Chapter 2

Genetic Disorders in Oman: A CTGA Perspective

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Introduction

The Sultanate of Oman is an Arab monarchy, located in the South East of the Arabian Peninsula. It shares its borders with Saudi Arabia, the United Arab Emirates, and Yemen, and has a coast line that stretches from the Arabian Sea and the Gulf of Oman to the Arabian Gulf (Figure 2.1). Apart from the mainland, several small islands in the Gulf of Oman and the Arabian Sea are also part of the Sultanate.

Oman has a total land area of about 310,000 square Km. About 82% of this is a desert, while the remaining area is principally mountainous in nature. Oman also has a beautiful coastline, which makes up for about 3% of the total land area (Ministry of Information, 2007). Thus, topographical features, ranging from valleys and mountains to plains, can all be seen within the boundaries of Oman. The climate in the country is as varied as its terrain and changes with regard to both season and geographical location. Along the coast, the weather is hot and humid, the interiors display a typical dry desert climate and regions at high-altitudes exhibit a moderate type of weather. The southern region of the country, typically the Dhofar province, is very unlike the rest of Oman, in that it receives the south-west summer monsoon from the Indian Ocean between June and September. Known locally as *Khareef*, this mon-

Figure 2.1. Sultanate of Oman and neighbouring countries.

soon provides heavy rainfall and lush green vegetation to the region. This is, in fact, one of only two places in Southern Arabia that catch this monsoon. The rest of the country receives scant and irregular rainfall.

For purposes of administration, the entire country has been divided into districts or *wilayats*, which in turn have been grouped into nine distinct regions. Of these, four regions, due to their populations, land areas, and/or strategic locations, have been accorded a special status of Governorates. These Governorates are:

Governorate of Muscat: This is Oman's most densely populated region, and contains the capital city of Muscat. It is, thus the political and administrative seat of the country. There are 32 governmental health institutions in this region, four of which are regional hospitals that serve also as national referral hospitals (Ministry of Health, 2006a).

Governorate of Dhofar: Located in the southern region of Oman and most known for the above-mentioned Khareef. Not surprisingly, the economy of Dhofar is supported by tourism and agriculture. The region is also host to a number of Semitic language speaking tribes. A total of 35 public health institutions serve this Governorate, the most for any region in the country (Ministry of Health, 2006a).

Governorate of Musandam: This is a small region in the extreme North of Oman that is interestingly, separated from the rest of the country by a strip of the United Arab Emirates. The strategic location of this region is highlighted by the fact that its coastline overlooks the navigable part of the Strait of Hormuz, a major transit point for oil. The beautiful fjords here also make for a great tourist attraction. Musandam is served by seven public health institutions (Ministry of Health, 2006a).

Governorate of Buraimi: This region, located in the North Western Oman, is famous for its historic forts and houses. Interestingly, just across the border, is the UAE city of Al-Ain. With regard to health administration, this region is clubbed together with the neighboring Ad-Dhahirah region (Ministry of Health, 2006a).

The remaining five regions, which have not been accorded Governorate status include the Batinah, Ad-Dhahirah, Dakhiliah, Sharqiyah, and Wusta regions. In terms of health administration, the Sharqiyah and Batinah regions have been further divided into two health regions each.

Of the total Omani population of 2.5 million (Table 2.1), the majority populate the plains of Muscat and Batinah regions. The Dhofar region is also fairly well-populated, whereas the hills and mountains of Oman are inhabited by only about 5% of the population (WHO, 2007). As in most other countries of the Gulf Cooperation Council (GCC), there is a sizable amount of expatriate work-force in Oman, reaching close to 700,000 in number (Ministry of Health, 2006a). Within the last decade, there has been a strong program aimed at improving the local human resource by the training of Omani personnel and the Omanization or localization of the workforce.

Although Omanis traditionally were seafarers and traders, the economy,

not unlike the rest of the Arabian Gulf region, is now more of an oil-based one. Infrastructural developments in the past few decades have touched almost every aspect of life, and have had a great impact on the health care system of the Sultanate too.

Health Care in Oman

Before 1970, the health care system in Oman was one of the poorest in the world. In 1970, the Omani Government undertook the responsibility of providing high-quality health care to all Omani people and citizens with the establishment of the Ministry of Health. Today, the Ministry of Health acts as the sole regulator of health care in the country, and is also the main health care provider, followed by the Ministry of Defense and the Sultan Qaboos University Hospital (SQUH). The efforts and achievements of the Ministry of Health in Oman throughout the past thirty years have had a positive impact on all health indicators. In 2006, the life expectancy at birth had increased to 74.29 years, the crude death rate had decreased to 2.48 per 1000 persons, and the infant mortality rate had declined to 10.3 per 1000 live births, from values of 67.4, 6.1 per 1000 persons, and 20.0 per 1000 live births, respectively for the same parameters in 1995 (Ministry of Health, 2007b; World health Organization, 2006). Accordingly, World Health Organization (WHO) ranked Oman as the first among emerging countries for excellence in health system performance (World Health Organization, 2000).

The Ministry of Health has established an extensive network of well-

Table 2.1. Major Health Indicators in Oman according to Ministry of Health (2007b) and Ministry of National Economy (2003).

