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CLINICAL STUDY

The most encountered groups of genetic disorders in Giza Governorate, Egypt

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Abstract: This study presents the prevalence, relative frequency, and analysis of genetic diseases/malformations in 73 260 individuals. Cases included were ascertained from: Pediatric outpatient clinics of two governmental hospitals and two primary health care centers (PHCCs) in Giza Governorate; Neonatal intensive care unit (NICU) in the selected hospitals and Outpatients Human Genetics Clinics (NRC). 62 819 persons visited the outpatients clinics of selected hospitals and PHCCs in Giza governorate. Out of these persons 731 cases (1.16 %) proved to have known genetic disorders or malformations. 7755 neonates were delivered in the selected hospitals. Out of these neonates 666 newborns entered NICU and 3 % (20 neonates) of them had genetic or congenital disorders. Also, 2686 patients were ascertained from the Human Genetics Clinics, NRC. The overall parental consanguinity rate among the 3417 diagnosed cases was 55 %, ranging from 29.5–75 %. The study showed a high prevalence of genetic/malformation disorders among Egyptians, with frequencies comparable to other Arab populations *(Tab. 4, Ref. 25)*. Full Text (Free, PDF) *www.bmj.sk.*
Key words: genetic disorders, classification, frequency, consanguinity, Egyptians.

In general, genetic diseases are relatively prevalent among the Arab population, and are a significant cause of morbidity and mortality (Teebi and Teebi, 2005) (1). The incidence of congenital malformations among Egyptians ranges from 1.16 to 3.17 % (Temtamy et al, 1998) (2). This is probably due to a high consanguinity rate (20–40 %) among Egyptians (3, 4).

A comprehensive classification system is necessary for the genetic diseases in order to provide a framework to scientifically study the etiology, pathogenesis and treatment of diseases. In addition, such system gives clinical geneticists a way to organize the health care needs for their patients.

Available classification systems for various disorders were reviewed, to determine which classification to follow. We revised classifications adopted by Ismail (5), Rimoin et al (6), ICD--10 – CM (7), and ICF (8). However these classifications were based on the etiological diagnosis, pathological diagnosis, phenotypic diagnosis and/or the mode of inheritance. Therefore, we established our own classification of genetic disorders, as a modification of the above mentioned classifications. The main purpose of our classification was to include four major descriptive categories (axes), that geneticists consider to identify different genetic disorders. These axes are the phenotypic axis, the etiologic axis, the differential diagnosis axis, and the referral axis, which includes patients seeking genetic counseling.

Our primary objective was to detect patients with genetic diseases and to estimate the prevalence of genetic diseases among the examined Egyptian patients in certain governmental clinics. This procedure, combined with a neonatal examination and increasing physician and public awareness of the genetic disorders, will have a positive impact on the overall health status of the community as well as on the psychological and financial aspects.

Subjects and methods

Cases included in this work were ascertained from:
- Pediatric Out-patients clinics of two governmental hospitals (Boulak El-Dakrour & Imbaba hospitals) in Giza Governorate.
- Outpatients clinics of two primary health care centers (El--Giza & El-Talbia PHCCs) in Giza Governorate.
- Neonatal care units (NICU) at the selected governmental hospitals in Giza Governorate.

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– Out-patients Human Genetics Clinics, National Research Centre (NRC).

A preparatory phase during the initial 4 months period included an extensive training (theoretically and clinically) for participating physicians (who were working in the selected places apart from the Out-patients Human Genetics Clinics at the NRC) to make them capable of identifying patients with possible genetic/malformation disorders. Clinical geneticists from the Department of Clinical Genetics, NRC, attended the chosen clinics with the trained physicians every day of the week for the period from July 2004 to June 2007. Any case with a suspected history or manifestations of genetic disorder was shown to our geneticists. He/she examined the case and if suspecting a genetic disorder, the case was referred to the Clinical Genetics Clinic, NRC, for further assessment and investigations. Also, specialized clinical geneticists examined neonates admitted to the selected NICU.

