Premarital counseling: an Experience from Bahrain

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التوعية قبل الزواج : تجربة من البحرين

شيخة سالم العريض وندى حفاظ وسميرة الصيرفي

خلاصة: أجريت هذه الدراسة لتحليل بيانات أول خمسمائة شخص تقدموا باختيارهم طالبين التوعية قبل الزواج خلال العامين 1993–1994. ولقد وجد أن 1و74% من المتقدمين لم يكونوا أقرباء لمن يزعمون الزواج منهم، بينما كان 2و23% من أقارب الدرجة الأولى، وكان . ووجد مرض الخلايا 5و1% من أقارب الدرجة الثانية. وكان الباقون من الأقارب البعيدين المنجلية في 6و1% من المتقدمين، وخلة الخلايا المنجلية في 0و13%، وخلة التلاسيمية بيتا في في 0و26%. ومن بين ثنائيات الأزواج المتقدمين للتوعية، تبين أن G6PD0و2% وعوز 1و8% كانوا معرضين لإنجاب أطفال غير أسوياء. وكان معدل القرابة بين ثنائيات الأزواج المعرضين لهذا الخطر 4و15%.

ABSTRACT The present study was conducted to analyse data of the first 500 clients who voluntarily attended premarital counseling during 1993-1994. It was found that 74.1% of clients were not related to their partner, 23.2% were first cousins in 1.6% of clients, sickle-cell trait in 13.0%, β-thalassaemia trait in 2.0% and glucose-6-phosphate dehydrogenase deficiency in 26.0%. Of the couples attending counseling, 8.1% were found to be at risk of having affected offecspring. The consanguinity rate among the couples at risk was 15.4%.

Consultations prenuptials: experience a Bahrain

RESUME La present etude a ete realisee pour analyzer les donnees relatives aux 500 premieres personnes qui not effectue une consultation prenuptiale volontairement au cours desannees 1993 et 1994. On a constate que 74,1% de ces personnes n'avaient pas de lien deparents avec leur partenaire, que 23,2% d'entre eux etaient cousins germains et 1,5% petits cousins. Les autres etaient des parents eloignes. La drepanocytose a ete depistee chez 1,6% de ces personnes, un trait drepanocytaire chez 13,0% dentre elles, un trait b-thalassemique chz 2,0% et l'anemie hemolytique enzymoprive chze 26,0%. On a trouver que 8,1% des couples quiont consulte risqaient d'avoir des enfante atteints. Le taux de consanguinite parmi les couoles arisqué s'elevait a 15,4%.

Introduction

The inherited haemoglobinopathies are a group of disorders that include thalasaemias and sickle-cell disease. These diseases are a major public health problem in the Mediterranean area, the Middle East, the Indian subcontinent, Asia, tropical Africa and the Caribbean. However, because of population flow, they are now widespread and occur in Europe and North and South America. According to the World Health Organization, the approximate estimates of affected individuals indicate that 240 million people are heterozygous for these disorders and at born annually, approximately equally divided between sick-cell anemia and Talassaemia syndromes [1,2].

The Cyprus Talassaemia Control programme has succeeded in reducing the incidence of β-thalassamia major in the country through measures such as health education, carrier screening, premarital counseling and prenatae diagnosis. This success has encouraged other countries to adopt the practice of premarital counseling. Countries or communities practising such as counseling, either voluntary or by law, are Italy and Greece for Talassaemia, the Ashkanzi Jews for Tay- Sachs Disease and some European communities for cystic fibrosis [3,4].

In Bahrain, the burden of genetic blood disorders has long been recognized, as studies have shown that 1%-2% of neonates have sickle-cell disease and the carrier state found in nearly 11% of neonates have sickle-cell disease and the carrier state is found in nearlt 11% of neonates; the β-thalassaemia rate is much lower at 2% [5,6].

In an attempt to reduce the incidence of babies born with sickle-cell disease and β-thalassaemia, the genetic clinic at the Salmaniya Medical Center initiated a premarital screening service in1985. Recognizing the importance of this clinic, the Ministry of Health decided in 1992 to expand the service and make it available as part of the general primary health care in all health center. Couples at high risk are identified, counseled and treated, and the those with an abnormal genetic history are referred to the Department of Genetic at Salmaniya Medical Center.

In the present study, data from premarital counseling clinics covering the period between 1993 and 1994 are presented.

Subjects and methods

The service was started on an expand basis in December 1992. It was preceded by an information and training course for all physicians, nurses and educators. The course included information about: common genetic disorders in the community, how to take a family genetic history, the basics and ethics of the techniques of genetic counseling, how to evaluate the risk of recurrence and the needs of the clients, how to discuss the risk and benefit burden, how to form a plan of action, giving advice and follow -up. The training course was followed by a mass media campaign on the availability of the service.

A special risk assessment sheet was designed for each sex separately. It includes information about sociodemographic data -sex, age, education, occupation, sequence of marriage, consanguinity, medical history, surgical history, infection history, history of sexually transmitted diseases, family genetic history, information on habits such as smoking, alcohol and drugs, pregnancy readiness, past obstetric history and contraception, if applicable. This is completed examination which includes measurement of height, weight, blood pressure, pulse and examination of other systems, such as the cardiovascular and respiratory systems. Investigations include a full blood count, blood group analysis, and screening for hemoglobin disorders, glucose-6-phosphate dehydrogenase deficiency(G6PD), rubella antibodies and syphilis [venereal disease research laboratory test(VDRL)]. Some cases are screened for human immino deficiency virus (HIV) and hepatitis B.

On the second visit, the results are discussed with the clinic and counseling and management are provided, such as immunization against rubella. An information booklet is given, which includes information about haemoglobinopathies, prevention of rhesus haemolytic diseases of neonates, the genetic risks associated with advanced maternal age, the effect of smoking, alcohol and drugs on conception, the effect of infection, including sexually transmitted diseases, on conception, sex education from the Islamic point of view, methods of contraception, and nutrion and its effect on conception. This educational during the screening programme as the counseller can save a great deal of time by giving people at risk written material to read and keep for future reference. The couples at risk are referred to the genetic clinic for further advice and management

Results

Of the first 500 clients who voluntarily at tended counseling during the period 1993 – 1994, the male/female ratio was 52.5/47.5 (262/238) The mean age for males was 26.5 years and females 21.9 years; the minimum age was 15 years and the maximum 45 years.

With regard to education, data on 495 clients showed that 340 (68.7%) were secondary school graduated and 15 (3.0%) primary- school educated or illiterate. Males were more likely to be primary- and secondary school aducated while females were more likely to be college educated.

Data on consanguinity revealed that 74.1% of clients were not related to their partner, 23.2% were first cousins, 1.5% were second cousins and 0.3% were distant relatives. It would be the first marriage for 97.6% of clients, the second marriage for 2.2% and the third marriage for the rest.

With regard to smoking and drinking habits, 88.5% (of 488) were nonsmokers and only 2.3% said that they drink alcohol. Normal appearance was found in 98.4% of the clients and abnormal features, such as extreme short stature, and skeletal deformity, in 1.6%. The cardiovascular system was normal in 99.8% of clients (one had a minor congenital abnormality); 11.9% (58/486) had high blood pressure. It was found that 7.8% were not immune to rubella and were in need of vaccination; all of them were females. VDRL was positive in 1.3% of clients (4/318).

Table 1 shows the frequency of blood diseases among the clients. Sickle-cell disease was found in 1.6% (8/500) of clients, sickle-cell trait in 13.0% and β-thalassaemia trait in 2.0%; the haemoglobin (Hb A2) average in β-thalassaemia was 5.6% G6PD deficiency was found in 26.0% (130/500) of clients; the male to female ratio among them was about 2:1 (86/44). Out of 161 couples who attended counseling, 13(8.1%) were at risk as both partners were carriers of the haemoglobinopathy gene. They either both had the sickle-cell trait or β-thalassaemia trait, or one partner had the sickle-cell trait and the other had the β-thalassaemia trait. Among couples at risk, only 2 of the 13 were related (15.4%).

	No.	%
Clients with sickle-cell disease	8/500	1.6
Clients with sickle-cell trait	65/500	13.0
β-thalassaemia carriers	10/500	2.0
Clients with G6PD deficiency	130/500	26.0
Couples at risk of having affected children	13/161	8.1
Consanguineous couples at risk	2/13	15.4
Nonconsanguneous couples at risk	11/13	84.6

Discussion

Because of the demographic factors and population strucure in Middle Eastrn countries, e.g. old paternal and maternal age and high frequency of counsangunieous marriages, there is a considerable need for genetic service in order to avoid misin-formation and mismanagement of counsan-guinity on genetic grounds. Premarital counseling is one of the important measures which can help reduce the incidence of genetic diseases in such circumstances [7-10].

Premarital counseling provides an opportunity to interven according to the identified risks. This intervention includes: treatment of diseases such as infections, modification of chronic disease medication to decrease teratogenic risks, vaccination, counseling regarding behavior, including those related to HIV

and other infections, nutrition counseling, advice regarding contraception or genetic counseling. The service in Bahrain is provided on a voluntary basis and clients come for counseling of their own accord. The counseling is nondirective and clints are free to act upon the advice as they see fit.

In the first tow years (1993-1994), 8.1% of couples were at risk of producing affected off sping. In the following year (1995), the rate increased, which suggests that the service was being utilized more by people at risk because they knew of the presence of an affected person(s) in their family and they went voluntarily for test family and they went voluntarily for testing. Among the couple at risk, only 15.4% were related whereas 84.6% were not. Thus, even if we advise against consanguineous marriage, this will not solve the problem of genetic blood disorders because of the high gene frequency in the population. The rates of sickle-cell trait (13%) and G6PD deficiency (26%) are similar to results in previous studies [3-6].