Demographic Indicators	
Population size	
Total population	2,577,062
Omani population	1,883,576
Expatriate population	693,486
Population growth rate (%)	2.2
Total fertility rate (children born per woman)	3.19
Age structure (% of population)	
0-14 years	33.8
15-64 years	56.2
65 years and over	3.2
Median age (years)	15.8
Sex ratio (male/female)	1.27
Health Status Indicators	
Life expectancy at birth (years)	
Total population	74.3
Male	73.2
Female	75.4
Death rate (deaths per 1,000 population)	2.5
Infant mortality rate (deaths per 1,000 infants)	10.3
Under-five mortality rate (per 1,000 live births)	11.1
Maternal mortality rate (per 100,000 live births)	15.4

equipped modern hospitals, health centers, and mobile units throughout the country, which have been divided administratively into 10 health regions. Each health region has a regional referral hospital supported by a network of primary and secondary health services (Grant and Al-Kindy, 2005). Currently, the Minstry of Health runs 49 hospitals and 140 health centers throughout the country (Ministry of Health, 2007a). Major hospitals include:

The Royal Hospital: Established in 1987, this is the largest tertiary health care institution in Oman with about 630 beds. It provides state-of-the-art services in the specialties and sub-specialties of medicine, surgery, pediatrics, obstetrics and gynecology, oncology and laboratory medicine. Additionally, it is a teaching hospital and conducts surgical training programs, among others.

Sultan Qaboos University Hospital: Opened in 1990, with a capacity of 532 beds, this is the prime teaching hospital in Oman. In addition to providing general health care services, it also offers certain specialized medical facilities that are unique in Oman, including the renal transplant and bone marrow transplant units.

Khoula Hospital: This is the first general hospital to be built by the Ministry of Health, and was opened in 1974. It is the main referral hospital for trauma and orthopedic surgery, neurosurgery, cosmetic surgery, burns, maternity and other cases.

Al Nahda Hospital: It is a specialist unit for ear, nose, throat, eye, dental surgery, and skin diseases.

The Ministry of Health also has a well established national health information system and cancer registry, and publishes a health survey report annually. Additionally, there are active continuing medical education programs in all hospitals, and specialty groups regularly organize local and international conferences and workshops (Grant and Al-Kindy, 2005). The private health sector is also playing an increasingly important role in providing advanced health services, under the supervision of the Ministry of Health. In 2005, there were four private hospitals and 713 private clinics in the country (Ministry of Health, 2007a).

As part of the developmental strategy of the country, medical education gets an important attention and has been one of the country's key pillars of growth since 1970. Higher education in Oman was initiated in 1986 with the establishment of the Sultan Qaboos University, with the college of Medicine as one of its seven constituent colleges. Prior to the establishment of the Sultan Qaboos University, students had to travel to neighboring Arab countries or overseas to pursue their higher education studies. Today, the College of Medicine at the University enrols up to 130 students per year and has graduated 764 physicians since 1993. In order to fill the need towards the increasing demand for medical education in Oman, Oman Medical College was established in 2001 as the first private medical school in the country. This college offers a 7-year integrated program leading to the Doctor of Medicine degree (Grant and Al-Kindy, 2005). Both these medical colleges follow the new trends in medical education, based on problem solving instead of the traditional method that depends on

memorization (Khalid, 2008). Besides these educational institutions, the Omani government also established the Oman Medical Specialty Board (OMSB) in 1994, which is the highest supervising body of all postgraduate medical training programs in Oman (Grant and Al-Kindy, 2005).

As a result of the development of education and initiation of these medical schools, medical research has shown considerable growth over the past decade (Deleu *et al*., 2001). The College of Medicine and Sultan Qaboos University Hospital are the main centers of medical research. Additionally, two peer-reviewed medical journals, both in English, are published regularly in Oman. These are the Oman Medical Journal and the SQU Journal for Scientific Research: Medical Sciences (Grant and Al-Kindy, 2005).

Genetic Services in Oman

Despite the improvement in the health care system in Oman, the incidence of children born with congenital or genetic disorders is as high as 7%, while about 21.6% of infant mortality in the country is attributed to congenital malformations (Alwan and Modell, 1997). This high incidence of genetic disorders has been credited to the high rate of consanguinity (24.1%; Rajab and Patton, 2000), the high prevalence of hemoglobinopathies and G6PD Deficiency (Al-Riyami *et al*., 2001), increased maternal age leading to chromosomal defects such as Down Syndrome and neural tube defects (Rajab *et al*., 1998), and the high total fertility rate (Ministry of Health, 2007b) in the country.

According to one estimate made in 1998, in the absence of a suitable prevention program, the number of individuals affected with genetic diseases in the country is expected to increase by up to 10 times in 50-years (Rajab, 1998). Keeping this in mind, the Ministry of Health has taken several steps to provide genetic services within the country. The objective of these steps is to provide effective preventive and curative medical care for genetic diseases and congenital abnormalities, as well as to provide premarital examination to reduce the incidence of such disorders (Ministry of Health, 2006b). The most important facet of these services was their integration into the primary health care of the country in order to ensure that they reached every single individual. The emphasis of this service has been on controlling hemoglobinopathies, preventing Down syndrome, providing clinical genetic services through a referral network connected to the Royal Hospital, and providing genetic laboratory services, especially by way of cytogenetic laboratories, DNA storage facilities, and molecular genetic tests for thalassemia and sickle cell disease (Please see Chapter 3). In 2000, a national facility for providing premarital counseling was also established in the country. Along with premarital clinics, this counseling facility has played a major role in reducing the occurrence of genetic disorders, especially the hemoglobinopathies prevalent in the country. Plans are also underway for the establishment of a National Centre for Medical Genetics in the country. This advanced genetic centre is hoped to perform the functions of data collection and situation analysis of genetic disorders, provide diagnostic facilities, conduct prevention programs, as well

as train Omani nationals in the field (Rajab, 2007). Apart from the Ministry of Health, the Genetics Department of the Sultan Qaboos University College of Medicine has also worked towards providing genetic services to patients and their families, as well as in undertaking research work on genetic disorders prevalent in the country.

