INCLEN Diagnostic Tool for Neuromotor Impairments (INDT-NMI) for Primary Care Physician: Development and Validation

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Objectives: To develop and validate a diagnostic tool for use by primary care physicians for diagnosing neuro-motor impairment among 2-9 year old children in primary care settings.

Study design: Modified Delphi technique involving national (n=49) and international (n=6) experts was used for development of INDT-NMI. The tool was then validated through a cross sectional study.

Setting: Neurology specialty clinics of three tertiary care pediatric centers in New Delhi, India.

Participants: 454 children aged 2-9 years [mean (SD) age: 60.4 (23.7) mo], selected through systematic random sampling, underwent assessment for identification and classification of neuromotor impairments (NMI).

Intervention: All study subjects were first administered INDT-NMI (candidate test) by a trained physician followed by expert assessment for NMI and other neurodevelopment disorders (NDD) by team of two pediatric neurologists (Gold standard).

Results: According to expert evaluation, 171 (37.8%) children had neuromotor impairments. There were four categories of subjects: NMI alone (n=66); NMI+other NDDs (n=105); Other NDDs without NMI (n=225) and ‘Normal’ group (n=58). Using expert evaluation as gold standard, overall sensitivity of the INDT-NMI was 75.4% and specificity was 86.8%. INDT-NMI helped graduate physicians to correctly classify 86.6% (112/129) children with NMI into different types (cerebral palsy, neuromotor diseases and other NMI). Graduate physicians assigned 40 children (8.8%) as ‘indeterminate’, 38 (95%) of whom had either NDD and/or NMI and thus merited referral. Misclassification of NMI occurred in those with mild changes in muscle tone, dystonia, or ataxia and associated NDDs.

Conclusion: Graduate primary care physicians with a structured short training can administer the new tool and diagnose NMI in 2-9 year old children with high validity. INDT-NMI requires further evaluation in actual primary care settings.

Keywords: Cerebral palsy, Disability, Diagnosis, Neuromuscular disorders, Resource constrained environments.

Primary care physicians frequently encounter children with neuromotor impairments who have difficulties of movement, posture and coordination in their day-to-day life. Neuromotor impairments (NMI) include a continuum of disorders caused by a wide variety of non-progressive and progressive conditions that affect body functions, activities, and quality of life. Cerebral palsy (CP) constitutes the bulk of NMI; progressive acquired or inherited neuromuscular disorders (NMD), and other NMI (not satisfying the definition of either CP or NMD) have to be considered in differential diagnoses as the approach to management and outcome varies significantly [1-3].

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Pediatric neurologists, developmental pediatricians and therapists with expertise in diagnosis and management must be able to obtain a relevant history and perform focused musculoskeletal, neurologic and functional physical examinations to diagnose NMI [4]. The availability and access to such expertise in resource-constrained environments like India and other...
developing countries is severely restricted and thus significantly increases the gaps in identification, and delivery of specific therapeutic and rehabilitative services for NMI [5,6]. Availability of a diagnostic tool for use by primary care physicians will considerably increase access to specific care and rehabilitation of children with NMI. Currently no validated tool is available for diagnosing NMI among 2-9 year old children in primary care settings. The demand for such a tool is further enhanced in the light of recently launched Rastriya Bal Swasthya Karyakram (RBSK) wherein diagnosis and management of neuro-developmental disorders within primary care settings is a core element of the program services [7].

To fill this gap, the INCLEN study group developed and validated a diagnostic tool for NMI (INDELN Diagnostic Tool for Neuromotor Impairments: INDT-NMI) that employs standardized and uniform diagnostic criteria for use in 2-9 year-old children. The tool is meant to be used by graduate physicians after a structured short training in primary care settings.

**METHODS**

**Study design:** Modified Delphi process for developing the tool, and diagnostic test evaluation by cross-sectional study design

The study was part of the INCLEN program to estimate the burden of Neuro-developmental Disorders (NDDs) in 2-9 year-old children at five sites across the country. As part of the larger study, specific diagnostic tools (for autism spectrum disorders [8], attention deficit hyperactivity disorder [9], epilepsy [10] and NMI) were developed and validated for use by different levels of health personnel. INDT-NMI is to be applied by primary care physicians for the diagnosis of NMI. The evaluation of INDT-NMI was conducted on 2-9 year-old children attending the pediatric neurology outpatient clinic of three public sector tertiary-care referral centers [All India Institute of Medical Sciences (AIIMS), Lady Hardinge Medical College (LHMC), and Maulana Azad Medical College (MAMC)] in New Delhi, India. The pediatric neurology specialty clinics in these hospitals attract a mix of complex neurology problems referred for diagnosis and management. Children of either gender in the age group 2-9 years coming for the first time in the pediatric neurology clinics of these hospitals were eligible for inclusion in the study. Children were excluded from the study if they had poor general condition (e.g. respiratory distress requiring supplemental oxygen, peripheral circulatory collapse, altered sensorium, or requiring care in intensive care), were not accompanied by primary caregiver, and if care provider refused consent. The tool development and validation exercise was conducted from June 2008 to April 2010. Ethical approval was obtained from INCLEN review board and ethics committees of all the sites.

