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Morbidity profile of children referred to Genetic Unit of Mansoura University Children's Hospital, Egypt

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ABSTRACT

Background: Genetic disorders remain a major cause of morbidity, mortality and handicap in Egypt. This study aims to describe the morbidity pattern of all children with suspected genetic disorders referred to a genetic unit in Egypt.

Methods: A retrospective hospital record-based descriptive study was carried out in the Genetic Unit of Mansoura University Children's Hospital, Mansoura, Egypt during a period of 13 years from 2003 up to 2015. The following data was collected for 3197 referred cases: child age at referral, sex, residence and karyotyping results.

Results: According to ICD-10 classification of congenital malformations the commonest diagnostic categories are congenital malformations, deformities and chromosomal abnormalities (79.7%) specially chromosomal malformations (73.5%) followed by endocrine, nutritional and metabolic diseases (8.6%), diseases of the nervous system (4.8%), mental and behavioral disorders (3.9%). Mucopolysaccharidosis is the most common type of endocrine, nutritional and metabolic diseases in referred cases. While mental retardation is the commonest mental and behavioral disorders; cerebral palsy and Duchenne muscular dystrophy were the commonest diseases of the nervous system. The commonest congenital malformations of the nervous system are microcephaly and congenital hydrocephalus. Achondroplasia and Osteogenesis imperfect are the most frequent congenital malformations of the musculoskeletal system. Down syndrome is the most common chromosomal abnormality (88.8%).

Conclusions: Primary prevention is the most cost effective method for prevention of these disorders. Pre-natal detection of disease should be more available. Educational efforts are needed to increase genetic literacy of the general public and healthcare workers.

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Congenital anomalies; ICD-10; Down syndrome; Egypt

Introduction

Congenital malformations, congenital anomalies and birth defects are synonymous terms used to describe structural, behavioral, functional and metabolic disorders present at birth [1]. These still remain a major cause of morbidity, mortality and handicap in Arab countries [2]. Genetic disorders can be caused by a mutation in one or multiple genes, by a combination of gene mutations and environmental factors or by damage to chromosomes [3]. The Egyptian population has a high frequency of genetic disorders. This is due to the high rates of consanguineous marriage and fertility, either early or late maternal age, lack of resources that deal specifically with genetic diseases, lack of public awareness of the significance of genetic disease, reluctance of couples to receive preconception counseling and prenatal diagnosis, religious and cultural concepts related to causation and dealing with diagnosed malformations as well as lack of public health measures directed towards prevention and control of congenital and genetic disorders [4-8].

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Analysis of the available epidemiological data clearly indicates that hereditary disorders and congenital anomalies are rapidly becoming a major public health concern in Egypt. The prevalence of congenital and genetic disorders among infants and young children in Egypt is estimated to range from 2.8% in urban areas in metropolitan governorates to 8.4% in rural areas in Upper Egypt [9]. The relative human and economic cost of these disorders are rising because of the decline in prevalence of infectious diseases and improved but expensive medical care available to affected people [10]. Because of underreporting, genetic disorders and birth defects are systematically underestimated in developing countries [11]. Genetic services available in Egypt are generally referral centers offering genetic counseling and diagnostic facilities. Despite this there is a dearth of studies about the magnitude of the genetic and congenital disorders in Egypt. There is no nationwide birth defect monitoring system. The magnitude of the problem is definitely unknown at both the community and clinic levels. Therefore this study aims to describe the morbidity pattern of all children with suspected genetic disorders referred to a genetic unit in Egypt.

Patients and Methods

This is a retrospective hospital record-based descriptive study carried out in the Genetic Unit of Mansoura University Children's Hospital, Mansoura, Egypt during a period of 13 years from 2003 up to 2015.

Genetic Unit of Mansoura University Children's Hospital is the only unit in Dakahlia governorate and one of the most important genetic centers in Egypt. The unit is responsible for diagnosis and treatment of genetic diseases, including prenatal diagnosis by clinical examination, necessary tests, and follow-up of patients. The official approval of the Hospital Director was obtained before data collection.

