RESEARCH PAPER

Diagnostic Accuracy of Indian Scale for Assessment of Autism in Indian Children Aged 2-5 Years

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Objective: To determine the diagnostic accuracy of Indian Scale for Assessment of Autism (ISAA) in children aged between 2-5 years.

Design: Study of diagnostic accuracy

Setting: Tertiary level hospital, (November 2015 – November 2017).

Participants*:* A consecutive sample of 500 children with suspected Autism (delay or regression of developmental milestones, delay or regression in speech, age-inappropriate understanding, behaviour, play and/or social interaction) was recruited.

Procedure: Each child underwent an expert comprehensive assessment of Autism (reference tool) that included history, observation, examination, diagnostic criteria for Autism Spectrum Disorder (ASD) of the Diagnostic and Statistical Manual of Mental Disorders', 5th edition, Childhood Autism Rating Scale-2 (CARS2), developmental status and adaptive function. This was followed by the administration of ISAA (test tool) in Hindi language. Parameters of diagnostic accuracy and Receiver Operating Characteristic curves were computed.

Main Outcome Measures: ASD based on (*i*) expert assessment, (*ii*) CARS-2, and (*iii*) ISAA.

Results: In children aged 2-3 years, sensitivity of ISAA was 100% (95% CI 98.2% -100%), specificity 28.9% (95% CI 17.7% to 43.4%), positive likelihood ratio 1.4 and negative likelihood ratio 0. In 3-5 year olds, sensitivity was 99.6% (95% CI 97.6% to 99.6%), specificity 33.3% (95% CI 15.1% to 58.3%), positive likelihood ration 1.5 and negative likelihood ratio 0.01. The degrees of autism based on the existing cut off values were inaccurate.

Conclusions: ISAA has sub-optimal performance in diagnosing and assessing severity in 2-5 year old children.

Keywords: *Autism Spectrum Disorder, Classification, Diagnosis*.

The prevalence of Autism spectrum disorders (ASD) is high in Indian children [1], but there is a scarcity of Indian mental health professionals and paraprofessionals skilled in their management [2]. As early detection and initiation of intervention before 4 years has a better prognosis [3], delayed diagnosis has far-reaching implications well in adulthood. There is a strong need to identify a tool best suited for diagnosing ASD in young children. Feasibility issues related to applying international practice parameters in the Indian population [4,5] prompted the development of the indigenous tools – Indian Scale for Assessment of Autism (ISAA) [6] and INCLEN Diagnostic Tool for ASD (INDT-ASD) [7]. Validation studies in diagnosis naive children are inadequate.

In 2016, the National Trust for Welfare of Children with Autism (India) recommended that after formal training, INDT-ASD should be used for diagnosing Autism, and ISAA should be restricted to certify disability in children ≥6 years [8-10]. The consensus statement of the Childhood Disability Group (Indian Academy of Pediatrics) listed ISAA in the assessment tools for ASD in children, but did not recommend any age criteria [11]. Pediatricians and paraprofessionals routinely use ISAA to diagnose Autism in children under 5 years of age. Prevalence studies have been published based on evaluation by ISAA, despite its uncertain accuracy [12-15]. These issues have serious implications in the management of pre-schoolers with ASD. Hence, we studied the diagnostic accuracy of ISAA in 2-5-year-old children and also assessed its level of agreement with Childhood Autism Rating Scale 2nd edition (CARS-2) and expert comprehensive assessment.

