



Teleneurology based management of infantile spasms during COVID-19 pandemic: A consensus report by the South Asia Allied West syndrome research group



Priyanka Madaan^{a,1}, Jitendra Kumar Sahu^{a,1,*}, Jithangi Wanigasinghe^b, Kanij Fatema^c, Kyaw Linn^d, Mimi Lhamu Mynak^e, Nicolás Garófalo Gómez^f, Pauline Samia^g, Prakash Poudel^h, Prem Chandⁱ, Raili Riikonen^j, for the South Asia Allied West Syndrome Research Group

^a Pediatric Neurology Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India

^b Department of Paediatrics, University of Colombo, Sri Lanka

^c Department of Pediatric Neurology, Bangabandhu Sheikh Mujib Medical University, Bangladesh

^d Pediatric Neurology Unit, Yangon Children Hospital, Myanmar

^e Department of Pediatrics, Jigme Dorji Wangchuck National Referral Hospital, Thimphu, Bhutan

^f Neuropediatric Department, Cuban Institute of Neurology and Neurosurgery, Havana, Cuba

^g Department of Pediatrics, Aga Khan University, Nairobi, Kenya

^h Department of Pediatrics, B.P. Koirala Institute of Health Sciences, Dharan, Nepal

ⁱ Department of Pediatrics and Child Health, Aga Khan University Hospital, Karachi, Pakistan

^j Child Neurology, Children's Hospital, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland

ARTICLE INFO

Article history:

Received 17 October 2020

Revised 8 December 2020

Accepted 12 December 2020

Available online 31 December 2020

Keywords:

Epileptic spasms

West syndrome

Teleneurology

Infants

COVID-19

ABSTRACT

With telehealth services rescuing patients with chronic neurological disorders during the COVID-19 pandemic, there is a need for simplified teleneurology protocols for neurological disorders in children. Infantile spasms is an epileptic encephalopathy where treatment lag is a significant predictor of outcome. It is one such condition where telemedicine can make a remarkable difference when in-person consultations are delayed or are not possible. However, the adverse effect profile of the first-line therapeutic options, the need for frequent follow-up, underdeveloped telemedicine services, lack of a rational protocol, poor awareness about infantile spasms, a lesser level of parental understanding, and scarcity of pediatric neurologists are the major hurdles in developing countries. This paper provides a teleneurology based approach for the management of infantile spasms in developing countries during the COVID-19 pandemic. The cornerstones of this approach include the fundamental principles of management of infantile spasms, decentralization of patient care to local health providers, efforts for improving sensitivity and specificity of diagnosis, early initiation of first-line therapeutic options, and constant motivation of parents and local health providers to be vigilant for therapeutic response, adverse effects of therapy, and infections.

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1. Introduction

The coronavirus disease-2019 (COVID-19) pandemic has significantly impacted the customary delivery of healthcare. Although children mostly remain asymptomatic, infants are particularly susceptible [1]. Negative consequences due to nationwide lockdowns, travel restrictions, and fear among patient families have affected the care of children with epilepsy like Infantile spasms (IS; includ-

ing West syndrome) [2]. Young age, comorbidities, need for hormonal therapy, and frequent healthcare visits are problems specific to children with IS [3]. Although the exact numbers are not known, the burden of IS and the treatment gap in developing countries is expected to be high considering the rampant causes of acquired brain injury such as hypoxic-ischemic brain injury, infections, etc., and relatively underdeveloped health infrastructure. Their management challenges are also distinct, e.g., a preponderance of structural etiology, significant lead-time-to-treatment, limited access to pediatric neurologists and specific investigations including electroencephalography (EEG), and problems with availability and licensing of first-line drugs [adrenocorticotropic

* Corresponding author.

E-mail address: jsh2003@gmail.com (J.K. Sahu).

¹ PM and JKS contributed equally and shared the first authorship.

hormone (ACTH) and vigabatrin] [4,5]. Moreover, the probable escalation of treatment lag (a significant predictor of outcome) due to prevalent travel restrictions is expected to adversely affect the outcome in children with IS [6]. Hence, the management protocols of the developed countries may not be entirely applicable to the developing nations.