This study included all cases (3197) referred to the unit during the study period. Data were extracted from patient's files kept in the patient's medical archive of the hospital.

The diagnosis of congenital anomalies was based on history, clinical examination, karyotyping and other appropriate investigations. All cases were diagnosed after birth. The patterns of congenital anomalies were classified according to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) Version for congenital malformations, deformations and chromosomal abnormalities [12]. The data were collected and data was analysis using Statistical Package for Social Sciences (SPSS for windows program version 16; SPSS Inc., Chicago, IL, USA) and presented as numbers and per cents in simple frequency tables.

Results

Males were more encountered than females with ratio 1.1:1. The age of referral age of referral ranged from 1 day to 356 months with median of 8 months. None of the cases were diagnosed in the prenatal period (data not shown in tables).

Table 1 shows that according to ICD-10 classification of congenital malformations the commonest diagnostic categories are congenital malformations, deformities and chromosomal abnormalities (79.7%) specially chromosomal malformations (73.5%), endocrine, nutritional and metabolic diseases (8.6%), diseases of the nervous system (4.8%), mental and behavioral disorders (3.9%).

The most common type of endocrine, nutritional and metabolic diseases in referred cases was Mucopolysaccharidosis type I Hurler (28.3%) followed by Glycogen storage disease (19.9%) and Familial Mediterranean fever (7.8%) (table 2).

Table 3 shows that mental retardation is the commonest mental and behavioral disorders (87.2), cerebral palsy and Duchenne muscular dystrophy are the commonest diseases of the nervous system (60% and 14.8%). Postural kyphosis is commonest musculoskeletal disease (38.5). Congenital rubella syndrome and congenital cytomegalovirus infection were the commonest perinatal conditions (44.4% and 33.3%; respectively).

The commonest congenital malformations of the nervous system are microcephaly (61.9%) and congenital hydrocephalus (15.9%). Achondroplasia (20.1%) and Osteogenesis imperfect (16.2%) are the most frequent congenital malformations of the musculoskeletal system. Down syndrome is the most common chromosomal abnormality (88.8%) (table 4).

Discussion

While Egypt has shown considerable progress in the prevention and combating of infectious disease, genetic disorders remain a major problem. Genetic disorders are chronic in nature and often require lifelong management with no definitive cure [13]. Primary prevention is the most cost effective method for prevention of these disorders. Sadly, in this study all cases were referred to the genetic unit

Table 1. Diagnostic categories of referred cases according to ICD-10.

Code	Categories	Number (%)
Total		3197 (100)
D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism*	6 (0.2)
E00-E90	Endocrine, nutritional and metabolic diseases	276 (8.6)
F00-F90	Mental and behavioral disorders	125 (3.9)
G00-G99	Diseases of the nervous system	155 (4.8)
H00-H59	Diseases of the eye and adnexa**	3 (0.09)
I00-I99	Diseases of the circulatory system***	18 (0.6)
M00-M99	Diseases of the musculoskeletal system and connective tissue	13 (0.3)
P00-P96	Certain conditions originating in the perinatal period	54 (1.7)
Q00-Q99	Congenital malformations, deformities and chromosomal abnormalities	2547 (79.7)
	-Congenital malformations of the nervous system	63 (2.5)
	-Congenital malformations of eye, ear, face and neck#	18 (0.7)
	-Congenital malformations of the circulatory system##	16 (0.6)
	-Congenital malformations of the respiratory system###	17 (0.7)
	-Congenital malformations of the digestive system@	21 (0.8)
	-Congenital malformations of genital organs@@	19 (0.7)
	-Congenital malformations of the urinary system@@@	20 (0.8)
	-Congenital malformations and deformations of the musculoskeletal system	308 (12.1)
	-Other congenital malformations	193 (7.6)
	-Chromosomal abnormalities	1872 (73.5)