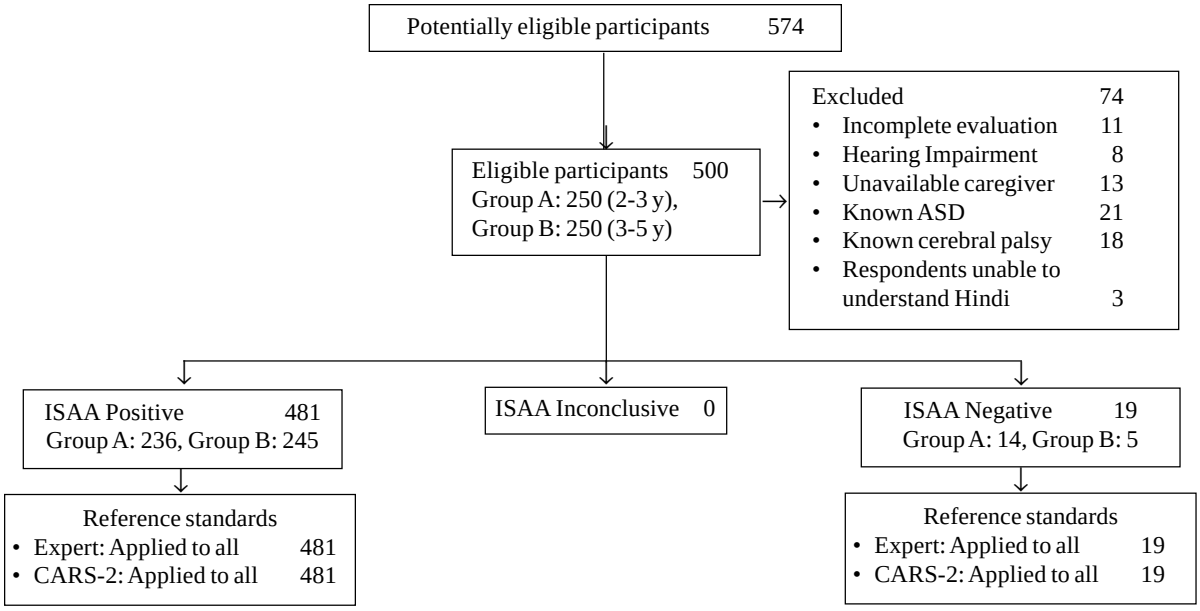
METHODS

This study of diagnostic accuracy was conducted over 2 years (November 2015 to November 2017) in a teaching hospital after obtaining approval from the Institutional ethics committee. Children aged between 2-5 years presenting with delay or regression of developmental

milestones, abnormal language, or age inappropriate understanding, behavior, play and/or social interaction were consecutively recruited from the pediatric outpatient department. Children with primary caregivers who were unavailable or did not understand Hindi language, had incomplete evaluations, or those with hearing impairment, known cerebral palsy, ASD or neurodegenerative disorders were excluded. An age-stratified sample size of 500 was calculated – 250 in Group A (2-3 years) and Group B (3-5 years) each – based on estimated 80% prevalence of ASD in 'high risk' referred population [4], 80% sensitivity and 80% specificity of ISAA with 10% attrition.

Each eligible child underwent evaluation for 1.5-2 hours after obtaining written informed consent. This included review of home videos, parental interview, observation of the child and administration of the following: (*i*) Developmental Profile, 3rd edition (DP 3) for evaluating developmental status by the General Developmental Score (GDS), wherein GDS <70 is a 'delay' [16]; (*ii*) Vineland Adaptive Behavior Scale, 2nd edition (VABS-II) for assessing adaptive function by the Adaptive Behavior Composite (ABC), wherein ABC <70 is 'low' [17]; (*iii*) Diagnostic criteria for ASD of 'Diagnostic and Statistical Manual of Mental Disorders', 5th edition (DSM 5), in which all criteria pertaining to persistent difficulty in social communication and social interaction, at least two out of four criteria pertaining to restrictive and repetitive patterns of behaviour, and all obligatory criteria need to be satisfied [18]; (*iv*) CARS 2 which rates severity of symptoms of ASD based on total scores, 'minimal-to-no-symptoms' if 15-29.5, 'mild-to-moderate' if 30-36.5 and 'severe' if >37 (reference tool 1) [19]; and (*v*) Brainstem evoked response auditory (BERA). The psychometric instruments were administered by a clinician psychologist. The final diagnosis (ASD/ No ASD) was established by a professor with 14 years of experience in developmental pediatrics based on a comprehensive assessment (reference tool 2). This comprised of a synthesis of the following; personal elicitation of history, review of home videos, observation, examination, confirmation of DSM 5 criteria and review of assessment scores.