Genetic Disorders in the Arab Population of Oman

In the first quarter of 2007, the CTGA Database Development Team of CAGS initiated an extensive data collection process for information on genetic disorders in the Sultanate of Oman. As in the CTGA Database's strategy for United Arab Emirates and the Kingdom of Bahrain, the source for this data came from two major searches. One was through a structured search of relevant records from internationally indexed databases, mainly Pubmed. The other, and perhaps more important one, was the search of relevant articles from local medical journals published in Oman. In this respect, Oman Medical Journal was chosen as the main source for data collection.

In the two previous projects of data collection completed by CAGS, all data were handled at the head office in Dubai. On the other hand, a major change in the management of the Omani data lay in the fact that for the first time, an on-site researcher in Oman dealt with the initial processing of data. This strategy worked very well, and enabled the processing of a large amount of data in a relatively short time. In fact, by the end of the project in mid-2008, the CTGA Database showed the presence of 282 genetic disorders (Table 2.2) and data on 56 related genes (Table 2.3) in the Arab population of Oman.

Table 2.2. Alphabetical listing of genetic disorders in the Arab population of Oman as indexed in the CTGA Database (October, 2008).

OMIM #	Name
246450	3-@Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency
250950	3-@Methylglutaconic Aciduria, Type I
100100	Abdominal Muscles, Absence of, with Urinary Tract Abnormality and Cryptorchidism
605552	Abdominal Obesity-Metabolic Syndrome
200400	Achalasia, Familial Esophageal
201460	Acyl-CoA Dehydrogenase, Long-Chain, Deficiency of
201910	Adrenal Hyperplasia, Congenital, due to 21-Hydroxylase Deficiency
304050	Aicardi Syndrome
225750	Aicardi-Goutieres Syndrome 1
607154	Allergic Rhinitis
203655	Alopecia Universalis Congenita
104290	Alternating Hemiplegia of Childhood
105250	Amyloidosis, Primary Cutaneous
300068	Androgen Insensitivity Syndrome
206500	Anencephaly
606788	Anorexia Nervosa, Susceptibility to, 1
107320	Antiphospholipid Syndrome
107600	Aplasia Cutis Congenita
207900	Argininosuccinic Aciduria
108120	Arthrogryposis, Distal, Type 1
108110	Arthrogryposis Multiplex Congenita
208300	Ascites, Chylous
208500	Asphyxiating Thoracic Dystrophy 1
600807	Asthma, Susceptibility To
108800	Atrial Septal Defect 1
209500	Atrichia with Papular Lesions
600309	Atrioventricular Septal Defect
143465	Attention Deficit-Hyperactivity Disorder
209900	Bardet-Biedl Syndrome
607483	Basal Ganglia Disease, Biotin-Responsive
130650	Beckwith-Wiedemann Syndrome
109650	Behcet Syndrome
113600	Branchial Cleft Anomalies
114480	Breast Cancer
211450	Bronchomalacia
211530	Bulbar Palsy, Progressive, with Sensorineural Deafness
607499	Bulimia Nervosa, Susceptibility to, 1
114290	Campomelic Dysplasia
114900	Carcinoid Tumors, Intestinal
115200	Cardiomyopathy, Dilated, 1A
255120	Carnitine Palmitoyltransferase I Deficiency
608836	Carnitine Palmitoyltransferase II Deficiency, Lethal Neonatal
115430	Carpal Tunnel Syndrome
212750	Celiac Disease
609222	Cephalocele, Atretic
608027	Cerebellar Atrophy with Progressive Microcephaly
603513	Cerebral Palsy, Spastic, Symmetric, Autosomal Recessive
214150	Cerebrooculofacioskeletal Syndrome
214800	CHARGE Syndrome
608911	Choanal Atresia, Posterior
200700	Chondrodysplasia, Grebe Type
215700	Citrullinemia, Classic
120000	Coarctation of Aorta
216550	Cohen Syndrome
212065	Congenital Disorder of Glycosylation, Type Ia
121050	Contractural Arachnodactyly, Congenital
122470	Cornelia de Lange Syndrome
217990	Corpus Callosum, Agenesis of
304100	Corpus Callosum, Partial Agenesis of, X-Linked

