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Cytogenetic profile of children with suspected genetic disorders referred to the Genetic Unit of Mansoura University Children's Hospital, Egypt

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ABSTRACT

Background: Cytogenetic has become an indispensable tool for the diagnosis of genetic disorders, paving the way for possible treatment and management. This study aims to describe the cytogenetic profile of cases referred to a genetic unit in Egypt.

Methods: This is a retrospective 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. The following data was abstracted from the files of 3,197 referred cases: child age at referral, sex, residence, and the results of karyotyping.

Results: Most of referred cases were from Dakahlia (60.9%). Males were more encountered than females with ratio 1.1:1. The age of referral ranged from 1 day to 1,530 months with mean ± SD of 20.4 ± 5.1. Karyotyping was not done or unrecorded in 27.8% of cases. Normal Karyotyping 46XY and 46XX was recorded in 8.5% and 6.9%, respectively. Chromosomal abnormalities were found in 56.8%. The most common autosomal abnormalities were Down syndrome non-disjunction (47, XY +21–47, XX +21) 30.2% and 17.2%, respectively. Classical type of Turner syndrome (45, X) was the commonest sex chromosomal abnormalities (1.8%). Numerical abnormalities were the most frequent (53.2%). Down syndrome accounted for 48.5% (for non-disjunction and mosaicism) and 3.5% (for translocation) of chromosomal abnormalities.

Conclusions: Karyotyping should be done for all cases with suspected genetic disorders. It provides the bases for clinical management and genetic counseling of parents.

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KEYWORDS

Cytogenetic; karyotyping; chromosomal anomalies; Down syndrome

Introduction

Genetic disorders will account for an increasing proportion of deaths and morbidity after the control of environment-related diseases. Despite this, they have not received much attention in developing countries because the prevailing burden of communicable diseases [1]. Reliable data about these disorders is not available in Egypt [2]. Genetic disorders are relatively frequent among neonates. A study in Giza hospitals, Egypt found that 3% of newborns entered neonatal intensive care units had genetic or congenital disorders [3].

Chromosomal abnormalities constitute a major category of genetic disorders. These abnormalities can be due to changes in the normal number or structure of chromosomes. They may involve one or more chromosomes and may involve only part of a chromosome or the whole chromosome [4].

Chromosome analysis is important to the diagnosis and evaluation of genetic disorders [1,5]. The phenotypes of chromosomal disorders vary considerably. Therefore, the cytogenetic analysis of children with suspected genetic disorder is important to establish the proper diagnosis, to provide information about prognosis and recurrence of risk for future siblings [6]. In Egypt, there are many studies about the cytogenetic profile of Down syndrome, with a study in the Genetic Unit of Mansoura University Children's Hospital [7], but none about the whole spectrum of genetic dis-

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orders. Therefore, this study aims to describe the cytogenetic profile 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.

This study included all cases (3,197) 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 collected data included child age at referral, sex, residence, and karyotyping results.

The study was approved the Research Ethics Committee of the Faculty of Medicine, Mansoura University. Confidentiality and anonymity of data were assured. The data were collected and analyzed using SPSS for windows program (version 16) using simple frequency tables.

Results

Most of the referred cases were from Dakahlia (60.9%) followed by Damitta (13.4%) and Kafr Elshikh (9.5%), nearby governorates. Males were more encountered than females with ratio 1.1:1. The age of referral ranged from 1 day to 1,530 months with mean ± SD of 20.4 ± 5.1. The majority of cases (64.3%) were referred during the first year of life (Table 1).

Karyotyping was missing in 27.8% of cases. Table 2 shows the results of 2,308 karyotypes. Normal Karyotyping 46XY and 46XX were recorded in 11.8% and 9.5%; respectively. Chromosomal abnormalities were found in 78.7%. The most common autosomal abnormalities were Down syndrome non-disjunction (47, XY +21 - 47, XX +21) 41.9% and 23.9%, respectively. Classical type of Turner syndrome (45, X) was the commonest sex chromosomal abnormalities (2%).

Table 1. Socio-demographic features of 3,197 referred cases.

	***N* (%)**
Governorate of origin	
Dakahlia	1,946 (60.9)
Damitta	427 (13.7)
Kafr Elshikh	305 (9.5)
Gharbia	275 (8.6)
Sharkia	120 (3.8)
Port Said	72 (2.3)
Menofia	17 (0.5)
Qaliobia	15 (0.5)
North Sinai	12 (0.4)
Others#	8 (0.3)
Sex	
Male	1,725 (54.0)
Female	1,472 (46.0)
Sex ratio	1.1:1
Age at referral (months):	
≤12 months	2,054 (64.3)
13–24 months	512 (16.1)
25–36 months	181 (5.7)
37–48 months	110 (3.5)
49–60 months	126 (3.9)
≥61 months	214 (6.7)
Mean ± SD	20.4 ± 5.1
Median (minimum - maximum)	(1 day – 1,530 months)

#Three cases from South Sinai, three cases from Cairo and two cases from Elwadi Elgadeid.

Table 3 shows that numerical abnormalities was the most common type of chromosomal abnormalities as it was reported in (93.6%) and structural abnormalities accounted for the remaining 6.4%. Down syndrome accounted for 85.4% (for non-disjunction and mosaicism) and 6.2% (for translocation) of chromosomal abnormalities.

Discussion

Mansoura University Children's Hospital is located in Mansoura City, the capital of Dakahlia Governorate, Egypt. So the majority of referred cases (60.9%) were from Dakahlia. This is a reflection of the physical accessibility to the genetic unit. Also, Dakahlia is one of the most populous areas in Egypt with a total population of more than six million. The remaining cases were from neighboring and even far away governorates. This is a reflection of the lack of specialized genetic units in the other governorates of Delta Region of Egypt. The preponderance of males may reflect inequality of care for children of different sexes. The culture of giving more value and care for males is common in traditional communities. More than one-third of cases were referred for genetic testing after one year of age. The causes of late referral are multiple such as unawareness of

Table 2. Karyotype of 2,308 referred cases#.