The Hindi version of ISAA (test tool) was then administered by a blinded social worker and trained pediatrician over 45-60 minutes. ISAA comprises of 40 items covering 6 domains; social relationship and reciprocity, emotional responsiveness, speech-language and communication, behavior patterns, sensory aspects and cognitive component [6]. Each item is assigned a Likert score ranging from 1 (rarely) to 5 (always) based on parental history and interviewer observations. The total score denotes the degree of autism and corresponding disability; ≤70 denotes no Autism (<40% disability), 71 to 106 mild (50-60%), 107 to 153 moderate (70-90%) and >153 severe (100%). Parental counseling was done by the expert, and the children were managed as per hospital protocol.



ASD: Autism Spectrum Disorder, CARS 2: Childhood Autism rating Scale, 2nd edition, ISAA: Indian Scale for Assessment of Autism

Fig. 1 *Flow of recruitment, selection and evaluation of study participants.*

TABLE I: CLINICAL AND PSYCHOMETRIC PROFILES OF STUDY POPULATION

Profile	*Descriptor*	*2-5 y (n=500)*	*A: 2-3 y (n=250)*	*B: 3-5 y (n=250)*	*P value A vs B*
Presenting	Developmental delay	235 (47.0)	106 (42.4)	129 (51.6)	0.04
complaints, *n* (%)	Age inappropriate. cognition	293 (58.6)	142 (56.8)	151 (60.4)	0.41
	Speech issues	356 (71.2)	165 (66.0)	191 (76.4)	0.01
	Regression	95 (19.0)	79 (31.6)	16 (6.4)	<0.05
	Age inappropriate play	184 (36.8)	73 (29.2)	111 (44.4)	0.05
	Age inapp. behavior / SI	276 (55.2)	98 (39.2)	178 (71.2)	<0.05
Co-morbid	Epilepsy	143 (28.6)	71 (28.4)	72 (28.8)	0.92
conditions, *n* (%)	Sleep related issues	337 (67.4)	179 (71.6)	158 (63.2)	0.04
	Feeding issues	334 (66.8)	172 (68.8)	162 (64.8)	0.34
Significant	Caesarean section	140 (28)	67 (26.8)	73 (29.2)	0.55
histories, *n* (%)	Preterm gestation	33 (6.6)	18 (7.2)	15 (6.0)	0.59
	Low birth weight	70 (14)	39 (15.6)	31 (12.4)	0.30
	Neonatal hospitalization	179 (35.8)	100 (40.0)	79 (31.6)	0.05
	Positive family history	61 (12.2)	32 (12.8)	29 (11.6)	0.68
Nutritional	Underweight	126 (25.2)	74 (29.6)	52 (20.8)	0.02
status, *n* (%)	Severe underweight	48 (9.6)	30 (12.0)	18 (7.2)	0.06
	Wasting	102 (20.6)	77 (30.8)	26 (10.4)	<0.05
	Severe wasting	10 (2)	6 (2.4)	4 (1.6)	0.5
	Stunting	123 (24.6)	64 (25.6)	59 (23.6)	0.6
	Severe stunting	69 (13.8)	38 (15.2)	31 (12.4)	0.36
Head	Microcephaly	128 (25.6)	72 (28.8)	56 (22.4)	0.1
circumference, *n* (%)	Macrocephaly	14 (2.8)	7 (2.8)	7 (2.8)	1.0
Dysmorphism, *n* (%)	Major physical anomalies	188 (37.6)	81 (32.4)	107 (42.8)	0.02
Development	Delay[#], *n* (%)	481 (96.2)	245 (98)	246 (98.4)	0.73
Adaptive function	Mean ABC (95% CI)	58 (56.9-59)	61.5 (59.9-63)	54.5 (53.2-55.9)	<0.05
Comp. Ass.	Low[$], *n* (%)	442 (88.4)	207 (82.8)	235 (94.0)	<0.05
	ASD, *n* (%)	440 (88)	205 (82)	235 (95)	<0.05
CARS-2:	No –minimal	22 (4.4)	15 (6)	7 (2.8)	0.08
symptoms of	Total score	21.7 (20.1-23.3)	19.7 (18.6-20.8)	25.9(23.6-28.2)	0.2
ASD, *n* (%) with	Mild to moderate	85 (17)	55 (22)	30 (12)	<0.05*
mean (95% CI) scores	Total score	31.6 (30.5-32.6)	31.5(30.5-32.5)	31.8(29.6-34)	<0.05*
	Severe	393 (78.6)	180 (72)	213 (85.2)	<0.05*
	Total score	43.5(43.1-43.9)	43.2(42.7-43.7)	43.8(43.2-44.4)	0.15
ISAA:	No Autism	19 (3.8)	14 (5.6)	5 (2)	0.04*
degree of	Total score	62.5(59.4-65.6)	62.9(59.4-66.4)	61.6(54.2-69.0)	0.45
Autism, *n* (%)	Mild Autism	127 (25.4)	66 (26.4)	61 (24.4)	0.6
with mean (95% CI)	Total score	94.4(92.4-96.4)	92.7(89.6-95.8)	96.3(93.9-98.7)	0.01*
total scores	Moderate Autism	349 (69.8)	168 (67.2)	181 (72.4)	0.2
	Total score	125.2 (124-126.4)	125.1 (123.4-126.8)	125.2 (123.6-126.8)	0.63
	Severe Autism	5 (1.0)	2 (0.8)	3 (1.2)	0.6
	Total score	154.6 (140.7-168.5)	145.5 (117.1-173.9)	160.7 (146.7-174.7)	0.48