*Aplastic anemia
**Blindness
***14 acute rheumatic fever, 4 rheumatic heart disease
#3 congenital cataract, 3 congenital cataract, 4 congenital, 3 congenital ectropion, 3 congenitaldeafness & 2 microtia.
##10 dextrocardia, 2 ventricular septal defect, 2 patent ductus arteriosus, 1 atrial septal defect, & 1 tricuspid atresia
###2 congenital cystic lung, 3 choanal atresia, 4 congenital laryngomalacia, 4 congenital cyst of mediastinum & 3congenital tracheomalacia
@3 congenital imperforate anus, 4 congenital megacolon, 5 macroglossia, 4 atresia of esophagus, 5 congenital hypertrophic pyloric stenosis.
@@3 agenesis & aplasia of uterus, 3 undescended tests, 3 congenital absence of vagina, 3 hypospadius, 2 congenital recto-vaginal fistulas & 5 hermaphroditism
@@@2 Potter syndrome, 9 polycystic kidney, autosomal recessive, 4 ectopic kidney & 5 atresia & stenosis of ureters

after birth and none of the cases were diagnosed during the prenatal period. The concept of primary prevention implies the prevention of the birth of an affected child prior to its occurrence in the family. The application of the community genetic will help in primary prevention of genetic diseases. It implies efforts to educate the public and patient. It should start at an early age and should focus on genetic information as a health promotional measure [14].

By employing the World Health Organization International Classification of Disease, version 10 (ICD-10), it is possible to categorize the distribution of genetic disorders in this study according to disease taxonomies. The commonest diagnostic categories are congenital malformations, deformities and chromosomal abnormalities (79.7%;

Table 2. Endocrine, nutritional and metabolic diseases in referred cases. (E00-E90,).

Code	Disease	Number (%)
E25.0	Congenital adrenal hyperplasia	7 (2.5)
E28.3	Hypogoanodism	3 (1.1)
E34.8	Progeria	8 (2.9)
E66.0	Primary obesity	1 (0.4)
E70.0	Phenylketonuria	12 (4.4)
E70.3	Oculocutaneous albinism	6 (2.2)
E71.0	Maple-syrup-urine disease	2 (0.7)
E71.1	Methylmalonic acidaemia	3 (1.1)
E72.2	Hyperammonemia	10 (3.6)
E72.3	Glutric acidaemia	9 (3.3)
E74.0	Glycogen storage disease	55 (19.9)
E75.0	Gangliosidosis	5 (1.8)
E75.1	Lipid storage disease	6 (2.2)
E75.2	Metachromatic leukodystrophy	5 (1.8)
E76.0	MPS, type I Hurler	78 (28.3)
E76.0	MPS, type I Hurler-Scheie	14 (5.1)
E76.2	MPS, type Maroteaux-Lamy	3 (1.1)
E76.2	MPS, type Morquio	4 (1.4)
E78.2	Familial hypercholesterolaemia	1 (0.4)
E80.2	Porphyria	3 (1.1)
E83.0	Familial hypophosphataemia	2 (0.7)
E83.5	Familial hypocalciuric hypercalcaemia	4 (1.4)
E85.0	Familial Mediterranean fever	24 (8.7)
E87.2	Lactic acidosis	6 (2.2)
E88.1	Lipodystrophy	5 (1.8)
Total		276 (100)

MPS=mucopolysaccharidosis

especially chromosomal malformations 73.5%), endocrine, nutritional and metabolic diseases (8.6%), diseases of the nervous system (4.8%), mental and behavioral disorders (3.9%). Few cases of hematological disorders were diagnosed as most of cases could be referred to pediatric hematology clinics, not the genetic unit.

Many previous studies in Egypt reported that neurological and chromosomal disorders were the most frequent. Afifi et al, [15] in their study in cases referred to the Clinical Genetic Clinic of National Research Center of Cairo reported that neurological disorders, chromosomal disorders, genetic syndromes, growth disorders and mental and behavioral disorder were the frequent diagnoses. In cases referred to the Division of Genetics of Ain Shams University, Cairo, neurologic disorders were the most common (31.38%), followed by hematologic disorders (18.48%) and chromosomal abnormalities (11.51%) [16].