Teleneurology is a well-established tool for epilepsy management, especially when face-to-face consultations are difficult (e.g., pandemic involving difficult access to care) [7]. In developing countries, the use of teleneurology is even more desirable during the COVID-19 pandemic to decentralize the patient care to community health services, promote healthcare access, reduce treatment lag, and cost of care [8]. However, considering the adverse effects associated with first-line therapeutic options for IS, reduced facilities, and lesser level of parental understanding in developing countries, a higher degree of vigilance is required during teleconsultations for IS. Therefore, a need for a simplified protocol for the management of IS via teleneurology exists.

2. Methods

The South Asia Allied West Syndrome Research Group developed an algorithm for teleneurology-based care of children with IS in developing countries. The initial research group had evaluated the management practices for West syndrome in South Asia and subsequently, developed a viewpoint statement on the management concerns during the COVID-19 pandemic [4,9]. The current study group initially searched the PubMed and EMBASE using the search terms “Infantile spasms OR West syndrome AND Teleneurology AND/OR COVID-19” until June 30, 2020, and later updated the literature review until September 20, 2020. The recommendations and guidelines developed by other societies/research groups were also searched.

Since the literature search did not reveal any specific recommendations or original research on teleneurology specific to IS during the COVID-19 pandemic, a simplified algorithmic teleneurology-based approach is being proposed keeping the general recommendations by the Child Neurology Society (CNS) and our group as the basis [3,9]. These recommendations and the concerns raised by the group members were discussed through multiple correspondences. The initial draft was formulated and revised on Google docs by authors based on the available evidence, expertise, practicality in their countries, and consensus. The concerns raised by group members in the algorithm were discussed and addressed through multiple emails and modifications were made in the algorithm based on suggestions.

3. Discussion and proposed approach

Fig. 1 illustrates a proposed simplified algorithm for teleconsultations for the management of IS.

3.1. Telemedicine tools

Despite the lack of organized telehealth facilities, there is easy access to smartphones in developing countries [7]. Tools with video modes of communication such as video-calls on a chat platform, Skype, video conferencing solutions, etc. may be the preferred options [7,9]. Unlike the USA, the South Asian and many developing countries don't follow Health Insurance Portability and Accountability (HIPAA) standards. However, country-specific recommendations for telemedicine need to be practiced. Patient confidentiality is of prime importance. WhatsApp, an end-to-end encrypted chat platform, may be useful in many developing countries since it ensures that the patient data is not available with any

private company. Hence, such tools may be used for interaction, sharing of patient videos, and providing prescriptions.

Some legal safeguards which may be helpful in the context of IS include proper documentation and recording of the consultation after parental consent, running a checklist of signs (including critical events) suggesting a need for an in-person consult before the beginning of teleconsult, maintaining a record of prescriptions, etc. Specific safeguards in each country also need to be considered [8,10].

3.2. First evaluation

At the first evaluation, video-teleconsultation or in-person consultation is preferred depending on travel restrictions and COVID-19 transmission in the region. Teleconsultation with the managing pediatrician or pediatric neurologist should be in liaison with a local health provider involved in the patient care. Each new consult should begin with general information (relevant history including clinical, family, past medical, perinatal, developmental, and treatment history; and focused physical/neurological examination). Detailed information on spasms, e.g., age at onset, clustering, type, relation with the sleep-wake cycle, burden, should be sought. Assessment of home videos of habitual events is strongly encouraged. Efforts should be made to determine the etiology [history of prior brain insult e.g., neonatal asphyxia, hypoglycemia, infections, or trauma; the presence of neurocutaneous abnormalities like ash-leaf spots (tuberous sclerosis complex), etc.]. Comorbidities should be looked for carefully. Besides a pretreatment screen to rule out any infections including tuberculosis, baseline parameters such as weight and blood pressure (BP) should be recorded. Baseline urine and blood sugar, electrolytes, liver enzymes, complete blood count, etc. should be recorded if possible.