OMIM #	Name
218030	Cortisol 11-Beta-Ketoreductase Deficiency
123400	Creutzfeldt-Jakob Disease
219050	Cryptorchidism, Unilateral or Bilateral
219200	Cutis Laxa, Autosomal Recessive, Type II
219250	Cutis Marmorata Telangiectatica Congenita
219700	Cystic Fibrosis
219730	Cystic Kidney Disease with Ventriculomegaly
220200	Dandy-Walker Syndrome
220500	Deafness, Congenital, and Onychodystrophy, Recessive Form
603165	Dermatitis, Atopic
607907	Dermatofibrosarcoma Protuberans
222100	Diabetes Mellitus, Insulin-Dependent
125853	Diabetes Mellitus, Noninsulin-Dependent
606176	Diabetes Mellitus, Permanent Neonatal
603933	Diabetic Nephropathy, Susceptibility to
142340	Diaphragmatic Hernia, Congenital
190685	Down Syndrome
225500	Ellis-van Creveld Syndrome
130710	Emphysema, Congenital Lobar
166000	Enchondromatosis, Multiple
226650	Epidermolysis Bullosa, Generalized Atrophic Benign
600669	Epilepsy, Idiopathic Generalized
606369	Epileptic Encephalopathy, Lennox-Gastaut Type
226980	Epiphyseal Dysplasia, Multiple, with Early-Onset Diabetes Mellitus
227090	Erythroderma, Lethal Congenital
133450	Ewing Sarcoma Breakpoint Region 1
227260	Facial Ectodermal Dysplasia
227600	Factor X Deficiency
227650	Fanconi Anemia
228520	Fibrochondrogenesis
305600	Focal Dermal Hypoplasia
300624	Fragile X Mental Retardation Syndrome
229400	Frontofacionasal Dysostosis
230400	Galactosemia
137215	Gastric Cancer
230750	Gastroschisis
230800	Gaucher Disease, Type I
231070	Geroderma Osteodysplastica
137750	Glaucoma 1, Open Angle, A
137800	Glioma of Brain, Familial
305900	Glucose-6-Phosphate Dehydrogenase
231670	Glutaric Acidemia I
266130	Glutathione Synthetase Deficiency
605899	Glycine Encephalopathy
232200	Glycogen Storage Disease I
232300	Glycogen Storage Disease II
232400	Glycogen Storage Disease III
232500	Glycogen Storage Disease IV
230500	GM1-Gangliosidosis, Type I
275000	Graves Disease
139393	Guillain-Barre Syndrome, Familial
141800	Hemoglobin - Alpha Locus 1
141900	Hemoglobin - Beta Locus
603553	Hemophagocytic Lymphohistiocytosis, Familial, 2
235510	Hennekam Lymphangiectasia-Lymphedema Syndrome
142623	Hirschsprung Disease, Susceptibility to, 1
236100	Holoprosencephaly
142900	Holt-Oram Syndrome
236200	Homocystinuria
143100	Huntington Disease
607014	Hurler Syndrome
236600	Hydrocephalus
236680	Hydrolethalus Syndrome 1
307030	Hyperglycerolemia
238320	Hypergonadotropic Hypogonadism
243700	Hyperimmunoglobulin E-Recurrent Infection Syndrome, Autosomal Recessive
256450	Hyperinsulinemic Hypoglycemia, Familial, 1
259900	Hyperoxaluria, Primary, Type I
145500	Hypertension, Essential
146110	Hypogonadotropic Hypogonadism
248250	Hypomagnesemia 3, Renal
241410	Hypoparathyroidism-Retardation-Dysmorphism Syndrome
241550	Hypoplastic Left Heart Syndrome
146450	Hypospadias, Autosomal
275200	Hypothyroidism, Congenital, Nongoitrous, 1
218700	Hypothyroidism, Congenital, Nongoitrous, 2
242300	Ichthyosis, Lamellar, 1
308350	Infantile Spasm Syndrome, X-Linked

OMIM #	Name
243200	Intracranial Hypertension, Idiopathic
147710	Intussusception
243310	Iris Coloboma with Ptosis, Hypertelorism, and Mental Retardation
243500	Isovaleric Acidemia
243600	Jejunal Atresia
213300	Joubert Syndrome 1
148000	Kaposi Sarcoma
300530	Kawasaki Disease
223000	Lactase Deficiency, Congenital
245800	Laurence-Moon Syndrome
601626	Leukemia, Acute Myeloid
608232	Leukemia, Chronic Myeloid
151600	Leukonychia Totalis
608594	Lipodystrophy, Congenital Generalized, Type 1
269700	Lipodystrophy, Congenital Generalized, Type 2
608154	Lipodystrophy, Generalized, with Mental Retardation, Deafness, Short Stature, and Slender Bones
607432	Lissencephaly I
192500	Long QT Syndrome 1
211980	Lung Cancer
605027	Lymphoma, Non-Hodgkin, Familial
607131	Macrocephaly with Multiple Epiphyseal Dysplasia and Distinctive Facies
248600	Maple Syrup Urine Disease
154700	Marfan Syndrome
125851	Maturity-Onset Diabetes of the Young, Type II
249000	Meckel Syndrome, Type 1
155600	Melanoma, Cutaneous Malignant
305800	Membranoproliferative Glomerulonephritis, X-Linked
156240	Mesothelioma, Malignant
250100	Metachromatic Leukodystrophy
251000	Methylmalonic Aciduria due to Methylmalonyl-CoA Mutase Deficiency
251200	Microcephaly, Primary Autosomal Recessive, 1
603802	Microcephaly with Simplified Gyral Pattern
252900	Mucopolysaccharidosis Type IIIA
253000	Mucopolysaccharidosis Type IVA
253200	Mucopolysaccharidosis Type VI
253220	Mucopolysaccharidosis Type VII
158330	Mullerian Aplasia
143400	Multicystic Renal Dysplasia, Bilateral
231680	Multiple Acyl-CoA Dehydrogenation Deficiency
265000	Multiple Pterygium Syndrome, Escobar Variant
254200	Myasthenia Gravis
160700	Myopia 2
310400	Myotubular Myopathy 1
161550	Nasopharyngeal Carcinoma
256300	Nephrosis 1, Congenital, Finnish Type
600995	Nephrotic Syndrome, Steroid-Resistant, Autosomal Recessive
256520	Neu-Laxova Syndrome
182940	Neural Tube Defects
601634	Neural Tube Defects, Folate-Sensitive
256550	Neuraminidase Deficiency
256540	Neuraminidase Deficiency with Beta-Galactosidase Deficiency
162200	Neurofibromatosis, Type I
101000	Neurofibromatosis, Type II
607847	Neutropenia, Nonimmune Chronic Idiopathic, of Adults
163950	Noonan Syndrome 1
257350	Nuchal Bleb, Familial
203100	Oculocutaneous Albinism, Type IA
311250	Ornithine Transcarbamylase Deficiency, Hyperammonemia due to
119530	Orofacial Cleft 1
166210	Osteogenesis Imperfecta, Type IIA
604370	Ovarian Cancer, Epithelial
167750	Pancreas, Annular
260350	Pancreatic Carcinoma
260500	Papilloma of Choroid Plexus
120330	Papillorenal Syndrome
118800	Paroxysmal Nonkinesigenic Dyskinesia 1
208150	Pena-Shokeir Syndrome, Type I
261550	Persistent Mullerian Duct Syndrome, Types I and II
101600	Pfeiffer Syndrome
261600	Phenylketonuria
261800	Pierre Robin Syndrome
263200	Polycystic Kidney Disease, Autosomal Recessive
174400	Polydactyly, Preaxial I
263630	Polysyndactyly with Cardiac Malformation
176000	Porphyria, Acute Intermittent
189800	Preeclampsia/Eclampsia 1
606054	Propionic Acidemia

