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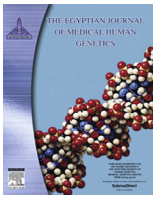

Original article

Yield of karyotyping in children with developmental delay and/or dysmorphic features in Sohag University Hospital, Upper Egypt

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ABSTRACT

Background: Global developmental delay (GDD) represents a measurable lag in a young child's achievement of developmental milestones compared to age matched children. Affection of two or more developmental domains is fundamental for assumption of GDD. Many chromosomal abnormalities are responsible for developmental delay or mental retardation and can be detected using G-banded karyotyping.

Aim of the work: This work aimed to determine the yield of karyotyping in children with GDD and/or dysmorphic features in Sohag University Hospital, Upper Egypt.

Subjects and methods: All children presenting with GDD and/or dysmorphic features, with abnormal karyotyping or other genetic testing were included. Full history, thorough clinical and detailed neurological examinations were done. The results of other investigations done for the patients, including neuroimaging and electroencephalography (EEG), were utilized (if available).

Results: The total number of patients included was 395 patients, out of 646 patients who did karyotype; the mean age of presentation was 24.7 ± 32.1 (SD) months, there were 243 (61.5%) males and 152 (38.5%) females. The positive yield of karyotyping in children with developmental delay and/or dysmorphic features, including classic Down features, was 61.1%; however, with exclusion of Down syndrome and other suspected trisomies, it became 7.4%. The most prevalent chromosomal abnormality was trisomy 21-Down syndrome (364 patients/92.2%), followed by structural chromosomal abnormalities and marker chromosome in 19 patients (4.8%) and, lastly, sex chromosome abnormalities (8 patients/2.0 %). The main complaint was GDD in half of the patients (205/51.9%), while the majority of patients had microcephaly.

Conclusion: G-banded karyotyping is a useful tool with reasonable yield in evaluation of children with developmental delay and/or dysmorphic features, especially in countries with limited resources.

1. Introduction

Global developmental delay (GDD) represents a measurable lag in a young child's achievement of developmental milestones compared to age matched children. Children aged less than six years are considered to have global developmental delay (GDD) if their performance was more than two standard deviations (SDs) below age-matched peers in two or more developmental domains [1–3]. It is considered a common problem, affecting 1–3% of children [4]. The American Academy of Neurology and the Child Neurology Society guidelines regarding evaluation of GDD clarified that several diagnostic tests had a greater than 1% yield. These tests include Giemsa-banded (G-banded) karyotyping, fragile X mental retardation 1(FMR1) gene testing, methyl-CpG binding protein 2(MeCP2) gene testing in girls with moderate to severe impairment, subtelomeric fluorescence in situ hybridization (StFISH) testing, neuroimaging and assessments for visual and hearing deficits. Genetic and metabolic testing were highlighted during the genetic era [5]. There are numerous and heterogeneous conditions causing GDD, with etiological yields ranging from 10 to 80% depending on variations in population characteristics, classification and diagnostic facilities available, such as genetic and imaging technology [6,7]. Retrospective and prospective studies found a yield of around 50% and the conditions were, in order of decreasing frequency; (1) genetic syndromes/chromosomal anomalies, (2) intrapartum asphyxia, (3) cerebral dysgenesis, (4) severe psychosocial deprivation and (5) ante-natal toxin exposure [5–7]. Conventional karyotyping using microscopy techniques or banding can initially detect duplication and recurrent deletions, which lead to many cases of mental retardation (MR). G-banding karyotype analysis

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is a famous technique used to identify individual human chromosomes in many laboratories worldwide and has an estimated yield of at 3% (excluding Down syndrome and other recognizable chromosomal syndromes) [8,9]. G-bands by trypsin using Giemsa (GTG), is performed by chromosome digestion with proteolytic enzymes, followed by Giemsa staining, leading to a characteristic pattern of light and dark bands (G bands) for each chromosome pair detected under a microscope [8]. Although karyotyping has been accepted as the standard for genetic assessment of children with GDD, it lacks the ability to capture chromosomal imbalances smaller than five to 10 Mb [10–12]. Smaller chromosomal gains and losses can be detected by fluorescence in situ hybridization (FISH) and multiplex ligation-dependent probe amplification. However, these techniques can be utilized only for a specific clinical suspicion or for the analysis of subtelomeric regions of the genome known to be frequently affected in developmentally impaired children [13]. There are demanding needs for accurate diagnosis and there is wide use of conventional karyotyping in our locality, in addition to few studies being conducted to address the value and yield of karyotyping in children with global developmental delay and/or dysmorphic features in Upper Egypt.