In our department, the patients were subjected to a complete personal-medical-family and developmental history, pedigree analysis and meticulous clinical examination of all body systems. Analysis of the clinical data and dysmorphic features were performed using the computer diagnostic software Data Bases (London Medical Databases, Dysmorphology and Neurogenetics: LMD version 1.0.6 (9); POSSUM version 5.7.3 (10) and OMIM site (11)). Also, a search for published literature and updated journal articles was done through navigating the various internet sites. To reach the final diagnosis various confirmation tests were done according to individual need e.g. chromosomal analysis, metabolic screening, enzyme assays, molecular analysis, psychological evaluation with IQ scoring, neuro-imaging, X-ray examination, etc..

Tab. 1. Distribution of cases attending the selected Hospitals and Primary Health Care Centers (PHCCs), number of suspected cases and number of cases with proved genetic disorder (1/7/2004–30/6/2007).

	Number of cases that attended the selected hospitals and PHCCs	Number of cases with suspected genetic disorders	Number of cases with proved genetic disorders
Hospital 1 (Bolak El-Dakrour)	37009	729	408
Hospital 2 (Imbaba)	13626	174	92
PHCC 1 (El-Talbia)	4767	166	96
PHCC 2 (El-Giza)	7417	226	135
Total & Percentage	62819	1295 (2.06 %)	731 (1.16 %)

Tab. 2. Distibution of cases according to their referral places (1/7/2004–30/6/2007).

Referral Place		Number of patients with suspected genetic disorders/ malformations that were referred to the Human Genetics Clinics, NRC	Number of patients who proved to have genetic disorders/ malformations	
			Number	%
1) Physicians, Self-referral, Universities, & Hospitals		2686	2686	100
2) Selected Hospitals & Primary Health Care centers (PHCCs)	Out-Patient Clinics	1275	711	55.8
	Neonates in ICU with genetic or congenital disorders	20	20	100
Total		3981	3417	85.8

Results

This study evaluted the prevalence, classification and relative frequency of genetic/malformation disorders in 73 260 individuals examined during the period from July 2004 till June 2007. Distribution of the cases is shown in the Table 1. 62 819 persons visited the Pediatric outpatients clinics of the selected hospitals and the PHCCs in Giza governorate. Out of these patients, 731 cases (1.16 %) proved to have genetic disorders or malformations. 7755 neonates were delivered in the selected hospitals. Out of these neonates, 666 newborns entered NICU and 3 % (20 neonates) of them had genetic or congenital disorders. Also, 2686 patients were ascertained from the Human Genetics Clinics, NRC. Out of the 3981 cases referred and examined for suspected genetic or congenital disorder, 3417 had genetic/malformation disorders (Tab. 2).

An accurate diagnosis needs a proper examination and classification of the patients. Therefore, we established an integrated classification for the genetic disorders referred to Out-patients Genetics Clinic at NRC. This classification considers the etiological, phenotypic, differential diagnosis and referral categories (axes), and is entitled "Genetic/Diagnostic/Referral Classification". It includes 18 disease groups (Tab. 3). Distribution of referred cases according to relative frequencies is shown in the Table 4.

According to this classification, the genetic counseling group represented the highest percentage (17 %) among the studied groups, followed by neurologic disorders (9.5 %), chromosomal disorders (9.3 %), genetic syndromes (8.3 %), growth disorders (8.2 %), and mental retardation and behavioral disorders (8.1 %). Neuromuscular disorders constituted 5.7 % of cases, metabolic disorders represented 5.3 % and cases with endocrinal abnormalities and skeletal disorders represented 4.9 % each of the total examined cases. Dermatological and renal disorders represented the least common causes of referral (1.1 % and 0.5 % respectively). 219 cases (6.4 %) could not be classified because their investigations were incomplete (158 patients=72.1 %) and 61 cases (27.9 %) had delayed milestones of motor and mental development for which the etiology was unknown.