OMIM #	Name
176807	Prostate Cancer
176860	Protein C Deficiency, Congenital Thrombotic Disease due to
176880	Protein S, Alpha
264350	Pseudohypoaldosteronism, Type I, Autosomal Recessive
264600	Pseudovaginal Perineoscrotal Hypospadias
178550	Pulmonary Hemosiderosis
178600	Pulmonary Hypertension, Primary
265430	Pulmonary Hypoplasia, Primary
265800	Pycnodysostosis
179010	Pyloric Stenosis, Infantile Hypertrophic 1
602722	Renal Tubular Acidosis, Distal, Autosomal Recessive
267450	Respiratory Distress Syndrome in Premature Infants
180200	Retinoblastoma
312750	Rett Syndrome
268210	Rhabdomyosarcoma 1
180300	Rheumatoid Arthritis
606072	Rippling Muscle Disease
268310	Robinow Syndrome, Autosomal Recessive
277000	Rokitansky-Kuster-Hauser Syndrome
268800	Sandhoff Disease
269160	Schizencephaly
162091	Schwannomatosis
255800	Schwartz-Jampel Syndrome, Type 1
210600	Seckel Syndrome 1
603903	Sickle Cell Anemia
270400	Smith-Lemli-Opitz Syndrome
270800	Spastic Paraplegia 5A, Autosomal Recessive
253300	Spinal Muscular Atrophy, Type I
253550	Spinal Muscular Atrophy, Type II
253400	Spinal Muscular Atrophy, Type III
164400	Spinocerebellar Ataxia 1
610685	Split-Hand/Foot Malformation with Long Bone Deficiency 2
106300	Spondyloarthropathy, Susceptibility to, 1
608637	Spondyloepiphyseal Dysplasia, Omani Type

OMIM #	Name
275355	Squamous Cell Carcinoma, Head and Neck
185100	Strabismus, Susceptibility to
601367	Stroke, Ischemic
185300	Sturge-Weber Syndrome
601559	Stuve-Wiedemann Syndrome
152700	Systemic Lupus Erythematosus
272800	Tay-Sachs Disease
187500	Tetralogy of Fallot
187600	Thanatophoric Dysplasia, Type I
249270	Thiamine-Responsive Megaloblastic Anemia Syndrome
273800	Thrombasthenia of Glanzmann and Naegeli
188030	Thrombocytopenic Purpura, Autoimmune
274150	Thrombotic Thrombocytopenic Purpura, Congenital
188550	Thyroid Carcinoma, Papillary
188580	Thyrotoxic Periodic Paralysis
106700	Total Anomalous Pulmonary Venous Return 1
189960	Tracheoesophageal Fistula with or without Esophageal Atresia
608808	Transposition of the Great Arteries, Dextro-Looped
154500	Treacher Collins-Franceschetti Syndrome
191100	Tuberous Sclerosis
276700	Tyrosinemia, Type I
191390	Ulcerative Colitis, Susceptibility to
606893	Vascular Malformation, Primary Intraosseous
192350	VATER Association
193000	Vesicoureteral Reflux 1
277440	Vitamin D-Dependent Rickets, Type II
193200	Vitiligo
277580	Waardenburg-Shah Syndrome
608710	Wegener Granulomatosis
277900	Wilson Disease
194200	Wolff-Parkinson-White Syndrome
222300	Wolfram Syndrome
278250	Wrinkly Skin Syndrome
214100	Zellweger Syndrome

Table 2.3. Alphabetical listing of gene loci studied in Arab individuals from Oman as indexed in the CTGA Database (October, 2008).

OMIM #	Name
603100	1-@Acylglycerol-3-Phosphate O-Acyltransferase 2
607093	5,10-@Methylenetetrahydrofolate Reductase
106180	Angiotensin I-Converting Enzyme
107680	Apolipoprotein A-I
611716	ATPase, H+ Transporting, Lysosomal, V0 Subunit A2
600355	Baculoviral IAP Repeat-Containing Protein 1
610148	BBS10 Gene
606158	BSCL2 Gene
603799	Carbohydrate Sulfotransferase 3
100730	Cholinergic Receptor, Nicotinic, Gamma Polypeptide
607817	COH1 Gene
120700	Complement Component 3
120810	Complement Component 4A
116899	Cyclin-Dependent Kinase Inhibitor 1A
600778	Cyclin-Dependent Kinase Inhibitor 1B
602421	Cystic Fibrosis Transmembrane Conductance Regulator
400003	Deleted in Azoospermia
604032	Eukaryotic Translation Initiation Factor 2-Alpha Kinase 3
134934	Fibroblast Growth Factor Receptor 3
121011	Gap Junction Protein, Beta-2
601146	Growth/Differentiation Factor 5
602302	Hairless, Mouse, Homolog of
147570	Interferon, Gamma
147679	Interleukin 1 Receptor Antagonist
147760	Interleukin 1-Alpha
147720	Interleukin 1-Beta
147680	Interleukin 2
147780	Interleukin 4
147620	Interleukin 6