3.3. Electroencephalogram

In agreement with the CNS recommendations, outpatient EEG comprising at least one sleep-wake cycle is advisable for confirmation of diagnosis, but treatment initiation should not be delayed if EEG is not feasible [3]. EEG should preferably be done at a place with expertise for hypsarrhythmia reporting. If conducted regionally, the technician and reporting person should be well-informed about the expectations from the report. Application of objective scoring for hypsarrhythmia may be considered based on feasibility and availability of expertise. Various available scores are Burden of Amplitudes and Epileptiform Discharges (BASED), score by Kramer and colleagues, score by Jeavons and Bower, etc. [11–13]. BASED score appears simple, feasible, and reliable tool with a favorable inter-rater agreement [11]. EEG confirmation of hypsarrhythmia would be useful for the initial diagnosis and the subsequent decision-making. However, it is important to note that hypsarrhythmia is not always present and is not essential to diagnose IS [14]. Availability of EEG and Magnetic Resonance Imaging (MRI) facilities is also a major limitation in many developing countries. Creation of this infrastructure will require funds and may not be possible acutely during this hour of crisis. Hence, gradual but persistent efforts towards creating a framework for the widespread availability of these investigations may be helpful.

3.4. Efforts to improve sensitivity and specificity of diagnosis and reduce treatment lag

In addition to objective EEG scoring, awareness regarding the semiology and development and validation of an objective clinical scoring system based on history and event videos may be beneficial. Also, easy access to this objective score in a smartphone application may ease the diagnostic process for local health providers and pediatricians. Furthermore, training of local health care providers and pediatricians through webinars for diagnosis and

