

lauded for designing a well thought out tool, certain deficiencies stand out. For example, many of the criteria for a convulsive seizure also apply to convulsive syncope where similar symptoms are seen in upto 90% of patients [3]. The diagnostic tool would have been more discriminatory between seizures and NEE had signs like open eyes in seizures and closed eyes in NEE, been included [9].

The diagnosis of epilepsy is not a trivial one to make. Besides the ensuing family stress and anxiety, restrictions in activities and overprotection by parents lead to unacceptable social consequences. Chronic exposure to unnecessary anti-epileptic drugs (AEDs) with their wide range of adverse effects especially on behavior and sleep could be often detrimental to school performance. This is worsened by the ease with which AEDs are prescribed because of the prevalent belief that seizures are dangerous and brain damaging and that lack of treatment would somehow perpetuate epilepsy. This view is no longer tenable as it has been demonstrated that long-term outcome is similar whether treatment is immediate or deferred [10].

In summary, misdiagnosis of epilepsy is common. To improve diagnostic accuracy of epilepsy, one would need to improve training of physicians not only during service but also by increasing exposure to subject of epilepsy in pre-service curriculum. Diagnostic tools like the INDT-EPI would further help this cause.

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REFERENCES

1. Kotagal P, Costa M, Wyllie E, Wolgamuth B. Paroxysmal nonepileptic events in children and adolescents. *Pediatrics*. 2002;110:e46.
2. Uldall P, Alving J, Hansen L, Kibaek M, Buchholt J. The misdiagnosis of epilepsy in children admitted to a tertiary epilepsy center with paroxysmal events. *Arch Dis Child*. 2006;91:219-21.
3. Hindley D, Ali A, Robson C. Diagnoses made in a secondary care “fits, faints and funny turns” clinic. *Arch Dis Child*. 2006;91:214-8.
4. Hamiwka LD, Singh N, Niosi J, Wirrell EC. Diagnostic inaccuracy in children referred with “first seizure”: Role for a first seizure clinic. *Epilepsia*. 2007;48:1062-6.
5. Seneviratne U, Rajendran D, Brusco M, Phan TG. How good are we at diagnosing seizures based on semiology. *Epilepsia*. 2012;53:e63-6.
6. Stroink H, van Donselaar CA, Geerts AT, Peters ACB, Brauwer OF, van Nieuwenhuizen, *et al*. *J Neurol Neurosurg Psychiatry*. 2004;75:241-5.
7. Ferrie CD. Preventing misdiagnosis of epilepsy. *Arch Dis Child*. 2006;91:206-9.
8. Konanki R, Mishra D, Gulati S, Aneja S, Deshmukh V, Silberberg D, *et al*. INCLIN Diagnostic tool for epilepsy (INDT-EPI) for primary care physicians: Development and validation. *Indian Pediatr*. 2014;51:539-43.
9. Korff C, Nordli D. Paroxysmal events in infants: persistent eye closure makes seizures unlikely. *Pediatrics*. 2005;116:e485.
10. Marson A, Jacoby A, Johnson A, Kim L, Gamble C, Chadwick D; Medical Research Council MESS Study Group. Immediate *versus* deferred antiepileptic drug treatment for early epilepsy and single seizures: a randomised controlled trial. *Lancet*. 2005;365:2007-13.

Diagnostic Questionnaire and its Validation

BIostatistician's PERSPECTIVE

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Epilepsy is a complex disease to diagnose in some cases because seizures occur in a variety of conditions. Fever, central nervous system (CNS) infections, head trauma or systemic illnesses can cause seizures, and seizures also mimic breath holding spells and syncopal attacks. Differentiation of symptomatic from epileptic seizures, and of seizures from disturbance due to other transient neurological conditions may be difficult [1]. Reports

suggest that misdiagnosis and missed diagnosis among pediatricians can occur in nearly one-third of cases [1,2]. In addition to expertise, neuroimaging and electroencephalography are often needed to confirm or exclude the disease. Would it not be nice if the diagnosis can be made by asking a few searching questions? No need of any examination, no need of any investigation – just binary yes/no type answer to a series of questions. If

successful, this questionnaire can be used in most peripheral settings. Perhaps any graduate can be trained to elicit the right answer to these questions, and there would be no need of any physician either. If this can be done for an intricate disease such as epilepsy in children, the value naturally multiplies. This is exactly what an INCLLEN sponsored study [3] tried to do, that too with somewhere near 90% success! This issue contains the details of this study that claims 86% sensitivity, 95% specificity, 94% positive predictivity and 88% negative predictivity of the questionnaire they developed for diagnosis of epilepsy [3].