The Table 3 shows that the overall parental consanguinity among the diagnosed 3417 cases was 55.9 %, ranging from 29.5–75 % according to the disease category. The highest percentage was among cases with deafness (75 %), cases seeking genetic counseling (74.3 %), metabolic disorders (72.8 %), dermatologic disorders (71.1 %), and ophthalmologic disorders (69.8 %). The lowest positive consanguinity was in the group with primary infertility (30 %) and chromosomal disorders (29.5 %).

Three hundred and nineteen patients had chromosomal anomalies, with the trisomy 21 being the most common anomaly

Tab. 3. Genetic /Diagnostic /Referral Classification of Patients (1/7/2004 - 30/6/2007).

Diagnosis	No. of Cases	Consan-guinity		Proband			No. & % of similarly affected family member(s)
		+ve Nº & %	-ve	Couple	Male	Female	
1- Genetic Syndromes	**283**	**143** ***50.5%***	**140**	**-**	**153**	**130**	**82** ***28%***
Known Dysmorphic Syndromes	196	112 (57%)	84	-	108	88	54
Multiple Congenital Anomalies not part of known syndromes	87	31	56	-	46	41	28
2- Neurologic Disorders	**324**	**224** ***69.1%***	**100**	**4**	**163**	**157**	**120** ***37%***
Developmental Brain Defects	139	102	37	-	75	64	43
Degenerative Brain Disorders	36	24	12	-	16	20	23
Ataxia / abnormal movements	20	17	3	-	8	12	8
Isolated Microcephaly	63	44	19	-	35	28	20
Neural Tube Defects	30	16	14	4	11	15	11
Epilepsies	36	21	15	-	18	18	11
3- Neuromuscular Disorders	**196**	**100** ***51%***	**96**	1	**142**	**53**	**76** ***38%***
Congenital Muscular Dystrophies	21	15	6	-	14	7	8
Congenital Myopathies	20	11	9	-	13	7	7
Duchenne Muscular Dystrophy	78	33	45	-	77	1	30
Hereditary Motor & Sensory Neuropathies	8	6	2	-	6	2	5
Muscular Dystrophy (Limb-Girdle)	12	8	4	-	6	6	5
Spinal Muscular Atrophy	56	27	29	1	26	29	21
Myasthenia Gravis	1	-	1	-	-	1	-

Diagnosis	No. of Cases	Consan-guinity		Proband			No. & % of similarly affected family member(s)
		+ ve N^{o} & %	- ve	Couple	Male	Female	
4- Mental and Behavioral Disorders	**276**	**135** ***48.9%***	**141**	**-**	**170**	**106**	**90** ***32%***
Attention Deficit Hyperacivity Disease	25	13	12	-	17	8	8
Autism	16	6	13	-	14	5	6
Fragile X Syndrome	19	6	10	-	16	-	7
Idiopathic Mental Retardation	138	77	61	-	71	67	45
Learning Disability	28	8	20	-	20	8	3
Speech Defects	50	24	26	-	33	17	21
5- Cardiovascular Disorders	**40**	**18** ***45%***	**22**	**-**	**23**	**17**	**12** ***30%***
6- Endocrinal Disorders	**169**	**86** ***50.9%***	**83**	**-**	**86**	**83**	**21** ***12%***
Diabetes Mellitus & Insipidus	4	2	2	-	1	3	3
Abnormal Sexual Differentiation							
- Female pseudoherma	32	16	16	-	-	32	2
- Male pseudoherma	47	22	25	-	47	-	7
- Hypogonadism & genital anomalies	86	40	46	-	51	36	9
7- Renal Disorders	**16**	**7** ***43.75%***	**5**	**-**	**9**	**7**	**5** ***31%***
8- Skeletal Disorders	**168**	**85** ***50.6%***	**83**	**-**	**83**	**85**	**40** ***23%***
Chondrodysplasias	64	26	38	-	39	25	20
Disorders of Bone Density	39	17	22	-	15	24	10
Limb anomalies	45	22	23	-	29	16	10

