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COUNTRY REPORT

Genetic services and testing in the Sultanate of Oman. Sultanate of Oman steps into modern genetics

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Abstract The Sultanate of Oman is a rapidly developing Muslim country with well-organised government-funded health care services, including primary, secondary and tertiary, and rapidly expanding medical genetic facilities. At the present time, the Omani population is characterised by a rapid rate of growth, large family size, consanguineous marriages, and the presence of genetic isolates. The preservation of a tribal structure in the community coupled with traditional isolation has produced unique and favourable circumstances for building genealogical records and the study of genetic disease. Genetic services developed in the Sultanate of Oman in the past decade have become an important component of health care. The recently constructed Genetic Centre in Muscat expects to meet the needs of the Omani population in provision of genetic services and research, in a manner deferential to the cultural and religious traditions of the country.

Keywords Genetic disease · Birth defects · Rare disorders · Sultanate of Oman

Introduction

Oman is situated in the South East of the Arabian Peninsula along the east coast of the Arabian Gulf. It has its borders with United Arab Emirates to the north, Saudi Arabia to the west and Yemen to the south west (Fig. 1).

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Oman is the second largest territory in the Arabian Peninsula with an area of 82,000 square miles and a coastline length of 1,300 miles.

After the accession of His Majesty Sultan Qaboos Bin Said in 1970, Oman opened the doors wide to the modern world after a long period of decline, debt and restrictions. Since 1970, progress has been extremely rapid. Schools, roads, hospitals, electricity and telecommunications have been brought to the remotest regions. Oman's income from oil is smaller than that of most of its neighbours in the Arabian Peninsula. Other sources of income come from fisheries, agriculture, industry and tourism.

The Sultanate of Oman is administratively divided into five regions and four governorates with 61 Wilayats. These regions are the following: Ad Dakhliyah, Ash Sharqiyah, Al Batinah, Adh Dhahirah and Al Wusta, and the governorates are as follows: Muscat, Dhofar, Musandam and Al Buraymi governorates. The regions of Ash Sharqiyah and Al Batinah have each been further subdivided into two health regions.

Demography and health indicators

The total population size of Omani nationals is 1,967,180, and the rate of natural increase is approximately 24 per 1,000 per year. Oman has a young population, about 11.58 and 36.2 % of the population are under 5 years and under 15 years, respectively, and only 3.7 % are 60 years and over (Fig. 2).

More than a quarter (28.1 %) of the total Omani population are females in the reproductive age group (15–49 years) according to the General Census of the Population conducted in 2007 (Ministry of National Economy Statistical Data). The fertility rate of Omani women was estimated from 1993 census data to be 6.9 but it has declined to 3.56 according to the 2003 census and has further declined to 3.13 during 2007.