Temtamy et al, [13] concluded that in Egypt central nervous system anomalies are the most prevalent congenital malformations as reported by numerous epidemiologic studies. Another Egyptian study in Zagazig University hospital, found that the most frequent congenital anomalies were musculoskeletal system (23%), followed by the central nervous system (20.03%), musculoskeletal system (19%) and gastrointestinal system (16.02%) [17]. Tadmouri [18] concluded that just over one-third of genetic disorders in Arab individuals result from congenital malformations and chromosomal abnormalities (34.6%). These are then followed by endocrine and metabolic disorders (17.8%) and diseases of the nervous system (9.9%). However, a considerable variation in the frequency of various genetic/malformations disorders had been previously reported in different Arab and Non-Arab countries [2,19-22]. Some studies, however, recorded higher proportions of central nervous

Table 3. Mental and behavioral disorders (F00-F90), diseases of the nervous system (G00-G99), diseases of the musculoskeletal system and connective tissues (M00-M99) and certain conditions originating in the perinatal period (P00-P96).

Code	Disorder/disease (Total)	Number (%)
Mental and behavioral disorders (125)		
F79.0	Mental retardation	109 (87.2)
F84.0	Childhood autism	4 (3.2)
F84.2	Rett syndrome	2 (1.6)
F90.0	Attention deficit hyperactivity disorder	6 (4.8)
F91.0	Nocturnal enuresis	1 (0.8)
F98.0	Post-encephalitic syndrome	3 (2.4)
Diseases of the nervous system (155)		
G11.1	Friedreich's ataxia	7 (4.5)
G11.3	Ataxia telangiectasia [Louis-Bar]	6 (3.9)
G12.1	Spinal muscular atrophy 1	6 (3.9)
G12.1	Spinal muscular atrophy 2	5 (3.2)
G23.0	Hallervorden spatz disease	4 (2.6)
G24.9	Dystonia musculorum congenita	3 (2.0)
G60.0	Charcot marie tooth disease	3 (2.0)
G71.0	Duchenne muscular dystrophy	23 (14.8)
G71.0	Becker muscular dystrophy	5 (3.2)
G80.0	Cerebral palsy	93 (60.0)
Diseases of the musculoskeletal system and connective tissues (13)		
M8.1.0	Juvenile ankylosing spondylitis	2 (15.4)
M40.0	Postural kyphosis	5 (38.5)
M40.3	Flatback syndrome	1 (7.7)
M61.1	Fibrodysplasia ossificans progressive	2 (15.4)
M88.9	Paget disease	3 (23.1)
Certain conditions originating in the perinatal period (54)		
P35.0	Congenital rubella syndrome	24 (44.4)
P35.1	Congenital cytomegalovirus infection	18 (33.3)
P35.2	Congenital herpes viral infection	2 (3.7)
P35.5	Congenital viral hepatitis	2 (3.7)
P35.8	Congenital varicella infection	4 (7.4)
P37.1	Congenital toxoplasmosis	4 (7.4)

system and cardiovascular system malformations followed by gastrointestinal tract and musculoskeletal systems [23-28].

But in contrast an Iranian study [29] reported genitourinary system as the one most often affected. Other studies from Iran [30,31] and one study from India [32] showed Musculoskeletal anomalies as the commonest. A study from Pakistan [33] reported gastrointestinal defects as the commonest.

This wide variability could be due to differences in population genetics, referral pattern which depends on the awareness of health care providers about genetic diseases, different classifications used in different studies, economic situation, accessibility of genetic services and social background of the community.

We found that mucoplysaccharidosis of different types and glycogen storage disease were the most frequent endocrine and metabolic diseases among the referred cases. No case of hypothyroidism was recorded. This is attributed to the nation-wide implementation of screening program for congenital hypothyroidism since 2003 with high coverage. In a previous study in Egypt mucopolysaccharidosis was the commonest metabolic disease [16].

This study revealed that mental retardation was the most frequent mental and behavioral disorders.