**Development of diagnostic tool:** Candidate test: As the first step, a consensus clinical criteria (CCC) for diagnosing NMI was developed by group of national (n=49) and international (n=6) experts consisting of pediatricians, developmental pediatricians, child psychiatrists, pediatric neurologists, pediatric oto-rhino-laryngologists, community physicians, clinical psychologists, special educators, specialist nurses, speech therapists, occupational therapists, and social scientists, for diagnosing NMI through a series of three 2-day workshops and web-based discussion using modified Delphi method. The CCC was then converted in to a diagnostic tool, INDT-NMI, for use by graduate physicians in primary care settings.

INDT-NMI is based on the definitions and classification proposed for cerebral palsy [11] along with questions to identify neuromuscular disorders (NMD) and other NMI that do not fit in to definition of either of these conditions (for practical reasons and simplification of the diagnostic process at primary level). The INDT-NMI thus developed comprises of three sections. Section-I (Triage questions) consists of four questions to elicit information from the parents/primary caregiver of the child regarding attainment of selected motor developmental milestones. Section-II (Observations): Physician makes three observations for assessing hand function, gait and muscle weakness. Section-III consists of six questions, and the operator (graduate physician) does the neurological examination necessary for confirmation of NMI. Thus final diagnosis of NMI is derived through an algorithm based on interpretation of three sections (i.e. 13 questions/items) and information on age at onset of symptoms, course of the illness and obvious clinical evidence of involvement of spinal cord (i.e. pilonidal sinus, tuft of hair). This tool requires approximately 20-25 minutes for assessing each child. Tool includes specific neurologic examination with interpretation but examination of cranial nerves and sensory neurologic system examination is not included in the tool as these are not directly relevant for making diagnosis of NMI. The final diagnosis informs whether the case has cerebral palsy (CP), neuromuscular disorders (NMD), Other NMI (that does not fit in to either CP or NMD), no NMI or an indeterminate clinical condition. The tool (Web Appendix I) was prepared in English, translated into Hindi and back translated to English before the study was undertaken.
At each of the three institutions, diagnosis of NMI was established by consensus of two pediatric neurologists with expertise in diagnosis and management of children with NMI and other NDDs. The clinical assessment included detailed history and physical examination with access to radiological and other relevant investigations whenever available.

Systematic random sampling of the children attending pediatric neurology clinics was followed for enrolment of study subjects. Daily, the principal investigator provided two computer-generated random numbers to the study coordinator in a sealed envelope. First random number (between 1 and 9) gave the serial number of first child to be recruited in the clinic and second random number was the nth number of patient (between 5 and 15 and represented interval between subjects as they came up in neurology specialty OPD at central registration) who was identified for the detailed evaluation. The identified subjects so enrolled were assessed for eligibility by site coordinator, and enrolled after obtaining written, informed consent until the final sample size was achieved. If consent or inclusion criterion was not achieved or if the child was not a first timer attendee, \((n+1)\text{th}\) child was enrolled. Subjects were recruited till the desired sample size was obtained in each category.

At each study site, a team of pediatric neurologists (at least two per site) with at least three years of experience in the diagnosis and management of children with NMI and other NDDs, one study coordinator and two graduate physicians (MBBS) undertook the study. Subjects were first administered the INDT-NMI (candidate test) by a graduate doctor (MBBS qualified) and later evaluated by the expert team of pediatric neurologists (gold standard). The findings of the graduate physician and expert group were separately placed in opaque envelopes, sealed and handed over to the coordinator. Evaluators of one category were blinded to the diagnosis of the other group. The children were given prescription and instructions for additional investigations as required and follow-up by the expert group. After initial assessment, the subjects were not allowed to interact with the graduate physician to avoid contamination and influence on the assessment of subsequently recruited subjects.

A standardized training manual with detailed instructions for administration of the tool was developed. Graduate physicians at each center administered the questionnaire verbatim, questioning the parents in the language they could understand (English or Hindi). These individuals were trained during a one-day hands-on structured workshop that included eight hours of didactic teaching and simulated administration of the tool in five cases of neuro-motor impairment. The training also involved interview skills and techniques of neurological examination of children.