The World Health Organization has recommended several measures for the prevention of genetic diseases, such as health education, screening to identify individuals or prenatal diagnosis. For these aspects of prevention to be applied to population, various ethical, legal, and cultural issues have to be taken into consideration. These arise because genetic prevention affects marriage habits, choice of partners and reproductive behavior. Any campaign must be tailored to the needs of each culture, and health education must be sensitive to these consederation, even though they may affect the final efficiency of the programme [1.2].

Many of the religious leaders in Bahrain are now convinced of the benefits of premarital counseling and are advocating that it should be made a legal requirement , as long as the client is free to take the medical advice and act according to his/her decision.

Recommendations

Premarital counseling should be compulsory by low but the freedom of couples to act upon the advice should be ensured. Appropriate and simple information on human genetics should be incorporated into the school curriculum so that all students are informed of issues. The puplic should be made aware of the fact that everyone may carry an inherited disease so as to prevent prejudice and misinformation. Professionals in genetics, health education and the media can work together to increase the awareness of the adult population, for example through television documentaries on specific disease or videos to watch prior to counseling.

MOLECULAR BASIS OF β- THALASSEMIA IN BAHRAIN, AN EPICENTER FOR A MIDDLE EAST SPECIFIC MUTATION

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Bahrain is an archipelago of 36 island in the Arabian Gulf. Until the era of Islam, Bahrain was influenced by the Babylonian, Assyrian and Greek Civilizations amongst other ancient civilizations. It was also an important commercial center on the major trade routes between the East and the West. Thus infiltration of different foreign cultures and civilization through time in Bahrain resulted in a cosmopolitan blend of present day genes.

Previous studies based on phenotype analysis showed that hemoglobinopathies represent one of the major genetic disorders in the population of Bahrain revealing high frequencies for sickle cell α- thalassemia and β-thalassemia genes (1). Consequently the hemoglopathies account for the major phenotype diagnostic requests in the hospital of Bahrain.

So far no molecular characterization of β-thalassemia in Bahrain had been performed although significant amount of data was available from the neighbouring countries. Given the geographical and historical particularities of Bahrain, we would predict that the spectrum of thalassemic defects in Bahrain may differ from other Middle East populations. Thus the objective of this study is to delineate the molecular lesions leading to β-thalasseamia in Bahrain. This is an essential prerequisite for evaluating the frequency of mutations as well for establishing an efficient prevention programme which includes carrier screening, premarital counseling and eventually offering prenatal diagnosis for couples at risk of having a child with thalassemia major syndrome.

We have studied a total of 80 individuals of whom 35 are transfusion dependent β-thalassemia trait and 8 S-β-thalassemia patients. All of them are Bahraini nationals followed-up in the pediatric clinics or consultees of genetics unit of Salmanyia Medical Center, Manama, Bahrain.

The DNA was extracted from whole blood (~ 5 ml) using the standard phenol-chloroform extraction method. The technique of reverse dot blot (RDB) was used initially to screen for the six commonest Indian and Mediterranean mutauions. The nucleotide sequences of each of these normal and mutant probes as well as the experimental conditions of polymerase chain reaction (PCR) and RDB procedure wrer as described Previously (2,3). The samples which provided no relevant signal in the RDB or signal for only one allele for with β-thalassemia major were further examined by denaturant gradient gel electrophresis (DGGE) analysis as described before (4). The samples exhibiting abnormal DGGE profiles were subjected to nucleotide sequencing using the dideoxy chain termination method.

A total of 67 β-thalassemic alleles have been deciphered which comprised of 12 differen mutauions. However four different mutations, namely IVS-I3 end (-25bp) CD 39 (C→t), IVSII,5(G→C) and IVSII,2(G→C),2(G→A) accounted for more than 80% of the total studied alleles. The frequency of each of these 12 β-thalassemic alleles in native Bahrainis is presented in table 1 along with a previously published datd for four neighbouring countries. Mutations common both to the Mediterranean basin [CD39(C→ T), IVS-I-1(G→ A), IVS-II-1 (G →A), IVS-I-110 (G→ A)] and Indla [CD8/9 (+G), IVS-I-5 (G→C),CD 15 (G→A), CD 41/42 (-TCTT)] were equally represented.

The most striking observation is the unprecedent high frequency of the 25bp deletion mutant in this country, the highest ever to be observed, including in the other Middle East countries. Interestingly the second major mutation (CD 39 C→T), a major Mediterranean allele and the third one (IVSI nt 5 G→C), amajor Indian allele are most likely to have been introduced into Bahrain respectively from the West and the East.

Some of our experience RDB for screening β-thalassemia in Bahrain is of particular interest. Screening for the Mediterranean type mutations by RDB revealed an individual as homozygous for Cd 39 (C → T) mutation. Further screening for Indian type mutations by RDB gave a positive heterozygous signal for Cd41/42 (-CTTT) mutation. We were able to assign this as compound hetrozygote for these two mutations and confirmed it by nucleotide sequencing. Such atypical data a raised because the design of the oligonucleotides in RDB were such that the deleted four nucleotides in Cd 41/42 mutation destabilized the hybridization with the normal Cd 39 probe. Similarly total absence of signal with normal IVSI, 110 (G → A) probe is a feature of the cases homozygous for IVSI 3 end (-25 bp) mutation because the RDB probe is within the deleted region. However precise diagnosis of mutation can be carried easily by siz-separation of the PCR product in an agarose gel electrophoresis.

Altogether (Table 1) our data reveal that in Bahrain, the IVSI3 end (-25 bp) mutation is largely predominant (36%) the highest frequency ever to be reported for this Middle –East specific mutation. Thus Bahrain appears to be the epicenter for this mutation in the Middle-East. In conclusion, this study will be of invaluable benefit for the precise, cost-effective DNA- based diagnosis and thus for future preventive programmes.

	Bahrain	SAUDI ARABIA	KUWAIT	UNITED ARAB EMIRATES (UAE)	SOUTH IRAN
No of chromosomes	66	158	96	185	108
IVSI 3 end (-25bp)	36.1	12.9	7.3	6.5	3.7
Cd39 (C→T)	24.2	12.9	7.3	5.4	5.5
IVSI, 1(G→A)	6.1	12.9	29	3.2	13.8
IVSI, 1(G→A)	3.0	-	7.3	-	3.7
Cd44(-C)	4.5	-	1	1.1	3.7
nt-88(C→A)	1.5	-	-	-	0.9
cds8(+G)	1.5	1.07	3.1	8.6	4.6
Cd15 (G→A)	1.5	-	-	2.2	-
IVSI,110 (G→A)	1.5	26.9	-	1.6	6.5
Cd35(-C)	1.5	-	-	-	-
Cds41/42 (-TCTT)	1.5	-	-	-	-
Others	0	20.43	26.1	17.3	50

Table1: Spectrum and distribution of b-thalassemic alleles in the Middle-East

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Case presentation
Fragile X syndrome in a Bahrain Family

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ABSTRACT

Fragile X syndrome (Martin Bell Syndrome) has been the subject of wide medical interest in the past decade. We are reporting the cases in Bahraini family documented to have fragile X syndrome. For sibs and a maternal brother have mental retardation with the typical clinical and cytogenetic picture of the syndrome.

The clinical picture, prenatal diagnosis and genetic counselling pertaining to this syndrome is discussed.

Fragile X syndrome is most commonly associated with moderate or profound mental retardation in affected males and some affected females. The frequency of fragile X syndrome is estimated to be 1 in 2,400 females. It estimated prevalence among mentally retarded individuals varies according to the type of population studied. A recent report estimates it to be 3.4% in males and 2.3% in females attending special schools for the mentally retarded; while in Swedish study the prevalence was found to be 16% in a group of males with infantile autism.

In 1969 Lubs demonstrated a fragile site which is seen as a gap or break at the end of the long arm of the X chromosome (Marker X) in four males with mental retardation. The fragile sight was present in few cells only in the affected males and in normal females who are obligatory of the same X chromosome5. Subsequently, it was found that the media with less fetal calf serum, minimal thymidine and no folic acid permitted better detection of many fragile sites5.

THE CASES

A Bahraini family with ten children and unrelated parents is reported. There are eight male members, four of whom are mentally retarded. While the two daughters are normal, the maternal brother is also mentally retarded, which indicates X-linked mental retardation. Although the mother is an obligatory carrier she is physically, mentally and cytogenetically normal. There is no history of mental retardation on the paternal side of the family (fig 1).

CASE 1

He was a product of full term normal delivery at Salmanyia Medical Center born on 12-1-86. pregnancy was uneventful apart from slight vaginal bleeding. A

pgat score at birth was 7&9 at 1 & 5 minutes respectively. Birth –weight was 2900 gm, head circumference 33.5cm. No physical abnormality apart from tongue tie was detected.

On the third post-natal day he was admitted to Special Baby Care Unit for neonatal jaundice, with bilirubin of 14.7 mg/dl and he received phototherapy. He sat and crawled at one year, walked alone at 18 months and had delayed language development.
At the age of three years, he was hyperactive, irritable and uncontrollable. His head circumference, length and weight were 47 cm, and 13.5 kg respectively. Abnormal features including strabismus, open mouth, big soft hands and feet, a palpable spleen, macro-orchidism and an ejection systolic murmur were present (Fig 2). Chromosomal studies revealed fragile (X) chromosome in about 70% of cells scored from low folate cultures.

CASE 2

He was product of full term normal delivery after an uneventful pregnancy . At birth he weighed 3.1 kg, head circumference was 35 cm, chest circumference 34 cm and length was 51cm. He was described as having odd features with big mouth, big ears, brachycephaly and strabismus. He had jaundice, which was treated with phototherapy. At the age of one month he was hospitalized for chronic gastroenteritis and bronchopneumonia. During childhood he was described as hyperactive and irritable. At the age of eight years his weight was 25kg, height 118 cm with long face, macrocephaly, large ears, big feet and hands, macro-orchidism were also present (Fig 3). He was reported to have short attention span and mild mental retardation needing institution care. Chromosomal studies revealed fragile (X) in 50% of cells scored from low folate culture.

