control of genetic diseases at population level through appropriate public health measures and programs and, at the same time, the delivery of genetics services (diagnosis and counseling) in the community for individuals and families. Thus, the term “community genetics services” is used interchangeably with community genetics (Ten Kate et al. 2010)

Spectrum of genetic diseases in the Lebanese

Currently, the CTGA represents a continuously updated catalogue of gene variants and heritable genetic diseases in Arab individuals. Starting at only 374 observations in 2004, the database now contains over 900 entries, showing major improvements in reporting discovered diseases. However, it was brought to our attention, by officials running the CTGA, that the data from Lebanon is not yet fully surveyed or compiled. CTGA lists 157 diseases reported in Lebanese; an OMIM search adds another 58 diseases, bringing the total to 215 diseases diagnosed in Lebanese individuals. Our PubMed search for articles, reviews, and book chapters yielded an additional 163 diseases not reported in any of the two major human genetic disease databases, all of which were identified in at least one Lebanese patient from Lebanon or the Lebanese Diaspora. Table 1 lists all 378 diseases, along with their OMIM numbers and the most recent publications linking

these diseases to Lebanese patients. The list of chromosomal abnormalities encountered is large due to the unpredictability of the mechanism by which these abnormalities arise. Table 1 lists the three chromosomal abnormalities reported in Lebanon and described in OMIM. Other common chromosomal abnormalities reported in Lebanon include trisomy 13 and trisomy 18, in addition to a number of sex chromosome abnormalities such as Turner syndrome and Klinefelter syndrome, among others (Mahfouz et al. 2001).

Classification according to mode of inheritance and affected systems

It is not surprising to conclude from the data that around 67 % of the reported genetic diseases follow autosomal recessive inheritance, a pattern similar to what is observed in the rest of the Arab world (Al-Gazali et al. 2006). This observation is most likely explained by the Arab region having among the highest rates of consanguinity in the world (Tadmouri et al. 2009). Several studies highlight the contribution of consanguinity in Lebanon to the high rate of autosomal recessive diseases, such as β -thalassemia (Inati et al. 2006), Familial Mediterranean fever (Mansour et al. 2001), phenylalanine hydroxylase deficiency (Karam et al. 2013a), and a broad category of aminoacidopathies and organic acidemias (Karam et al. 2013b). Out of all the reported cases of the abovementioned autosomal recessive diseases, 63, 33, 43, and 60 % of cases, respectively, were found to be due to consanguinity. Autosomal dominant disorders are less common representing 17 % of all reported genetic diseases, followed by X-linked diseases being the least common at around 6 % (Fig. 1).

According to WHO-International Classification of Disease (WHO-ICD10), congenital malformations and chromosomal abnormalities are the most common around 32 % of all reported diseases. Endocrine, nutritional, and metabolic disorders represent about 29 %, which compared to other Arab countries shows an increase most likely due to two major centers in Lebanon focused on identifying biochemical disorder causing an over reporting of this category.

Incidence of genetic diseases in the Lebanese

Genetic diseases in Lebanon, like other Arab countries, are frequent with an incidence among the highest in the world (Tadmouri et al. 2009). Several factors contribute to this high incidence (Hamamy and Alwan 1994; Lindner et al. 2007). These include the limited availability of genetic services and public health programs aimed at the prevention and care of genetic diseases; the high rates of consanguinity, which specifically increase the incidence of recessive diseases, and the

Table 1 List of genetic disorders in Lebanese population

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
610006	2-Methylbutyrylglycinuria	Autosomal recessive	(Sass et al. 2008)
250950	3-Methylglutaconic aciduria, type I	Autosomal recessive	Wiley et al. (1999); Wortmann et al. 2010)
100100	Abdominal muscles, absence of, with urinary tract abnormality and cryptorchidism	Autosomal dominant and Autosomal recessive	CTGA
200100	Abetalipoproteinemia	Autosomal recessive	(Khachadurian et al. 1971)
100800 ^a	Achondroplasia	Autosomal dominant	CTGA
201100	Acrodermatitis enteropathica	Autosomal	(Der Kaloustian et al. 1980)
602875	Acromesomelic dysplasia, Maroteaux type	Autosomal recessive	CTGA
201470	Acy-CoA dehydrogenase, short-chain, deficiency of	Autosomal recessive	(Mikati et al. 2007)
175100	Adenomatous polyposis coli	Autosomal dominant	(Biagini et al. 1992)
201910	Adrenal hyperplasia, congenital, due to 21-hydroxylase deficiency	Autosomal recessive	(Delague et al. 2000b)
300100	Adrenoleukodystrophy	X-linked	CTGA
118450	Alagille syndrome	Autosomal dominant	CTGA
203500	Alkaptonuria	Autosomal recessive	(Zouheir Habbal et al. 2013)
203750	Alpha-methylacetoacetic aciduria	Autosomal recessive	(Zhang et al. 2004)
609889	Alpha/beta T-cell lymphopenia with gamma/delta T-cell expansion, severe cytomegalovirus infection, and autoimmunity	Autosomal recessive	(de Villartay et al. 2005)
301050	Alport syndrome	X-linked	(Ernisch et al. 2000)
105250	Amyloidosis, primary localized cutaneous, I	Autosomal dominant	CTGA
300068	Androgen insensitivity syndrome	X-linked recessive	CTGA
207500	Anus, imperforate	Autosomal recessive	(Soussou et al. 1974)
101200	Apert syndrome	Autosomal dominant	CTGA
177400	Apnea, postanesthetic	Autosomal recessive	(Der Kaloustian et al. 1980)
207800	Arginemia	Autosomal recessive	(Karam et al. 2013b)
207900	Argininosuccinic aciduria	Autosomal recessive	(Khneisser 2012)
610001 ^c	Arthrogryposis multiplex with deafness, inguinal hernias, and early death	Autosomal recessive	(Tiemann et al. 2005)
208085	Arthrogryposis, renal dysfunction, and cholestasis I	Autosomal recessive	(Mikati et al. 2007)
208230	Arthropathy, progressive pseudorheumatoid, of childhood	Autosomal recessive	CTGA
208500	Asphyxiating thoracic dystrophy 1	Autosomal recessive	CTGA
208900	Ataxia-telangiectasia	Autosomal recessive	(Fares et al. 2004)
108800 ^a	Atrial septal defect 1	Autosomal dominant	CTGA
611363	Atrial septal defect 4; ASD4	Unknown	(Posch et al. 2010)
603642 ^d	Atrial septal defect, secundum, with various cardiac and noncardiac defects	Autosomal dominant	CTGA
240300		Autosomal recessive	(Traboulsi et al. 1985a)