There have been many attempts in the past of developing a diagnostic questionnaire. One can appreciate the prominent role of a questionnaire for diagnosing a predominantly behavioral disease such as anxiety disorder in adults [4] and fetal alcohol spectrum disorders in children [5] but the attempts to diagnose clinically-interactive conditions such as chronic obstructive pulmonary disease through a short questionnaire was not particularly successful [6]. Thus there is a need to be extra careful in taking questionnaire route for diagnosing such a disease.

Developing a questionnaire containing items that are believed to have differential value for diagnosis apparently looks easy but could actually turn out to be a tall order. First is the choice of questions and the second is their correct framing. In the INCLLEN tool [3], Delphi method was adopted but that has not prevented discrepancies to creep in. To a third person like me, some questions are not as specific as I would have liked them to be in a questionnaire such as this. For example, Q4 asks the duration between the first and the last episode of seizure. The options for recording are 'less than 24 hours', 'more than 24 hours' and 'not applicable'. The age group covered by this study is 2 to 9 years; thus theoretically this gap between the first and the last episode could be as much as 8 years when a 8½-year old child had an episode recently and the first when the child was 6 months. The gap of 2 days is also more than 24 hours and the gap of 5 years is also more than 24 hours. Experts could tell how differential it is to club 2 days and 5 years together for diagnosis of epilepsy in children, and whether the gap between last two episodes could be a more revealing question. Similarly, Q3 asks the number of episodes the child had, and the options are 'one' and 'more than one'. In the absence of specification of the applicable duration, they are to be presumably counted since birth. I am not sure if that is what this question is designed for. If the parents of a child of age 8 years who has had episodes of seizures 5 years ago and thought of going to a clinic now, how this questionnaire will handle

this information? Some other 'discrepancies' of this type can be identified in this questionnaire.

In addition to the precision in framing questions in a diagnostic questionnaire, developing an algorithm that minimizes both false positives and false negatives can be nerve wrecking. In case of the INCLLEN tool [3], it seems from what is stated that Yes to Q10 or Q11 is enough for diagnosing epilepsy since the first condition regarding Q2, 3, 4 and 5-9 is not necessarily required. Q10 is on frequent episodes of 'going blank' or lose awareness of his/her surroundings, and Q11 is on presence of any of (i) sudden or unexplained episodes of falling to the ground, (ii) sudden head drop, and (iii) sudden jerking movement with bending of body. By the way these questions also do not specify the durations. They may have occurred 4 years ago. Q10 and Q11 can be easily combined in to a single question and, according to this questionnaire, positive answer to any of these items will identify epilepsy, although they will not be sufficient to exclude the disease. Experts will decide the validity of this assertion.

Next challenge in developing a successful questionnaire for diagnostic purposes is its validation. Sensitivity, specificity, positive predictivity and negative predictivity are indeed valid measures. But sensitivity and specificity are used in retrospective setups where the disease status is already known, and predictivities in prospective setup where the disease status is elicited. It is only for representative cross-sectional studies that both can be used on the same data [7]. For any such tool, internal consistency and external validation are also important prerequisites for its usability. In addition, a clear distinction must be made between a screening tool and a diagnostic tool. If the objective is to reduce the burden on the secondary level of care, the focus clearly is on screening and not on diagnosis.

Despite such limitations, any attempt for developing a questionnaire-based diagnostic tool is welcome because of its wide applicability. Few such attempts have been made in India and they need encouragement. The tool can be subsequently modified as feedback is received on its merits and demerits.

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REFERENCES

1. Chadwick D, Smith D. The misdiagnosis of epilepsy. *BMJ*. 2002;324:495-6.
2. Uldall P, Alving J, Hansen LK, Kibaek M, Buchholt J. The misdiagnosis of epilepsy in children admitted to a tertiary epilepsy centre with paroxysmal events. *Arch Dis Child*. 2006;91:219-21.
3. Konkani R, Mishra D, Gulati S, Aneja S, Deshmukh V,

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- Silberberg D, *et al.* INCLIN diagnostic tool for epilepsy (INDT-EPI) for primary care physicians: Development and validation. *Indian Pediatr.* 2014;51:539-43.
4. Norton PJ, Robinson CM. Development and evaluation of the anxiety disorder diagnostic questionnaire. *Cogn Behav Ther.* 2010;39:137-49.
 5. Fitzpatrick JP, Latimer J, Ferreira M, Martiniuk AL, Peadar E, Carter M, *et al.* Development of a reliable questionnaire to assist in the diagnosis of fetal alcohol spectrum disorders (FASD). *BMC Pediatr.* 2013;13:33.
 6. Stanley AJ, Hasan I, Crockett AJ, van Schayck OC, Zwar NA. Validation of the COPD Diagnostic Questionnaire in an Australian general practice cohort: A cross-sectional study. *Prim Care Respir J.* 2014;23:92-7.
 7. Indrayan A. *Medical Biostatistics, Third Edition*, Chapman & Hall: CRC Press, 2012.
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