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Original article

Value of clinical assessment in the diagnostic evaluation of Global Developmental Delay (GDD) using a Likelihood Ratio Model ☆

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Abstract

Objective: A selective approach is recommended for investigating children with GDD. Our objective is to identify clinical markers to improve the diagnostic yield of evaluation of children with GDD.

Method: Children with GDD (delay > 2 S.D. in > 1 domain) followed up in our centre were reviewed retrospectively. We selected nine clinical markers (sex, severity of GDD, parental consanguinity, family history, behavioral problems, head size, facial dysmorphism, non-facial anomalies and neurological deficits) and looked into the likelihood of finding an underlying etiology during follow-up.

Results: There were 577 children with 63%, 33% and 4% having mild, moderate and severe grade GDD. An identifiable etiology is detected in 53%. Genetic disease (25%) was the commonest cause identified. We have found that severity of GDD (severe and moderate versus mild grade [LR+ = 1.92 (95% C.I. = 1.49–2.48); LR− = 0.72(0.64–0.81)], behavioral problems [LR+ = 0.24 (95% C.I. = 0.17–0.34); LR− = 1.67 (1.48–1.88)], facial dysmorphism [LR+ = 2.66 (95% C.I. = 1.10–3.54); LR− = 0.65 (0.58–0.73)] and neurological deficits [LR+ = 2.85 (95% C.I. = 2.32–3.50); LR− = 0.31(0.25–0.39)] were clinical markers associated with increased chance of identifying an underlying etiology by multivariate analysis.

Conclusion: These four clinical markers are useful in selecting patients with GDD for further diagnostic tests. Using the LR model, clinical markers in the first clinical evaluation of any child with GDD can potentially improve the etiological yield using targeted investigations.

Keywords: Likelihood Ratio Model; Global Developmental Delay; Children; Clinical assessment

1. Introduction

Developmental delay (DD) is present in 10% of pre-school children [1] and one of the commonest developmental problems encountered by general medical practitioner or paediatrician in their practice. Children with DD might later evolve into different neurodevelopmental disorders e.g. specific language impairment, developmental coordination disorder, specific learning disability, learning disability, attention deficit hyperactivity disorder, autism spectrum disorder, dyslexia,

Abbreviations: GDD, Global Developmental Delay; LR+, positive likelihood ratio; LR−, negative likelihood ratio

☆ **Institutional Review Board (IRB)**: This study had been approved by the HKU–HKWC IRB.

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specific motor impairment, visual or hearing impairment, cerebral palsy or even neurometabolic or neurodegenerative diseases.

Global Developmental Delay (GDD) is a subgroup of developmental disorders defined as delay in two or more of the following domains including (1) gross motor, (2) fine motor, (3) language or speech, (4) social personal activities of daily living, and (5) cognition. Significant delay is defined as delay in more than two standard deviations from the population norm [2,3].

After confirming a child has GDD, searching for the underlying etiology is the next logical step. Etiologic determination has important implications in treatment, prognosis and family counseling concerning recurrence risk. The chance of finding a diagnosis for GDD in children is variable, ranging from 22–72% [4]. Evidence-based research has provided strategies to optimize diagnostic yield when investigating for GDD. Prominent examples include the practice parameter in evaluating GDD issued by the American Academy of Neurology (2003) [3] and a systematic review for the diagnostic evaluation of mental retardation by van Karnebeek et al. (2005)[5].

However, successful application of these evidence-based strategies in daily clinical practice might be affected by various factors. In particular, access to modern diagnostic techniques including subtelomeric deletion studies, molecular genetic tests, neuroimaging or recently, the Comparative Genomic Hybridization (CGH) microarray [3,6–10].Resource allocation by the government for public health distribution is also an important issue to be considered. At present, these investigations have relatively low diagnostic yield (all <20%) and are relatively expensive in terms of cost per diagnosis made. In our locality, with a diagnostic yield for cytogenetics of around 3.7% [3], it costs US $1500 for every diagnosis made. The cost per diagnosis made is even higher for other investigations like subtelomeric deletion studies (US $4100) and fragile X studies (US $7500) due to lower diagnostic yield.

Apart from financial aspects, unnecessary investigations at the first stage during the initial consultation often create anxiety for families. Thus, a selective approach, using key clinical features, has been advocated for investigating children with GDD e.g. clinical checklists for fragile X syndrome and subtelomeric studies [11,12]. However, a "syndromic" diagnosis for children with GDD is often difficult to make for non-geneticists during the first assessment and this limits the application of these syndrome-based clinical checklists. Therefore, looking for key features (i.e. markers) in the initial evaluation with history taking and physical examination will improve evaluation strategies for increasing the diagnostic yield.

In this study, our objective is to identify useful clinical markers to improve diagnostic yield in the initial evaluation of a child with GDD by using the "Likelihood Ratio Model" [13].

2. Method

2.1. Developmental assessment program for children with DD in Hong Kong

In Hong Kong, we have adopted the United Kingdom model for the assessment of children with developmental disorders since 1977 [14]. Developmental screening and surveillance program had been provided by the Maternal Child Health Centers (MCHC). Until 2004 September, developmental screening had been conducted in 3 stages by trained nurses at 3 months, 6–9 months and 3 years in conjunction with the immunization programs to improve the compliance rate. Screening includes assessment on the gross motor, fine motor, vision, hearing, speech and behavioral adaptability via observation and interviews. This screening service is targeted to all children born in Hong Kong, both in the public and private sectors. It is free-of-charge and no referral is required. Only a small percentage (<1%) of children born in private hospitals would not attend these MCHCs as the parents preferred to bring their children to their own private paediatricians for health care. In 2005 October, Developmental Surveillance Program was conducted in phases in Hong Kong to replace the developmental screening program.

2.2. Referral for any cases with suspected developmental problems in Hong Kong

After developmental screening, any child from birth to 12 years with suspected DD will be referred to Child Assessment Centers (CAC) for comprehensive developmental and behavioral assessment. Currently, there are seven CACs in Hong Kong. Apart from MCHC, referrals from clinicians and clinical psychologists from both public and private sectors are accepted based on regional distribution. A multidisciplinary assessment team consisting of developmental paediatricians, clinical psychologists, speech therapists, occupational therapists, physiotherapists, audiologist, optometrists, medical social workers and nurses provide comprehensive assessment for diagnosis and functional evaluation of the disabilities. When necessary, referral will be made to other specialists including child neurologists, clinical geneticists for further evaluation.

The Clinical Genetics Service (CGS), under the Department of Health, provides free-of-charge counseling and genetic diagnostic service to Hong Kong citizen. Conventional karyotype has been available since late 1970s and molecular studies for fragile X syndrome and various genetic studies were available in early