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
180500	Autoimmune polyendocrinopathy syndrome, type I, with or without reversible metaphyseal dysplasia	Autosomal dominant	(Der Kaloustian et al. 1980)
209900	Axenfeld-Rieger syndrome, type 1	Autosomal recessive	CTGA
602522	Bardet-Biedl syndrome	Autosomal recessive	CTGA
109650	Barter syndrome, infantile, with sensorineural deafness	Autosomal recessive	(Tohme et al. 2009)
231200	Bechet's syndrome	Autosomal recessive	(Mahfouz et al. 2012)
613985	Bernard-Soulier syndrome	Autosomal recessive	(Makhoul et al. 2005)
210370	Beta-thalassemia	Autosomal recessive	(Haddad et al. 2012)
210550	Bietti crystalline corneoretinal dystrophy	Autosomal recessive	(Mikati et al. 1984)
253260	Biliary malformation with renal tubular insufficiency	Autosomal recessive	(Khneisser I)
184095	Biotinidase deficiency	Autosomal dominant	CTGA
609166 ^d	Brachyolmia type 2	Autosomal dominant	CTGA
113620	Branchiogenic deafness syndrome	Autosomal dominant	CTGA
114480	Branchiooculofacial syndrome	Autosomal dominant	(Jalkh et al. 2012)
604370	Breast cancer	Autosomal dominant	(Nasser 2009)
612555	Breast-ovarian cancer, familial, 1	Autosomal dominant	(Nasser 2009)
614707	Breast-ovarian cancer, familial, 2	Autosomal	(Johnson et al. 2012)
211530	Brown-Vialetto-Van Laere syndrome 2	Autosomal recessive	CTGA
613779	Bulbar palsy, progressive, with sensorineural deafness	Autosomal recessive	(Pussell et al. 1980)
211900	C3 deficiency	Autosomal recessive	CTGA
271900	Calcinosis, tumoral, with hyperphosphatemia	Autosomal recessive	(Karam et al. 2013b)
237300	Canavan disease	Autosomal recessive	(Klaus et al. 2009)
212112	Carbamoylphosphate synthetase I deficiency	Autosomal recessive	CTGA
192600	Cardiomyopathy, congestive, with hypergonadotropic hypogonadism	Autosomal dominant	CTGA
212140	Cardiomyopathy, familial hypertrophic	Autosomal recessive	(Khneisser I)
NA	Carnitine deficiency, systemic primary	Autosomal recessive	(Khneisser I)
212138	Carnitine translocase deficiency	Autosomal recessive	(Khneisser et al. 2008)
201000	Carnitine-acylcarnitine translocase deficiency	Autosomal recessive	CTGA
610623	Carpenter syndrome	Autosomal dominant	(Bidinost et al. 2006)
212500	Cataract 11, multiple types	Autosomal dominant	(Baghdassarian and Tabbara 1975)
603116	Cataract, congenital or juvenile	Autosomal recessive	(Chouery et al. 2013)
212750	CDAGS syndrome	Autosomal recessive	(Barada et al. 2012)
224050	Celiac disease, susceptibility to	Autosomal dominant	(Delague et al. 2001)
204500	Cerebellar hypoplasia and mental retardation with or without quadrupedal locomotion 1	Autosomal recessive	CTGA
	Ceroid lipofuscinosis, neuronal, 2	Autosomal recessive	

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
204200	Ceroid lipofuscinosis, neuronal, 3	Autosomal recessive	(Sarpong et al. 2009)
214400	Charcot-Marie-Tooth disease, type 4A	Autosomal recessive	CTGA
614895	Charcot-Marie-Tooth disease, type 4 F	Autosomal recessive	(Delague et al. 2000a)
609311	Charcot-Marie-Tooth disease, type 4H	Autosomal recessive	CTGA
608911	Choanal atresia, posterior	Autosomal recessive	CTGA
613320 ^c	Chondrodysplasia, Megarbane-Dagher-Melki type	Autosomal recessive	(Megarbane et al. 2008b)
604213	Chudley-McCullough syndrome	Autosomal recessive	(Alrashdi et al. 2011)
215518 ^d	Ciliary discoordination due to random ciliary orientation	Autosomal recessive	CTGA
215700	Citrullinemia	Autosomal recessive	(Khneisser et al. 2008)
216400	Cockayne syndrome, type A	Autosomal recessive	(Khayat et al. 2010)
216550	Cohen syndrome	Autosomal recessive	CTGA
614337	Colorectal cancer, hereditary nonpolyposis, type 4	Autosomal dominant	(Tan et al. 2008)
609060	Combined oxidative phosphorylation deficiency 1	Autosomal recessive	(Coenen et al. 2004)
602579	Congenital disorder of glycosylation, type Ib	Autosomal recessive	(Jaeken et al. 1998; Niehues et al. 1998)
306955	Congenital heart defects, nonsyndromic, 1, X-linked	X-linked	(Megarbane et al. 2000)
217095	Conotruncal heart malformations	Autosomal recessive	CTGA
217400	Corneal endothelial dystrophy and perceptive deafness	Autosomal recessive	(Abramowicz et al. 2002)
219200	Cutis laxa, autosomal recessive, type IIA	Autosomal recessive	(Megarbane et al. 2009)
605685 ^d	Cutis verticis gyrata, retinitis pigmentosa, and sensorineural deafness	Autosomal recessive	CTGA
219700	Cystic fibrosis	Autosomal recessive	CTGA
220210	Dandy-Walker-like malformation with atrioventricular septal defect	Autosomal recessive	CTGA
278800	De Sanctis-Cacchione syndrome	Autosomal	(Der Kaloustian et al. 1980)
601386	Deafness, autosomal recessive 12	Autosomal recessive	(Chaib et al. 1996b)
603098	Deafness, autosomal recessive 13	Autosomal recessive	CTGA
603678 ^d	Deafness, autosomal recessive 14	Autosomal recessive	CTGA
220290	Deafness, autosomal recessive 1A	Autosomal recessive	CTGA
603629	Deafness, autosomal recessive 21	Autosomal recessive	CTGA
600971	Deafness, autosomal recessive 6	Autosomal recessive	(Chaib et al. 1996b)
601071 ^b	Deafness, autosomal recessive 9	Autosomal recessive	CTGA
221300	Deafness, conductive, with malformed external ear	Autosomal recessive	(Megarbane et al. 2005)
125630 ^d	Dermatostrophic urticaria	Autosomal dominant	CTGA
125700	Diabetes insipidus, neurohypophyseal	Autosomal dominant	(Najjar and Mahmud 1968)
222100	Diabetes mellitus, insulin-dependent	Autosomal recessive	CTGA
125853 ^a	Diabetes mellitus, noninsulin-dependent	Autosomal dominant	CTGA
222600	Diastrophic dysplasia	Autosomal recessive	(Megarbane et al. 1999)