CASE 3

Figure 4 shows a thirteen year old boy, who is 50 kg in weight and 132 cm in height. His features were coarse, with long face, macrocephaly, large ears, big nose, big hands and feet and macro-orchidism. Although mildly mentally retarded, he is still attending regular school where his performance is reported to be poor. Chromosomal studies revealed fragile (X) in 20% of cells scored from low folate cultures.

CASE 4

Figure 5 shows a twenty-year-old man who is 65 kg in weight and 157 cm in height. He has prominent jaws, hypotelerism, strabismus, large ears, big nose, big hands and feet with brachydactly, and macro-orchidism.

He is also hyperactive child with attentional deficit and is now enrolled in the Hope Institute for the handicapped children. Chromosomal studies revealed the presence of fragile (X) in 10% of cells scored in low folate cultures.

Cytogenetic studies were performed for the other sibs, and all of them showed normal karytypes except the elder daughter who is carrier of the marker X, as fragile X was shown in 25% of the cells studied.

DISCUSSION

The fragile X syndrome is a common genetic condition characterized by normal life expectancy and mental retardation that affects some 80% of male and 30% of females needing special education and support from social agencies. 6,7 Approximately 25% to 50% of all cases of X-linked mental retardation are caused by this syndrom.8.9

The usual presenting syndrome is developmental delay and a family history of mental retardation. The majority of affected males have a characteristic appearance, which includes large ears, rominent forehead and jaw and large testes. In adult life there is decrease of stature involving upper limb length and upper face height with increase in jaw length, chest circumference and waist width in affected men and women. There is increase in palpebral fissure length and decrease in the inter-canthal distance. There are special dermatoglphic changes. Macro-orchidism is present in most post-pubertal manes.

Most of these patients have learning disability, attentional defects and hyperactive behavior with autistic features. A characters tics from of speech has been described by many authors. IQ in such patients ranges from 20-80, but in most instances it is in the 50-60 range. Verbal IQ is more depressed than performance IQ, but there are considerable variation as some affected males may by be completely normal physically and mentally.

Table 1 and 2 show the comparison between our cases and those reported from Australia. It was noticed by many authors that sudden unexpected infant death is frequently observes in the progeny of obligate females.

Physical Traits from Possum Checklist	Case 4
(Occurring in over 50%)	
Long face	**+**
	-
Big ears	**+**
Big hands and feet	**+**
Photosensitivity	**+**
	-
Blond hair, light skin	**-**
Multiple pigmented Nevi	**-**
Narrow bifrontal diameter	**-**
Strabismus	**+**
Macrocephaly	**+**
Soft skin	**+**
	-
Hypotonia	**-**
(Occurring in fewer than 50%)	**-**

epicanthic folds	
Patchy skin rash	-
Eunuchoidal build	+
Myopia	+
Gynecomastia	-
Hypotel0rism	+
Narrow shoulder	+
Big (broad) nose	+
Ptosis	+
Skull asymmetey	-
Genua valga	-

TABLE 2
Physical traits Found in Young Pre-Pubertal Children
Finding in Cases 1, 2& 3

Findings	Case 1	Case 2	Case 3
Puffy face	+	+	+
Narrow palpebral fissures			
- Big head relative to body	+	+	+
- High arched eyebrows	-	-	-
- Abnormal eyes	+	-	-
- Winged neak	-	-	-
- Puffy fingers	+	+	+

It was also observed that individuals with FRA X Syndrome may be at increased risk of developing cancers, especially the unusual types such as Ewing's sarcoma, seminoma, sperm granuloma, malignant ganglioma.18 Many cases of prenatal fragile (X) diagnosis have been confirmed and reported. Amniotic fluid, fetal blood and chorionic villus samples (CVS) have exhibited FRA (X g 27.3) in culture. Where fragile (X) is not present or is in very low frequencies in CVS and/or amniotic fluid cultures molecular methods by means of recombinent DNA technology can be resorted to using specific probes. 19,20 Gestational age dating by ultarsonography is recommended as early as possible.

CONCLUSION

This is a report of the first family in Bahrain with fragile X syndrome. The diagnosis is important because many members of the family will be at risk, and the possibility of prevention aiming at reduction of mental retardation through genetic counseling, prenatal diagnosis is there. Therefore we recommend genetic counseling and cytogenic studies for

all mentally handicapped, especially when there is positive family history of mental retardation and/or autism.

Genetics and Anaesthesia: Malignant Hyperpyrexia

Dr Shaikha Al Arrayed*

Malignant hyperpyrexia1 is a potentilly fatal complication of general anaesthesia. In the affected individuals Suxamethonhum and/or Halothane and other drugs can trigger a sudden rise in body temperature which unless rapidly corrected is followed by convulsion and death in 60% of cases. The reaction dose not seems to depend upon any particular anaesthetic agent nor on the type of surgery being performed. It has often developed in previously healthy individuals undergoing relatively minor surgical procedure. The tendency to develop this complication is inherited as an autosomal dominant characteristic.

Soon after induction of anaseathesia the muscles go into massive spasm, the body temperature quickly rises to a high level and the patient becomes acidotic. It is probably the cardiac effect of the acidosis which often causes sudden death.

Malignant hyperyrexia is accompanied by the following biochemical changes: serum creatine phosphlinase (CPK) reaches high level within three hours after induction of anaesthesia which is explained by muscle injury and damage; high level of serum glutamic oxalacetic transuminase (SGOT) and lactate dehydrogenase (LDH); high level of serum phosphate which results in a fall of serum calcium; and high levels of serum potassium and serum aldolase.

Denborough et al studied the family and three close relatives of a patient who had survived malignant hyperpyrexia. They were found to have a very high level of serum creatine phospokinase (CPK). Although the patient's muscles seemed normal, two of the three relatives had a mild but definite myopathy, affecting predominantly the lower muscles of the thigh. It seems that malignant hyperpyrexia develops in individuals with a myopathy which is inherited as an autosomal dominant, 4 and which may be sub clinical. Therefore, all patients with myopathy ad their relatives may be at risk of malignant hyperpyrexia (indeed this syndrome was described first in a patient with myotonia congenital).

Fortunately, affected individuals can be detected by a serum CPK estimation, all blood relatives of the patient who had malignant hyperpyrexia should be examined clinically and screened for raised scrim CPK levels. It was advised that all individuals having general anaesthesia be screened by a serum CPK estimation because the myopathy causing malignant hyperpyrexia may not be detected clinically, and a family history of this rare disorder is usually not given. Whenever serum CPK level is elevated from some other causes, the body temperature should be monitored during anesthesia so that hyperpyexia can be corrected at an early stage.

Muscle contracture tests to be the corner stone for diagnosing patients with malignant hyperyrexia, the test is not easy and it can be done only in few cenres in the world, while serum CPK can be estimated in most Medical Centres.

Whenever faced with an unexpected attack, all anaesthetic agent should be discontinued at once and Dantrolene administered by rapid IV push, starting with 1mg/kg and continue until the symptom begin to subside.5,6 It is also advised to reduce the temperature by vasodilator drugs, cool the patient, correct acidosis and any electrolyte disturbance (hyperkalaemia), and support the circulation.

ASURVEY OF PATIENTS WITH SICKLE CELL CRISIS PRESENTING TO ACCIDENT AND EMERGENCY DEPARTMENT OF SALMANYIA MEDICAL CENTER, BAHRAIN

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ABSTRACT

احتلت أمراض فقر الدم الوراثية في عام 1990 المركز الثالث بين عشـــرة أمراض اســـتدعت مراجعة مركز السـلمانية الطبي . وقد تمت دراسـة وتقويم الأعراض السـريرية والمراحل العلاجية ل 200 شـخص بحريني مصاب بفقر الدم المنجلي ممن راجعوا قسم الطوارئ بمستشفى السلمانية خلال نوبة انسداد الأوعية الدموية . كما أن عدد الذكور فاق عدد الإناث بنســبة 1 : 2 وإن 60% من هؤلاء ضــمن المجموعة العمرية (30-15) عاما وتظاهر معظم (86%) بألم الأطراف يتبعه ألم في البطن وآلام جســمية متعممة. وقد اســتجاب المرضــى للعلاج بالاماهة ومسـكنات الألم المخدر أو بالعقاقير المضـادة للالتهاب غير السـيترودية وقد غادر (83%) منهم قسم الطوارئ. ويبدو أن المرضى البحرينيين مصابين بنوع متوسط من فقر الدم المنجلي.

وبائيات الشذوذات الخلقية في دولة البحرين
شيخة سالم العريض

أجريت هذه الدراسة لمعرفة معدل وقوع الشذوذات الخلقية في البحرين. وتمت دراسة إحصائيات وزارة الصحة خلال السنوات العشر من 1980 إلى 1990 ووجد أن معدل وقوع هذه الشذوذات في البحرين يبلغ 7و2% من المواليد الأحياء. وتم بحث كل شذوذ بمفرده وقورن بمعدلات حدوثه في البلدان الأخرى كلما أمكن. وتبين أن معدل شذوذات الجهاز الحركي كان أعلى المعدلات (28و2 في الألف) وجاءت من بعدها شذوذات الجهاز البولي (13و2 في الألف) بينما بلغ معدل حدوث الاضطرابات في الصبغيات 9و0في الألف.

This study was carried out in order to find out the incidence of congenital in anomalies in Bahrain. Statistics of the Bahrain Ministry of Health for 11 years from 1990 were studied. The overall incidence rate of congenital anomalies in Bahrain was found to be 2.7% of live births. Each anomaly was studied separately and compared with the incidence in other countries, whenever possible. It was found that anomalies of the musculoskeletal system have the highest incidence if chromosomal disorders was 0.9 per 1000.

