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INVITED COMMENTARY

Neurodevelopmental and Behavioral Outcomes of Very Low Birth Weight Children: A Call for Early Intervention

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Prenatal, natal, and postnatal determinants of physical, psychological, and mental health issues of later childhood have been undermined for too long. The concept of 'first 1000 days' including the 270 intrauterine days and the 'next 1000 days' have brought in a new impetus to habilitation—prevention of impairment going on to disability through neuro-developmental follow-up and early stimulation. Very low birth weight (VLBW) babies including preterm and intrauterine growth retardation (IUGR) represents a major perinatal challenge for future health outcomes.

Neuroimaging of VLBW babies in childhood and later life reveals reduced total brain volume, decreased neuronal density, altered cortical folding/structure, abnormal neuronal migration, deficient myelination, and dendritic arborization—all of which may lead to deficits in cognition, memory, motor skills, and executive functioning that persist into school-age [1]. A systematic review and meta-analysis of studies from South Asia, showed that low birth weight (LBW) babies particularly those < 2000 g, scored significantly lower in cognitive domain compared with normal birth weight (NBW) peers at 10 years [2]. Other systematic reviews have shown that children with higher birth weight and larger head circumference, independent of environmental influences, demonstrated superior attention, memory, and executive functioning during school years [3].

Preterm and extremely LBW children, exhibit increased rates of attention-deficit hyperactivity disorder (ADHD), anxiety and communication difficulties during school years [4]. Children born extremely preterm (EP) or ELBW show deficits in self-regulation and executive function, disproportionate to the general cognitive impairment [5]. Adolescents born ELBW continue to have behavioral problems similar to those evident at a younger age, but these problems are not evident in behavioral self-ratings.

It was also shown that the percentage of parent ratings meeting DSM-5-TR symptom criteria for inattentive ADHD were also higher for the ELBW group (33% vs 13%); ELBW group had lower symptom severity scores on self-ratings than controls using several scales and group differences in parent ratings decreased over time for ADHD, especially among females, but were stable for anxiety and social problems [6].

Although, more than half of preterm children were shown to have minimal or no difficulties in various domains, viz., emotional symptoms, conduct problems, hyperactivity/inattention, and peer problems, during school years but those with the characteristic 'preterm behavioral phenotype' were over-represented by the ELBW/EP group which further was associated with poor academic performance and cognitive outcomes in later childhood [7]. LBW and VLBW groups remained at risk for school difficulties into late childhood, even when not neurologically impaired. Arithmetic, vocabulary, concentration, non-verbal intelligence, and attention problems were significant mediators of the effect of LBW on the school performance score [8]. A meta-analysis of very preterm and/or VLBW children showed moderate-to-severe deficits in academic achievement, attention problems, internalizing behavioral problems, and poor executive function—all strongly correlated to their immaturity at birth [9].

A meta-analysis found that children born preterm had significantly higher odds of developing anxiety, generalized anxiety disorder, and specific phobias compared to their term-born peers. The study concluded that preterm birth is associated with a greater prevalence of anxiety—but not depressive disorders—between the ages of 3 and 19 years, indicating potentially distinct etiological pathways in this high-risk population [10]. Furthermore, executive function difficulties in children born very preterm or with VLBW may manifest differently across settings. While these children exhibited clinically significant problems in the behavioral

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regulation index at home, the difference was no longer significant after adjusting for paternal education. The study concluded that executive function challenges vary between home and school environments, with particular emphasis on working memory difficulties observed in school settings [11].

In this context, the article by Mukhopadhyay et al. is both important and timely [12]. It presents an observational study involving 50 VLBW children and 50 age- and sex-matched NBW controls, assessed between 6 and 11 years of age. Outcome measures were evaluated by a certified psychologist using several standardized tools: Malin's Intelligence Scale for Indian Children (MISIC), the Childhood Psychopathology Measurement Schedule, the Children's Self-Concept Scale, the Preadolescent Adjustment Inventory, and the PGI Memory Scale for Children (PGIMC). The study largely adheres to the *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) guidelines. It features a clear title and abstract, a well-articulated background and rationale, explicitly stated objectives, and a detailed description of the study design, setting, and participants. Variables, outcome measures, and tools are appropriately defined, data sources and measurements are adequately described, statistical methods are appropriately applied, and the discussion effectively addresses the key findings.

A major strength of this study lies in its comprehensive evaluation using multiple assessment tools and parameters. However, its limitations include being a single-center study with a relatively small sample size. The findings revealed that, compared to NBW children, those born VLBW had significantly lower verbal, performance, and full-scale intelligence quotients (IQ). Additionally, the VLBW cohort demonstrated poorer scores in remote memory, mental balance, attention, visual retention, recognition, self-concept, and adjustment, along with higher levels of psychopathology and anxiety. These cognitive impairments are attributed to early disruptions in brain development, underdeveloped white matter, and cortical abnormalities. Deficits in arithmetic and digit span performance suggest difficulties in working memory and executive function, while challenges in spatial reasoning, motor coordination, information processing, and verbal reasoning may persist into later childhood. Combined with increased behavioral problems, anxiety, and depression, these deficits can contribute to withdrawal, social isolation, and academic difficulties.

Although significant progress has been made in reducing overt disabilities such as cerebral palsy and intellectual developmental disorders, the growing burden of autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), learning disabilities, executive function deficits, and behavioral issues calls for early intervention.

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