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
188400	DiGeorge syndrome	Autosomal dominant	CTGA
222748	Dihydropyrimidinase	Autosomal recessive	CTGA
603133 ^d	Dislocated elbows, bowed tibias, scoliosis, deafness, cataract, microcephaly, and mental retardation	Unknown	CTGA
126300	Distichiasis	Autosomal dominant	(Shammas et al. 1979)
246200	Donohue syndrome	Autosomal recessive	CTGA
190685 ^a	Down syndrome	Isolated cases	CTGA
223400	Duodenal atresia	Autosomal recessive	CTGA
223800	Dyggve-Melchior-Clausen disease	Autosomal recessive	CTGA
224400	Dyssegmental dysplasia, rolland-desbuquois type	Autosomal recessive	CTGA
224410	Dyssegmental dysplasia, Silverman-Handmaker type	Autosomal recessive	CTGA
612406 ^c	Dystonia-17, primary torsion	Autosomal recessive	CTGA
NA	Early-onset dementia without bone cysts	Autosomal recessive	(Chouery et al. 2008)
305100	Ectodermal dysplasia 1, hypohidrotic, X-linked	Autosomal recessive	(Chouery et al. 2008)
224900	Ectodermal dysplasia 10B, hypohidrotic/hair/tooth type, autosomal recessive	X-linked recessive	(Tomb et al. 2009)
129500	Ectodermal dysplasia 2, Clouston type	Autosomal recessive	(Megarbane et al. 2008d)
224800	Ectodermal dysplasia and sensorineural deafness	Autosomal dominant	(Fujimoto et al. 2013)
602401	Ectodermal dysplasia, hidrotic, autosomal recessive	Autosomal recessive	(Mikaelian et al. 1970)
129600	Ectopia lentis, familial	Autosomal recessive	CTGA
601552 ^d	Ectopia lentis, spontaneous filtering blebs, and craniofacial dysmorphism	Autosomal dominant	(Baghdassarian and Tabbara 1975)
130050	Ehlers-Danlos syndrome, type IV	Autosomal recessive	CTGA
600791	Enlarged vestibular aqueduct	Autosomal dominant	(Der Kaloustian et al. 1980)
226150	Enterocolitis	Autosomal recessive	CTGA
226700	Epidermolysis bullosa, junctional, Herlitz type	Autosomal recessive	(Megarbane and Sayad 2007)
600513	Epilepsy, nocturnal frontal lobe, 1	Autosomal recessive	CTGA
266100	Epilepsy, pyridoxine-dependent	Autosomal dominant	(Hwang et al. 2011)
NA	Familial Laugier-Hunziker syndrome	Autosomal recessive	CTGA
249100 ^b	Familial Mediterranean fever, AR	Unknown	(Makhoul et al. 2003)
227650	Fanconi anemia, complementation group A	Autosomal recessive	CTGA
228400 ^d	Fever, familial lifelong persistent	Autosomal recessive	(Rizk et al. 2013)
228520	Fibrochondrogenesis 1	Autosomal recessive	CTGA
300624	Fragile X mental retardation syndrome	Autosomal recessive	CTGA
249420	Frank-ter Haar syndrome	X-linked dominant	CTGA
229700	Fructose-1,6-bisphosphatase deficiency	Autosomal recessive	(Iqbal et al. 2010; Megarbane et al. 1997)
229800	Fructosuria	Autosomal recessive	(Alexander et al. 1985)
		Autosomal recessive	(Der Kaloustian et al. 1980)

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
230400	Galactosemia	Autosomal recessive	(Khneisser et al. 2008)
608013	Gaucher disease, perinatal lethal	Autosomal recessive	(Lui et al. 1988) (Stone et al. 2000)
230800	Gaucher disease, type I	Autosomal recessive	(El-Zahabi et al. 2007)
143500	Gilbert syndrome	Autosomal recessive	(Der Kaloustian et al. 1980)
231300	Glaucoma 3A, primary open angle, congenital, juvenile, or adult onset	Autosomal recessive	(Noureddin et al. 2006)
305900 ^a	Glucose-6-phosphate dehydrogenase	X-linked	CTGA
231680	Glutaric acidemia II	Autosomal recessive	(Karam et al. 2013b)
231670	Glutaric aciduria, type I	Autosomal recessive	(Alexander 1986)
605899	Glycine encephalopathy, GCE	Autosomal recessive	(Karam et al. 2013b)
232200	Glycogen storage disease Ia	Autosomal recessive	(Trioche et al. 1999)
232500	Glycogen storage disease IV	Autosomal	(Wakid et al. 1987)
275000	Graves' disease	Autosomal recessive	(Nakkash-Chmaisse et al. 2004)
234100	Hallermand-Streiff syndrome	Autosomal recessive or Autosomal dominant	(Baghdassarian and Tabbara 1975)
141900 ^a	Hemoglobin-beta locus	Autosomal dominant and Autosomal recessive	CTGA
267700	Hemophagocytic lymphohistiocytosis, familial, 1	Autosomal recessive	(Alsaied et al. 2011)
306700	Hemophilia A	X-linked	(Djambas Khayat et al. 2008)
235550	Hepatic venoocclusive disease with immunodeficiency	Autosomal recessive	CTGA
114550	Hepatocellular carcinoma	Somatic mutation	CTGA
235800	Histidinemia	Autosomal recessive	(Karam et al. 2013b)
602782	Histiocytosis-lymphadenopathy plus syndrome	Autosomal recessive	(Hussain et al. 2009)
142900	Holt-Oram syndrome	Autosomal dominant	CTGA
236200 ^b	Homocystinuria due to cystathionine beta-synthase deficiency	Autosomal recessive	CTGA
228600	Hyaline fibromatosis syndrome	Autosomal recessive	(Fayad et al. 1987)
231090	Hydatidiform mole	Autosomal recessive	CTGA
236600 ^a	Hydrocephalus	X-linked	CTGA
147060	Hyper-IgE recurrent infection syndrome	Autosomal dominant	(Jiao et al. 2008)
143890 ^a	Hypercholesterolemia, familial	Autosomal dominant	CTGA
603813	Hypercholesterolemia, familial, autosomal recessive	Autosomal recessive	(Lind et al. 2004; Naoumova et al. 2004)
238600	Hyperlipoproteinemia, type I	Autosomal recessive	CTGA
238700	Hyperlysinemia	Autosomal recessive	(Karam et al. 2013b)
250850	Hypermethioninemia, persistent, autosomal dominant, due to methionine adenosyltransferase I/III deficiency	Autosomal recessive	(Khneisser I)
238970	Hyperornithinemia-hyperammonemia-homocitrullinemia syndrome	Autosomal recessive	(Khneisser et al. 2008)
259900	Hyperoxaluria, primary, type 1	Autosomal recessive	(Traboulsi et al. 1985b)