Epidemiologie des anomalies congenitales a Bahrain
Cette etude a ete relisee afin de determiner l'incidence des anomalies congenitales a Bahrain. Les statistiques produites par le Ministere de la Sante de Bahrain sur une periode de 11 ans de 1980 a 1990 ont ete examinees. On a trouve que le taux global de l'incidence des anomalies congenital a Bahrain s'elevait a 2,7% des naissances vivantes. Chaque anomalies a eteetudiee et son incidence a ete comaree avec celle d'autres pays, Chque fois que possible. Cette etude a montre que l'incidence la plus elevee etait celle concernant les anomalies du systeme osteo-articulaire et musculaire (2,28 pour 1000), tandis que l'incidence des anomalies chromosomiques s'eleit a 0,9 pour 1000.

Introduction

Because of the decline in fatal infectious disease, in the near future congenital abnormalities will become one of the major causes of infant mortality in Bahrain, as is the case in developed countries.

Methods

Deliveries in state hospital constitute more than 80% of the deliveries in the country; the rest of the deliveries are conducted at home or in private hospitals. The statistics of the Ministry of health for 11 years (1980-1990) were classified and analysed to find out the incidence of each anomaly separately. The classification of congenital malformations presents certain difficulties, as other investigators in this field have found. The following classification has been adopted to maximize the information available[7].

Every malformation was classified, ac-cording to the system, as follows:

1. central nervous system
2. cardiovascular system
3. musculoskeletal system
4. genitourinary system
5. gastrointestinal system
6. respiratory system
7. chromosomal disorder.

This covers all the abnormalities that were diagnosed in the delivery suites immediately after birth, together with cases that were diagnosed by a pediatrician during the first year of life. However, the statistics may not represent the actual number of cases [7}, because of underdignosis and underreporting of some types of malformations on account of the following:

• Lethality of these disorders, causing death before birth or before diagnosis is made.
• Impossibility of diagnosis of certain disorders that manifest themselves with the functional development of the infant, e.g. mental retardation, eye and ear abnormalities.
• Difficulty of diagnosing internal organ abnormalities as a compared with external organs.

Result and discussion

Table 1 shows the number of deliveries and the incidence of congenital anomalies each year, together with the overall incidence.

Table 2 shows the incidence of these diseases every year, as well as the average incidence.

Table incidence of congenital anomalies in Bahrain, 1980-1990

	No. of birth	No. of abnormal cases	Percentage
1980	10097	86	0.9
1981	11248	159	1.4
1982	11248	148	1.3
1983	11633	161	1.4
1984	12254	189	1.5
1985	12394	230	1.9
1986	8544	355	4.2
1987	9809	463	4.7
1988	9978	489	4.9
1989	10063	348	3.5
1990	10230	248	2.4

Overall incidence 2.5%

Table 2 The annual incidence (per thousand births) of each anomaly

Anomaly	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	Averag incide
NTD	2.18	1.01	1.24	1.46	1.14	1.21	0.54	0.49	0.42	0.44	0.35	0.95
CHD	0.49	2.03	2.22	1.63	2.53	2.5	0.53	0.75	0.90	0.58	0.38	1.32
Respiratory	-	-	0.26	0.34	0.16	0.24	0.07	0.08	0.04	0.03	0.05	0.12
Cleft palate	0.39	0.55	0.53	0.52	0.73	0.81	-	-	0.25	0.07	0.05	0.35
Gastrointestinal	0.59	1.02	0.98	1.03	0.98	2.02	0.50	0.66	0.66	0.24	1.27	0.90
Genitourinary	0.89	3.69	3.02	2.41	2.36	3.87	0.93	1.27	1.33	0.90	0.65	1.93
Undescended testicle	0.37	1.29	0.89	0.69	0.73	1.53	0.35	0.46	0.37	0.18	0.27	0.65
Hypospadias	0.39	2.03	1.24	1.03	0.82	1.13	0.16	0.49	0.50	0.45	0.13	0.76
Chromosomal	0.79	1.01	0.89	0.77	1.14	1.13	0.42	0.45	0.79	1.06	0.20	0.79Mu
Musculoskeletal	1.78	3.50	2.49	3.00	3.75	4.03	0.90	0.89	0.90	1.06	0.47	2.07
TEV	0.59	2.03	-	1.20	1.22	1.05	0.39	0.42	0.32	0.39	0.18	0.71

NTV=Neural tube defects
CHD= Congenital heart defects
TEV= Talipes equinovarus

Central nervous system

The incidence of neural tube defects (NYD), which include anencephaly, spina bifida and encephalocele, was found to be 0.95 per 1000, which is considence. Low incidence. The incidence of NTD in the United Kingdom (in certain parts of Wales, Ireland and Scotland) is as high as 4-8 per 1000. in general, most NTD are of multifactorial inheritance[4].

Cardiovascular system

Table 2 shows the overall incidence of congenital heart defects to be 1.32 per 1000 in Bahrain. In the United Kingdom the incidence is 8.14 per 1000. the cause of the low incidence here is under diagnosis and not merely rare occurrence. More of these malformations are development of the infant. The malformation of great vessels is underreported because usually it can be diagnosed only at autopsy. The majority of cardiovascular system anomalies have a multifactorial mode of inheritance [5].

Musculoskelatal system

The anomalies involving this system are the most common of all anomalies. The overall incidence was found to be 2.07 per 1000.The most common category of these is talipes equinovarus (TEV), which had an incidence of 0.87 per 1000.

Genitourinary system

The incidence was found to be 1.93 per 1000, which ranks second in frequency after musculoskeletal disorders. The most frequent types found were un descended testes (0.65 per 1000) and hypospadias (0.76 per 1000). The reasons for this may be the easy diagnosis of these disorders in comparison with the diagnosis of kidney abnormalities.

Gastrointestinal system

The average incidence of anomalies involving this system was 0.90 per 1000. In 1985 the incidence was 2.02 per 1000 . The incidence of cleft palate and lip was found to be 0.35 per 1000[8].

Respiratory system

We found that the incidence of anomalies involving this system was 0.12 per 1000. The same was noticed in other studies(0.2 per 1000) [7]. Due to the lethality and difficulty of diagnosis of this anomaly, this is usually an underestimation.

Chromosomal disorders

Chromosomal disorders had an incidence of 0.79 per 1000. The most common category was Down syndrome. In 1984 the incidence was 1.14 per 1000, compared to the international incidence of 1.4 per 1000.

Conclusion

We found from our study that the incidence of congenital malformations in Bahrain falls within the world range of 2.5-6%, even for individual anomalies[4]. It is thought that the majority of such anomalies have multifactorial origin, caused by the joint action of a genetic liability (polygenic inheritance) and environmental factors. The recurrence risk depends on the number of affected individuals in the family, the serverity of the disorder and the sex of the index case. For an isolated case

The recurrence risk varies between 1% and 7% depending on the type of malformation that occurs in more than one member in the same family can have at least four causes: teratogens, an inherited chromosome abnormality, multifactorial inheritance and Mendelian inheritance [8]. The first of these may be established by taking a careful history of the pregnancy, and the second by chromosomal analysis. However, to ascertain whether two affected sibling or an affected parent and affected child reflect multifactorial or Mendelian inheritance we need to collect data from a large number of the members of the affected family [9].

The above frequencies are an underestimation since not all congenital malformations can be detected at birth or shortly thereafter. Some may not be diagnosed in the first year. In other studies, researchers have found that they diagnosed 43% of

malformation at birth and 82% during the first 6 months[9].

Incidence of cystic fibrosis in Bahrain

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ABSTRACT

التكيس الليفي هو مرض وراثي متعدد يتم توريثه بصبغات متنحية مؤديا إلى مرض رئوي مزمن ونقص في الأنزيم البنكرياسي, واضطراب في الشوارد السكرية. ويعتبر هذا المرض سائد بين العرق القوقازي المنحدر من العرق الأوروبي.
وتعود دراسة المراجعة هذه إلى بحث مكثف لهؤلاء المرضى عن طريق المعلومات السريرية وسجلات المستشفى في مركز السلمانية الطبي وذاك بهدف تحديد نسبة الإصابة بالتكيس الليفي في البحرين.
يحتوى التقرير على 27 إصابة مؤكدة بالتكيس الليفي لأطفال ولدوا بين عام 1987 و1994 وقد تأكد التشخيص من وجود نسب عالية لشوارد الصوديوم والكلورايد السكرية (>70mml/L الإصابة نسبة بلغت.) خلال هذه الفترة إصابة واحدة بين كل 7700 وقد تم تشخيص جميع الحالات خلال السنة الأولى بعد الولادة.
كما تم تشخيص 60% من الحالات خلال الثلاثة شهور الأولى. بلغت نسبة الذكور إلى 13/14(1:1)..
وبلغت نسبة العلوص العقي (16%) . أما نسبة الوفيات في فترة ما بعد الولادة(60%). كما باغت نسبة التزاوج بأبناء الخالات والعمات والعموم والأخوال بين هذه العائلات نسبة (63%).

Cystic Fibrosis (CF) is a hereditary multi system disease transmitted as an autosomal recessive, leading to chronic pulmonary disease, pancreatic enzyme deficiency and abnormally high sweat electroytes. It is considered predominantly a disorder of Caucasians of European descent. The following study refers to an intensive retrospective search for patients with cystic fibrosis from clinical data, hospital record in Salmanyia Medical (SMC), with the aim of determining the incidence of cystic fibrosis in Bahrain. The survey included 27 confirmed cases of cystic fibrosis born during the period 1978-1994. diagnosis was established by sperence of a high sweat sodium and chloride (70 mmol/1). The mean incidence during this period was found to be one in 7,700, all cases were diagnosed during the first year of life, and 60% were diagnosed in the first three months of life. Male and female ratio was found to be 14/13 (1:1). The incidence of meconum ileus was 16%. Mortality in the neonatal period was 60%. First cousin marriage rate among these families was 63%.