**Sample size:** We expected four categories of subjects in whom INDT-NMI was to be evaluated: NMI alone, NMI along with other NDD, Other NDDs without NMI and children without NMI or other NDDs (Normal). Assuming sensitivity and specificity of INDT-NMI to be 85% with ±10% precision at 95% confidence level, sample size was calculated to be 50 subjects in each category of patients. To account for 10% drop-outs, it was decided to enroll at least 55 children in each category. The sample size was calculated using Epi info software [12].

**Statistical analysis:** The data were analyzed using STATA 10 software. The psychometric properties of INDT-NMI were calculated against the assessment done by team of pediatric neurologists (Gold standard).

**RESULTS**

A total of 454 children (mean ± SD age: 60.4 ± 23.7) were enrolled from three centers: AIIMS 354; MAMC 46; and LHMC 54. The subjects included 308 (68%) boys and 146 (32%) girls; 40.3% \((n=183)\) were 24-48 month old, 43.2% \((n=196)\) were aged between 49-84 months, and 16.5% \((n=75)\) belonged to 85-108 month category. According to expert evaluation, 66 children had NMI alone (CP=39; NMD 20; other NMI 7), 105 had NMI with other NDDs (CP 95; NMD 3; other NMI 7) 225 with Other NDDs without NMI, and 58 subjects were normal (without NMI or any other NDD). Thus, 171 (38%) children had NMI (CP 134; NMD 23 and other NMI 14) and remaining 283 (62.3%) were without NMI. Out of 134 children with CP, 95 (70.9%) had one or more comorbidities like epilepsy, global developmental delay and intellectual disability.

Using INDT-NMI, graduate physicians were able to assign NMI (yes/no) label to 414 subjects: remaining 40 out of 454 (8.8%) subjects were categorized as ‘indeterminate’ (Fig. 1). The overall sensitivity of the tool was 75.4% (95% CI: 68.0-81.3) and specificity was 86.6% (95% CI: 82.1-90.1). Out of 129 NMI cases detected true positive, 112 (86.8%) were correctly classified by INDT-NMI to a specific neuro-motor impairment type (CP, NMD or other NMI).

**Table 1** provides validity of the tool for various groups of subjects without taking indeterminate cases in to consideration. Sensitivity of the tool was between 89.7% and 83.7% for two groups of NMI; while the specificity among normal children or those with other NDDs was 96.4% and 91.8%, respectively.
**Fig. 1 INCLEN Diagnostic Tool for Neuromotor Impairment (INDT–NMI): Subject recruitment and assessment.**

The expert (gold standard) diagnostic labels of 40 subjects categorized as ‘indeterminate’ by the INDT-NMI were: NMI alone 8; NMI + other NDD 13; NDD other than NMI 17; and Normal (without NMI or any NDD) 2. Failure to identify hypotonia, mild spasticity, dystonia and ataxia by the graduate physicians were the frequent reasons for NMI cases being labeled as indeterminate. Twenty-one children (52.5%) had intellectual disability/global development delay. Overall, out of 40 indeterminate cases, 38 (95%) had other NDDs with or without NMI; remaining 2 children were from ‘Normal’ group and had moderate undernutrition.

False negative cases had hypotonia (4 patients),
spasticity (14 patients), ataxia (2 patients) and dystonia (one patient). Over two-third of these (15/21) were associated with other NDDs as well. The neuro-motor impairment was mild in most of these children. There were 19 false positives: 17 with different NDDs and 2 from normal category. Eleven of these children had varying degree of intellectual disability and 2 had autism. Seizure disorder was also present either as isolated condition (N=3) or with other NDDs (N=5). Two children without any NDD had rickets (N=1) and moderate under-nutrition (N=1). INDT-NMI categorized the false positives as having CP in 17 cases and one each with NMD and other NMI.

**DISCUSSION**

The diagnosis of neuro-motor impairments including cerebral palsy is essentially clinical. In this study on development and validation of a simple clinical tool (INDT-NMI), good psychometric properties (sensitivity 75.4% and specificity 86.6%) were observed. About 9% subjects were categorized as ‘indeterminate’ and most of these (95%) were having either NMI or had another NDD.