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
145000	Hyperparathyroidism, familial primary	Autosomal dominant	(Der Kaloustian et al. 1980)
261640	Hyperphenylalaninemia, BH4-deficient, A	Autosomal recessive	(Karam et al. 2013b)
223910	Hyperphenylalaninemia, BH4-deficient, B	Autosomal recessive	(Karam et al. 2013b)
261630	Hyperphenylalaninemia, BH4-deficient, C	Autosomal recessive	(Karam et al. 2013b)
239500	Hyperprolinemia type I	Autosomal recessive	(Karam et al. 2013b)
145900	Hypertrophic neuropathy of Dejerine-Sottas	Autosomal recessive	CTGA
240200	Hypoadrenocorticism, familial	Autosomal recessive	(Najjar and Jarrar 1964)
145980	Hypocalcemic hypercalcemia, type I	Autosomal dominant	(Fuleihan Gel 2002)
NA	Hypogonadism, primary, and alopecia	Autosomal recessive	(Siti and Salem 1979)
241090	Hypogonadism, primary, and partial alopecia	Autosomal recessive	CTGA
NA	Hypokalemic salt-losing tubulopathy with chronic renal failure and sensorineural deafness.	Unknown	(Jeck et al. 2001)
241520	Hypophosphatemic rickets, AR	Autosomal recessive	(Feng et al. 2006)
307800	Hypophosphatemic rickets, X-linked dominant	X-linked dominant	CTGA
241550	Hypoplastic left heart syndrome	Autosomal recessive	CTGA
218700	Hypothyroidism, congenital, due to thyroid dysgenesis or hypoplasia	Autosomal recessive or Autosomal dominant	(Najjar 1974)
275200	Hypothyroidism, congenital, nongitrous, 1	Autosomal recessive	(Khneisser et al. 2008)
308205	Ichthyosis follicularis, atrichia, and photophobia syndrome	X-linked recessive	CTGA
604777	Ichthyosis, congenital, autosomal recessive 5	Autosomal recessive	(Lefevre et al. 2006)
615468 ^e	Immunodeficiency 2	Autosomal recessive	(Jabara et al. 2013)
614069	Immunodeficiency-centromeric instability-facial anomalies syndrome-2	Autosomal recessive	(Chouery et al. 2012)
615207 ^c	Immunodeficiency, primary, autosomal recessive, IL21R-related	Autosomal recessive	(Kotlarz et al. 2013)
613148	Inflammatory bowel disease 28, early onset, autosomal recessive	Autosomal recessive	(Glocker et al. 2009)
614328 ^c	Inflammatory skin and bowel disease, neonatal	Autosomal recessive	(Blaydon et al. 2011)
243110 ^d	Interleukin 1, defective T-cell response to	Autosomal recessive vs. X-linked	CTGA
243150	Intestinal atresia, multiple	Autosomal recessive	CTGA
243500	Isovaleric acidemia	Autosomal recessive	(Khneisser I)
217080	Jalili syndrome	Autosomal recessive	CTGA
243600	Jejunal atresia	Autosomal recessive	CTGA
220400	Jervell and Lange-Nielsen syndrome 1	Autosomal recessive	CTGA
612347	Jervell and Lange-Nielsen syndrome 2	Autosomal recessive	CTGA
308700	Kallmann syndrome 1	X-linked	(Schulze-Bahr et al. 1997)
148000	Kaposi sarcoma	Autosomal	CTGA
156550	Kniest dysplasia	Autosomal recessive	(Hale and Kelly 1998)
245200	Krabbe disease	Autosomal recessive	(Frayha et al. 1979)
			(Zlotogora et al. 1985)

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
236792	L-2-Hydroxyglutaric aciduria	Autosomal recessive	(Rzem et al. 2004)
223100	Lactase persistence/nonpersistence	Autosomal recessive	(Nasrallah 1979)
245570	Landau-Kleffner syndrome	Autosomal recessive	CTGA
204000	Leber congenital amaurosis 1	Autosomal recessive	(Yzer et al. 2006)
535000	Leber optic atrophy	X-linked recessive	(Der Kaloustian et al. 1980)
308905	Leber optic atrophy, susceptibility to	X-linked	(Baghdassarian and Tabbara 1975)
150600	Legg-Calve-Perthes disease	Autosomal dominant	CTGA
150800	Leiomyoma, hereditary multiple, of skin	Autosomal dominant	CTGA
150900 ^d	Lentigenes	Autosomal dominant	CTGA
269700	Lipodystrophy, congenital generalized, type 2	Autosomal recessive	CTGA
247100	Lipoid proteinosis of Urbach and Wiethe	Autosomal recessive	CTGA
609192	Loeys-Dietz syndrome, type 1A	Autosomal dominant	CTGA
309000	Lowe oculocerebrorenal syndrome	X-linked recessive	CTGA
309520	Lujan-Fryns syndrome	X-linked recessive	CTGA
153400	Lymphedema-distichiasis syndrome	Autosomal dominant	(Der Kaloustian et al. 1980)
615122	Lymphoproliferative syndrome 2	Autosomal recessive	(Salzer et al. 2013)
120435	Lynch syndrome I	Autosomal dominant	CTGA
602501	Macrocephaly-Capillary malformation	Autosomal dominant	CTGA
154570 ^d	Mannose 6-phosphate receptor recognition defect, lebanese type	Autosomal dominant	CTGA
248600	Maple syrup urine disease	Autosomal recessive	(Mamo and Tabbara 1971)
248700	Marden-Walker syndrome	Autosomal recessive	(Jaatoul et al. 1982)
248770	Marfanoid mental retardation syndrome, autosomal	Autosomal recessive	CTGA
236700	McKusick-Kaufman syndrome	Autosomal recessive	CTGA
249000	Meckel syndrome 1	Autosomal recessive	(DerKaloustian 2010)
607361	Meckel syndrome, type 3	Autosomal recessive	CTGA
604004	Megalencephalic leukoencephalopathy with subcortical cysts	Autosomal recessive	(Koussa et al. 2005)
261100	Megaloblastic anemia 1	Autosomal recessive	(Rossler et al. 2003)
606527	Megabane syndrome	Autosomal recessive	CTGA
612785 ^c	Megabane-Jalkh syndrome	Autosomal recessive	(Megarbane et al. 2008c)
305800	Membranoproliferative glomerulonephritis, X-linked	Autosomal recessive	CTGA
611091	Mental retardation, autosomal recessive 5	X-linked	CTGA
606220 ^d	Mental retardation, short stature, facial anomalies, and joint dislocations	Autosomal recessive	CTGA
250100	Metachromatic leukodystrophy	Unknown	CTGA
609989	Metaphyseal chondrodysplasia with cone-shaped epiphyses, normal hair, and normal hands	Autosomal recessive	(Harvey et al. 1993; Zlotogora 2010)
250400	Metaphyseal chondrodysplasia, Spahr type	X-linked	(Kozlowski et al. 1995)
N/A	Methylmalonic acidemia	Autosomal recessive	(Megarbane et al. 2008a)
		Autosomal recessive	(Karam et al. 2013b)