Introduction

The State of Bahrain consist of a group of islands with a total area of approximately 695.26 square kilometers. Kilometers. It is roughly half-way down the Arabian Gulf. It has a population of 519,000 (medium projection for 1992), approximately 36% of the population is non-Bahraini. The overall crude birth rate is 26.7% per 1000, and the infant mortality rate is 20.5% per thousand of newborns1. Cystic fibrosis is the most frequent lethal genetic disease among white Caucasian children. The commonest syndrome is a triad of chronic lung disease, pancreatic insufficiency, and elevated sweat electrolytes. The disease was first described in 1936, and its prevalence among Caucasian in Europe

and North America is estimated between 1 in 1600 to 1 in 2000, it reported to be very rare amongst American Blacks (1in 17,000) and Orientals (1 in 90,000)2-8.

The first Arab child with the disease was documented by Salem from Lebanon in 1962 9. Recently cases were reported from Iraq, Kuwait, Palestine and Jordan. Saudi Arabia and Bahrain. But the incidence in the Arab population is still unknown 10-16. This study is an attempt to find the incidence of cystic fibrosis in Bahrain. It is a retrospective study which include 17 years review case notes of patients diagnosed for cystic fibrosis from SMC, which is the main hospital in Bahrain with a bed capacity of nearly 700.

Patients and Methods

This survey included all cystic fibrosis cases born in Bahrain in the years 1978-1994 and registered in the record department in SMC. The survey included statistical information on the births, date of confirmed diagnosis, date of death where applicable , sex, nationality, family data including consanguinity and affected sibships, clinical picture including meconeum ileus, and information about investigation and treatment. All the data were confirmed from the original medical record for each patient. The clinical diagnosis of cystic fibrosis was confirmed by a sweat chloride test. The mean incidence of cystic fibrosis in Bahrain was calculated indecently for each year from the ratio of the number of children born in each year who were ascertained to have CF to the total number of live births in that year.

Results

The survey included a total of 27 patients (14 male/13 females) born between January 1978- and December 1994 and confirmed to have cystic fibrosis. The series included 13 families each having one affected child and 7 families each having , two affected children. Thirteen of those families had history of early child hood deaths(28 infants) these cases were not included in the study as they were not confirmed to have CF. the minimum incidence of CF was found to be one in 7,700 over the 17 years period (table 1). All these patients were Bahraini except two, one was Saudi the other Syrian.

The sex ratio was found to be M/F 1:1 (14:13), all patients were diagnosed within the first year of life, and 60% were diagnosed by 3 month of age. The consanguinity rate was high among the parents (80%). First cousin marriage accounted for 63% of the total (Fig 2). Average birth weight was 1.5 kg. Six out of 27 (22%) had sickle cell trait one patients had sickle beta thalasaemia and 98% of patients had glucose six phosphate dehydrogenase deficiency. Mean hemoglobin concentration was 9.8 gm/dl. Meconium ileus was reported in 4 of the 27 patients giving an overall incidence of meconeum of 15% in patients with cystic fibrosis. The most common pathogens found in the sputum were pseudomonas, Kelebsiella and Candida. Table 2 shows the common signs and symptoms found in these patients. The mortality rate was60% as only eleven patients are still alive. The eldest patient is now nine years old.

TABLE 1
Incidence of Cystic fibrosis in Bahrain
Between 1978 and 1994

Year	No. of birth	No. of cases	Incidence per Thousand
1978	9,398	22	¼,700
1979	9,395	0	0
1980	10,097	0	0
1981	11,248	1	1/1,100
1982	11,248	2	1/5,600
1983	11,633	3	1/3,900
1984	12,254	2	1/6,100
1985	12,394	1	1/12,000
1986	893	2	1/6,400
1987	12,699	3	¼.000
1988	12,555	0	0
1989	13,611	1	1/13,600
1990	13,370	1	1/13,000
1991	13,229	3	¼,000
1992	13,874	2	1/7,000
1993	14,234	3	¼,700
1994	13,941	1	1/13,000
Total	208,663	27	1/7,700

TABLE 2
Clinical picture & Complications Observed
In Cystic fibrosis Cases in Bahrain
Between 1978 and 1994

SIGN & SYMPTOMS	NO.	PERCENT
Failure to thrive	**18**	**66%**
Pneumonia	**7**	**62%**
Hypochloraemic alkalosis	**12**	**44%**
Anaemia	**10**	**37%**
Malobsorption	**10**	**37%**
Oedema	**6**	**22%**
Meconium ileus	**4**	**16%**
Hydrocoele	**2**	**7%**

Pneumothorax	**2**	**7%**
Bleeding diathesis	**2**	**7%**
Inguinal hernia	**1**	**3%**

Discussion

From this study the incidence of CF in Bahrain is estimated to be 1/7,700. this represents a minimum incidence for Bahrain. Not accounted for in this estimate are undiagnosed patients, patients who died before diagnosis and patients with milder forms of the disease who may not be diagnosed until later in life. Until a widespread screening programme is established for CF, it will not be possible to determine the actual incidence of this disease in Bahrain or elsewhere. Warwick 1980 has proposed that the actual incidence of cystic fibrosis may be tow to three times greater than the minimum incidence. We found that the consanguinity rate was high among the families studied. First cousin marriages accounted for 63% of the total as compared to 21% in the general population. This is consistent with an autosomal receive inheritance pattern. the common presentating clinical was failure to thrive 66%, pneumonia62%, hypochloremic alkalosis 44%, and aaemia 37% (table 2).

Our study chows that the incidence of meconium ileus in cystic fibrosis is 16% which is similar to other studies, as earlier reports describe the incidence of meconium ileus in a range from 7-25% of CF subject 19. Sixty percent of CF patients died (16 patients) and (70%) of these died before the first year of life (11 patients). While 11 are still alive. Pneumonia in the first place as a cause of death which is expected 20-21. these patients were treated by using chest physiotherapy, Salbutmol, Hydrocortisone, Panox capsules 10% Propylene glycol, and vitamins and different types of antibiotics.

Conclusion

The minimum incidence of CF in Bahrain is 1/7,700 and the mortality rate is high. Registration for theses cases together with molecular genetic studies to identify the defect causing the disease in our population is needed. Early diagnosis and management together with early genetic counseling may improve the outcome for CF patients.

Book review

Control of hereditary diseases. Report of a WHO Scientific Group. World Health Organization, Geneva 1996 (Technical Report Series, No. 865)

It is difficult to review a publication about genetics because of the extraordinary pace at which new concepts are being introduced. One can appreciate the considerable effort the authors have expended in writing this report. It contains a great deal of information, as well as recommendations on how to integrate genetic services into a community's general health services. The publication of the report is timely. Many developing countries are beginning to recognize how genetic disorders are responsible for a large proportion of infant mortality and childhood disability, and how genetic predisposition may lead to premature onset of common disorders in adulthood, which places a significant burden on health care delivery systems.

The report begins by providing an overview of the genetic basis of diseases, and a summary on molecular genetics, the human Genome Project and gene therapy. The epidemiology, management and prevention of congenital abnormalities are considered, as is the role of genetic predisposition in common disorders.

Part of the report focuses on prevention issues such as public health measures, carrier detection, genetic family studies and population screening. Costs and benefits of genetic services are compared and genetic counseling and consanguineous marriage are discussed. Prenatal diagnostic techniques and current research in fetal therapy are also considered. Genetic services in primary and secondary health care and in health education are reviewed, emphasizing the need for public health action to control genetic and congenital disorders. The final chapters include a good review of the ethical, social and legal aspects of genetic technology in medicine and provide a number of recommendations.

The authors have succeeded in covering most of what is important in the field, in a way that will appeal to a diverse audience. However, some of the statistics used in the figures are only estimated values, possibly not reflecting the real situation in each country. This

highlights the importance of performing standardized epidemiological studies in each country to obtain actual frequency figures.

The report might have given more emphasis to the importance of premarital counseling, especially in Islamic countries where the acceptability and availability of prenatal diagnosis is limited, and consanguineous marriages are common.

Greater emphasis could also have been given to preimplantation diagnosis, practice that may be more acceptable in some societies if the technical difficulties could be overcome.

Overall, the WHO report is an excellent, concise treatment of a broad subject, providing an outline of public health interventions that can be integrated into existing health care systems. It is an important work for clinicians, health workers and administrators _ useful for increasing awareness of the rapidly changing advances in the field of genetics.

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The Genetics of Sickling

By Shaikha Al Arrayed*

It is known that Bahrain is one of the countries where haemoglobinopathies (especially sickilling) form real health problems. This drains the health drastically affects family and personal life. It is essential that there is far more understanding of sickle cell disease.

The sickle cell disease patient differs from the normal human only in the structure of the haemoglobin is a tetramere with a molecular weight of 64,500. it consists of two non-alpha globin polypeptide chains, each of which has a single covalently bound haem groups. Each of the four haem groups is made of an iron atom within a protopotphyrin ring.

In sickle cell disease, when oxygenated, the cells are biconcave discs like red blood cells of a normal individual. However, when they are deoxygenated, they become elongated, filamentous and sickle shaped.

Heterozygous individuals who receive the abnormal gene from one parent but its normal allele from the other, would be expected to have sickle cell trait. homozygous individuals who receive the abnormal gene from each parent, would develop sickle cell anemia. When mating occurs between two individuals with sickle cell trait, the ratio between normal children, children with sickle cell anemia is 1:2:1:

Hb S differs in its electrophoresis from Hb A. The difference lies in the protein part. The nature of the difference was found by Ingram (1957-1959). That a particular position in the amino acid sequence of the B-polypeptide chain, which is occupied by a glutamic acid residue in Hb A, is occupied by a valine resdue in hb S. If normal Hb a is written as Alpha 2 Beta 2, the structure of Hb S may be written as Alpha 2 Beta 2 6 glu→ val. And it was found to be due to a single mutational step which is the smallest unit difference in the primary structure of a specific protein.