ABC: Adaptive Behavior Composite, ASD: Autism Spectrum Disorder, CARS-2: Childhood Autism Rating Scale, 2nd edition, ISAA: Indian Scale for assessment of Autism, SES: Socio-economic status, SI: social interaction, Comp.Ass: Comprehensive assessment; [#]Development has a Delay' when General Developmental Score <70. [$]Adaptive Function is 'Low' when ABC <70.

TABLE II: PARAMETERS OF DIAGNOSTIC ACCURACY OF ISAA IN CHILDREN AGED 2-5 YEARS

Parameter	*2-3 years (n=250)*		*3-5 years (n=250)*		*2-5 years (n=500)*	
	Comp. Ass.	*CARS-2*	*Comp. Ass.*	*CARS-2*	*Comp. Ass.*	*CARS-2*
Sensitivity	100	97.6	99.6	98.7	99.8	98.1
Specificity	28.9	53.3	33.3	28.6	30	45.5
Posivitive predictive value	86.5	97.2	95.9	97.9	91.3	97.5
Negative predictive value	100	57.1	83.3	40	94.7	52.6
Positive likelihood ratio	1.4	2.1	1.5	1.38	1.4	1.8
Negative likelihood ratio	0	0.1	0.01	0.04	0	0.04
Diagnostic accuracy	87.2	95.0	95.6	96.8	91.4	95.8

CARS-2: Childhood Autism Rating Scale (2nd edition); Comp. Ass: Comprehensive assement.

TABLE III: SENSITIVITY AND SPECIFICITY OF ISAA IN CHILDREN AGED 2-5 YEARS AT DIFFERENT LEVELS AND CUT-OFF SCORES

Cut-off on ROC curve	*Cut-off score*	*2-3 years*		*3-5 years*		*2-5 years*	
		Sn (%)	*Sp (%)*	*Sn (%)*	*Sp (%)*	*Sn (%)*	*Sp (%)*
≥Level 1	71	100	28.9	99.5	33.3	99.7	30
≥Level 2	107	79.5	82.2	77.9	100	78.6	86.7
≥Level 3	153	1.5	100	0.85	100	1.1	100

ISAA: Indian Scale for Assessment of Autism, ROC curve: receiver operating characteristic curve, Sn: Sensitivity, Sp: specificity

The outcome measures were: children diagnosed with ASD based on expert assessment, CARS-2 and ISAA. Statistical analysis was performed *by the STATA software package*, version 10.1, 2011. Standard parameters of diagnostic accuracy and Receiver Operating Characteristic (ROC) curves (Open 80 software) were determined.