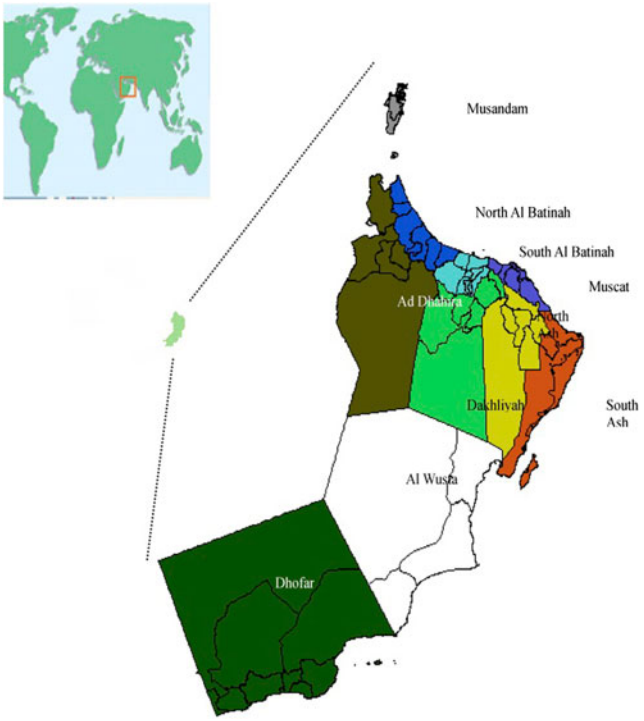

Fig. 1 Map of Oman. Oman divided into heath regions and governorates

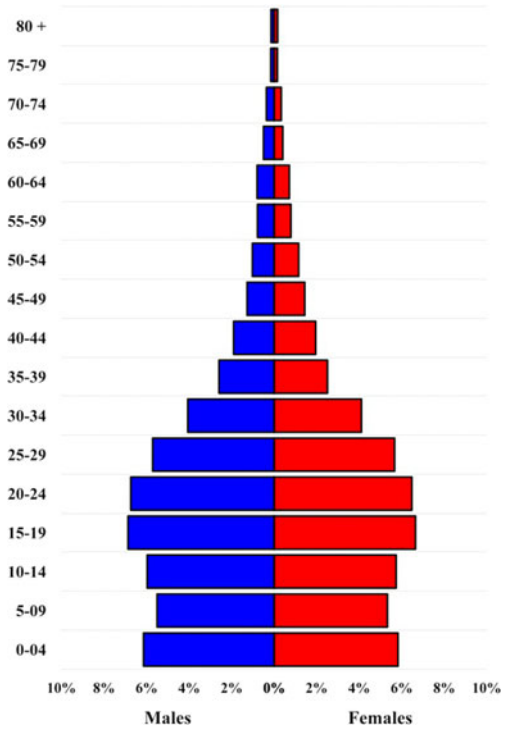

Fig. 2 Population pyramid of the Omani nationals 2010 (males in *blue*; females in *red*)

The crude birth rate was estimated to be 2. The Ministry of Health (MoH) provides free of charge health services to Omani nationals. Primary care is a first point of consultation for nationals provided in 200 health centres. It includes outpatient curative services, health promotion and health education. Secondary care is provided in 50 hospitals with nearly 5,000 beds. Ten regional hospitals provide specialised care in their corresponding health region. Tertiary care is available in four dedicated National Referral Tertiary Care Hospitals and the Sultan Qabus University Hospital. More than 30 directorates for health affairs of the MoH are responsible for the development and implementation of health policies such as family and community health, school health, communicable disease surveillance and control, non-communicable disease surveillance and control, health education, public health, hospital affaires, nursing affaires, community participation, nutrition, primary health care, environmental health, quality and patient safety and others.

Over 95 % of deliveries take place in government hospitals while vaccinations coverage in Oman is 95 %. Fortification of the flour with folate, commercial oils with vitamin A, and salt with iodine is regulated by the MoH.

Consanguinity and population structure

The custom of consanguineous marriages in Muslim communities is deeply rooted in Arab culture, and the balance of opinion in the Middle East still remains in favour of consanguinity irrespective of increased risk of autosomal recessive diseases, congenital malformations and mental retardation (Alwan and Modell 1997; Bittles 1989; Bittles 2003; Al-Gazali et al. 2006).

Consanguinity data were collected on 60,635 Omani couples of childbearing age, which represented around 20 % of the total female population of childbearing age or 32.3 % of married women in Oman in 1996 (Rajab and Patton 2000). In terms of its coverage of the population, this study is one of the largest and most comprehensive so far conducted (Table 1).

The findings showed that 56.4 % of the sample were in consanguineous marriages. However, more recent data suggest that there is a reduction in the frequency of consanguineous marriages particularly in the urban areas of Oman.

Oman has a unique population structure with preservation of rural tribal communities and their original places of residence. A tradition of tribal organisation and a Sheik's leadership of the tribe is still preserved and directed towards justice and care of those in need. Family and tribal pedigrees have great importance and command respect in the Arab culture. The inclusion of the tribal name in national identity cards and medical records creates favourable circumstances for linking medical conditions with the tribe (Ministry of Health Annual Health Report 2010; Rajab and Patton 1999a).

Table 1 Consanguinity figures in Omani population (Rajab and Patton 2000)

Coefficient of inbreeding is defined as the probability that the individual will haven at a given locus, two genes identical by descent from a common ancestor. The amount of consanguinity in a population is expressed as the average inbreeding coefficient (0.0198).

Type of union	No. of couples studied, % of total	Coefficient of inbreeding
Double first cousins	2,945 (4.8 %)	0.006
First cousins	10,205 (16.8 %)	0.0104
First cousins once removed	1,575 (2.6 %)	0.0008
Second cousins	7,186 (11.8 %)	0.0018
Marriages within the same tribe	12,459 (20.4 %)	0.0008
Unrelated	26,525 (43.6 %)	–
Total	60,895 (100 %)	0.0198

Congenital and genetic disease burden

Centralised notification of birth defects and genetic conditions is currently being developed in Oman. However, there is a wealth of data on genetic diseases available through publications (Tadmouri et al. 2008; Rajab 2010; Rajab and Patton 2012) and the MoH information system. In 2008, the MoH reported that 39 % of perinatal deaths in hospitals were caused by malformations and genetic diseases.