At the chromosomes level, there are 6 globin genes coding for the 6 globin chains, Alpha, Beta, Gamma, Delta, Epsilon, Zeta. Epsilon, Gamma, Delta chains are similar to a Beta chain. While Zeta is similar to an alpha chain. There are 9 different genetic loci which code for the 6 globin genes. In addition, there are at least 3 pseudo genes which have sequences similar to other globin genes, but which differ in that they are not expressed into globin protein.

The region of chromosome 11 coding for Beta and Beta like genes (Epsilon, Gamma A, Gamma G, Delta) has been thoroughly mapped by restriction endonuclease analysis, and these genes have been sequenced.

At the DNA level, the full base sequence messenger RNA fro the polypeptide chain has now been determined. Starting from the 5 end it consists of a sequence of 50 bases which are not translated into aminoacid sequence, the intiator codon (AUG) which codes for methionine and is later removed from the polypedtide chain, the sequence of 438 bases which code in triolets for the sequence of the 146 aminoacide of the normal Beta polypeptide, the chain termination codan (UAA), a sequence which is also not translated.

The DNA base sequence is even longer because it includes two interveining sequences (IVS). These IVS in the DNA are transcribed into RNA but are removed during processing. So, they are not represented in the final messenger RNA molecule which binde to the ribosomes and serves as a template for polypeptide synthesis.
Sickle cell mutation which results in substitution of glutamic acid by valine at position No. 6 in the polypeptide chine can be attributed to a change from RNA codon GAG to GUG. This change, resulting from the substitution of A (Adenine) by U (Uridine) at position No. 20 in the massenger RNA sequence, can in turn be attributed to a mutational sequence of the gene itself. So, all the sickling phenomena is a result of a single base change at the level of DNA.

The antenatal diagnosis of sickle cell disease can be used to detect the status of the fetus early in pregnancy. The parents then know the exact condition of the fetus, whether it is normal, a carrier or diseased. Provided whith this

information, they have the right to decide whether to continue the pregnancy or not.

Fetal blood sampling: The antenatal diagnosis of sickling has been carried out by fetoscopy, fetal blood sampling and analyzing the globin chain synthesis since 1975. It requires a very specialised technique carried out in very few medical centers. It can only be done after 18 weeks of gestation and it has a 5-10%b risk of fetal mortality.

DNA analysis of amniotic fluid cell : a) By using HpaI endonuclease. In 1978 Kan and Dozy described polymorphism located extremely close to the Beta globin gene on chromosome 11. the DNA was digested with restricted endonuclease HpaI, Beta globin gene was contained in a fragment of DNA 7.6 kilobase in length. We expect the person with Hb A to have only the 7 or 7 Kb fragments, while persons with sickle cell trait will have the 7 Kb and 13 Kb fragments. Those with sickle cell disease will have only the 13 Kb fragment.

b) By using mst II endonuclease. It was mentioned that Hb S results from a single base mutation from an A to a T. this base change happens to occur in the middle of a recognition site for the restriction endonuclease Mst II. This enzyme recognizes the sequence CCTNAGG (N is any base) in the normal Beta globin chain. Mst II normaly cuts 5 to the B globin gene and at the GAG codon to generate a 1.1 Kb fragment. The base change from A to T destroys the recognition site resulting in a larger fragment of 1.3 Kb. Therefore, Mst II can be used to diagnose sickle cell anemia directly, and we can expect to see the 1.15 Kb fragment in the AA genotype. The 1.35 Kb fragment in the SS and both the 1,15 Kb and the 1.35 Kb fragment in the HbAS.
Chorionic villa biopsies and the first trimester diagnosis of the sickling 8. Dr. J.M. old developed a method of extraction of a small amount of fetal DNA from chronic villi biopsies which can provide a first trimester (8-10 weeks) antenatal diagnosis by DNA analysis. The DNA was best prepared from a fresh chorionic villi biopsy or one that had been quickly frozen and transported in dry ice. This DNA is then subjected to endonuclear Mst II for analysis.

From this we can see that the genetic clinic has a major role to play in preventing this disorder. It's aim is to provide genetic counseling to all those who need it. Carry out prenatal diagnosis. Administer the new technology in investigating and treating this disorder. Perform new born screening and carrier detection. And increase the awareness of the public regarding methods to avoid bringing sick children into their families and the community.

EDITORIAL

Genetics, Epidemiology and Ethics.

Shaikha Salim Al Arrayed, MBChB, DHCG, PhD*

The human genome project is a $3 billion global project. The goal is to map and sequence 100,000 genes that make up each individual. This project is already transforming health care regardless of specialty.

Genetic factors contribute to nearly every common disease. New genes linked to specific conditions are discovered and reported every day. We are bombarded by this genetic information through the media, the Internet, support groups and advertising agencies.

Worldwide, according to world health organization, about 5% of children are born with hereditary disorders, and 40% of adults are genetically predisposed to common diseases during their lifetime.

In developed countries congenital and congenital disorders account for 25% of deaths under the age of one. An estimate of 250 million people, or 4.5% of the world population, carry a potentially pathological haemoglobinopathy gene. Prevalence varies from under 0.1 births per thousand in some parts of the world to more than 20 births per thousand in parts of Africa and Asia.

More than 9,000 single gene condition have been identified. Some are more common in certain ethnic groups or geographic areas due to certain demographic and cultural factors, such as maternal age group or the prevalence of cousin marriages.

By implementing the new genetic approaches, it is expected to reduce the mortality and disability caused by genetic diseases. About 50% of congenital abnormalities, 10% of inherited diseases and 2% of congenital abnormalities, 10% of inherited diseases and 2% of chromosomal disorders can be treated or prevented.

Among the new techniques described will be Gene therapy the introduction of a gene sequence into a cell with the aim of modifying the cell behavior, either to correct a genetic mutation, or to destroy a cell, or to modify susceptibility to diseases.

Before the end the century genetic screening and counseling will become major components of the both public health and individual medical care. This includes prenatal diagnosis, newborn screening, carrier screening, forensic screening and susceptibility screening.

Soon, we will be able to predict a patient's risk for a disease by using genetic information encoded on a small and inexpensive chip. This new information is forcing new fundamental changes in our view about health and disease, and in our practice of medicine.

Now we are asking, what is the disease? And how can we treat it ? Soon, we will be asking why the disease occurs in an individual at a specific time? How health can be restored in that individual? Answering these questions can help to maintain health and prevent disease. This can produce a change in medical taking.

The patient will be viewed not as a case, but as an environmental and development causes has developed a disease. As it is known now, that all genetic disease have a genetic base that involve many genes interacting together, and interacting with the environment.

Controversies arise over issues such the ethics of genetic testing, gene therapy and cloning . All physicians should be aware of these ethical problems, and the damage that can be caused by misusing or misunderstanding the genetic information 2,3.Human dignity and well being are at the center of these ethical, legal and social issues. It is recommended now that genetic services should be available to all patients. Adequate information should be ensured before testing. Appropriate, non –directive counseling should be offered. equality of access should be provided, respecting the self- determination of those tested.

Genetic data must not be used to stigmatize or discriminate. It should b e used for the advantage of the patients and family. Information should kept confidential and should not be given to a third person such as insurers or employers, without the consent of the person tested.

At this stage, all physicians need to understand genes and genes interactions in order to manage and counsel patients with common disease, hypertension, asthma, diabetes, and rheuatios arthritis etc.,

For this reason, integration of the new genetic knowledge into routine practice is needed. Unfortunately , few are prepared for this revolution, and current educational efforts are inadequate in this respect. This why some universities in USA are developing new genetic curriculum. This is to combine teaching of genetics, epidemiology and ethics in one curriculum.

These new ways of thinking about illness need to be incorporated into all medical education for future physicians. Continuing educational programs are essential for all health care personnel. We need to prepare the future physicians and health care personnel to meet both the preset and future challenges of new genetics5.

CHROMOSOMAL ABNORMALITIES IN 500 REFERRED CASES IN BAHRAIN

SHAIKHA SALIM AL ARRAYED, MD, PHD*

Objective: Study the incidence and pattern of major chromosomal abnormalities in a Bahraini population suspected of having chromosomal abnormality on the basis of physical and /or development clinical features.

Design: Cytogeneic studies were performed on five hundred patients.

Setting: genetic clinic, Salmaniya Medical Center, Bahrain during the period from 1984-1991.

Main Outcome: 134(27%) patients had abnormal karyotype, 97(19%) patients had numericalities and 37(7%) had structural chromosomal abnormalities. The majority of patients (66%) with numerical abnormalities had trisomy 21, 4% had trisomy 13, and 4% had trisomy 18. cases of X chromosome abnormalities were found in 13% of the abnormal cases, while 12% were having abnormality of other chromosomes.

Coclusion: this study demonstrates the spectrum of chromosomal abnormality in Bahrain but not the prevalence of these abnormalities in the country as it was only performed on a small number of patients. Bahrain Med Bull 1996; 18 (1): 2-4

It is well known that too many or too few copies of genes can upset the normal process of development. These abnormalities result from gross imbalances in the number and action of genes. A general rule is that the greater the imbalance, the more severe is the abnormality. Some imbalance is sufficiently small to have almost no effect on development, while other larger ones are lethal and may lead to death of an embryo or a child at an early age 1-5.