OMIM #	Name
146930	Interleukin 8
124092	Interleukin 10
243400	Isoniazid Inactivation
604945	Killer Cell Immunoglobulin-Like Receptor, Two Domains, Long Cytoplasmic Tail, 4
607900	Kindlin 1
151443	Leukemia Inhibitory Factor Receptor
153440	Lymphotoxin-Alpha
142800	Major Histocompatibility Complex, Class I, A
142830	Major Histocompatibility Complex, Class I, B
142840	Major Histocompatibility Complex, Class I, C
142860	Major Histocompatibility Complex, Class II, DR Alpha
609023	Myofibrillogenesis Regulator 1
300415	Myotubularin
170280	Perforin 1
605925	Pericentrin 2
176741	Proliferation-Related Ki-67 Antigen
602337	Receptor Tyrosine Kinase-Like Orphan Receptor 2
111680	Rhesus Blood Group, D Antigen
182205	Sex Hormone-Binding Globulin
126455	Solute Carrier Family 6 (Neurotransmitter Transporter, Dopamine), Member 3
600354	Survival of Motor Neuron 1, Telomeric
601627	Survival of Motor Neuron 2, Centromeric
609884	Transmembrane Protein 67
191160	Tumor Necrosis Factor
134637	Tumor Necrosis Factor Receptor Superfamily, Member 6
191170	Tumor Protein p53
164870	V-ERB-B2 Avian Erythroblastic Leukemia Viral Oncogene Homolog 2

Classification and Molecular Complexity of Genetic Disorders in Oman

The CTGA Database data analysis reveals that congenital malformations and chromosomal abnormalities form the major chunk (37%) of genetic disorders from Oman (Figure 2.2). Endocrine, nutritional and metabolic disorders are also quite numerous, making up for almost 24% of the genetic disorders in Oman. Additionally, the percentages of both these categories of genetic disorders are higher than the average values for the Arab population as a whole (35% and 19%, respectively). Neoplasms form another category of genetic disorders that shows a significant increase in the number of disorders in Oman as compared to the Arab average (8.9% vs. 5.3%). On the other hand, diseases of the eye and adnexa are significantly lower than the Arab average in Oman (1.1% vs. 2.8%). Genetic disorders of the ear and mastoid process have not been reported from Oman at all. These features could in part be explained by the availability or lack of skilled practitioners in these specific medical specialties. However, a more proper and complete explanation can only be provided once detailed data collection projects have been completed for all Arab countries.

Autosomal recessive disorders are numbered higher than the autosomal dominant disorders in Oman. However, when compared to the data for Arabs as a whole, the Omani data shows a comparatively lower percentage of autosomal recessive diseases (54.6% vs. 62.6%) and a corresponding increase in the number of autosomal dominant disorders (Figure 2.3). The relatively lower consanguinity rate in Oman compared to other GCC countries could have some bearing on this difference (Please see 'Consanguinity and Reproductive Health' in Chapter 1).

More than 57% of the genetic disorders seen in the Omani Arab population are due to single gene defects. Incidentally, this compares well to the Arab average. With each successive increase in the number of genetic loci, the percentage of disorders is significantly reduced. A little more than 10% of disorders in Oman are attributed to two gene loci, while only 5% are disorders linked to three genetic loci (Figure 2.4).

Incidence of Genetic Disorders in Oman

Of the 282 genetic disorders described in Oman, the CTGA Database also contains information regarding the incidence of some of these disorders in the country (Table 2.4). Apart from the extremely common diseases, such as the hemoglobinopathies, including beta-thalassemia and sickle cell disease, and other disorders such as favism, the highest incidence is noted for genetic diseases such as hypospadias, orofacial cleft, and neural tube defects, and chromosomal aberrations, such as Down syndrome.

Overview of Medical and Genetic Research in Oman

By studying biomedical research productivity in Oman, the general trends and directions of medical

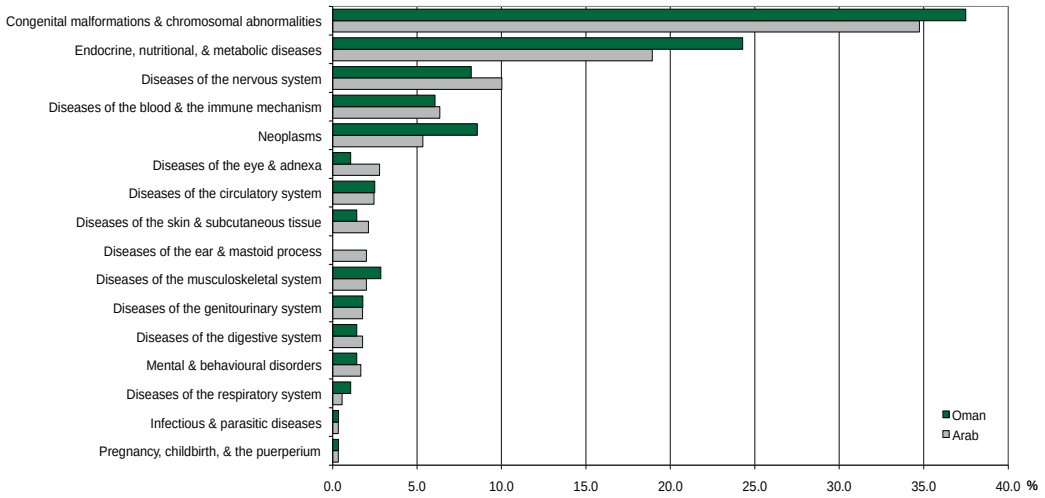

Figure 2.2. Classification of genetic disorders in the Arab population of Oman compared to rates recorded in the Arab World using the WHO ICD-10 system (August, 2008).

