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Prevalence of Genetic Disorders in Pediatric Emergency Department Al Galaa Teaching Hospital

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Abstract: To determine the prevalence and patterns of presentation of cases with suspected genetic disorders among neonatal pediatric emergency department. A retrospective and prospective review of pediatric emergency department admissions at Al Galaa Teaching Hospital among one year; suspected infants with genetic disorder are prone to full clinical evaluation with special emphasis on any associated anomalies or facial malformations, meticulous pedigree construction, chromosomal analysis for karyotyping and metabolic studies when indicated. Infants with suspected genetic diseases represent 11.1% among patients admitted to PED. Of these 50% were related to single gene disorders, 22% had chromosomal aberrations, 20% were due to multifactorial etiology and 8% had sporadic isolated anomalies. Parental consanguinity was found in 40% of these cases. We concluded that genetic disorders due to single gene defect are the most common pattern of malformations. This could be related to the high consanguinity rate among Egyptian population. Also emphasized that it is important for emergency physicians, neonatologists and pediatricians to be familiar with common genetic diseases, their acute presentations and complications. Awareness of underlying genetic disorders and accurate diagnosis are required for appropriate management and proper counseling.

Key words: Genetic disorders, neonates, Egypt

INTRODUCTION

Patients with genetic conditions constitute an important portion of world population with special health care needs. The complexity of these patients' health needs in conjunction with social and economic factors make medical follow up difficult.

Al Galaa Teaching Hospital is a large ministerial health center with at least eleven thousands deliveries/year and the emergency department (ED) is a major source of primary care.

Using our hospital's ED data as a starting point we sought to design modified guidelines covering detailed history and genetic examination to delineate different types of genetic conditions and the vast array of common presentations that they manifest, diagnosis and management options. To our knowledge, no other studies have detailed contribution of genetic conditions to ED.

Patients and methods: Among one year retrospective and prospective admissions were reviewed to identify infants with known cases or suspected genetic disorder. Selected and suspected genetic disease cases were subjected to the following:

- Maternal age, parity and health including maternal illness and medications used.
- Onset and quality of fetal movements throughout pregnancy.
- Teratogenic exposure such as tobacco, drugs and medications.
- Periconceptional supplementation with folate.
- Prenatal testing.

Perinatal history: Duration of pregnancy, Presentation and mode of delivery, Complications of delivery and description of the placenta

Family history: A three generation family history including consanguinity in parents with health information about relatives and similarly affected cases or other genetic disease, still births or neonatal deaths.

Physical examination: Particular attention to major and minor malformations and to physical variations.

Growth parameters: Length, weight and head circumference, with percentiles Assessment of proportionality and symmetry

General appearance: Tone, positioning, alertness, color…

Detailed examination: Skin- pigmentation pattern, excessive peeling and vascular lesions Head-shape, symmetry, fontanelles Scalp-hair patterning and location of hair whorls

Facial features

Eyes : Palpebral fissure inclination and length.
Ears : location and configuration
Nose : nares, nasal bridge and columella
Mouth : philtrum, intra-oral examination
Mandible : shape and symmetry

Neck : posterior hair line, redundant skin or webbing
Chest : shape, symmetry, location of nipples or accessory nipples
Cardiovascular : heart murmurs
Lungs : symmetry of breath sounds
Abdomen : umbilicus, integrity of wall, enlarged organ or masses
Genitalia : size, appearance, presence of ambiguity
Anus : location and patency
Back : symmetry, spine, sinuses or hair tufts
Extremities : proportions, motion, reduction or duplication of segments
Hands and feet : nails, creases, phalanges and toes
Neurological : tone, alertness, reflexes.

Diagnostic evaluation:

- Chromosomal analysis using G-banding technique (Arakaki and Sparkes, 1963) using Giemsa and Trypsin G-banding techniques (Verma and Babu, 1995). Fifty metaphase spreads were analyzed under microscope. Breaks, gaps and abnormal cells were photographed and karyotyped using Image Analyzer. Insitu hybridization technique was applied for some cases using satellite centromeric probes or whole painting probes (Oncor, Cambio).
- Metabolic screening by fluorometry immune assay (Bellisario *et al.,* 1987; Gerasimova *et al.,* 1989) when indicated.
- Diagnostic imaging when indicated.

RESULTS

Out of 900 infants visited the ED, 100 infants (11.1%) were diagnosed or suspected of having genetic diseases. Known genetic disorders were further classified into single gene disorders in (50%) of cases, chromosomal disorders in (22%), multifactorial in (20%) and others in (8%). Table 1 describes the categories of genetic disorders. While Table 2 listed the presenting complaints or systemic presentation which could be suggestive of an underlying genetic disorder requiring further evaluation.