Table 4. Congenital malformations, deformities and chromosomal abnormalities (Q00-Q99).

Code	Malformations/deformities (Total)	Number (%)
Congenital malformations of the nervous system (63)		
Q02.0	Microcephaly	39 (61.9)
Q03.0	Congenital hydrocephalus	10 (15.9)
Q03.1	Dandy-Walker syndrome	2 (3.2)
Q04.2	Holoprosencephaly	4 (6.3)
Q04.3	Lissencephaly	2 (3.2)
Q04.6	Schizencephaly	4 (6.3)
Q07.0	Arnold-Chiari syndrome	2 (3.2)
Congenital malformations and deformations of the musculoskeletal system (308)		
Q68.0	Congenital torticollis	2 (0.6)
Q69.0	Polydactyly	37 (12.0)
Q70.0	Syndactyly	17 (5.5)
Q73.1	Phocomelia	25 (8.1)
Q74.3	Arthrogryposis multiplex congenital	24 (7.8)
Q74.8	Larsen syndrome	3 (0.97)
Q75.0	Craniosynostosis	25 (8.1)
Q75.1	Cruozon disease	9 (2.9)
Q75.4	Treacher Collins syndrome	3 (0.97)
Q75.8	Frontonasal dysplasia	3 (0.97)
Q77.3	Chondrodysplasia punctate	2 (0.6)
Q77.4	Achondroplasia	62 (20.1)
Q77.4	Hypochondroplasia	9 (2.9)
Q77.5	Dystrophic dysplasia	5 (1.6)
Q77.6	Chondroectodermal dysplasia (Ellis-van Creveld syndrome)	7 (2.3)
Q77.8	Kniest dysplasia	3 (0.97)
Q78	Osteogenesis imperfect	50 (16.2)
Q78.8	Multiple epiphyseal dysplasia	16 (5.2)
Q79.6	Ehlers-Danlos syndrome	1 (0.3)
Q79.8	Multiple pterygium syndrome	1 (0.3)
Q89.8	Sacrum agenesis (Caudal Regression Syndrome)	4 (1.3)
Other congenital malformations (193)		
Q80.1	X-linked ichthyosis	2 (1.0)
Q80.2	Collodion baby	2 (1.0)
Q81.0	Epidermolysis bullosa	2 (1.0)
Q82.1	Xeroderma pigmentosum	2 (1.0)
Q82.3	Incontinentia pigmenti	1 (0.5)
Q82.4	Ectodermal dysplasia	5 (2.6)
Q82.8	Cutis laxa	3 (1.6)
Q82.8	Kindler syndrome	1 (0.5)
Q85.0	Neurofibromatosis	24 (12.4)
Q85.8	Sturge weber syndrome	2 (1.0)
Q87.0	Congenital malformation syndromes predominantly affecting facial appearance*	29 (15.0)
Q87.1	Congenital malformation syndromes predominantly associated with short stature**	52 (26.9)
Q87.2	Congenital malformation syndromes predominantly involving limbs***	24 (12.4)
Q87.3	Congenital malformation syndromes involving early overgrowth#	26 (13.5)
Q87.4	Marfan syndrome	7 (3.6)
Q87.8	Other specified congenital malformation syndromes, not elsewhere classified##	11 (5.7)

Table 4. Congenital malformations, deformities and chromosomal abnormalities (Q00-Q99) (cont.)

Code	Malformations/deformities (Total)	Number (%)
Chromosomal abnormalities (1872)		
Q90	Down syndrome	1663 (88.8)
Q91.3	Edwards syndrome	68 (3.6)
Q91.7	Patau syndrome	6 (0.3)
Q92	Trisomy8	9 (0.5)
Q93.3	Wolff-Hirschorn syndrome	1 (0.05)
Q93.4	Cri-du-chat syndrome	5 (0.27)
Q93.5	Angelman syndrome	6 (0.3)
Q93.8	Williams syndrome	13 (0.7)
Q96	Turner syndrome	55 (2.9)
Q98	Klinefelter syndrome	16 (0.85)
Q99.2	Fragile X chromosome	30 (1.6)