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
277400	Methylmalonic aciduria and homocystinuria, cblC type	Autosomal recessive	(Karam et al. 2013b)
210720	Microcephalic osteodysplastic primordial dwarfism, type II	Autosomal recessive	CTGA
251200	Microcephaly 1, primary, autosomal recessive	Autosomal recessive	(Mikati et al. 1985)
206920	Microphthalmia with limb anomalies	Autosomal recessive	CTGA
251600	Microphthalmia, isolated 1	Autosomal recessive	(Der Kaloustian et al. 1980)
156900	Microphthalmia, isolated, with corectopia; MCOPCR	Unknown	(Baghdassarian and Tabbara 1975)
615453 ^c	Mitochondrial complex III deficiency, nuclear type 6	Autosomal recessive	(Gaignard et al. 2013)
615084 ^c	Mitochondrial DNA depletion syndrome 11	Autosomal recessive	(Kornblum et al. 2013)
NA	Mitochondrial respiratory chain disorders	Autosomal or Mitochondrial	(Skladal et al. 2003)
252350	Moyamoya disease 1	Autosomal recessive	CTGA
607014	Mucopolysaccharidosis 1h	Autosomal recessive	(Salam and Idriss 1964)
252920	Mucopolysaccharidosis type IIIB (Sanfilippo B)	Autosomal recessive	(Mossman et al. 1983)
608840	Muscular dystrophy-dystroglycanopathy (congenital with mental retardation), type B, 6	Autosomal recessive	(Clarke et al. 2011)
608446 ^a	Myocardial infarction, susceptibility to, 1	Unknown	CTGA
604363	Myoclonic epilepsy, congenital deafness, macular dystrophy, and psychiatric	Autosomal recessive	CTGA
613561 ^c	Myopathy, lactic acidosis, and sideroblastic anemia 2	Autosomal recessive	(Riley et al. 2010)
161950	Nephropathy, IgA type	Autosomal	(Karnib et al. 2007)
256690	Neurofaciodigitorenal syndrome	Autosomal recessive	(Megarbane 2001)
201300	Neuropathy, hereditary sensory and autonomic, type II	Autosomal dominant	(Riviere et al. 2004)
257270	Night blindness, congenital stationary (complete), 1B, autosomal recessive	Autosomal recessive	(Audio et al. 2012)
614565	Night blindness, congenital stationary (complete), 1E, autosomal recessive	Autosomal recessive	(Audio et al. 2012)
163950 ^b	Noonan syndrome 1	Autosomal dominant	CTGA
257400	Nystagmus, congenital, autosomal recessive	Autosomal recessive	(Khawam et al. 1992)
601665 ^a	Obesity	Autosomal recessive	CTGA
164185	Ocular cicatricial pemphigoid	Autosomal dominant	CTGA
203100	Oculocutaneous albinism, type IA	Autosomal recessive	CTGA
257850	Oculodentodigital dysplasia, autosomal recessive	Autosomal recessive	(Traboulsi et al. 1986a)
257980	Odontonychoodermal dysplasia	Autosomal recessive	CTGA
165500	Optic atrophy 1	Autosomal dominant	(Der Kaloustian et al. 1980)
258500	Optic atrophy 6	Autosomal recessive	(Baghdassarian and Tabbara 1975)
258870	Ornithine aminotransferase deficiency	Autosomal recessive	CTGA
311250	Ornithine transcarbamylase deficiency	Autosomal recessive	(Karam et al. 2013b)
258860	Orofaciodigital syndrome, type IV	Autosomal recessive	CTGA
NA		Autosomal recessive	(Megarbane 2007)

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
166210	Ossous dysplasia, severe short stature, multiple dislocations, delayed bone age	Autosomal dominant	CTGA
259700	Osteogenesis imperfecta, type IIa	Autosomal recessive	CTGA
259720	Osteopetrosis, autosomal recessive 1	Autosomal recessive	(Pangrazio et al. 2006)
166710	Osteopetrosis, autosomal recessive 5	Autosomal dominant	CTGA
602080	Osteoporosis	Autosomal dominant	(Hale and Kelly 1998)
NA	Paget disease of bone	Unknown	(Zein et al. 2007)
245000	Painful subacute thyroiditis associated with human leukocyte antigen-B35	Autosomal	(Kurban et al. 2009)
606324	Papillon-Lefevre syndrome	Autosomal recessive	CTGA
270300	Parkinson's disease 7, autosomal recessive early-onset	Autosomal recessive	(Kurban and Azar 1969)
274600	Peeling skin syndrome	Autosomal recessive	(Mustapha et al. 1998)
260800	Pendred syndrome	Autosomal recessive	CTGA
261550	Pentosuria	Autosomal recessive	(Der Kaloustian et al. 1980)
175200	Persistent Mullerian duct syndrome, type I or II	Autosomal recessive	(Der Kaloustian et al. 1980)
261600	Peutz-Jeghers syndrome	Autosomal dominant	(Der Kaloustian et al. 1980)
300661	Phenylketonuria	Autosomal recessive	(Khneisser et al. 2008)
301220	Phosphoribosylpyrophosphate synthetase superactivity	X-linked	(Der Kaloustian et al. 1980)
219090	Pigmentary disorder, reticulate, with systemic manifestations	X-linked	CTGA
263200	Pituitary adenoma, ACTH-secreting	Unknown	(Sali and Mufarrij 1981)
612674	Polycystic kidney disease, autosomal recessive	Autosomal recessive	CTGA
263700	Polycystic kidney disease, autosomal recessive	Autosomal recessive	(Eisenberger et al. 2012)
176261	Polycystic kidney disease, autosomal recessive	Autosomal recessive	(Maakaron et al. 2012)
300604 ^e	Polycystic kidney disease, autosomal recessive	Autosomal recessive	CTGA
264090	Pigmentosa, and cataract	Unknown	(Lacombe et al. 2006)
113900	Porphyrin, congenital erythropoietic	Autosomal recessive	CTGA
604559	Potassium channel, voltage-gated, ISK-related subfamily, member 1	Autosomal recessive	CTGA
170100	Premature ovarian failure 2B; POF2B	Unknown	(Lacombe et al. 2006)
606054	Progeroid syndrome, neonatal	Autosomal recessive	CTGA
264600	Progressive familial heart block, type IB	Autosomal dominant	CTGA
264800	Progressive familial heart block, type IB	Autosomal dominant	(Stephan 1978; Stephan et al. 1997)
265100	Prolidase deficiency	Autosomal recessive	(Freij and Der Kaloustian 1986)
606963 ^a	Propionicacidemia	Autosomal recessive	(Khneisser I)
264600	Pseudovaginal perineoscrotal hypospadias	Autosomal recessive	(Hochberg et al. 1996)
264800	Pseudoxanthoma elasticum	Autosomal recessive	(Abbas et al. 2010)
265100	Pulmonary alveolar microlithiasis	Autosomal recessive	CTGA
265950	Pulmonary disease, chronic obstructive	Autosomal	CTGA
266200	Pyloric atresia	Autosomal recessive	CTGA
266200	Pyruvate kinase deficiency of red cells	Autosomal recessive	CTGA
233100	Renal glucosuria	Autosomal recessive or Autosomal dominant	(Der Kaloustian et al. 1980)