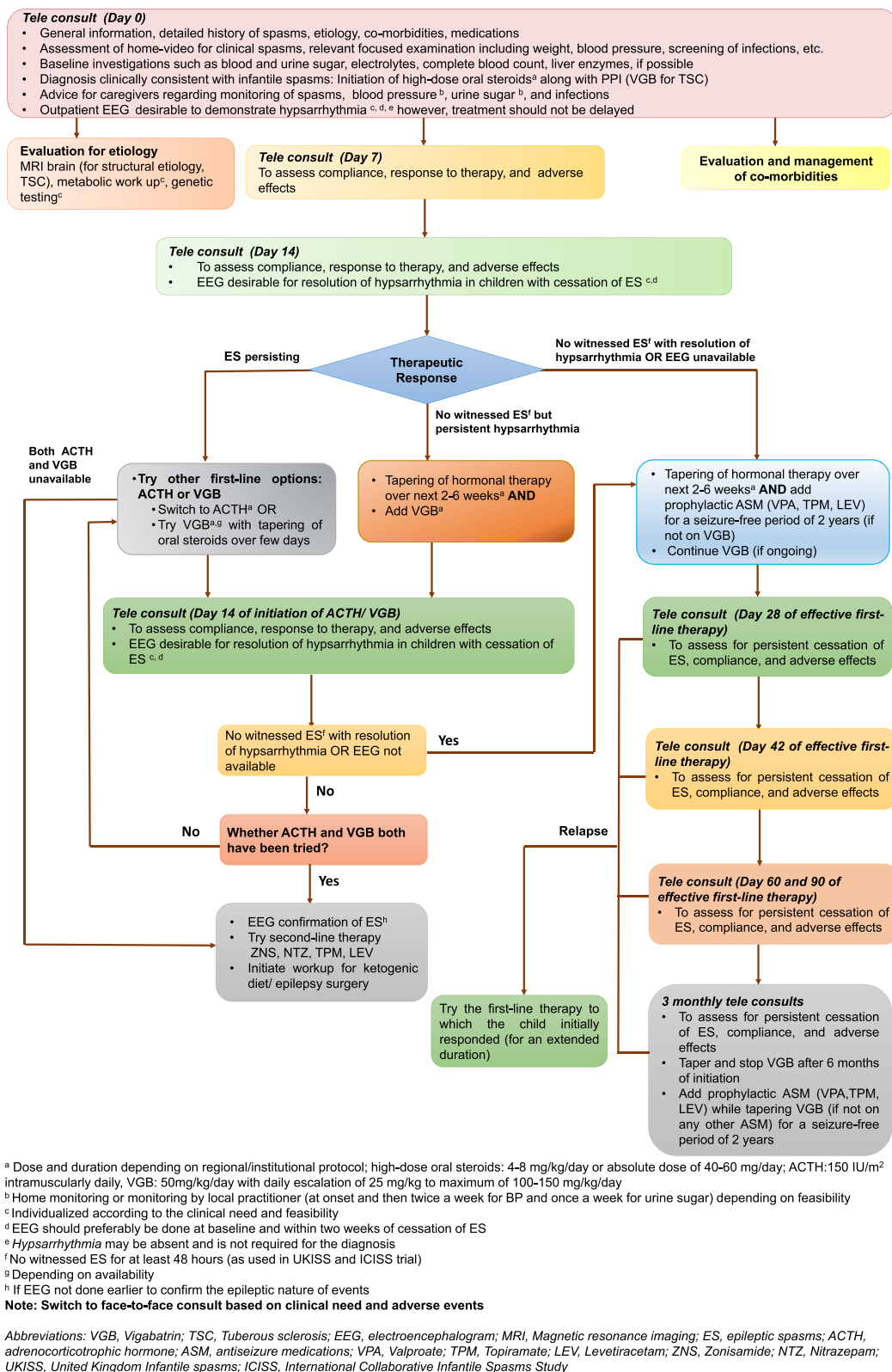


Fig. 1. Algorithm for tele-neurology-based care of children with Infantile spasms in developing countries during the COVID-19 pandemic.

management of IS will also be advantageous. Establishing a linkage facility for paediatricians to reconfirm their observations and management decisions with Paediatric neurologists may also be helpful. Besides, creating awareness among parents through mass media (screening children with neonatal brain injury during visits for immunization) will probably reduce the treatment lag.

3.5. Initial treatment advice

The initial choice should be one of the standard first-line medications: ACTH, prednisolone, and vigabatrin. Contraindications for high-dose hormonal therapy include acute infections, a history of clinical infection caused by herpes or cytomegalovirus, and

congestive heart failure. In accord with the CNS recommendations, high-dose oral prednisolone may be the preferred initial therapy during the COVID-19 pandemic [3]. Preferably syrups/ suspensions should be prescribed, and printed advice regarding dispensing and administration of liquid formulation using a syringe and possible adverse effects of medications and danger signs should be provided. Caregivers should be advised to record the daily burden of spasms, change in seizure types, and adverse effects of antiseizure medications (e.g. irritability, sleep disturbances, any new-onset symptoms of infections like fever, cough, respiratory distress, etc.). There is a risk of hypertension with hormonal therapy requiring BP monitoring [3,15]. Availability of appropriate-sized BP cuff for infants is an issue. Further, BP monitoring at home is challenging, hence may be done at a nearby healthcare facility. Urine sugar may be monitored at home. Besides, repeated emphasis should be given on general precautions such as the use of masks, social distancing, and hand hygiene.

3.6. Follow-up

The first follow-up should be scheduled after a week (or earlier depending on clinical need) of treatment initiation for assessing compliance, tolerability, and response to therapy. The next teleconsultation should be at two weeks of therapy. EEG is desirable to demonstrate resolution of hypsarrhythmia at this point, however, the feasibility and access may be issues. Depending on the therapeutic response, the initial therapy may be continued or switched to or supplemented with another first-line drug. Subsequent follow-up should be scheduled once in two weeks for assessment of therapeutic response, drug compliance, adverse effects, and need for modification of therapy. All the available first-line options need to be exhausted before going to second-line therapies. It is important to reiterate that teleconsultation should be switched to in-person consultation in the event of a diagnostic or management uncertainty.

4. Conclusion

Despite the innumerable pros of telemedicine, there are some limitations such as lack of detailed examination, limited access to investigations, problems with infrastructure and internet facilities, confidentiality, and legal implications involved. However, it seems to be a simple and convenient tool during the COVID-19 pandemic to provide optimal care while minimizing hospital visits. Although formal evaluation of the effectiveness of this approach is evolving, the advantages of early diagnosis and reduction in treatment lag are presumed to outweigh this limitation. Future studies should be done to validate this approach and algorithm in developing countries.