Diagnosis	No. of Cases	Consan-guinity		Proband			No. & % of similarly affected family member(s)
		+ ve N^{o} & %	- ve	Couple	Male	Female	
9- Growth Disorders	**279**	**130** ***46.6%***	**149**	**-**	**115**	**164**	**63** ***22%***
Growth Retardation	57	31	26	-	31	26	14
Short Stature (non-specific)	197	89	108	-	65	132	41
Obesity	25	10	15	-	19	6	8
10- Hematologic Disorders	**54**	**37** ***68.5%***	**17**	**-**	**34**	**20**	**15** ***27%***
Hemoglobinopathies & Thalassemias	15	8	7	-	10	5	5
Hemophilias & other disorders of hemostasis	2	1	1	-	2	-	-
Hereditary RBC Disorders	2	2	-	-	2	-	2
Fanconi Anemia	27	22	5	-	14	13	6
Leukemias / aplastic anemia	8	4	4	-	6	2	2
11- Dermatologic Disorders	**38**	**27** ***71.1%***	**11**	**1**	**18**	**19**	**19** ***50%***
12- Ophthalmologic Disorders	**53**	**37** ***69.8%***	**16**	**1**	**35**	**17**	**24** ***45%***
13- Deafness	**52**	**39** ***75%***	**13**	**-**	**28**	**24**	**23** ***44%***
14- Primary Infertility with normal Karyotype	**80**	**24** ***30%***	**56**	**1**	**32**	**47**	**17** ***21%***
Primary Female Infertility	48	13	35	1	-	47	10
Primary Male Infertility	32	11	21	-	32	-	6

Diagnosis	**No. of Cases**	**Consan-Guinity**		**Proband**			**No. & % of similarly affected family member(s)**
		+ ve **N^{o} & %**	**- ve**	**Couple**	**Male**	**Female**	
15- Chromosomal Disorders	**319**	**94** ***29.5%***	**225**	**1**	**149**	**169**	**38** ***11%***
Sex Chromosome abn. - Numerical - Structural	48 -	18 -	30 -	- -	19 -	29 -	5 -
Autosomal Chromosome abn. - Numerical - Structural	253 18	67 9	186 9	- 1	121 8	132 9	30 3
16- Inherited Metabolic Disorders	**180**	**131** ***72.8%***	**49**	**-**	**108**	**72**	**73** ***40%***
17- Environmental Etiology	**90**	**41** ***45.5%***	**49**	**-**	**45**	**45**	**6** ***6%***
Prenatal	12	6	6	-	6	6	3
Natal	29	15	14	-	12	17	1
Postnatal	49	20	29	-	27	22	1
18- Genetic Counseling	**581**	**432** ***74.3%***	**149**	**473**	**19**	**89**	**192** ***33%***
Premaital/ Preconception	222	175	47	207	7	8	90
Previous child with query genetic disorder	138	100	38	97	8	33	47
Repeated Abortions	103	59	44	79	-	24	24
Repeated IUFD/ SB / Infant deaths	118	98	20	90	4	24	31
Unclassifiable *	**219**	**118**	**101**	**10**	**114**	**95**	**32**
Total	**3417**	**1912** ***55.9%***	**1505**	**492**	**1527**	**1398**	**947** ***27.7%***

* Unclassifiable group included 158 cases with incomplete investigations and 61 cases with non-specific delayed motor and mental developmental milestones.

Tab. 4. Distribution of all referred cases according to relative frequency (1/7/2004–30/6/2007).