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
602722	Renal tubular acidosis, distal, autosomal recessive	Autosomal recessive	CTGA
180200	Retinoblastoma	Autosomal dominant	(Traboulsi et al. 1986b)
268050	Retinopathy, pigmentary, and mental retardation	Autosomal recessive	CTGA
312750	Rett syndrome	X-linked	(Corbani et al. 2012)
180300	Rheumatoid arthritis	Unknown	(Darwish and Armenian 1987)
610319 ^c	Rhizomelic dysplasia, scoliosis, and retinitis pigmentosa	Autosomal recessive	(Megarbane et al. 2006)
268310	Robinow syndrome, autosomal recessive	Autosomal recessive	(Mehawej et al. 2012)
268400	Rothmund-Thomson syndrome	Autosomal recessive	CTGA
180849	Rubinstein-Taybi syndrome	Autosomal dominant	CTGA
268800	Sandhoff disease	Autosomal recessive	CTGA
269000	SC phocomelia syndrome	Autosomal recessive	CTGA
102700	Severe combined immunodeficiency due to ADA deficiency	Autosomal recessive	(Der Kaloustian et al. 1980)
601457	Severe combined immunodeficiency, B cell-negative	Autosomal recessive	(DerKaloustian 2010)
609654 ^d	Short stature and facioauriculothoracic malformations	Autosomal recessive	CTGA
182212	Shprintzen-Goldberg craniostosis syndrome	Isolated cases	CTGA
603903	Sickle cell anemia	Autosomal recessive	(Inati et al. 2007)
180860	Silver-Russell syndrome	Isolated cases	CTGA
270200	Sjogren-Larsson syndrome	Autosomal recessive	(Pigg et al. 1999)
609047 ^d	Skeletal dysplasia, rhizomelic, with retinitis pigmentosa	Autosomal recessive	CTGA
270400	Smith-Lemli-Opitz syndrome	Autosomal recessive	(Nezarati et al. 2002)
604320	Spinal muscular atrophy with respiratory distress 1	Autosomal recessive	CTGA
607088	Spinal muscular atrophy, distal, autosomal recessive	Autosomal recessive	CTGA
213200	Spinocerebellar ataxia, autosomal recessive 2	Autosomal recessive	CTGA
606937 ^d	Spinocerebellar ataxia, autosomal recessive 5	Autosomal recessive	CTGA
271310	Spinocerebellar degeneration and corneal dystrophy	Autosomal recessive	(Der Kaloustian et al. 1985)
119100	Split-hand/foot malformation with long bone deficiency 1	Autosomal dominant	(Der Kaloustian et al. 1980)
106300 ^b	Spondyloarthropathy, susceptibility to, 1	Autosomal dominant	CTGA
106300	Spondyloarthropathy, susceptibility to, 1	Autosomal dominant	(Frayha and Nasr 1971)
272460	Spondylocarpotarsal synostosis syndrome	Autosomal recessive	CTGA
608681	Spondylocostal dysostosis, autosomal recessive 2	Autosomal recessive	CTGA
609813	Spondylocostal dysostosis, autosomal recessive 3	Autosomal recessive	(Sparrow et al. 2006)
603546	Spondyloepimetaphyseal dysplasia with multiple dislocations	Autosomal dominant	CTGA
143095	Spondyloepiphyseal dysplasia with congenital joint dislocations	Autosomal	(Megarbane and Ghanem 2004)
248200	Stargardt disease 1	Autosomal recessive	(Der Kaloustian et al. 1980)
152700	Systemic lupus erythematosus	Autosomal dominant	CTGA
207600 ^a	Takayasu arteritis	Autosomal recessive	CTGA

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
272800	Tay-Sachs disease	Autosomal recessive	CTGA
187100	Teeth, supernumerary	Autosomal dominant	CTGA
273150	Testes, rudimentary	Autosomal recessive	CTGA
273395	Tetra-Amelia, autosomal recessive	Autosomal recessive	CTGA
187500 ^b	Tetralogy of fallot	Autosomal dominant	CTGA
249270	Thiamine-responsive megaloblastic anemia syndrome	Autosomal recessive	(Bergmann et al. 2009)
313900	Thrombocytopenia, X-linked	Autosomal dominant	(Ho et al. 2001)
188030	Thrombocytopenic purpura, autoimmune	Autosomal	(Yamout et al. 2009)
612304	Thrombophilia due to protein C deficiency, autosomal recessive	Autosomal recessive	(Tjeldhorn et al. 2010)
188050	Thrombophilia due to thrombin defect	Autosomal dominant	(Kreidy et al. 2012)
275350	Transcobalamin II deficiency	Autosomal recessive	(Haberle et al. 2009)
608808 ^b	Transposition of the great arteries, dextro-looped	Unknown	CTGA
605067	Tricuspid atresia	Unknown	(Abdul-Sater et al. 2012)
276700	Tyrosinemia I	Autosomal recessive	(Karam et al. 2013b)
276600	Tyrosinemia, type II	Autosomal recessive	(Khneisser I)
191440	Ulnar hypoplasia	Autosomal dominant	(A. Megarbane and Ghanem 2005)
138900	Uric acid concentration, serum, QTL1	X-linked dominant	(DerKaloustian 2010)
276900	Usher syndrome, type 1B	Autosomal recessive	(Mouglabey et al. 1998)
276904	Usher syndrome, type 1C	Autosomal recessive	(DeAngelis et al. 2001)
276901	Usher syndrome, type 2A	Autosomal recessive	(Saouda et al. 1998)
276902	Usher syndrome, type 3A	Autosomal	(Eisenberger et al. 2012)
201475	Very long-chain acyl-CoA dehydrogenase deficiency	Autosomal recessive	(Karam et al. 2013b)
277350 ^d	Vitamin A metabolic defect	Autosomal recessive	CTGA
607473 ^d	Vitamin K-dependent clotting factors, combined deficiency of, 2	Autosomal recessive	CTGA
277450	Vitamin K-dependent coagulation defect	Autosomal	(Fregin et al. 2002)
201475	VLCAD deficiency	Autosomal recessive	(Khneisser I)
193300	Von Hippel-Lindau syndrome	Autosomal dominant	CTGA
193510	Waardenburg syndrome, type 2A	Autosomal dominant	(Haddad et al. 2011)
277580	Waardenburg syndrome, type 4A	Autosomal recessive	(Haddad et al. 2011)
600118	Warburg micro syndrome	Autosomal recessive	CTGA
613398	Warsaw breakage syndrome	Mutations	(Capo-Chichi et al. 2013)
277600	Weill-Marchesani syndrome, autosomal recessive	Autosomal recessive	CTGA
277900	Wilson disease	Autosomal recessive	CTGA
301000	Wiskott-Aldrich syndrome	X-linked recessive	(Der Kaloustian et al. 1980)
222300	Wolfram syndrome	Autosomal recessive	

Table 1 (continued)

OMIM phenotype no.	Disorder name	Mode of inheritance	Source
278300	Xanthinuria, type I	Autosomal recessive	(Medlej et al. 2004; Zalloua et al. 2008a)
278700	Xeroderma pigmentosum, group A	Autosomal recessive	CTGA (Afifi et al. 1972)

N/A subtype of disease not specified by reference

^a Very Common

^b Common

^c Lebanon only

^d Lebanon only in the Arab world

common large family sizes which increase their occurrence within one family; the high frequency of advanced maternal age, increasing the predisposition to chromosomal trisomies; and advanced paternal age, increasing the risk of autosomal dominant disorders through the occurrence of new mutations.