Autosomal recessive disorders

A recently completed population-based study (Rajab et al. 2013, in preparation) confirmed that autosomal recessive disorders are by far the commonest of the genetic disorders and remain the major contributor to childhood mortality, morbidity and handicap in Oman. The complexity of dealing with autosomal recessive disorders is that they constitute a large number when a great variety of rare disorders are put together.

More than 600 rare genetic disorders have been published so far (Tadmouri et al. 2008; Teebi 2010; www.cags.org.ae). A number of new genetic diseases and genetic variants have been described in Omanies (Rajab 2010; Rajab and Patton 2012).

Various groups of genetic disorders have been observed such as haemoglobin disorders; inborn errors of metabolism; congenital malformations syndromes; brain structural anomalies;

Table 2 Commonly ascertained autosomal recessive diseases in the Sultanate of Oman among 420,000 live births (hospital data 1993–2002)

Autosomal recessive diseases	No. of patients born 1993–2002	Observed birth incidence
Spinal muscular atrophy (Werdnig–Hoffmann disease)	56	1 in 10,000
Congenital adrenal hyperplasia	55	1 in 10,000
Polycystic kidneys	34	1 in 12,000
Cystic fibrosis	32	1 in 15,000
Primary microcephaly	31	1 in 15,000
Renal tubular acidosis	28	1 in 20,000
Congenital nephrotic syndrome (Finnish type)	25	1 in 20,000
Nesidoblastosis	24	1 in 20,000
Apple-peel bowel syndrome	21	1 in 20,000
Zellweger syndrome	19	1 in 20,000
Metachromatic leukodystrophy	18	1 in 25,000
Congenital generalised lipodystrophy	18	1 in 25,000
Ellis–Van Creveld syndrome	18	1 in 25,000
Schwartz–Jampel syndrome	15	1 in 30,000
Bardet–Biedl syndrome	14	1 in 30,000
Robinow syndrome	12	1 in 35,000
Oculocutaneous albinism	14	1 in 30,000
Epidermolysis bullosa	15	1 in 30,000
Galactosialidosis	9	1 in 50,000
Cerebro-oculo-musculo-skeletal syndrome	9	1 in 50,000
Meckel–Gruber syndrome	9	1 in 50,000
Carbohydrate deficient glycoprotein syndrome	8	1 in 50,000
Mucopolysaccharidosis	8	1 in 50,000

neurodegenerative conditions; non-syndromic mental retardation; skeletal dysplasias; disorders involving the liver, kidneys, gut and skin; and congenital blindness and deafness.

Hospital-based data on recessive disorders frequently ascertained in paediatric practice, derived from the years 1993–2002, are presented in Table 2 (from Rajab et al. 2005). Individual genetic disorders can be often linked to tribal origin and geographical areas of tribal territories (Rajab et al. 2005; Rajab and Patton 1997).

Haemoglobinopathies and red cell disorders

The haemoglobinopathies are one of the most prevalent single gene disorders in the Middle East. At present, there are around 400 patients with thalassaemia major and around 3,000 with sickle cell disorders cared for in the Sultanate. The birth prevalence of infants with haemoglobin disorders was 3.5–4.7/1,000 (Rajab and Patton 1997; Rajab and Patton 1999b). Around 10 % of Omani nationals are carriers of the gene for sickle cell anaemia, 2–3 % carry the gene for β-thalassaemia and 45 % are carriers of the α-thalassaemia gene (Alkindi et al. 2010; White et al. 1993; Daar et al. 1998, 2000). The high frequency in some areas may reflect natural selection due to advantage for survival, in the heterozygous state, against malaria and also to genetic drift in small isolated populations.

The other red cell abnormality that is common in Oman is G6PD deficiency which is found in 28 % of males and 12 % of females (Daar et al. 1996; Alkindi et al. 2010).

Inborn errors of metabolism

There have been a number of hospital-based studies of metabolic disease in Oman (Bappal et al. 1999, 2001; Joshi et al. 2002; Joshi and Venugopalan 2007). A wide variety of metabolic disorders have been observed, e.g. disorders of amino acids, organic acids, long chain fatty acids, lysosomal storage disorders, mitochondrial disorders and metabolic endocrinopathies.