Table 1: Diagnostic Genetic Classification of the studied cases

Categories	Diseases	No. of cases
Single gene disorders		
* Autosomal recessive	Holoprosencephaly	2
	Neu laxova	2
	Congenital adrenal hyperplasia	2
	Fanconi syndrome	1
	Seckel syndrome	2
	Cutis aplasia	1
	Palistar Hall syndrome	1
	Meckel syndrome	1
	Phenyl Ketonuria (PKU)	1
	Hypothyroidism	3
	Achondrogenesis (Fig. 1)	4
	Galactosemia	3
	Arthrogryposis	1
	Camptomelic dysplasia	4
	COFS	2
	Incontinentia Pigmenti	1
	Penoscrotal transposition	1
	Osteogenesis imperfecta	1
* Autosomal dominant	Frontonasal dysplasia	2
	Neurocutaneous	2
	Congenital polycystic kidney	2
	Crouzan syndrome	1
	Ellis-van Creveld	1
	Achondroplasia	2
* X-linked	Testicular feminization	3
	Hydrocephalus	1
	Hemophilia	2
	Osteogenesis imperfecta	1
Chromosomal Disorders	Down's syndrome	17
	Trisomy 18	2
	Trisomy 13	2
	Cri du chat (Fig. 2)	1
	Pierre robian anomaly	1
Multifactorial	Cleft palate	2
	NTD	7
	VATER association	1
	TAR syndrome	1
	Exomphalus major (Fig. 3)	1
	Conjoined twin	1
	Amnionotic band	1
	Diaphragmatic hernia	2
	Doudenal atresia	2
	Cauda regression	1
Others	MCA / MR	1
	Genu recurvatum	2
	Omphalocele	1
	Rib gab	1
	Talipus equino varus	1
	Secrococcygeal teratoma	1
	Subcostal fistula	1

DISCUSSION

Major malformations are common, they are the leading cause of neonatal mortality, contribute substantially to chronic disease morbidity and have a

Table 2: Systemic Presentation of Genetic Disorders

Systemic Presentation	Diagnosis	Management
Dysmorphic Features	Holoprosencephaly, cerbro-oculo-facial syndrome, frontonasal dysplasia and Crouzon syndrome	Neuroimaging, referral to genetics.
Hydrocephalus	Hydrocephalus	Determine isolated or not and referral to genetics.
Microcephaly	Chromosomal, Metabolic, Congenital infection	Chromosomes, Amino acid study TORCH
Dermatologic	Neu-Laxova, Cutis aplasia, Incontinentia pigmenti syndrome.	Dermatologic and Genetic evaluation
Neurologic	Neurocutaneous and chromosomal	Chromosomal analysis.
Cardiac	Chromosomal, VATER association	Isolated cardiac or not, chromosomal
Abdominal	Polycystic kidney, Exomphalus major, Omphalocele	Abdominal sonar Referral to genetics
Respiratory	Cleft lip/palate Holoprosencephaly, Frontonasal dysplasia	Check for NTD Neuroimaging study, Referral to genetics
Hematologic	TAR syndrome, Fanconi anemia	Hematologic investing. Radial rays anomaly, Referral to genetics
Metabolic	Phenylketonuria, Hypothyroidism, Galactosemia	Enzyme assays, Amino acid studies T3, T4 and TSH
Limb anomalies and fractures	Meckel,Ellis-van Creveld syndrome, amniotic band, fanconi anemia, ost. imperfecta, Achondroplasia, genu recurvatum	Chromosomal study, Radiologic evaluation, Referral to genetics
Ambiguous genitalia	Penoscrotal transposition, congenital adrenal	Metabolic acidosis, Chromosomal study, Psychiatric evaluation

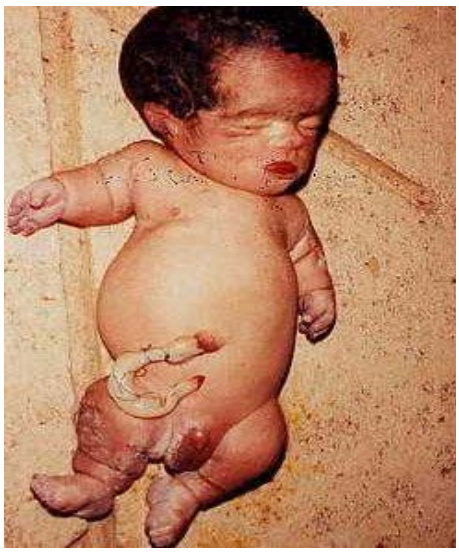
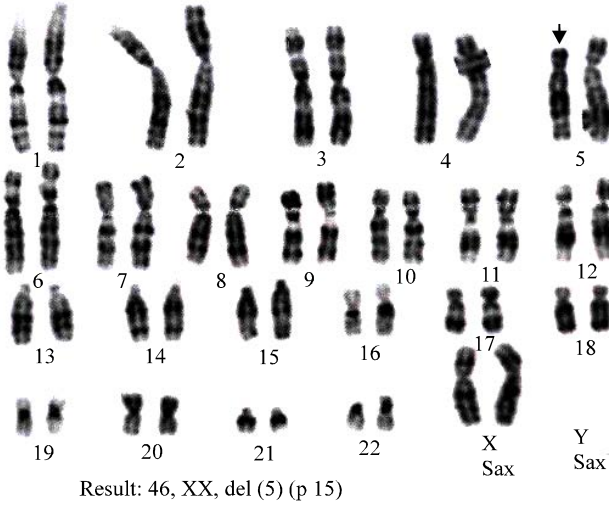


