Global Developmental Delay and Intellectual Disability in Indian Children – Where do we Stand?

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The original research papers that were published in the last issue of Indian Pediatrics in 1968, covered heterogeneous fields ranging from surgery (pancreatic pseudocysts), biochemistry (serum glycoprotein levels in health and disease), and infections (Tuberculosis and Rabies) to neuro-development (Mental Retardation). Out of these, we selected the study 'Some etiological problems in mental retardation: solved and unsolved' [1] to highlight that researchers in those days were cognizant of the fact that determining cause in these children with special needs could translate into finding a cure or treatment options, identification of children at high risk, looking for preventive strategies, and prediction of recurrence.

Mental retardation (MR) is now referred to as Global developmental delay (GDD) when applied to children under five years and Intellectual Disability (ID) in older individuals. Through this communication, we present the salient changes in nomenclature, understanding of the etiopathogenesis, and clinical approach to establishing diagnosis in this condition in the last five decades.

THE PAST

Historical background and past knowledge: In the fifth century, Hippocrates stated that MR resulted from a physiological imbalance of four humors in the brain. Thomas Willis (1621-1675) described it as a disease resulting from structural problems in the brain. At the time when this study was published, the systems of classification included Tretgold's that categorized MR as primary, developmental (genetic, chromosomal and epigenetic) and environmental (traumatic, infective and deprivative), the WHO system (not particularly in favor), and that proposed by the American Association of Mental Deficiency (which was modified and used in the study).

The study: Somasundararm conducted this retrospective observational study [1] in a Child Guidance Clinic, which was incidentally located in the 'Government Mental Hospital', Madras. During the study period of 11 months 1,818 children (87% boys) under the age of 18 years visited the hospital, out of which 238 (65% boys) were enrolled in the child guidance clinic and 126 children (sex ratio unavailable) were diagnosed with MR. On applying the aforementioned modified American classification based purely on history, examination and occasionally electroencephalography (EEG), the distribution of causes were determined to be: (*i*) Infective (33, 26%), congenital (2) and postnatal (31); (*ii*) Intoxication due to post vaccination encephalopathy (3, 2.4%); (*iii*) Cerebral palsy resulting from trauma or physical agents (21, 16.6%); (*iv*) Metabolic disorders (hypothyroidism, gargoylism) (4, 3.2%); (*v*) Unknown prenatal causes with microcephaly (6, 4.8%) or mongolism (3, 2.4%); (*vi*) Structural defects of central nervous system resulting in epilepsy (27, 21.4%); (*vii*) Childhood schizophrenia (3, 2.4%); and (*viii*) Unknown etiology (18, 14.3%).

The author acknowledged that the lack of neurochemical and neurophysiological tests was a major limitation. Though he stated that because of these reasons, it was scientifically inaccurate to compare his observations with the larger British series of Penrose [2] and Kirman [3], it was evident that the major difference was a preponderance of non-infective and neuro-metabolic causes from the Western world. Though not based on the study findings, at the end of the paper, the

author opined that more medical professionals (physicians, pediatricians, neurologists, pathologists, psychologists and psychiatrists) should become involved in management of MR; more funds and advanced tests (genetic, biochemical and neuropathological) should become available for research; and MR should not be considered to be an isolated medical problem, but one in which the psychological, psychiatric, educational and sociological aspects should be considered concurrently.

THE PRESENT

The term 'Mental Retardation' was used in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision (DSM-4 TR) and International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10: codes F70–F79). Subsequently, in lieu of the negative connotations associated with this nomenclature, it was replaced by 'Intellectual disability (intellectual developmental disorder)' in DSM-5 (2013), as well as 'Disorders of intellectual development' in ICD-11 (6A00–6A04 and 6A00.Z for unspecified diagnosis). Thankfully, nowadays children at least are now being seen by paediatricians and are not being shunted off to psychiatric wards.

The diagnosis of ID has been based upon observing sub-optimal intelligence based on scores of cognitive ability obtained on assessment by standardized and validated psychometric tools since the early 1900's. The concept of concurrently assessing adaptive function was included in 1959, when it was understood that the mere ability to perform a skill was not holistic enough, but that the typical performance of an individual in his daily life and the amount of support that one required for functioning was also important. DSM5 states that adaptive behavior should be assessed in various settings to see whether the person has skills that cover abilities in the conceptual (extent of understanding and using concepts like pre-academic/academic or numeric skills), social (extent and quality of social interaction and communication) and practical (extent of support required) aspects of activities of daily living.