Genetic Disorders	Number of cases	Percentage %
Genetic Counseling	581	17.0
Neurologic Disorders	324	9.5
Chromosomal Disorders	319	9.3
Genetic Syndromes	283	8.3
Growth Disorders	279	8.2
Mental Retardation and Behavioral Disorders	276	8.1
Neuromuscular Disorders	196	5.7
Inherited Metabolic Disorders	180	5.3
Endocrinologic Disorders	169	4.9
Skeletal Disorders	168	4.9
Environmental Etiology	90	2.6
Primary Infertility with normal karyotype	80	2.3
Hematologic Disorders	54	1.6
Ophthalmologic Disorders	53	1.5
Deafness	52	1.5
Cardiovascular Disorders	40	1.2
Dermatologic Disorders	38	1.1
Renal Disorders	16	0.5
Unclassifiable*	219	6.4
Total	3417	100.0

* Unclassifiable group included 158 cases with incomplete investigations and 61 cases with non-specific delayed motor and mental developmental milestones.

(250 cases), followed by numerical sex chromosome abnormalities (48 cases).

One hundred and eighty patients had metabolic disorders, with phenylketonuria (PKU) being the most common disorder (48 cases) followed by mucoploysaccaroidoses (36 cases) and mitochondrial diseases (17 cases).

Statistical analysis

For the statistical analysis of data, the Package for Social Science (SPSS for Windows Release 10; SPSS Inc., Chicago, IL, USA) was used. For the evaluation of groups' variables, Chi square test was used. All tests were two sided and P values <0.05 were considered significant.

Discussion

The focus of clinical genetics, and thus genetic counseling, is the prediction of common, often treatable or preventable conditions. Accordingly, genetic research must first characterize the common genetic diseases in small communities (12).

Our data indicate that the prevalence of genetic/malformation disorders among hospitals and PHCCs Egyptian patients was 1.16 % (731/62 819). In a recent study of an Iranian population of Ghazvin Province, the incidence was 2.9 % (13), while another study in Kuwait documented 1.25 % of children with congenital malformations (14). Considerable variation in frequency in different populations has been reported, from as low as 1.07 % in Japan (15) to as high as 4.3 % in Taiwan (16). This wide variability could be due to the difference in population genetics. In this study the overall rate of genetic/ malformation disorders in males (1527 cases) was higher than in females (1398 cases), as M/F was 1:0.9. This finding is in accordance with the Iranian study (13).

Three percent of all neonates admitted to the NICU in this series proved to have genetic/malformation disorders. Mkandawire and Kaunda (17) reported a 7.5 % in Malawi, which is much higher than our results. The difference may be attributed again to the considerable variation in frequency between different populations in addition to the number and availability of places in NICU, the financial situation and social background of parents.

The patients that were picked-up from the non-genetic outpatients clinics, when re-examined and investigated meticulously at the NRC specialized genetics clinics, only 56 % of them proved to have genetic/malformation disorders. However, all neonates in the NICU, that were examined meticulously by our experienced geneticists, and suspected to have genetic/malformation disorders, proved to have one. This emphasizes the importance of trained physicians in picking-up and diagnosing patients with genetic disorders. Family history, meticulous examination and a proper differential diagnosis remain of paramount importance in accurate genetic diagnosis and proper genetic counseling. Al--Gazali et al (18) stated that genetic services did not cover all population in Arab countries. The authors also suggested and summarized a strategy to spread genetic services and prevent genetic diseases. This strategy may be adopted in Egypt.

The analysis of data revealed an overall parental consanguinity rate of 55.9 %. This consanguinity rate is significantly higher than the documented parental consanguinity rate among Egyptians (3, 4). The increased parental consanguinity rate among Egyptians and Arabs is considered as a risk factor for inherited disorders, especially the autosomal recessive traits (14, 18, 19).