Information on the individual incidence rates is not readily available for all the listed diseases. However, the groups of diseases commonly identified and determined by CTGA database to be of relatively high incidence are shown in Table 1. It is also noteworthy to mention that around 30 diseases in the literature are only reported in the Lebanese population and not in any of the other Arab countries. Moreover, a few other diseases are strictly confined to patients of Lebanese origin and have not even been reported in any other genome around the world. These diseases have been given OMIM numbers and are reported either in OMIM or the CTGA database (Table 1).

Genetic services

Comprehensive genetic services, capable of delivering proper diagnosis, care, and prevention of genetic diseases at the community level, must include the following: (i) clinical and laboratory diagnostic services provided by clinical geneticists (physicians who specialize in genetic disorders), nurse geneticists (RN with genetics training), and laboratory geneticists (PhDs or MDs who are trained and certified to perform and interpret genetic tests in one or more of the three clinical genetics laboratory specialties—Clinical Molecular Genetics, Clinical Cytogenetics, or Clinical Biochemical Genetics; (ii) genetic counseling, ideally delivered by trained genetic counselors; and (iii) prevention programs including premarital and carrier screening, prenatal screening and newborn screening (NBS), and prenatal and preimplantation genetic diagnosis (PGD) (Christianson and Modell 2004; health, W. s. d. o. 2008; Modell 1997; Organization 2010). Despite the above reported numbers of congenital and genetically determined disorders and the high incidence of recessive disease directly linked to the increased rate of consanguinity, genetic services vary greatly in nature and location leading to their selectivity, inadequacy, and insufficiency to cover high-risk communities. Most of the available services are focused on clinical and laboratory diagnosis. Although those services available insure high standard genetic diagnosis in the rapidly expanding world of genetic technology, community genetic services focusing on early detection, prevention, knowledgeable counseling, and care are almost nonexistent.

Here, we report on the availability, or lack thereof, of the abovementioned genetic services in Lebanon. We contacted the Ministry of Public Health (MOPH), private and public hospitals, and private medical laboratories. We also conducted a search on several governmental websites such as that for the

Fig. 1 Classification according to mode of inheritance in Lebanon compared to the Arab world

order of physicians and the hospital and laboratory registries. This yielded contact by phone with around 180 private and public hospitals and about 50 private labs. In addition, the authors surveyed the official websites of the ministry of education, ministry of advertisement, and the Lebanese national council for scientific research to gain information on government-led education or research campaigns on genetic diseases. This does not represent a structured needs assessment but provides general information on available genetics units and the services they provide, as well as the availability of prevention and screening programs. However, the report does not provide information on the treatment, management, and care options available for people with genetic conditions.

1. Clinical and laboratory diagnostic services. Diagnostic services for genetic diseases in Lebanon have been present for over 40 years. These genetic services abide by law #625/11198 that protects the right of the individual to consent to genetic testing and protects the individual from prejudice based on genotypic information. Some of the diagnostic centers in academic institutions currently have state-of-the-art equipment and means of identification in both cytogenetic and molecular diagnostic units. After contact with almost all registered private and public hospitals (149 private hospitals and 29 public hospitals), as well as private medical laboratories, it was clear that the majority of units capable of diagnosing cytogenetic and molecular genetic diseases are located in the Capital, Beirut. Those hospitals with the major workload include the American University of Beirut Medical Center (AUBMC), University of Saint Joseph—Medical Genetics Unit (USJ-MGU), Saint Georges University Medical Center, Clemenceau Medical Center, and Chronic Care Center. The abovementioned are hospitals that provide laboratory diagnostic services under the supervision of a clinical laboratory geneticist who is qualified to interpret and communicate results to the relevant party and sometimes provide limited counseling services. A few other hospitals provide the laboratory diagnostic service to the patient; however, most of the laboratory tests are

performed elsewhere, and there are no clinical geneticists on board. The hospitals, which outsource the testing, include a couple of hospitals in the Beirut area, about three private hospitals in Mount Lebanon, and about five hospitals in south Lebanon. To the best of our knowledge, none of the public hospitals that we contacted attested to providing any form of genetic diagnosis (with the exception of forensic genetics taking place at Rafic Hariri Governmental Hospital). A few private labs also provide genetic testing services, most of which are outsourced. In addition to the abovementioned, it is noteworthy to mention that, according to the order of physicians, there are only five registered clinical geneticists, who are qualified to care for patients with genetic diseases, follow up on their diagnoses and treatment, and provide limited genetic counseling. All five registered clinical geneticists currently practice at AUBMC or USJ-MGU.

2. Knowledgeable counseling and support. Our brief survey showed that there is complete absence of trained and dedicated genetic counselors in Lebanon. Genetic counseling is an essential component in the process of genetic testing and screening. The WHO recommends against genetic testing and screening unless comprehensive genetic services (including counseling units) are available and recommends that these services should be accessible to the entire population. Private hospitals and laboratories in Lebanon, especially those that outsource testing, offer diagnostic services without the availability of a specialized health care professional to interpret or relay information to those that receive unfavorable results. Affected and at-risk individuals, families, and communities are limited to the expensive services provided by a few specialists, most of whom are localized in Beirut and are overbooked most of the time. Diagnostic units are not even spread to the North or South of Lebanon, nor are they present in most areas of Mount Lebanon. As a result, it is often the primary care physicians, medical laboratory doctors, laboratory technicians, and nurses (often without any, or inadequate training in genetic counseling) who take on the role of counseling the patient and the family.

Furthermore, individuals in high-risk communities, with increased prevalence of genetic diseases and high rates of consanguinity, endogamy, and arranged marriages, are in utmost need for genetic counseling. However, these communities are often in rural areas where genetic services do not exist.

3. Prevention and control. Patients suffering from genetically determined disorders have to deal with the burden of the increased frequency and length of hospital admissions and more surgeries (McCandless et al. 2004), in addition to the high cost of ongoing management of genetic disorders. As reported by the WHO in 1996, prevention can help alleviate the significant cost of health care and the psychological burden not only on the affected individual and family but also on the society as a whole.

