Half a Century With Pediatric Viral Encephalitis

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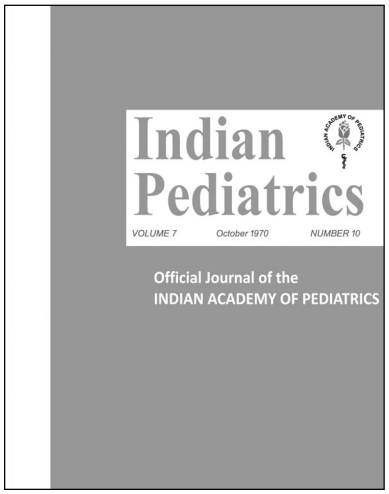
Periodic outbreaks of acute encephalitis regularly occur across India, leading to substantial mortality [1]. Japanese encephalitis (JE) has been the leading cause for the same [2,3], but the incidence of non-JE etiologies has been steadily increasing as well [1,4]. Even half a century back, pediatricians were struggling with this disease entity. We came across two articles from *Indian Pediatrics* archives dating back to 1970, and endeavor to describe the change in epidemiology and approach to viral encephalitis, over the past five decades.



THE PAST

Soon after Independence, there were many outbreaks of acute encephalitis in India. In 1954, Dr. Khan, while working at Tata Main hospital, Jamshedpur, described an epidemic, from Uttar Pradesh, Bengal and Bihar, of an acute encephalitic disease process, that predominantly affected children and had a high mortality rate. He undertook this work with Dr. Seal (Kolkata) and Dr. Work (Pune) [5,6]. This was the first reported epidemic of encephalitis from India.

Indian pediatricians have always been intrigued by this disease entity. During 1966-68, Balakrishnan, *et al.* [7] came across 72 consecutive pediatric cases of viral encephalitis. They published their experience in the April, 1970 edition of *Indian Pediatrics* [9]. They presented a case series of 19 clinically diagnosed pediatric viral acute encephalitis syndrome (AES) from Pondicherry. Cerebrospinal fluid examination was normal in a third of their cases, while echovirus-7 was isolated from CSF in 37% cases. Treatment offered by them 50 years back, was quite similar to what we offer today, including rehydration, nutrition by intravenous/enteral routes (nasogastric), antibiotics (tetracycline) and corticosteroids. But unfortunately, their mortality rate was quite high (79%).

Later, the same year (October, 1970), Athavale, *et al.* [8] published their experience with 125 children, who presented with meningoencephalitis, from erstwhile Bombay. Infectious etiological agents reported, included coxsackie (B4/B6) (12.8%), and echovirus (19/21) (12.8%). Their patient population had fever (91.2%, 45.8% high grade), altered sensorium (98/125) and convulsions (91/125) (1/3rd had persistent seizures). They observed that both presence of meningeal signs and absence of altered sensorium were associated with a better prognosis. They also defined a unique entity, acute fulminant meningoencephalitis (AFE) (disturbance in sensorium within 24 hours of onset), which was associated with terminal outcome.

Since then, acute encephalitis, predominantly attributed to Japanese encephalitis, has been reported from almost all states in India [3]. Enteroviruses [7,8] and Kyasanur forest disease [7] have also resulted in several outbreaks since independence.

THE PRESENT

This disease rattles the best brains even today. Worldwide, AES incidence varies between 3.5 and 7.4 per 100,000 patient-years [9]. But the mortality rate, has fortunately come down, to around 6% (National Vector Borne Diseases Control Programme (NVBDCP,2018) [3].

Across half a century, the etiology of AES is still predominantly viral. JE has continued to remain active, with recent outbreaks in Malkangiri [2012], Manipur (2016) and Delhi (2011) [10]. Amongst non-JE etiologies, enteroviruses (EV-71, coxsackie, echoviruses) [11,12], Nipah [13], Chandipura [14] and even dengue virus [12] are on the rise. Herpes simplex virus (HSV), the commonest cause of sporadic encephalitis worldwide, is still not as common in India [15]. Non-infectious causes have also been identified, as due to consumption of plant toxins (seeds of *Cassia occidentalis*, Cassia beans) (*kasondi* plant associated acute hepatomyoencephalopathy

[16] and litchi fruits (containing hypoglycin A and MCPG) (Muzaffarpur encephalitis) [17].

Pinpointing an etiological agent for acute encephalitis continues to be challenging, and may remain inconclusive in many cases. A detailed history, thorough physical examination focusing on level and localization of brain function, laboratory investigations, especially lumbar puncture, are very important in the treatment of the disease [15]. Nowadays, techniques such as enzyme-linked immunosorbent assay, molecular techniques like polymerase chain reaction (PCR) and dot blot hybridization are being increasingly used [18]. Advancement in radiological imaging has tremendously helped clinical decision making. Computed tomography scans in emergency situations, and magnetic resonance imaging when patients are more stable (especially with a diffusion weighted imaging and a gadolinium enhanced study), can help identify cerebral edema, and point towards a specific diagnosis.

Since viral encephalitis has a substantially high morbidity and mortality rate, primary prevention through immunization, holds a far greater promise than targeted therapy after disease infliction. Subsequent to the longest epidemic of JE in Gorakhpur (2005), mass vaccination against the same was introduced in endemic districts [10]. NVBDCP, launched in 2003-4, focusses on training staff at ground level (PHCs and CHCs) for early diagnosis and management. It also focusses on source reduction, especially vector control measures as water and hygiene practices, fogging, space spraying and antilarval measures [3].

THE FUTURE

Newer techniques as matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS), unbiased high-throughput sequencing (HTS) and VirCapSeq-VERT (virome capture sequencing for vertebrate viruses) may hold promise for the future, in providing accurate and rapid epidemiological and virological data for acute meningoencephalitis patients [20,27]. More research is still needed for development of more robust vaccines with improved immunogenicity. Further strengthening of NVBDCP programs and surveillance measures will contribute towards controlling arboviral encephalitis.

Though, over past half century, we have progressed and reduced case fatality, the basic tenets of medicine, a good clinical history, and detailed serial neurological examinations and testing as CSF examination, remain the backbone for treating viral meningoencephalitis.

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