Birth defects

The prevalence of various common birth defects and trisomy 21 has been investigated and the results are presented in Table 3.

History of genetic services in Oman

In the past 30 years, Oman has witnessed remarkable social and economic growth, which is best reflected in the well-organised and efficient health care system. With these achievements, the country has had a shift in the pattern of disease. There has been a significant decrease in the incidence of communicable diseases and in the mortality and morbidity rates of infants and children under 5 years (Fig. 3). In the past, the scale of the problem of congenital/genetic disorders was hidden in the high infant mortality rate because most affected infants died without being diagnosed. At present, the majority are diagnosed and provided with the best possible treatment. As a result, the number of surviving affected children increases every year causing a considerable burden on the health care services (Alwan and Modell 1997; Rajab et al. 2013, in preparation).

Genetic services in the Sultanate of Oman were pioneered in the 1990s when individuals attempted to improve the care of children with genetic disease since many admissions in paediatric wards were affected. The registration of families affected by genetic diseases started at the same time, for health information and planning purposes.

The central cytogenetic service in the country was set up under the auspices of the MoH in the year 2000 with the equipment procured from charitable donations. It grew over the years with the introduction of skilled national personnel and presently has the capacity to perform 2,000 tests per year. The development of two molecular genetic laboratories was supported by donations from Oman LNG (Oman Liquefied Natural Gas Company). Diagnostic services for haemoglobin disorders were established in 2006 and a molecular genetics/FISH facility to support cancer care was set up in 2010.

Table 3 Published figures of birth defects and Down syndrome from Oman

No	Condition	Birth prevalence per 1,000 live births	Reference
1	Neural tube defects	1.25	Rajab et al. (1998)
	Anencephaly	0.69	Rajab et al. (1998)
	Myelomeningocele	0.45	Rajab et al. (1998)
2	Facial clefts	1.5	Rajab and Thomas (2001)
3	Hirschsprung's disease	0.3	Rajab et al. (1997)
4	Congenital heart disease	7.1	Subramanyan et al. (2000)
5	Posterior urethral valves	1 in 2,000 males	Rajab et al. (1996)
6	Down syndrome	2.9	Rajab et al. (2013), in preparation

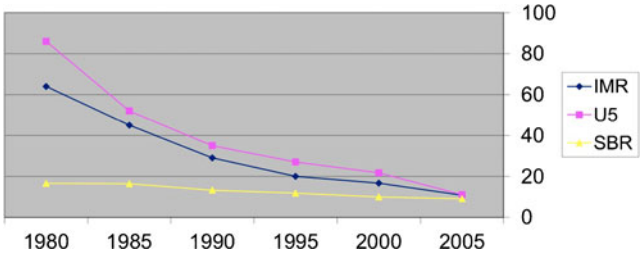

Fig. 3 Changes in mortality rates in Oman (per 1,000 live births). Infant mortality rates (IMR), mortality rates under 5 (U5) and stillbirth rates (SBR) at 5 year intervals from the years 1980-2005. Data from the Ministry of Health Information System

The first community genetic programme started in 1999 as the National Program for the Control of Genetic Blood Disorders. It operates in eight regional hospitals through regional teams providing care, genetic counselling, premarital screening and education in genetic health.

Special support for genetic services in Oman came from international bodies: the World Alliance of Organisations, March of Dimes and UK Genetic Alliance organised a national workshop in 2006 to support development of local facilities and training of national personnel. Also, World Health Organisation provided consultants to assess genetic service needs.

Oman has contributed considerably to research, in collaboration with C. Walch Laboratory at Harvard Institute of Neurology (USA), Weill Cornell College (USA), Institute of Human Genetics at Humboldt University (Berlin, Germany), Genetic Department of St-George's Hospital Medical School (UK) and Leiden University (Netherlands).

Present and future of genetic services

The main drivers for the development of medical genetic services are the increasing recognition of community needs for genetic services, the availability of new genetic information developing from the advancement of the science of genetics and the improved understanding of genetic predisposition to adult-onset disorders.

Birth defects and suspected genetic conditions seen in primary care are referred to secondary and tertiary referral centres for care and counselling.