One of the areas in the field of clinical genetics is the concept of primary prevention. It implies prevention of the birth of an affected child prior to its occurrence in any family. Primary prevention requires targeting of preventive measure(s) to the entire population or to high-risk individuals, if the latter can be identified by suitable screening strategies. Our study showed that in 27.7 % of cases, there was another affected family member, with higher percentage values in specific groups of genetic disorders. Prevention of recurrence of the disease after birth of one affected child is known as secondary prevention. This is the usual recourse available for prevention of most genetic disorders. Individuals seeking genetic counseling represented the most frequent group (17 %) in our study. Obviously, both primary and secondary prevention are cost and effort intensive activities. Increased cost-effectiveness due to better targeted interventions may be counterbalanced by the price of the new technologies and an expanding indicated population (20). A newly emerging area in the field of genetics is the concept of community genetics. It implies efforts to educate the public and (potential) patients, which should start at an early age, and must focus on what (future) health care users need for a balanced appraisal of genetic information and for optimal decision making in health promotion and health care (21).

Identifying and knowing the most common inherited disorders are the first step in planning preventive strategies for genetic/malformation disorders. According to our classification the

genetic counseling category was the commonest, followed by the neurological disorders and chromosomal aberrations, while the least common were dermatological and renal disorders. A considerable variation in the frequency of various genetic/malformation disorders has been reported (14, 18, 19). This wide variability could be due to the different methodologies and classifications of disorders used in the different studies.

Chromosome analyses were performed in cases with recognizable clinical manifestations including mental retardation, dysmorphic features, multiple congenital anomalies, primary infertility or primary amenorrhea of unknown etiology, abnormal sex differentiation and abnormal sex development. Chromosomal disorders were detected in 9.3 % of examined patients. Trisomy 21 was the most common chromosomal anomaly in our study. It represented 78 % of karyotyped cases. Down syndrome has always been the most frequent chromosomal anomaly (22, 23). Technical advances in cytogenetic and molecular cytogenetic techniques will detect complex chromosomal re-arrangement aberrations which might explain some of the undiagnosed cases in the study.

Inherited metabolic disorders (IMD) represented 5.3 % of studied cases. IMD is a complex and heterogeneous group of monogenic disorders. Clinical consequences of IMD are often severe and constitute an important cause of morbidity and mortality in clinical practice, especially in pediatrics (24). Although each disorder is individually rare, their cumulative incidence is substantial (Sanderson et al, 2006) (25). However, the most published studies have focused on special disorders or group of disorders (18, 24, 25).

Of all studied cases, 6.4 % could not be classified as their investigations were incomplete or they had non-specific delayed motor and mental development. This percentage is acceptable compared to published reports (18, 20). With technical advances of diagnostic tools and a higher compliance of patients to complete their investigations, this percentage may decrease.

In conclusion, findings of our study showed a high prevalence of genetic diseases/malformations among Egyptians with frequencies comparable to other studies in Arab population. Physicians' knowledge of genetic disorders needs to be clarified and expanded. Increasing public awareness of genetic diseases and establishment of databases for genetic disorders, together with premarital diagnosis, carrier detection and genetic counseling are important preventive measures. Establishing a genetic preventive strategy including neonatal mass screening programs is of utmost importance, especially for prevalent disorders among Egyptians.

References

1. Teebi AS, Teebi SA. Genetic diversity among the Arabs. Community Genet 2005; 8: 21—26.

2. Temtamy SA, Meguid N, Mazen I, Ismail SR, Kassem NS, Bassouni R. A genetic/epidemiological study of malformations at birth in Egypt. East Mediter Health J 1998; 4: 252—259.

3. Hafez M, El-Tahan H, Awadallah M, El-Kayat H, Abdel-Gafar A, Ghoneim M. Consanguineous mating in the Egyptian population. J Med Genet 1983; 20: 58—60.

4. Temtamy SA, Kandil MR, Demerdash AM, Hassan WA, Meguid NA, Afifi HH. An epidemiological / genetic study of mental subnormality in Assiut governorate, Egypt. Clin Genet 1994; 46: 347—351.

5. Ismail S. Genetic Diagnostic classification of patients seen in the Human Genetics Clinic, National Research Centre. Ph.D. Thesis, in Childhood Studies, Medical Department, Ain Shams University, 1996.