RESULTS

The flow of participants from recruitment till diagnosis is depicted in ***Fig.* 1**. The mean age of the entire group, group A and group B was 37.8 , 28.6 and 47.1 months respectively. The sex ratio was 7:3 in each. The distribution of socio-economic strata was similar, predominantly upper and middle socio-economic strata. An age-wise comparison of the clinical and psychometric profiles of the study population is presented in ***Table* I**. Diagnostic accuracy of ISAA (test tool) with respect to expert and CARS-2 evaluation are compared in ***Table* II**.

ROC curves to determine overall accuracy of ISAA for discriminating between ASD and Non-ASD across the ISAA cut-off scores are displayed in ***Fig.* 2** and ***Web Fig.* 1**. The optimal threshold point (closest to 0,1) was observed at a total ISAA score of 107. The discriminatory power was good in group A with area under curve (AUC) 0.83 (95% CI 0.78, 0.90), excellent in group B with AUC 0.92 (95% CI 0.89, 0.96) and good (collectively) with AUC 0.85 (95% CI 0.8, 0.9). The age-wise sensitivity and specificity at different cut-off scores at different levels are presented in ***Table* III**. The comparative ROC of the discriminatory power of CARS-2 and ISAA with the comprehensive assessment was good: AUC 0.88 (95% CI 0.84, 0.93) for CARS-2 and AUC 0.85 (95% CI 0.80, 0.90) for ISAA.

DISCUSSION

In our study of the diagnostic accuracy of ISAA (test tool) in 2-5-year-old children against a comprehensive expert assessment (reference tool 1) and evaluation by CARS-2 (reference tool 2), sensitivity was acceptable (>80%), but specificity was very low. The ROC also revealed that the optimal sensitivity and specificity in differentiating between ASD and non-ASD children differed from the existing cut-offs resulting in inaccurate assessment of the extent of Autism.

The strength of this study was age-stratification, which ensured adequate representation of 2-3 year olds. Since validity was questionable from the onset, reliability was not assessed. Limitations include the study being restricted to a single center. In addition, referral bias due to hospital having a neuro-developmental center may also be an issue. We tried to minimize evaluation bias by deferring parental disclosure of diagnosis till final

WHAT IS ALREADY KNOWN?

- The 2016 National Trust (India) guidelines recommend that ISAA be used only for certification of disability due to ASD in children 6 years and above.

WHAT THIS STUDY ADDS?

- The specificity of the Hindi version of ISAA is low for diagnosis of Autism in children aged 2-5 years.

counseling and blinding the person who administered ISAA to the expert diagnosis. However, there may be a possibility of conceptual priming influencing of the respondent, which may occur when two similar evaluations are done successively on the same day.

The high sensitivity (>90%) of ISAA found in the present and earlier studies is explainable by similarity of content (autistic symptoms) of the reference tools used (CARS-2 and DSM V) [6,18,19]. Comparison of previous studies with our results revealed a significant difference in specificity at different ages of the participants–92 in 3-22 year olds (mean age 9.4 years) (6), 97 in 2-9 year olds (mean age 4.5 years) (4), 33.3 in 3-5 year olds (mean age 3.9 years), and 28.9 in 2-3 year olds (mean age 2.3 years) in the present study. Specificity becomes sub-optimal (<80%) when the study population is restricted to children under 5 years. Also, a low possible likelihood ratio means that this may lead to significantly large numbers of children incorrectly identified as ASD.

