

Developmental delay & mental retardation

Global developmental delay (GDD) and mental retardation (MR) affect 1-3% of children of which 40 - 70% have an identified etiology (1-3). Several environmental factors, such as congenital infections (i.e. rubella, toxoplasmosis, cytomegalovirus) and hypothyroidism, associated with physical and intellectual disabilities, are potentially modifiable. Others, like genetic factors, even if not modifiable are treatable if an early diagnosis is made (4,5).

Various studies have reported that Down syndrome is the leading genetic cause of GDD/MR, followed by the Fragile X mutation. Despite this, information regarding the genetic etiology of these disabilities in Ecuador is lacking (3,6-10). The aim of this study was to determine the genetic etiology of subjects with GDD/MR in whom the possibility of perinatal, post-natal or environmental etiology had been previously ruled out.

From April 1st to December 31st 2006 subjects with GDD/MR admitted to the Clinical Genetic Service of the Roberto Gilbert Elizalde Children's Hospital, Guayaquil-Ecuador were identified in whom perinatal, post-natal or environmental causes of their disabilities had been previously ruled out. Medical records were reviewed and after a careful multi-specialized clinical and genetic examination the obtained information was analyzed.

During the study period, 120 subjects with GDD/MR (68 males and 52 females) were identified. Ages ranged from 3 months to 17 years (mean 3 years). The majority of the patients with GDD/MR of prenatal origin (n=120) had a genetic origin (77%; n=92). There were 28 patients with GDD/MR of unknown etiology. Genetic causes were chromosomal (66%; n=61), monogenic (33%; n=30) and multifactorial (1%; n=1). The only case diagnosed as a multifactorial disease was autism (Table 1). The most frequently involved genetic diseases were Down (63%; n=58) and Fragile X syndrome (14%; n=13). Our results were similar to that of other studies reporting Down syndrome as the leading genetic cause of GDD/MR followed by the Fragile X syndrome (3,6-10). This information justifies the implementation of educational and other training programs regarding Down and Fragile X syndromes especially focused to primary health care providers. Despite the fact that these are non curable conditions, early intervention and appropriate multidisciplinary management would significantly improve prognosis. To the best of our knowledge this is the first series to report the genetic of GDD/MR drawn from the Ecuadorian population. We recommend the initiation of a similar analysis however with a multicentric modality.

References

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Table 1. Genetic diagnosis in subjects with GDD/MR

Genetic Etiology	Number	%
Chromosomal aberration		
Down syndrome	58	63%
Other*	3	3%
Subtotal	61	66%
Monogenic disorders		
Fragile X syndrome	13	14%
Cornelia De Lange syndrome	3	3%
Rett syndrome	2	2%
Prader-Willy syndrome	2	2%
Goldenhard syndrome	2	2%
Other**	8	8%
Subtotal	30	33%
Multifactorial		
Autism	1	1%
Subtotal	1	1%
Total	92	100%

*Patau, Edwards * Klinefelter's

**Wolf, Treacher Collins, Caudal regression, Moebius, Pierre Robin, Ceroid lipofuscinosis neuronal, Achondroplasia, & Glycogenosis type I

NT – Mixed model

At the July 2007 World Congress of Fetal Medicine in Croatia, Dave Wright presented a new model for Down's syndrome risk calculation from NT and CRL measurements, using data from the large UK FMF studies. Briefly, the model fits two log Gaussian distributions to NT values in unaffected pregnancies at each CRL; similarly two log Gaussian distributions are fitted in Down's syndrome pregnancies. One of the distributions is major, accounting for most values, and one minor. In unaffected pregnancies, the mean value in the major distribution increase with CRL whilst the minor distribution mean is invariate with CRL. In Down's syndrome pregnancies the reverse is the case. It is hoped that detailed model including all the parameters will be published.