Current genetic testing facilities within the MoH include the National Cytogenetic Service Laboratory with the Cytogenetic European Quality Assessment certification, and two molecular genetic diagnostic laboratories. The molecular genetic laboratory for haemoglobin disorders is providing services for patients with genetic blood disorders and for premarital counselling clinics. The Laboratory for Haematological Cancer Care performs molecular tumour markers and minimal residual disease diagnostics with FISH, sequencing, PCR and RT-PCR.

Premarital genetic counselling clinics for haemoglobin disorders are operational in the regional hospitals and in primary health care in the regions with a high prevalence of haemoglobin disorders. The National Program for the Control of Genetic Blood Disorders includes improvement of care, premarital screening, counselling, health education and data collection starting from the year 2000. The programme had served as a model for the prevention of other genetic disorders.

At the Sultan Qabus University in Muscat, haematology–immunology, biochemistry and various other fields are emerging as genetic research facilities. Tandem MS diagnostics have been established at the Sultan Qabus University Hospital and are to be expanded to the national service of newborn screening.

A number of biochemical and genetic diagnostic tests are currently being purchased from laboratories abroad. However, the situation is changing. New facilities are being developed and a number of Omani specialists who have been trained and have graduated abroad are now returning possessing new service skills and new research ideas. The interest in genetic research and application of genetic testing for numerous medical conditions is increasing among Omani professionals. Research activities in paediatric genetics, oncology, cardiogenetics, nephrogenetics, neurogenetics and genetics of deafness have been initiated and are expanding in other medical fields.

The health policy of the MoH includes education and training for health professionals with focus on national human resources. The MoH Health supports education in wide range of disciplines, locally and overseas, at both undergraduate and postgraduate levels. Great attention has been given to capacity building and training of Omani nationals in genetic technologies and the latest diagnostic techniques. The Ministry of Higher Education and the MoH provide scholarships for training abroad.

The MoH in the Sultanate of Oman wishes to reap the potential benefits of the genomic advances for the Omani population and recognises the urgent need for the local application of genomic knowledge. The MoH acknowledges the need for a national biomedical infrastructure and therefore is presently developing policies for translating genomic knowledge into public health care. A new National Genetic Center equipped with modern diagnostic and educational facilities has recently been established in the capital (Muscat).

The challenges for the National Genetic Center involve developing the infrastructure, tools, resources, guidelines and procedures leading to the establishment and provision of quality genetic services, competence in testing for a variety of genetic disorders and research.

Neonatal screening is currently provided for hypothyroidism. The preferred policy for genetic service provision in the Sultanate of Oman is providing community genetic services which combine the skills of community medicine and medical genetics.

Emerging new technologies, like pre-implantation genetic diagnosis, maternal serum screening and premarital diagnostic chips, are planned to be introduced and may offer new

solutions for the prevention of the genetic diseases, thereby reducing the burden on the health care system.

However, the application of new genetic technology needs to be explained to the population and medical professionals. Strengthening genetic literacy among the population about genetic health and genetic disease avoidance is planned in the Education Unit of the new National Genetic Center. At present, the decision about interruption of pregnancy is not easily accepted by families.

National guidelines and recommendations for the provision of medical genetic services are structured along ethical guidelines of the World Health Organisation 1999.

The national strategies for the prevention and management of genetic and congenital disorders are taking into account local needs, priorities and resources. At the present time, the Oman policy for prevention of genetic disorders includes early identification and prevention of genetic risk including the avoidance of marriages between carriers of the same genetic disorder.

The current strategies are compatible with the cultural and social make up and religious beliefs of the population, and the legal system of the country. The existing national policies are embedded within a framework of Muslim Law (Sharia) which forbids the interruption of pregnancies, except for cases where the mother's life is endangered or permission have been granted by Joint Committee of Medical and Religious experts. Termination of pregnancies is considered on parental request when anomalies incompatible with life are detected.

The estimated potential for reducing the proportion of infant deaths due to congenital/genetic disorders would include provision of genetic diagnostic and preventive facilities, increasing population literacy regarding how to avoid genetic disease, reduction in premature births and improvement of antenatal care in diabetic mothers (4.8 % of pregnant mothers were diabetic in 2009). Encouraging family planning may prove beneficial as advanced maternal age is common (age over 35 years is observed in 17.3 % of pregnancies).

Respect for the traditions set up in an Islamic community and understanding the social beliefs, and psychological difficulties faced by families affected by genetic disease, are essential for planning care and prevention (Rajab and El-Hazmi 2007).

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Declaration This is the declaration that the experiments described in current paper comply with the current laws of the Sultanate of Oman in which they were performed.

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