2. Aim of the work

This work aimed to determine the yield of karyotyping and to explore the pattern of chromosomal abnormalities in children with GDD and/or dysmorphic features in Sohag University Hospital, Upper Egypt.

3. Subjects and methods

3.1. Study design

This study was both prospective and retrospective, observational hospital based study done in the Pediatric Neurology Clinic, Pediatric Department, Sohag University Hospital, Upper Egypt, over a one year period from January 2016 through December 2016. Informed consent of the parents of the children coming for follow up was taken prior to conducting this research and was approved by the Faculty of Medicine, Sohag University Ethics Committee. In addition, it was carried out in accordance with The Code of Ethics of The World Medical Association (Declaration of Helsinki) for experiments in humans.

3.2. Patients

This study included all children who presented to us with global developmental delay, dysmorphic features, hypotonia and or intellectual disability and had abnormal karyotyping in the last eight years. For those children still coming for follow up in our clinic, data was taken from the patients and their parents, whereas for those who missed follow up data was extracted from the patient's files. Exclusion was done for cases that did not have karyotyping; meanwhile, those with normal findings were used only as a reference for positive yield (Fig. 1).

3.3. Methods

The results of karyotyping were reviewed and confirmed. In all cases, routine GTG (Giemsa banding technique) karyotyping was done, in five cases FISH test (fluorescence in situ hybridization) was performed, while in only three cases, studying for fragile-X syndrome was conducted. Karyotyping was requested previously for the patients as part of their diagnostic evaluation.

Patients data were reviewed and clinical history including age, sex, birth order, consanguinity, family history, perinatal, neonatal and developmental history were collected. History of behavioral problems like hyperactivity, aggression and autistic features were also included.

The details of patients examinations took into account general look and the presence of dysmorphic features (slanting eyes,

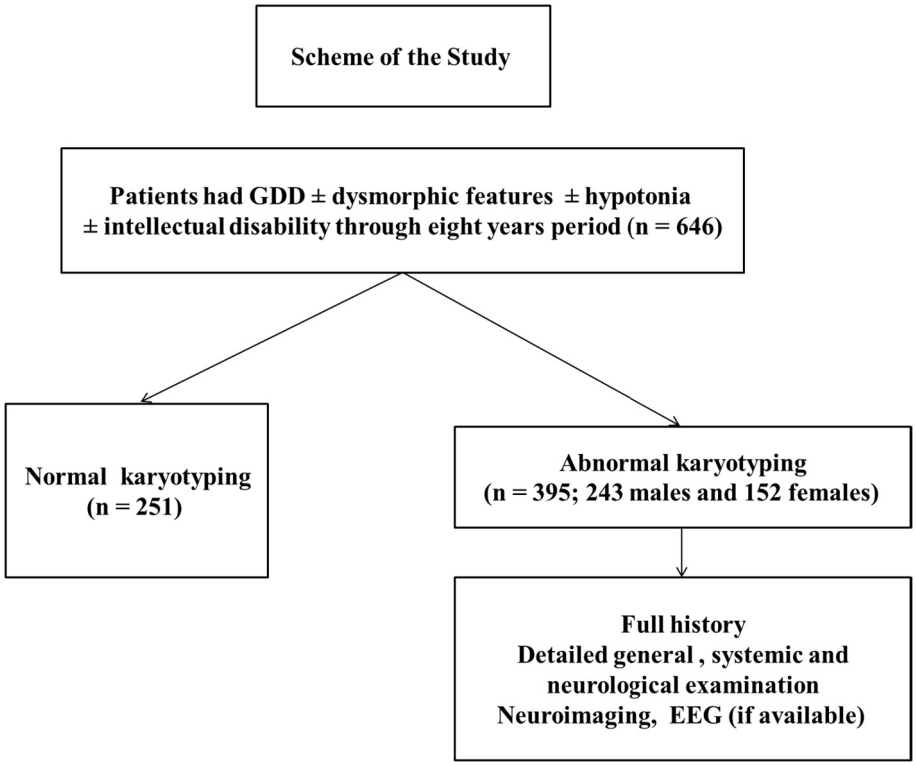

Fig. 1. Scheme of the study.