Singh in 1977 investigated 451 referred cases suspected in South Carolina, USA of having chromosomal abnormalities, due to physical and/or developmental abnormalities, and he found changes in 28.8%. in a comparable study, Verma in 1980 investigated 57 referred cases from New York, USA and found chromosomal abnormalities in 27.2% of these cases, while Shah in Ahmedbad in India studied 205 referred cases and reported 39.58% (Table 1).

Table 1
Abnormal karyotypes in referred cases

	Year	*No of cases*	*% of chromosomal abnormalities*
Sing et al	1977	451	28.8
Shah et al	1990	205	39.58
Verma et al	1980	357	27.2
Present study	1992	500	27.0

The present study describes the frequency and the incidence of major chromosomal abnormalities in a Bahraini population suspected of having chromosomal abnormalities on the basis of physical and/or developmental clinical features.

METHODS

Patients were referred to the Genetic Clinic from the Pediatric Clinic, gynaecology Clinic and Medical Clinic, Salmaniya medical Center, Bahrain, during the period between 1984-1991. The majority of cases were suspected of having chromosomal abnormalities because of abnormal clinical features such as mental retardation, dysmorphic features or multiple congenital abnormalities, ambiguous genitalia etc. In case of gynaecology patients, couples with foetal loss, delayed puberty and primary or secondary amenorrhoea were the basis of referrals. Blood samples were collected in heparinised bottles and send to JSPS Cytogenetic Laboratory, London, United Kingdom where conventional karyotyping and fragile Xstudies were performed as appropriate.

RESULT

Of the 500 patients investigated 134 (27%) patients showed abnormal karyotypes and 366(73%) showed normal findings. Of the abnormal karyotypes there were 97(19%) patients with numerical abnormalities and 37(7%) patients with structural abnormalities.

Some patients had combined abnormalities of more than one chromosome. The incidence of individual chromosome abnormalities was as follows: abnormalities of chromosome 21 was seen in 86 patients, of chromosome 13 in 7 patients, of chromosome 18 in 5 patients, of sex chromosome in 19 patients, and of other chromosomes in 16 patients. The type of chromosome aberration in Down syndrome patients was as follows: 86 (97%) patients with triosomies and 3(3%) with translocation.

Table 2 shows the rare structural abnormalities.

DISCUSSION

In the present cytogenetic survey, the observed frequency of chromosomal abnormalities was the same as reported earlier by Singh in 1977 from South Carolina and by Verma in 1980 from New York, USA.

Down syndrome forms the majority of patients in this series and its incidence of 1.4/1000. Again, the majority (97%) of the Down syndrome patients were trisomy, while 3% were translocation cases. According to different surveys, trisomies occur on 92.5% to 95% of the cases. It results from non-disjunction during meiosis in one of the parents and is correlated with advanced maternal age, while cases due to translocations are not. Translocation can either appear de novo in the newborn, or be transmitted from one of the parents. It is

interesting to find in this survey a three year old girl with the rare karyotype of 47, XX, +21/47, XX, +12, +r(22) and with clinical features of Down syndrome. Both parents are above 40, and both have normal karyotype. The child had ring chromosome 22.

Some studies suggest that the distal part of the long arm of chromosome 21, and especially the band 21q22 is responsible for the characteristic phenotype of down's A great variety of biochemical markers have been investigated in trisomy 21. the first gene localized with certainty was that of superoxide dismutase 1 (SOD 1). This gene has been assigned to band 21q22.1 and as a result of the trisomies gene dosge effects are observed. The enzymatic activity of SOD 1 is increased by a ratio of 3:2 in trisomy 21 and decreased by half in monosomic patients with and 21q22.1.

Table 2

Patients with rare abnormal karyotype

No	*Age (yrs)*	*Sex*	*Karyotype*	*Phenotype*
1	3	f	46, XX,+21 74,XX-2122+r22	Down's syndrome features
2	NB	M	47,X, -4T(4:13) (q35:q220 MAT	Micrognathia, undesended testis, polydactyly all limbs, hepatosplenomegealy
3	8	F	46,XX Sex DEL 17P	Mental retardation, obesity, brochydactyly, congenital heart disease
4	6	F	46,XX DEL (9) (P22> PTER)	Mental retardation, speech defect, syndromes, anteverted nares
5	7	M	46, XY, DEL(21) (q1212> PTER)	Microcepha, growth and mental retradtion, underceconded testis
6	7	M	46, XY, DEL(8) (q23:q24.1)	Marasmic, inguinal hernia, mental retardation, Café-au-lait spot
7	3	F	46, XX, T(6-10) (q15:q21-20)	Microcephaly, developmental retardation

Patient with a mild clinical picture of Down's syndrome was found to have mosaicism (46,XX/46,XX, +21). Mosaics are individuals with two or more genetically different cell population. They are observed in 2.7% of case of trisomy 21. Down's syndrome children with mosaicism are less severely retarded when compared to non-mosic trisomic cases3.

Down's syndrome has recurred in one family who had two affected children. The mother was 21 year old and these were her first and second children. Both parents' karyotypes were repeatedly studied and found to be normal. In this

family it is possible that the mother is a mosic, although she is mentally normal, with upward slanting eyes.

Trisomy 13 was present in 4% of the abnormal cases. The major features of trisomy 13 are microphthalmia, harelip and polydactyly. A high proportion of these zygotes are eliminated as spontaneous abortions. All our patients died either immediately after birth or during the first year of life 10.11.
Trisomy 18 was present in 4% of the abnormal cases. The sex ratio of patients shows an excess of females and it is lethal3. Turner's syndrome (XO) was identified in three girls, with gonadal dysgenesis. Embryos with 45, X are very prone to be aborted.

Sex chromosome aneupresent in 3% of our numerical abnormalities, 2% of them had XYY, and 1% had Klinefelter Syndrome (XXY). Non-disjunction at the first meiotic division of the mother is believed to the chief mechanism of origin.

We also found cases of discrepancy between the karyotype and the sex phenotype, with cases of XY females being diagnosed in early childhood because of the ambiguity of the genitalia. One of these cases reached puberty and was married for 6 years before she was diagnosed during investigation of her infertility. Ambiguity in the appearance of the external and /or internal genitalia, with or without ambiguity in the secondary sex characteristics can be due to a considerable number of different mechanisms.

Some of 46, XY women with pure gonadal dysgenesis are the result of the loss of the testis determining factor (TDF) on the Y chromosome in the majority of XY women with pure gonadal dysgenesis, a female or somewhat eunuchoid habitus and normal or above normal height is found. There is primary amenorrhoea, streak gonads and infantile or sometimes relatively normal appearing external and internal female genitalia. Secondary sex characteristics particularly breast development are poor and the oestrongen is low and gonadotrophin is high.

Families aggregation of XY gonadal dysgenesis has been documented. Therefore the existence of an autosomal recessive gene causing gonadal dysgenesis is regarded as established.

CONCLUSION

This study shows the significantly high rate of chromosomal abnormalities found in referred population, which demonstrates the importance of cytogenetic evaluation in patients who have abnormal clinic features. It also shows that chromosomal studies are mandatory in most mentally retarded children.

In Bahrain

By Shaikha Al Arrayed*

ABSTRACT

This study was carried out in order to find the incidence of congenital anomalies in Bahrain, we studied the statistic of the ministry of Health for 8 years from 1978 to 198. we found that the incidence rate of congenital anomalies in Bahrain is 20%. We studied each anomaly separately and compared it with the incidence in other countries whenever possible, together with the mode of these disorders as known from literature1,2,3. we found that anomalies of the musculoskeletal system have the highest rate (2.8 per thousand), following that, the genitourinary system (2.5 per thousand) and chromosomal disorders (0.9 per thousand). We also noticed that the anomalies are o f increasing frequency.

Due to the decline in fatal infectious diseases, congenital abnormalities will, in the near future, be one of the major causes of infant mortality, as is the case in developed countries. We studied the congenital anomalies during the last eight years to find the incidence of these diseases in Bahrain. We did not attempt to differentiate between the major and the minor anomalies, i.e. major anomalies, those malformations having a detrimental effect on either the physical function or social acceptability of the individual, in contrast to minor malformations which have neither medical or cosmetic consequences for the patient.

METHODS

Deliveries in the M.O.H hospitals from more then 80% of the deliveries on the island. These statistics of the m.O.H for the past eight years were classified and analysed to fined the incidence of each anomaly separately. The problem of classification of congenital malformations presents certain difficulties, as other investigators in this field have found. The following classification has been adopted which maximizes the information available.

Every malformation was classified according to the system as follows:

1. **Central nervous system.**
2. **cardiovascular system**
3. **musculoskeletal system**
4. **Geniourinary system**
5. **Gastrointestinal system**
6. **Respiratory system**
7. **eye.**
8. **Ear.**
9. **Skin.**
10. **miscellaneous.**

This covers all the abnormalities which were diagnosed in the delivery suites immediately after birth, together with cases which were diagnosed by a pediatrician during the first year of life.

The statistics may not represent the actual number of cases, due to under diagnosis and under reporting of some types of malformations due to the following:

1. Lethality of these disorders, causing death before birth or diagnosis is made.
2. Impossibility of diagnosis of certain disorders which manifest themselves with the functional development of the infant, e.g. mental retardation, eye and ear abnormalities.
3. Difficulty of diagnosing internal organ abnormalities as compared with external organs.

RESULTS

Table 1. Shows the number of deliveries and the incidence of congenital of congenital anomalies each year.