*3 Acrocephalopolysyndactyly (carpenter) Syndrome, 8 Acrocephalosyndactyly (Apert) Syndrome, 7 Goldenhar Syndrome, 7 Pierre Robin Syndrome, 1 Ritscher–Schinzel syndrome, 2 Whistling face &1 Cerebro-oculo nasal syndrome.
**1 Aarskog Syndrome, 10 De Lange Syndrome, 10 Noonan Syndrome, 3 Prader-Willi Syndrome, 2 Russell-Silver Syndrome, 23 Seckel Syndrome & 3 Smith-Lemli-Opitz Syndrome.
***7 Holt-Oram Syndrome, 9 Klippel-Trénaunay-Weber Syndrome, 3 Rubinstein-Taybi Syndrome, 3 Thrombocytopenia with absent radius (TAR) Syndrome & 2 VATER association.
#3 Beckwith-Wiedemann Syndrome, 3 Soto's Syndrome & 20 Hemihypertrophy.
3 Laurence-Moon(-Bardet)-Biedl Syndrome, 3 Zellweger Syndrome, 1 Coffin–Lowry syndrome, 2 Cohen syndrome, 1 Langer–Giedion syndrome & 1 Congenital microgastria limb reduction complex.

This is in agreement with previous studies in other localities of Egypt [15,16].

This study revealed that cerebral palsy and Duchenne muscular dystrophy were the most frequent disease of the nervous system. A previous study in Egypt reported that developmental brain disorders are commonest neurologic disorders [15]. However, in Iran the most prevalent disorders were identified as inherited deafness, spinal-muscular atrophy, Duchenne muscular dystrophy [34].

In Tanzania, Mashuda et al, [22] found that the most frequent congenital anomalies of the central nervous system were among hospitalized children were spina bifida and hydrocephalus.

This study revealed that achondroplasia and osteogenesis imperfect were the commonest congenital malformations of the musculoskeletal system. This agrees with previous studied in Egypt [15,16].

In Iran the most prevalent disorders were identified were spinal-muscular atrophy, Duchenne muscular dystrophy [34]. In Tanzania, Mashuda et al, [22] found that the most frequent congenital anomalies of the musculoskeletal system among hospitalized infants were omphalocele and gastroschisis.

Congenital rubella syndrome accounted for more than two-fifths of conditions originating in the perinatal period. Rubella is an absolutely preventable disease. It is hoped the high coverage of rubella vaccination will prevent the occurrence of this syndrome.

Down syndrome accounted for 88.8% of the chromosomal abnormalities. In previous study in Egypt Down syndrome was the commonest chromosomal abnormalities [15,16]. The same finding was reported in Barbados [28].

There is a need for national projects aimed at controlling genetic disorders. Pre-natal detection of disease should be more available while early diagnosis was essential in treating many disorders. Screening potential spouses for defective recessive genes will contribute to preventing autosomal recessive diseases. Aside from improvements to medical services, educational efforts are needed to increase genetic literacy of the general public, and primary healthcare workers should undertake comprehensive courses and campaigns improve counseling skills specifically related to consanguineous marriages [2,35].

Reliable epidemiologic and burden of diseases data collection, along with proper analysis of the situation would help policy makers, priorities

planning and implementing community genetic services at the primary healthcare level.

There is a need to establish a network of genetic units in all governorates to cover the needs of all population, children and adults, for genetic testing. Constructing an electronic data base for genetic disorders in Egyptians will help in monitoring trends in incidence of these disorders. A nation-wide community survey will highlight the magnitude and the underlying factors of genetic disorders and help in formulation a national policy for their prevention and control.

Study limitations

This is a retrospective single center study on selective group of children suspected to have genetic disorders. The results reveal the relative frequency of different morbidities in this group of children. So it cannot be generalized to the whole population.

Ethical approval

not applicable

Sources of funding

none

Conflict of interest

none

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