The reason for poor specificity and low positive likelihood ration could be related to inaccuracy of existing cut-off scores for classifying extent of autism. This is supported by the significant discrepancy in proportion of cases of severe ASD identified individually by CARS-2 and ISAA. Previously identified issues related to construct and content [4,6] of the score could also be responsible. Three domains ('speech, language and communication', sensory aspects' and 'cognitive component') and certain items have consistently demonstrated sub-optimal correlation across studies irrespective of age [4,6,14]. Some items become irrelevant when applied in younger children as they either do not appear at that age, while some are developmentally normal within 2-5 years (though considered abnormal when they persist in older individuals). As these issues are not due to translation, the sub-optimal diagnostic accuracy may extend to all versions.

We also observed that the discriminatory power of ISAA and CARS-2 were comparable and acceptable. This can be explained by the overlapping content of both instruments and acquisition of similar levels of competence of the interviewers after training. Although their performance was not on par with the,expert, it was satisfactory (≥80%). The possibility that para professionals involved in the care of children with ASD can become adept in administering a validated tool (with acceptable psychometric properties) for evaluation of ASD after appropriate training is definitely worth studying in-depth, especially given the lack of mental health professionals in our country.

We conclude that the sensitivity of ISAA (Hindi version) has acceptable sensitivity when used in children referred to a developmental clinic or tertiary hospital setting but the specificity is very low in children under 5 years of age. This may result in children being inaccurately labeled as ASD by this tool. We suggest that a modified pediatric version of the score be developed for under-five children by developmental experts maintaining a similar format but ensuring age-appropriate content. This should be followed by a multi-centric validation study of ISAA in all languages, before being recommended for nationwide use.

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Contributors: SBM, SA: conceptualized the study. SBM, SA, SS: were the neuro-developmental experts; SBM: performed the comprehensive evaluation and quality check; MS: helped in collection and analysis of the data pertaining to ISAA; SBM: carried out the literature search, interpreted the data and drafted the manuscript which underwent a critical appraisal by SA, SS and MS. All the authors approved the final version of manuscript, and agree to be held accountable for all aspects of the work.
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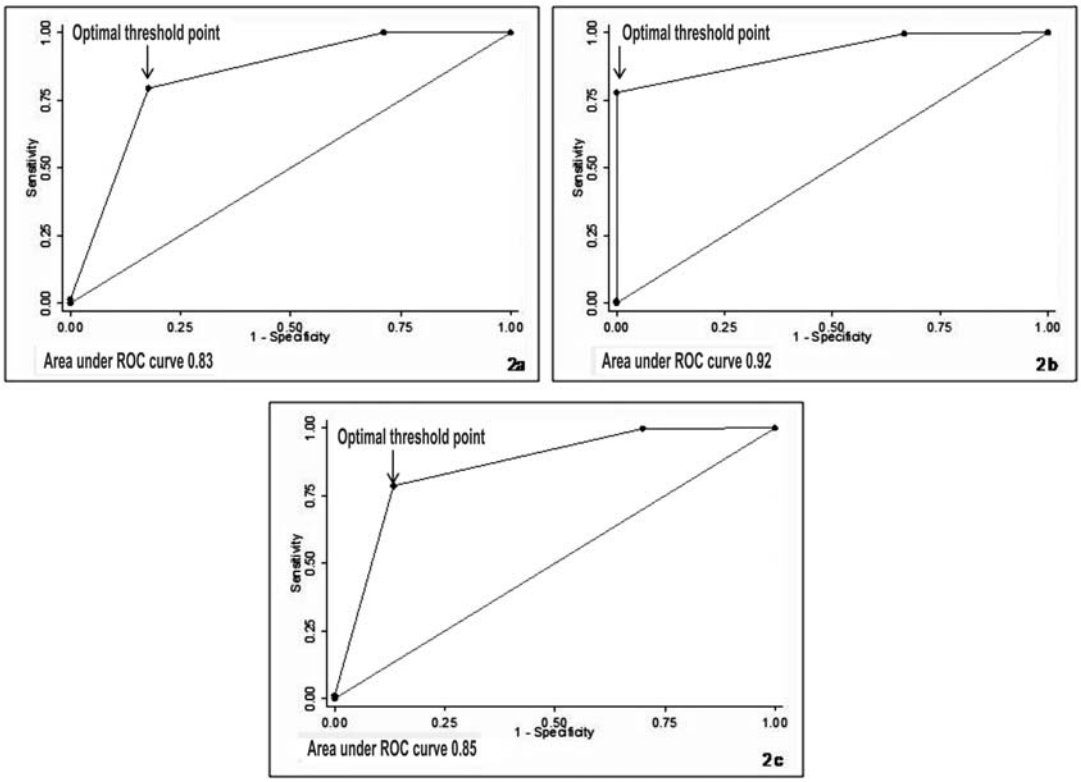
REFERENCES