	Total *N* (%)
Total	2,308 (100)
Normal karyotype	491 (21.3)
46XY	272 (11.8)
46XX	219 (9.5)
Chromosomal abnormalities	1,817 (78.7)
Autosomal chromosomal abnormalities	
47, XY +21	966 (41.9)
47, XX +21	551 (23.9)
46, XY, t(21q; 21q)	17 (0.74)
46, XX, t(21q; 21q)	9 (0.4)
46, XY, t(13q; 21q)	30 (1.3)
46, XX, t(13q; 21q)	14 (0.6)
46, XY, t(14q; 21q)	14 (0.6)
46, XX, t(14q; 21q)	12 (0.52)
46, XY, t(15q; 21q)	6 (0.3)
46, XX, t(15q; 21q)	10 (0.4)
47, XY, +21/46, XY	15 (0.5)
47, XX, +21/46, XX	19 (0.8)
47 XY, +18	44 (1.9)
47 XX, +18	24 (1.0)
47 XY, +8	5 (0.2)
47XX, +8	4 (0.17)
47 XY, +13	4 (0.17)
47 XX, +13	2 (0.09)
Sex chromosomal abnormalities	
45, X	47 (2.0)
45, X/46, XX	4 (0.17)
46, X, Xp	4 (0.17)
47 XXY	12 (0.52)
48 XXXY	4 (0.17)

#Karyotype was missing in 889 cases.

Table 3. Types of chromosomal abnormalities according to karyotyping results of 1,817 karyotypes#.

Type	Total *N* (%)
Total	1,817 (100)
Numerical abnormalities	1,701 (93.6)
Autosomal	
Down (non-disjunction + mosaicism)	1,551 (85.4)
Edward syndrome	68 (3.7)
Patau syndrome	6 (0.3)
Trisomy 8	9 (0.5)
Sexual	
Turner syndrome (monosomy + mosaicism)	51 (2.8)
Klinefelter syndrome	16 (0.9)
Structural abnormalities	116 (6.4)
Autosomal	
Down (translocation)	112 (6.2)
Sexual	
Turner syndrome (Xp)	4 (0.2)

#Karyotype was missing and normal in 889 and 491 cases, respectively.

the family and healthcare providers, inaccessibility of genetic services. Utilization of genetics services are restricted by certain cultural, legal, and religious limitations, such as the cultural fear of families with genetic diseases being stigmatized within their community [8,9]. A previous study on Down syndrome in the same unit found that the age at referral ranged from 3 days after birth up to the age of 168 months, with a mean of 12.2 months [7].

Karyotyping was missing in the files of 27.8% of referred cases. It is not clear whether it was not done at all or not recorded. The possibility of unaffordable cost cannot be excluded as a barrier for karyotyping.

In the current study, chromosomal abnormalities were detected in 78.7% of karyotypes. Previous studies in different countries reported different proportion of abnormal karyotypes among referred cases to genetic testing. Much lower proportions were reported in different countries, e.g., 22% in Sudan [10]; 27% in Morocco [11]; 33.3% in Nepal [6]; 29.3% and 28.6% in Brazil [1,12]; 32.2% in Turkey [13]; 50.6% in Sri Lanka [14]; and 28.3% in Oman [5]. A much lower proportion of 3.8% have been reported in the USA [15]. This wide range of proportions could reflect variations in the criteria for referral to cytogenetic investigations, age at referral, and the cytogenetic methods used. It has been noticed that some clinicians refer cases for cytogenetic study before exhausting other less expensive and time-consuming tests that may lead to the final diagnosis. In some instances, the patients were referred just to exclude the possibility of having an associated chromosomal abnormality [16]. In Egypt, referral to genetic specialist is considered when a health care worker or a family member notices that the child has dysmorphic features or delayed physical or mental milestones. There is no national or local guideline for referral of such cases to genetic testing. In the developed countries, the trigger of referral may be different, e.g., families with history genetic disease.

The current study revealed that 93.6% and 7.4% of abnormal karyotypes showed numerical and structural abnormalities, respectively. The same proportions were reported in Sudan [10]. The corresponding figures were 90.8% and 9.2% in Sri Lanka [14]. Down syndrome is the most common autosomal syndrome with non-disjunction as the most common type of Down syndrome. This agrees

with previous studies [6,7,10,11,14,17]. This could be attributed to its easy clinical suspicion/diagnosis. On the other hand, Turner syndrome is the most common sex chromosomal abnormalities. This agrees with previous studies [6,10,11].

A note to be mentioned is that chromosomal microarrays (CMAs) were not used for genetic testing. They are more advanced technique than conventional karyotyping showing not only chromosomal abnormalities (numerical and structural) but also submicroscopic abnormalities; however, they are expensive and cannot be afforded by the majority of families. Most of the Egyptians are not covered by the ongoing health insurance system.

Karyotype should be done routinely and recorded for all referred cases. It should be available free of charge or at affordable cost for all cases. Including CMA test will be an advantage. The newly adopted health insurance program in Egypt can cover its high cost. Efforts should be made to raise awareness of parents and healthcare providers, especially those working in primary health care, for early suspicion of genetic disorders and referral for genetic testing. Developing a national guideline for referral to genetic specialist will improve the timely referral of suspected cases. 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 among 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 single center study on selective group of children suspected to have genetic disorders. So, its results cannot be generalized to the whole population.

Ethical Approval

Not applicable

Sources of Funding

None

Conflict of Interest

None

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