ID is a non-communicable health disorder that has become a public health concern worldwide. A systematic review from the United States reported a prevalence of 0.66% in children and adolescents in 2012 [4]. There is paucity of community-based data from developing countries, but it stands to reason that the prevalence would be similar, if not considerably higher. The main reason for this is the logistic challenges that arise in establishing diagnosis in the community using valid and reliable tools. For instance, in India, the prevalence of individuals with MR according to the 2011 census is reported as 5.6%, but further age stratification is unavailable. The accuracy of diagnosis remains questionable as this categorization is based on a few questions out of a series reserved for disability that are asked by door-to-door brief interviews. It is quite possible that these may not be answered accurately in our settings, given the social taboo that is associated with any sort of disability. A multi-centric study that evaluated the prevalence of Neurodevelopmental disorders in children between 2-9 years belonging to both rural and urban backgrounds was conducted by the International Clinical Epidemiology Network-India (INCLEN). This project used proper interviewing methods, validated tools and consensus criteria and reported a prevalence of 3.1% in children between 2 to 6 years and 5.2% in children between 6 to 9 years [5]

The identification of underlying etiology in individuals with GDD/ID is extremely important for several reasons that go way beyond immediate management. It enhances the planning of long-term goals, prognostication, monitoring, genetic counseling and prenatal diagnosis in subsequent pregnancies. The change in the diagnostic yield pertaining to the etiological profile of GDD/ID in the last five decades is a reflection of the advances in medical technology and advent of sophisticated investigations, be it in neuroimaging, metabolic or genetic. The 2008 guidelines of the American Academy of Pediatrics (AAP) followed a tiered approach that was based on history, examination and investigations based on suspected diagnosis and specific indications for further assessment if there was no clear differential. In the last decade it has become evident that up to 50 percent of cases of GDD/ID have an underlying genetic etiopathogenesis [6]. This is reflected in the change in the contents of the AAP guidelines. The latest version (2014) now directs that if a clinical gestalt is not immediately recognized, molecular and cytogenetic investigations should be considered the first line of testing, starting with chromosomal microarray [7].

Obviously this cannot be adopted in a resource-limited setting such as ours. We have to use a clinical approach that is eclectic and that is still chiefly directed by the clinical diagnosis that has been made by based on information obtained from a detailed history (including drawing a third degree pedigree tree), examination (including assessment of dysmorphism), diligent literature searches of genetic and dysmorphism databases, supported by investigations that are dependent on availability, cost and parental wishes. We present the findings of three Indian studies that have been conducted in the last decade based on this Tikaria, *et al*. [8] examined

100 children with GDD under 5 years of age and arrived at the following four common diagnostic categories-chromosomal disorders including Down syndrome (20%), hypoxic-ischaemic encephalopathy (15%), multiple malformation syndromes (14%) and cerebral dysgenesis (11%). Jain, *et al*. [9] used a stratified approach (the algorithm of which has been outlined in the article) for determining the etiological profile of children aged 3 months to 12 years with GDD/ID. Genetic causes were the most common category accounting for 51/83 (61.4%) of causes followed by perinatal causes (17, 20.4%), CNS malformations (10, 12%), external prenatal (3, 3.6%) and postnatal causes (2, 2.4%) [9]. Ali, *et al*. [10] enrolled 150 children with suspected unexplained non-syndromic ID ranging from 5 to 17 years in age and found metabolic cause in 9.3% of the cases. Though there were differences in study populations, definitions used and criteria defining the outcome variables, nonetheless with an expert-guided systematic predominantly clinical-based approach supplemented by individualized and rational investigations, the etiological yield was as high as 70-80%, which does not differ significantly from Western literature.

Though we have come a long way in the last 50 years in recognizing the medical and social needs of children with GDD/ID and related disorders [11,12], we still have a long way to go until we reach the goals that the author had envisioned at the end of his paper. There is still a need for dedicated and experienced medical professionals and paraprofessionals in management of this vulnerable population; funds are still restricted and largely unavailable for research; tests are costly and still not easily available or widely accessible; management is still not widely multi-dimensional that addresses the needs of both the affected individual and also the family; and sensitization and active involvement of the society still needs to be scaled up. Let us hope for a better update when a tale of 100 years is published.

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