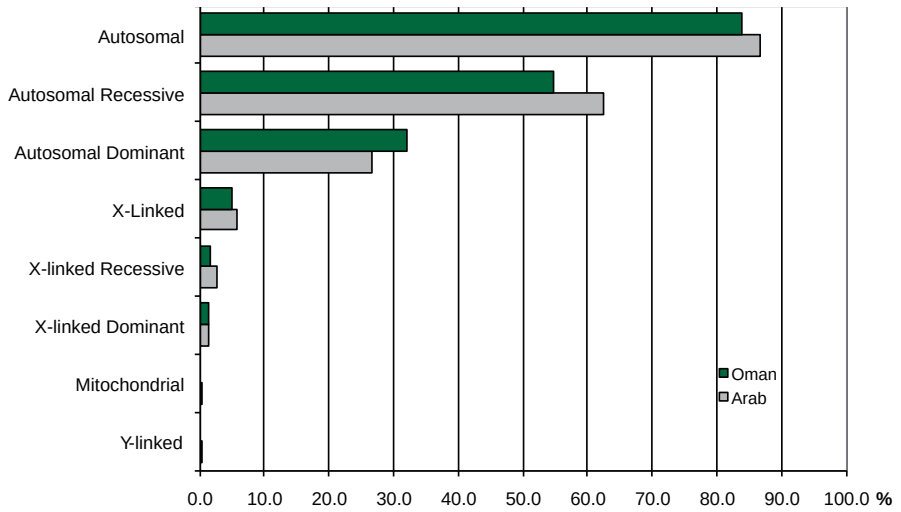

Figure 2.3. Classification of genetic disorders in the Arab population of Oman compared to rates recorded in the Arab World according to mode of inheritance (August, 2008).

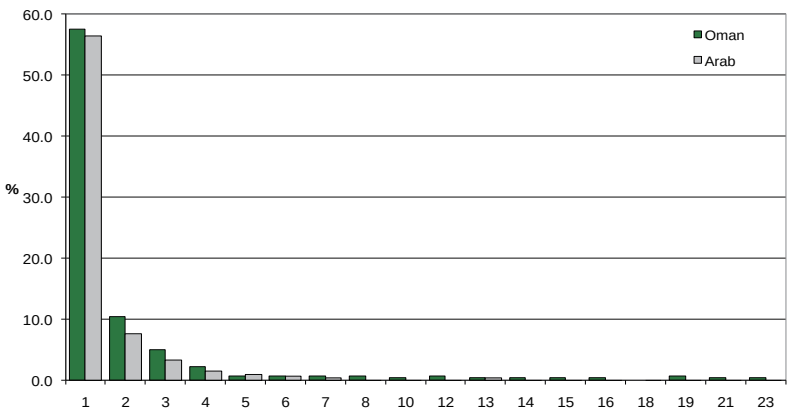

Figure 2.4. Classification of genetic disorders in the Arab population of Oman compared to rates recorded in the Arab World according to number of causative gene loci (August, 2008).

Table 2.4. Rates per 10,000 births of cases with congenital abnormalities and genetic disorders in Oman as constructed from the CTGA Database (August, 2006).

Disease	Rate	References
Hypospadias, Autosomal	33.10	Sawardekar, 2005
Down Syndrome	20.01	Sawardekar, 2005
Orofacial Cleft 1	19.55	Rajab and Thomas, 2001; Sawardekar, 2005
Neural Tube Defects	16.71	Rajab *et al*., 1998; Sawardekar, 2005
Anencephaly	12.73	Sawardekar, 2005
Neural Tube Defects, Folate-Sensitive	12.50	Rajab *et al*., 1998
Cryptorchidism, Unilateral or Bilateral	11.40	Sawardekar, 2005
Diaphragmatic Hernia, Congenital	6.82	Sawardekar, 2005
Atrial Septal Defect 1	6.24	Subramanyan *et al*., 2000; Sawardekar, 2005
Hypothyroidism, Congenital, Nongoitrous, 1	4.65	Elbualy *et al*., 1998
Hirschsprung Disease, Susceptibility to, 1	3.26	Rajab *et al*., 1997
Coarctation of Aorta	3.18	Sawardekar, 2005
Thanatophoric Dysplasia, Type I	3.18	Sawardekar, 2005
Meckel Syndrome, Type 1	2.82	Rajab *et al*., 2005; Sawardekar, 2005
Osteogenesis Imperfecta, Type IIA	2.27	Sawardekar, 2005
Melanoma, Cutaneous Malignant	2.20	Sawardekar, 2005
Pierre Robin Syndrome	1.82	Sawardekar, 2005
Ichthyosis, Lamellar, 1	1.82	Sawardekar, 2005
Hypoplastic Left Heart Syndrome	1.82	Sawardekar, 2005
Arthrogryposis, Distal, Type 1	1.82	Sawardekar, 2005
Noonan Syndrome 1	1.82	Sawardekar, 2005
Adrenal Hyperplasia, Congenital, due to 21-Hydroxylase Deficiency	1.41	Rajab *et al*., 2005; Sawardekar, 2005
Transposition of the Great Arteries, Dextro-Looped	1.37	Sawardekar, 2005
Pulmonary Hypoplasia, Primary	1.36	Sawardekar, 2005
Holoprosencephaly	1.36	Sawardekar, 2005
Aplasia Cutis Congenita	1.36	Sawardekar, 2005
Polycystic Kidney Disease, Autosomal Recessive	1.33	Rajab *et al*., 2005; Sawardekar, 2005
Ellis-van Creveld Syndrome	1.11	Rajab *et al*., 2005; Sawardekar, 2005
Epidermolysis Bullosa, Generalized Atrophic Benign	1.08	Rajab *et al*., 2005; Sawardekar, 2005
Spinal Muscular Atrophy, Type I	1.00	Rajab *et al*., 2005
Absence of Abdominal Muscles with Urinary Tract Abnormality and Cryptorchidism	0.91	Sawardekar, 2005
Beckwith-Wiedemann Syndrome	0.91	Sawardekar, 2005
Tetralogy of Fallot	0.91	Sawardekar, 2005
Pena-Shokeir Syndrome, Type I	0.91	Sawardekar, 2005
Cerebrooculofacioskeletal Syndrome	0.91	Sawardekar, 2005
CHARGE Syndrome	0.91	Sawardekar, 2005
Cystic Kidney Disease with Ventriculomegaly	0.91	Sawardekar, 2005
Microcephaly, Primary Autosomal Recessive, 1	0.67	Rajab *et al*., 2005
Cystic Fibrosis	0.67	Rajab *et al*., 2005
Renal Tubular Acidosis, Distal, Autosomal Recessive	0.50	Rajab *et al*., 2005
Hyperinsulinemic Hypoglycemia, Familial, 1	0.50	Rajab *et al*., 2005
Nephrosis 1, Congenital, Finnish Type	0.50	Rajab *et al*., 2005
Jejunal Atresia	0.50	Rajab *et al*., 2005
Zellweger Syndrome	0.50	Rajab *et al*., 2005
Focal Dermal Hypoplasia	0.45	Sawardekar, 2005
Smith-Lemli-Opitz Syndrome	0.45	Sawardekar, 2005
Multiple Pterygium Syndrome, Escobar Variant	0.45	Sawardekar, 2005
Neu-Laxova Syndrome	0.45	Sawardekar, 2005
Hydrolethalus Syndrome 1	0.45	Sawardekar, 2005
Pfeiffer Syndrome	0.45	Sawardekar, 2005
Campomelic Dysplasia	0.45	Sawardekar, 2005
Cornelia de Lange Syndrome	0.45	Sawardekar, 2005
Holt-Oram Syndrome	0.45	Sawardekar, 2005
Treacher Collins-Franceschetti Syndrome	0.45	Sawardekar, 2005
Nasopharyngeal Carcinoma	0.45	Sawardekar, 2005
Sturge-Weber Syndrome	0.45	Sawardekar, 2005
VATER Association	0.45	Sawardekar, 2005