The concept and definition of CP has changed over years reflecting the evolving understanding of causative mechanisms and varied manifestations [11,13-16]. To the best of our knowledge, no validated tools for diagnosing and categorizing neuro-motor impairments for children older than two years are available. Several assessment tools are however, available to quantify and monitor developmental milestones and skills in children with CP and other NMI after initial diagnosis has been made and to assess the quality of life of patients and their caregivers [17-20]. Tiered approach involving initial community screening followed by diagnostic assignment by an expert have been applied in epidemiologic studies [21-23]. Use of motor developmental milestones to screen for delays and identify children with CP has been evaluated in a group of high-risk, prematurely born infants below two years of age [18-20]. Kuban, et al. [24] incorporated selected components from standard neurological examination to an algorithm for identifying cerebral palsy in 2-year-old children who were born at extremely low gestational age, in a multi-centric epidemiological study. The minimum threshold criteria for identifying cerebral palsy were specified but the diagnosis of CP using this algorithm was not validated using any reference standard assessment. Similar to our study, efforts to strengthen primary care have been made in China with recent validation of Chinese version of INFANIB for assessing infants with neuromotor abnormalities in primary care setting [25].

In the current study, over 86% of true positives were correctly classified in to the various sub-types of NMI. Clinically, it is important to differentiate CP from other neuromotor impairment and neuromuscular disorders for deciding the line of investigations, specific therapeutic and rehabilitative interventions, and counseling. In our patients, 70% children with NMI had other co-morbidities like epilepsy, global developmental delay and intellectual disabilities. Similar findings have been described in other studies and therefore there is need for a

<table>
<thead>
<tr>
<th>Categorization as per Candidate Test</th>
<th>Neuromotor Impairment Alone (N= 58)</th>
<th>#Neuromotor Impairment + Other NDDs (N=92)</th>
<th>NDDs without NMI (N=208)</th>
<th>Children without NMI and NDDs (normal) (N=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroromotor impairment</td>
<td>52</td>
<td>77</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>No neuro-motor impairment</td>
<td>6</td>
<td>15</td>
<td>191</td>
<td>54</td>
</tr>
<tr>
<td>Sensitivity % (95% CI)</td>
<td>89.7 (78.8-96.1)</td>
<td>83.7 (74.8-90.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity % (95% CI)</td>
<td>–</td>
<td>91.8 (87.3-95.2)</td>
<td>96.4 (87.7-99.6)</td>
<td></td>
</tr>
<tr>
<td>+Likelihood Ratio (Group I and III)</td>
<td>11 (6.9-17.4)</td>
<td>–</td>
<td>0.1 (0.05-0.24)</td>
<td></td>
</tr>
<tr>
<td>+Likelihood Ratio (Group I and IV)</td>
<td>25.1 (6.4-98.2)</td>
<td>–</td>
<td>0.1 (0.05-0.22)</td>
<td></td>
</tr>
<tr>
<td>+Likelihood Ratio (Group II and III)</td>
<td>10.2 (6.4-16.3)</td>
<td>–</td>
<td>0.1 (0.1-0.28)</td>
<td></td>
</tr>
<tr>
<td>+Likelihood Ratio (Group II and IV)</td>
<td>23.4 (5.9-91.7)</td>
<td>–</td>
<td>0.1 (0.1-0.26)</td>
<td></td>
</tr>
</tbody>
</table>

Figures in parenthesis are 95% CI; * Out of 454 subjects, 40 (8.8%) were categorized as Indeterminate; 38/40 (95%) had NMI with or without NDD and were referred for further workup. Details of indeterminate cases are given in the text; 9 These are the diagnostic categories as per expert evaluation (Gold Standard).
comprehensive assessment of all these subjects. In any situation, once diagnosis of NMI is made in primary care, physiotherapy can be initiated early while detailed specialist assessment is underway. Triage questions of the INDT-NMI can potentially be evaluated in future studies for screening of NMI in the community by non-physician healthcare personnel.

Analysis of false positives and negatives indicated that there is need to emphasize identification of mild changes in tone, and dystonia through demonstration and actual hands-on practice during training. This aspect may require extending the training by a few hours and ensuring some patients with subtle findings for training of the graduate physicians. Misclassification of a few moderately malnourished children – who can have hypotonia – in to false positives is another limitation of the tool. The performance of the tool may be better in the hands of physicians with longer experience and among those who continue to use it for some time. Another limitation of the study was that expert groups adopted a clinical rather than a protocol based approach to establish the NDD diagnosis and obtained special investigations as and when these were considered relevant. The tool was evaluated in tertiary care clinics while INDT-NMI is meant to be used in primary care settings. The performance of INDT-NMI therefore needs to be systematically evaluated in primary care of different geographic regions and general practice environment for its diagnostic capability.

In conclusion, graduate primary care physicians with a structured short training can administer the new tool and diagnose NMI in 2-9 year old children with high validity. INDT-NMI requires further evaluation in actual primary care settings. The tool will help early diagnosis of NMI in primary care and institution of physiotherapy and assignment to a specialist for detailed evaluation and management.

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