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Study funding

None.

Authors' contribution

Priyanka Madaan and Jitendra Kumar Sahu contributed by planning of the study, literature search, participated as an expert, preparation of initial draft of manuscript and its revision for intellectual content.

Jithangi Wanigasinghe, Kanij Fatema, Kyaw Linn, Mimi Lhamu Mynak, Nicolás Garófalo Gómez, Pauline Samia, Prakash Poudel, Prem Chand, and Raili Riikonen contributed by participating as an expert and by a critical review of the manuscript for intellectual content.

All authors approved the final version of the manuscript to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors have agreed to the submission.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

None.

References

- [1] Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020;109:1088–95.
- [2] Wirrell EC, Grinspan ZM, Knupp KG, Jiang Y, Hammeed B, Mytinger JR, et al. Care delivery for children with epilepsy during the COVID-19 pandemic: an international survey of clinicians. *J Child Neurol* 2020. <https://doi.org/10.1177/0883073820940189>. in press.
- [3] Grinspan ZM, Mytinger JR, Baumer FM, Ciliberto MA, Cohen BH, Dlugos DJ, et al. Management of infantile spasms during the COVID-19 pandemic. *J Child Neurol* 2020;35:828–34.
- [4] Madaan P, Chand P, Linn K, Wanigasinghe J, Mynak ML, Poudel P, et al. Management practices for West syndrome in South Asia: a survey study and meta-analysis. *Epilepsia open* 2020;5:461–74.
- [5] Vaddi VK, Sahu JK, Dhawan SR, Suthar R, Sankhyan N. Knowledge, attitude and practice (KAP) study of pediatricians on infantile spasms. *Indian J Pediatr* 2018;85:836–40.
- [6] O'Callaghan FJK, Lux AL, Darke K, Edwards SW, Hancock E, Johnson AL, et al. The effect of lead time to treatment and age of onset on developmental outcome at 4 years in infantile spasms: evidence from the United Kingdom Infantile Spasms Study. *Epilepsia* 2011;52:1359–64.
- [7] Patterson V. Managing epilepsy by telemedicine in resource-poor settings. *Front Public Health* 2019;7:321.
- [8] Reddy C, Madaan P, Saini L. Tele-child-neurology in the era of COVID-19: A developing nations' perspective. *Ann Indian Acad Neurol* 2020; under issue preparation. doi: 10.4103/aian.AIAN_786_20.
- [9] Sahu JK, Madaan P, Chand P, Kumar A, Linn K, Mynak ML, et al. Management of west syndrome during COVID-19 pandemic: A viewpoint from South Asian West Syndrome Research Group. *Epilepsy Res* 2020;167:106453.
- [10] Telemedicine Practice Guidelines Enabling Registered Medical Practitioners to Provide Healthcare Using Telemedicine [Internet]. [cited 2020 September 20]. Available from: <https://www.mohfw.gov.in/pdf/Telemedicine.pdf>
- [11] Mytinger JR, Hussain SA, Islam MP, Millichap JJ, Patel AD, Ryan NR, et al. Improving the inter-rater agreement of hypsarrhythmia using a simplified EEG grading scale for children with infantile spasms. *Epilepsy Res* 2015;116:93–8.
- [12] Kramer U, Sue WC, Mikati MA. Hypsarrhythmia: frequency of variant patterns and correlation with etiology and outcome. *Neurology* 1997;48:197–203.
- [13] Bower BD, Jeavons PM. Infantile spasms and hypsarrhythmia. *The Lancet* 1959;273:605–9.
- [14] Caraballo RH, Ruggieri V, Gonzalez G, Cersósimo R, Gamboni B, Rey A, et al. Infantile spasms without hypsarrhythmia: A study of 16 cases. *Seizure* 2011;20:197–202.
- [15] McGarry L, Messer R, Cree-Green M, Ray K, Knupp K. Incidence of hypertension among children treated with adrenocorticotropic hormone (ACTH) or prednisolone for infantile spasms. *J Child Neurol* 2020;35:215–20.