Genetic screening is at the core of any proper prevention program, yet it is very recent, primitive, and almost nonexistent in Lebanon. Genetic screening is testing individuals for the risk or the probability of developing a disease or the risk of having diseased offspring. Genetic diseases can be screened for at the level of the family with high risk for disease or the couple prior to marriage (carrier or premarital screening), the offspring prior to implantation (PGD), or prior to birth (prenatal screening), and the newborn (NBS). At each level, an intervention can be implemented to alleviate the burden of the expected outcome.

NBS is defined as the early detection of infants at increased risk for selected treatable diseases, mostly biochemical genetic diseases (inborn errors of metabolism (IEM)), through a nationally mandated public health program. The importance of NBS stems from the need for fast and early intervention in most of the identified IEMs, thus avoiding child mortality and in some instances morbidity. Screening for G6PDH deficiency, which is available at USJ, for example, decreases the chances of children having an anemic crisis in early childhood from 70 to below 10 % (Khneisser et al. 2007).

AUBMC is one of the few hospitals with a hospital-based registry for congenital abnormalities that helped guide its NBS program testing for a few diseases. However, AUBMC sends samples from neonates of in-house deliveries to be tested at collaborating centers in Europe. The only two centers in Lebanon that offer on-site NBS for a few of these diseases are the Analytical Testing Laboratories (ATL), which is affiliated with the American University of Science and Technology (AUST), and the Newborn Screening Laboratory (NSL) at the Saint Joseph University (USJ). The NSL at USJ alone screens samples from 40 hospitals across Lebanon, for about 15,000 out of 74,000 newborns a year, and is now considered a reference laboratory for a well-established NBS program (Khneisser et al. 2008). The abovementioned local laboratories are limited in technical expertise to tandem mass spectrometry (TMS), which is mostly used for screening purposes.

Due to the lack of a well-established comprehensive Biochemical Genetics Laboratory in Lebanon, cases that are positive on NBS or those that are suspected on a clinical basis to have an IEM are mostly confirmed by sending testing to certain European laboratories. This delays diagnosis by a significant amount of time and delays the timely initiation of treatment that is crucial in achieving satisfactory clinical outcomes in these cases.

The available NBS in Lebanon is, however, not mandatory, not publically funded, not re-reimbursed by health insurance plans, not available at any public institution, and not guided by a proper research assessment of the national incidence of IEMs. Most of the hospitals we contacted do not offer NBS, and those that outsource it do not inform the parents about the test unless there are unfavorable results. NBS should be implemented as a public health program, run by the public health system, and covering all steps in the prevention process: screening of all newborns for the most common and nationally relevant diseases, diagnostic confirmation of those newborns who screen positive (requires biochemical genetics laboratories, which are to date unavailable in Lebanon), referral for proper care (usually lifelong), and genetic counseling for the parents and family members.

As for the other aspects of a prevention program, although some are available, they are not being utilized in the context of a national prevention plan. The Lebanese government enforced premarital screening for several infectious diseases in 1994. However, among all the common genetic diseases, only thalassemia is screened for indirectly (measuring Hgb and MCV). This disease has also been ameliorated due to awareness campaign and the establishment of a tertiary care center for medical and emotional support (Inati et al. 2006). Even if the couple chooses to undergo premarital genetic testing, there are no genetic counselors available to advise them toward an informed decision. Furthermore, carrier screening on the population level is not available as there has not been an assessment study for the most prevalent genetic diseases.

The technology for prenatal screening is also partially available in Lebanon ranging from ultrasound scanning accessible to almost everyone (detecting major congenital abnormalities such as neural tube defects and congenital heart malformations), to the less readily available assessment of maternal serum markers. Advanced prenatal diagnosis is even less available with invasive testing such as amniocentesis and chorionic villus sampling, available particularly at a few private hospitals at a relatively high cost. Despite availability, since selective termination of pregnancy is not legal and genetic counseling is absent, invasive procedures are not as effective in the prevention process. PGD, on the other hand, is more favorable as it allows the termination of the embryo prior to implantation and is available only at certain in vitro fertilization (IVF) centers in Lebanon. The costly and ethically

challenging PGD along with IVF programs however is not under any public or governmental supervision or financial support.

Education in genetics

In addition to diagnostic services, sufficient clinical specialists, genetic counselors, and proper prevention plans, education in genetics is a major requirement in the proper implementation of community genetics services. There is a major deficit in genetic literacy at all levels including high-risk families, the general public, and even health care providers. Even institutions such as private hospitals and laboratories, when contacted directly and asked about the services which they claim to offer, could not properly define or differentiate between these genetic services (mostly laboratory testing). To the best of our knowledge, besides the hemoglobinopathy awareness campaigns conducted by the chronic care center, there are no other national awareness campaigns for the diagnosis, care, and prevention of genetic diseases.

Research in genetics

A quick look at the references (albeit not in a systematic manner) shows that most mechanistic analyses for genetic diseases are reported from the Lebanese Diaspora. Publications from Lebanon are mostly clinical, peer-reviewed reports with no dwelling on mechanisms or molecular analyses. Even for diseases that have only been reported in the Lebanese genome, mechanism studies are minimal. The lack of these studies prevents the international scientific community from obtaining valuable information about the function of many genes and pathways that may be beneficial in delineating other genetically transmitted conditions and diseases.

Concluding remarks

In light of the high number of genetic disorders in the Lebanese population and the lack of proper genetic services and knowledge, medical and research genetic societies in Lebanon have to play an urgent and important role in opening the dialogue with public health professionals and decision makers to initiate a process whereby Lebanon goes through a needs assessment and establishes preventive genetic programs and interventions with population health benefits. There is a need to nurture public health interest and participation in medical genetics. Currently, existing research data sets are not being used to increase public awareness and formulate intervention or strategic planning to decrease the burden in any manner. Efforts in that direction are minimal and personal.

Geographic and financial barriers to the utilization of available genetic services have to be addressed. The quality and availability of community genetics services, including counseling and screening programs, need to be enhanced. The MOPH has to initiate a national birth defect registry and launch a mandatory national NBS program accordingly. Introduction of counseling services has to follow a national dialogue to define ethical, legal, religious, and cultural factors that would guide interventions, such as those for prenatal genetic diagnosis and termination of the affected pregnancy. Carrier screening programs have to be evaluated in context of the prevalent genetic diseases. There is also a tremendous need to educate all sectors of the population about the role of genetics in health and disease, including related ethical, legal, and social issues perhaps through the introduction of scientifically based mass media campaigns and providing the public with a national source of information about genetic diseases, resources, and services. Finally, one could implement high impact action plans to increase awareness and training for primary health care providers including obstetricians and pediatricians to provide the necessary information and counseling to patients until proper strategies are drawn and put into action.

Compliance with ethics guidelines The experiments performed during the study comply with the current laws of Lebanon.

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