Fig. 1: Achondrogenesis



Result: 46, XX, del (5) (p 15)

Fig. 2: Cri du chat

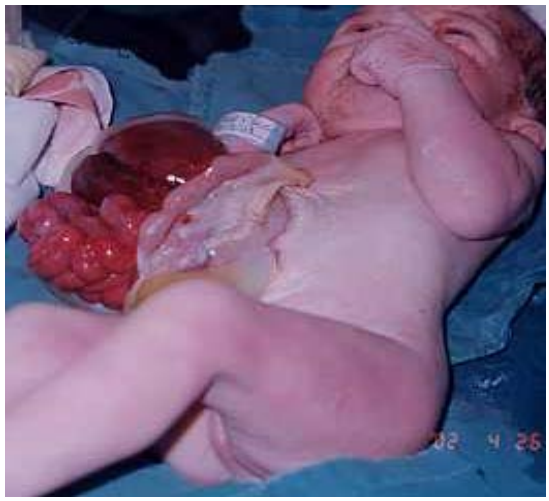


Fig. 3: Exomphalus major

high social cost. Primary care providers, physicians and pediatricians when encounter newborns with malformations or suspected genetic disease should be able to deal with their medical needs as well as the impact of the disease on the family. Several studies on patients with genetic disorders have been done in the past, addressing the frequency of hospital admissions and mortality. The prevalence of genetic disease ranged from 4.5 to 12% of total admissions (Childs *et al.*, 1972; Fitz Ptrick *et al.*, 1991; Yoon *et al.*, 1997). A prevalence of 30% was documented by Scriver *et al.*, 1995 and by Hall, 1997 by using a broad definition of genetic conditions. In the present work, infants with genetic disorders represent 11.1% among patients admitted to emergency department where the prevalence was 18%.

The data presented in Table 2 support the view that genetic conditions should be included in the differential diagnosis of various presentations. Consideration of an

appropriate genetic diagnosis should be indicated based on the practitioner or pediatrician's assessment of the patients medical, family history and findings on physical examination. These will guide selection of preliminary tests followed by diagnostic evaluation (Zitelli and Davis, 1999). Consultations with specialists in pertinent fields may clarify diagnostic possibilities. Medical genetics consultation is highly recommended when a clear working diagnosis is not evident, to confirm the diagnosis or to provide detailed genetic counseling.

The present work is limited by several factors. We relied on written documentation in the Emergency Department record. Since the Emergency Department records may be incomplete, not containing complete information about the underlying disorder, some cases with underlying genetic disorders may have been missed. Our study provide a guideline description (modified from Winter and Baraitser, 2000; Human Genetics Clinic, National Research Center and New York state Genetic Services Program). This guideline is intended to cover common situations and providers needed to consider their personal level of comfort and expertise as well as their specific practice setting when evaluating complex cases. If significant components of the process can not be accomplished in the primary care setting, referral should be made to medical genetics specialist.

In the present study, single gene defect represent the most prevalent cases (50%) (Table 1). This could be explained by the high consanguinity rate in Egypt (36.8%) reported by Temtamy *et al.* (1996). Consanguinity rate is high in the general population of all Arab countries. In Saudi Arabia, the consanguinity rate was 57.7% (El-Hazmi *et al.*, 1995), while in Kuwait it was 54% (Al-Awady *et al.*, 1995). Even monogenic disorders which affect a small number of newborns (2-3%), have a greater impact on childhood diseases (Albar, 2002). Therefore, it is imperative to scrutinize the available methods of prevention and management of genetic disorders. The recent Online Mendelian Inheritance in Man indicates a total of 11,553 autosomal entries, 681 X-linked entries, 37 Y-linked entries and 60 mitochondrial entries (OMIM, 2002). As a result of the continued increase in clinical genetics knowledge, educational strategies is need to be developed for clinicians to incorporate genetic advances into their daily patient diagnosis and management.

Chromosomal group represent 22% of the studied cases, where Down syndrome is the most frequent aberration. There are almost 1000 chromosomal syndromes reported in the literature (Muller and Young, 2000). Higher percentage of Down syndrome among the chromosomal aberration group was also reported by Butler and Hamill (1995) where it represent 34% of chromosomal abnormalities. Major birth defects among cases with Down syndrome such as cardiac and gastrointestinal anomalies have been reported as a result of gene-environment interaction (Hassold *et al.*, 2001).

In conclusion, since the Emergency Department provides both primary and subspeciality care for many patients, it is important for emergency physicians, pediatricians and other primary care practitioners to be familiar with common genetic diseases, their acute presentations and complications. Our study emphasized the higher burden of genetically determined than environmental disorders and the major contribution of recessive genes.

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