6. Rimoin DL, Connor JM, Pyeritz RE, Korf BR. Principles and Practice of Medical Genetics, Fourth Edition, Churchill Livingston, London, Edinburgh, New York, 2002.

7. ICD-10-CM. International classification of diseases, 10th version, clinical modification, 2003. World Web site: http://www. cdc.gov/nchs/icd9.htm.

8. ICF, 2004. World Web site: http://www.who.int/classifications/icf/en/.

9.Winter R, Baraitser M. London Medical Two Databases: Dysmorphology and Neurogenetics. Version 1.0.10. Oxford University Press. UK, 2007.

10. Possum Program, version 5.7.3 for **W**indows, Murdoch Children's Research Institute, Australia, 2006. http://www.possum.net.au.

11. OMIM. Online Mendelian Inheritance in Man. Center for Medical Genetics, John Hopkins University (Baltimore, M.D.) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, M.D.), 2009. http:// www.ncbi.nlm.nih.gov/OMIM.

12. Port KE, Mountain H, Nelson J, Bittles AH. Changing profile of couples seeking genetic counseling for consanguinity in Australia. Amer J Med Genet, 2005; 132A: 159—163.

13. Movafagh A, Zadeh ZP, Hajiseyed-Javadi M, Mohammed FM, Ghaderian SMH, Heidari MH, Barghi GR. Occurrence of Congenital Anomalies and Genetic Diseases in a Population of Ghazvin Province, Iran: A study of 33380 cases. Pak J Med Sci 2008; 24: 80—85.

14. Madi SA, Al-Naggar RL, Al-Awadi SA, Bastaki LA. Profile of major congenital malformations in neonates in Al-Jahra Region of Kuwait. East Mediter Health J 2005; 11: 700—706.

15. Imaizumi Y, Yamamura H, Nishikawa M, Matsuoka M, Moriyama I. The prevalence at birth of congenital malformations at a maternity hospital in Osaka City, 1948–1990. Jinrui Idengaku Zasshi 1991; 36: 275—287.

16. Chen CJ, Wang CJ, Yu MW, Lee TK. Perinatal mortality and prevalence of major congenital malformations of twins in Taipei city, Taiwan. Acta Genet Med Hemellologiae (Roma) 1992; 41: 197—203.

17. Mkandawire M, Kaunda E. An audit of congenital anomalies in the Neonatal Unit of Queen Elizabeth Central Hospital. One-year study period: 1st November 2000 to 31st October 2001. East Centr Afr J Surg 2002; 7: 29—33.

18. Al-Gazali L, Hamamy H, Al-Arrayad S. Genetic disorders in the Arab world. Brit Med J 2006; 333: 831—834.

19. Al-Arrayed SS. Review of the spectrum of genetic diseases in Bahrain. East Mediter Health J 1999; 5: 1114—1120.

20. Cavalli P. Genetic counseling: a medical approach. Genet Test Mol Biomarkers 2009; 13: 1—5.

21. Knottnerus JA. Community genetics and community medicine. Fam Pract 2003; 20: 601—606.

22. Al-Arrayed SS. Chromosomal abnormality in 500 referred cases in Bahrain. Bahrain Med Bull 1996; 18: 1—5.

23. Mosquera Tenreiro C, Ariza Hevia F, Rodriguez Dehli C, Fernandez Toral J, Garcia Lopez E, Riano Galan I. Prevalence and secular trend of Down syndrome in Asturias (Spain), 1990—2004. Med Clin (Barc) 2009; 132 (15): 580—584.

24. Das SK, Biswas A, Roy T, Banerjee TK, Mukherjee CS, Raut DK, Chaudhuri A. A random sample survey for prevalence of major neurological disorders in Kolkata. Indian J Med Res 2006; 124: 163—172.

25. Sanderson S, Green A, Preece MA, Burton H. The incidence of inherited metabolic disorders in the West Midlands, UK. Arch Dis Child 2006; 91: 896—899.

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