Incidence of Congenital Anomalies

years	No. of Birth	No. of Abnormal Cases	Incidence
1978	9398	68	7.24
1979	9985	120	12
1980	10097	86	8.5
1981	11248	159	14.13
1982	11248	148	13.16
1983	11633	161	13.8
1984	12254	189	15.4
1985	12394	230	18.5

Table II

No. of Anomalies per Year

TYPE	1978	1979	1980	1981	1982	1983	1984	1985
NTD	17	20	22	11	14	17	14	15
CHD	4	14	5	22	25	19	31	31
RESP	0	0	0	0	3	4	2	3
CLEFT	4	6	4	6	6	6	9	10
GASTRO	8	8	6	11	11	12	12	25
GENETO	10	25	9	40	34	28	29	48
UNDESEDED	3	10	4	14	10	8	9	19
HYPOSPADIUS	3	8	4	22	14	12	10	14
CHROM	4	11	8	11	10	9	14	14
MUSCLESK	17	22	18	38	28	35	46	50
TEV	7	8	6	22	0	14	15	13

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TABLE III

INCIDENCE OF EACH NAOM ALU PER YEAR

TYPE	1978	1979	1980	1981	1982	1983	1984	1985
NTD	17	20	22	11	14	17	14	15
CHD	4	14	5	22	25	19	31	31
RESP	0	0	0	0	3	4	2	3
CLEFT	4	6	4	6	6	6	9	10
GASTRO	8	8	6	11	11	12	12	25
GENETO	10	25	9	40	34	28	29	48
UNDESEDED	3	10	4	14	10	8	9	19
HYPOSPADIUS	3	8	4	22	14	12	10	14
CHROM	4	11	8	11	10	9	14	14
MUSCLESK	17	22	18	38	28	35	46	50
TEV	7	8	6	22	0	14	15	13

Table 2. shows the actual numbers of these disease every year.

Table 3. shows the incidence of these diseases every year together with the overall incidence.

DISCUSSION

We noted the following:

1. CENTRAL NERVOUS SYSTEM

The incidence of neural tube defects (N.T.D) which include; anencephaly, spina bifida and encsidered to be within the low group. The incidence of N.T.D. in the United Kingdom, in certain parts pf Wales, Ireland and Scotland is as high as 4-8 per thousand. Moat of the N.T.D. are of multifactorial inheritance.

2. CARDIOVASCULAR SYSTEM

Table 3. shows the overall incidence to be 1.6 per thousand in Bahrain. In the United Kingdom the incidence is 8.14 per thousand. The cause of the low incidence here is due to under diagnosis of these disorders and not due to the rare occurrence. More of these malformations are diagnosed later in the development of the infant. the malformation of great vessels are under reported because most of them can only be

diagnosed at autopsy. the majority of cardiovascular system anomalies have a maltifactorial mode of inheritance.

3. MUSCULOSKELETAL SYSTEM

The anomalies involving this system are the most common of all anomalies. The average incidence was found to be 2.8 per thousand. It is of increasing frequency as in 1985 the incidence was 4.1 per thousand. We found that the most common category of these is the talipes equinovars (T.E.V) which had the incidence of 0.96 per thousand. The incidence of T.E.V. in the literature is 0.5 – 1.0 per thousand.

4. GENITOURINARY SYSTEM

The incidence was found to be 2.5 per thousand which comes second in frequency only to musculoskeletal disorders. The most frequent types that were found were undescended testes, 0.86 per thousand and hypospadias, 0.97 per thousand. The reason for this may be the easy diagnosis of these disorders in compatison with the diagnosis of kindly abnormalities. It was noticed that these disorders are increasing in frequency, in 1985 the incidence was 3.9 per thousand.

5. GASTROINTESTINAL SYSTEM

The average incidence of amoralities involving this system is 1.1 per thousand. The incidence was 2.17 per thousand. The incidence of cleft palate and lip was found to be 0.6 thousand. In Europe it is 1.22 per thousand.

6. RESPIRATORY SYSTEM

we found that the incidence of the anomaly involving this system is 0.13 per thousand. The same was notice in other studies, 0,02per thousand6. due to the lethality and difficulty of diagnosis of this anomaly, this is usually an underestimation.

Chromosomal disorders had the frequency of 0.91 per thousand. The most common category was Downs syndrome. In 1984 the incidence was 1.14 per thousand, the international incidence of this disorder is 1.4 per thousand9.

We found from our study that the incidence of congenital malformations in Bahrain falls within the world range, even for individual anomalies. We noticed that most of them are of increasing frequency. The majority have a malt factorial origin, caused by the joint action of a genetic liability (polygenicinheritance) and environmental factors. The recurrence risk depends on the number of affected individuals in the family the severity of the disorder and the sex of the index case. For an isolated case the recurrence risk varies between 1%

and 7% depending on the type of malformation. The malformation that occurs in more than one member in the same family can have at least four causes8: teratogens, an inheritable chromosome abnormality , multifactoral inheritance and mendelian inheritance. The first of these can be established by carefully taken history of the pregnancy, and the second by chromosomal analysis. However, to ascertain whether two affected siblings or an affected parent and affected child reflect multifactorial or mendelian inheritance we need to collect data from a large number of the members of a family10.
The above frequencies are an underestimation since not all congenital malformations could be detected at birth or shortly thereafter. Some may not be diagnosed in the first year. McIntosh et al. found that they diagnosed 43% of malformations at birth and 82% during the first 6 months10.

CONCLUSION

From our study we found that the incidence of congenital malformations in Bahrain lies within the world range of 0.57% - 4.93% 4. that they are of increasing frequency, and that anomalies of the musculoskeletal system had the highest rate. Many of these anomalies create major problems for the family, society and the health services. That is why we recommend the following:
To register properly and monitor all congenital malformations in order to initiate treatment as soon as possible. To provide the parents with genetic counseling before another pregnancy is started. genetic counseling is essential in these cases so that the parents will know the risk of having another affected baby, the ways of avoidance, and, even for the low risk group, alleviation of anxiety about further pregnancy 5,11,12.

CASE PRESENTATION

Bardet-BiedlSyndrome in a Bahraini Family

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Bardet-Biedl syndrome (BBS) is a rare autosomal recessive disorder characterized by five cardinal signs: retinal pigmentary degeneration, obesity, hypogonadism, mental retardation and polydactly.1,2 In this review, we are reporting the first family in Bahrain with BBS. Two members of the family are affected, they manifest the typical signs of BBS.

THE CASES

A Bahraini family with eight sibs, six males and two females, has been investigated. Two of the males are affected with BBS, the others are normal. The parents are first cousins and there has been no previous family history of the same disorder in both sides of the family for at least three generations.

CASE 1

This 25-year-old male patient is short (163 cms in height) and very obese, weighing 160 kg at the time of the investigation (fig 1). He had polydactyly in both hands and left foot which was excised at the age of twenty. He developed severe pain at the excision site of the toe and had another operation for the excision of an extra metatarsal bone. he had a pilonidal sinus which was excised but developed a fistula which requited fistulectomy.sigmoidoscopy showed normal mucosa with no polyps. he had poor vision especially at night with visual acuity was 6/36, in the right and left
eyes(with no error of refraction).

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Fundus showed narrow retinal vessels, especially the arterioles with moderate tapetoretinal degeneration in mid periphery and slight pallor of optic disc. He was diagnosed as having retinitis pigmantosa (RP) (Fig 2). He also complained of difficulty in hearing. Examination of sexual characteristics reveled a very small phallus but normal hair distribution, and no urinary symptoms. His blood pressure, pulse rate, respiration and hematological and biochemical investigations were within normal limits. Chest X-rays showed cardiomegaly and increased vascular marking. Abdomanal ultrasound showed a large liver with normal Abdomanal organs.

CASES 2

Mentally retarded, this 18-year-old male patient is short in stature (161 cms in height) and obese, weighing 148 kg at the time of the investigation (Fig3). He had polydactyly in both hands and feet which was excised in early childhood. He had poor vision and was diagnosed as having retinitis pigmantosa. His visual activity, as measured by Catfordmethod, was 6/60 in both eyes (refraction-4.00 in the right eye and-3.00 in the left). Fundus examination showed narrowed retinal vessels, especially arterioles, very mild tapetoretinal degeneration in mid periphery (Fig4). Examination of external genitalia

revealed a small phallus; his secondary sexual characteristics revealed hypogonadism as evidenced by scanty hair growth in the face and body.

DISCUSSION

BBS can be detected usually in childhood or early adolescence. It is thought to result from an autosomal excessive gene. The prevalence rate of this syndrome is 160,000 with a primary sex ratio of one. Pigmantary retinal degeneration occurs in 90% of those patients 3-6 with never loss of peripheral and central vision as well as pigmentry changes in the fundus.the age at which the degenerative retinal changes begins varies widely; approximately 75% of those who have Pigmantary changes are legally blind by the age of 20 and 87%by age of 30 years. Night blindness may be the presenting sign. Electroretinnopathy shows the pattern of tapetoretinal degeneration. Early detection can be facilitated by performing electroretinogram (ERG) in offspring and younger siblings of patients with RP. The finding of subnormal or extinguished ERG have been documented in as early as 7 months old babies.

Generally, obesity in BBS has its onset in infancy or early childhood and progresses with age. Some degree of mental retardation is found in 86% of patients with this condition.1.7 Digital anomalies include syndactly with or without polydactyly and may occur on any or all limbs. Short and broad fingers and toes may occur .1 Both of our patients have shown hypogonadism, delayed or incomplete pubertal development, as well as a wide variety of genital defect including small phallus, bifid scroum, hypospadias, and cryptorchidism as expected of patients with BBS.

Endocrine disturbances are not frequent but include diabetes insipidus, tall and short stature and rarely abnormal glucose tolerance. Renal abnormalities are frequent. Cardiovascular defects are common. Other associated defects include anal atresia, progressive nerve deafness.

The prognosis is good, and life span is good if no cardiac or renal abnormality is expected, if these are present, then prognosis depends upon severity of associated complication.

CONCLUSION

We recommend the establishment of a proper genetic registry for all Bahraini families with positive history of retinitis pigmentosa for early diagnosis and treatment of those family members with BBS and to provide them with the necessary genetic counselling at the appropriate time.
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