Disease	Rate	References
Asphyxiating Thoracic Dystrophy 1	0.45	Sawardekar, 2005
Seckel Syndrome 1	0.45	Sawardekar, 2005
Lipodystrophy, Congenital Generalized, Type 1	0.40	Rajab *et al*., 2005
Schwartz-Jampel Syndrome, Type 1	0.39	Rajab *et al*., 2005; Sawardekar, 2005
Oculocutaneous Albinism, Type IA	0.33	Rajab *et al*., 2005
Bardet-Biedl Syndrome	0.33	Rajab *et al*., 2005
Robinow Syndrome, Autosomal Recessive	0.28	Rajab *et al*., 2005
Diabetes Mellitus, Permanent Neonatal	0.20	Bappal *et al*., 1999; Soliman *et al*., 1999
Neuraminidase Deficiency with Beta-Galactosidase Deficiency	0.20	Rajab *et al*., 2005
Congenital Disorder of Glycosylation, Type Ia	0.20	Rajab *et al*., 2005
Retinoblastoma	0.05	Khandekar *et al*., 2004

research in the country over the last few decades can be easily deduced. A total of 1242 articles were obtained from a targeted search strategy of PubMed, adapted from Tadmouri and Bissar-Tadmouri (2004), which included only those articles where the principal investigators were affiliated to Omani institutions. In terms of journal destination, the most popular subject oriented journals among researchers in Oman were inferred to be those dealing with pediatrics (11.4%), neuroscience (6.5%), and transplantation (3.1%). A similar trend is reflected in the analysis of the source of publications. Pediatric and child health departments account for more than 13% of these publications, followed by the departments of neurology (6.3%), anesthesia (3.2%), hematology, and ophthalmology (3.1% each). The increased activity of pediatric departments could be due to the heightened importance being afforded to child and adolescent health development in the country. In fact, the Ministry of Health formally endorsed the WHO's strategy for Integrated Management of Child Health in 2001, and by 2005, all of the Governorates had been covered under this scheme. A more focused look at the keyword data in biomedical articles from Oman indicates that genetic studies are a popular theme. Other conditions that generate a considerable amount of interest among researchers in Oman include pregnancy and pregnancy related complications, congenital abnormalities, kidney diseases, and diabetes mellitus. Interestingly, most Omani authors do prefer regional journals over international publications. The two most popular journal destinations, Saudi Medical Journal and the Annals of Saudi Medicine, by themselves accounted for more than 12% of the publications from Oman (data not shown).

With the increase in incidences of known genetic disorders in the country, a need has emerged for novel research to understand the etiology of these disorders and to work towards their management. Genetic researchers from Oman, especially from the Ministry of Health and the Sultan Qaboos University have, either on their own, or in collaboration with various international institutions, worked towards a better understanding of the genetic disorders present in the country (Rajab *et al*., 2005; Sawardekar, 2005; Bayoumi *et al*., 2007).

One of the projects carried out by the College of Medicine at SQU, known as FamGUARD, undertakes

studies on autosomal recessive genetic disorders and the kind of clinical and laboratory services that the patients with such disorders and their families require. The University has also undertaken several studies focusing on chromosomal rearrangements and mutations in cancerous conditions, especially in leukemia (Udayakumar *et al.*, 2007; Al-Lamki *et al.*, 2005). On the other hand, the University has collaborated with several international institutions to further genetic research. One of such programs is the Oman Family Study research program, which conducts studies on complex diseases, mainly hypertension, diabetes, obesity and the metabolic syndrome, aiming at investigating the role of genetic and environmental factors in these diseases (Please see Chapter 4).

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