1. Arora NK, Nair MKC, Gulati S, Deshmukh V, Mohapatra A, Mishra D, *et al.* Neurodevelopmental disorders in children aged 2-9 years: Population-based burden estimates across five regions in India. Available from: *https://doi.org/10.1371/journal.pmed.1002615*. Accessed August 10, 2018.
2. MoHFW. National mental health survey of India, 2015-2016: summary. Available from: *http://indianmhs.*

nimhans.ac.in/Docs/Summary.pdf. Accessed January 1, 2019.
3. Elder JH, Kreider CM, Brasher SN, Ansell M. Clinical impact of early diagnosis of autism on the prognosis and parent-child relationships. Psychol Res Behav Manag. 2017;10:283-92.
4. Mukherjee SB, Malhotra MK, Aneja S, Chakraborty S, Deshpande S. Diagnostic accuracy of Indian scale for assessment of autism (ISAA) in children aged 2-9 years. Indian Pediatr. 2015,52:212-16.
5. Volkmar F, Siegel M, Woodbury-Smith M, King B, McCracken J, State M, *et al*. Practice Parameter for the Assessment and Treatment of Children and Adolescents with Autism Spectrum Disorder. J Am Acad Child Adolesc Psychiatry 2014;53:237- 57.
6. Ministry of Social Justice and Empowerment. Scientific Report on Research Project for Development of Indian Scale for Assessment of Autism. New Delhi: Government of India; 2009.
7. Juneja M, Mishra D, Russell P, Gulati S, Deshmukh V, Tudu P, *et al.* INCLEN diagnostic tool for Autism Spectrum Disorder (INDT-ASD): Development and validation. Indian Pediatr. 2014;51:359-65.
8. Ministry of Social Justice and Empowerment. The National Trust for Welfare of Persons with Autism, Cerebral Palsy, Mental Retardation and Multiple Disability, The National Trust Regulations, 2001. Available from: *www. socialjustice.nic.in*. Accessed June 23, 2014.
9. Notification: Guidelines for evaluation and assessment of Autism and procedure for certification. The Gazette of India, Extraordinary 2016 Apr 25; New Delhi: p. 1 (sec 1).
10. Press Information Bureau, Government of India, MOSJE, 31st August, 2016. National Workshop for Training Master Trainers in Autism Tools INCLEN and ISAA begins. Available from: *http://pib.nic.in/newsite/mbErel.aspx. relid.149368.* Accessed November 19, 2016.
11. Dalwai S, Ahmed S, Udani VU, Mundkur N, Kamath SS, Nair MKC, *et al*. Consensus Statement on Evaluation and Management of Autism Spectrum Disorder. Indian Pediatr. 2017 54:385-93.
12. Patra S, Arun P. Use of Indian Scale for Assessment of Autism in Child Guidance Clinic: An Experience. Indian J Psychol Med. 2011:33;217-9.
13. Raina SK, Kashyap V, Bhardwaj AK, Kumar D, Chander V. Prevalence of autism spectrum disorders among children (1-10 years of age)- Findings of a mid-term report from Northwest India. J Postgrad Med. 2015;61:243-6.
14. Chakraborty S, Thomas P, Bhatia T, Nimgaonkar VL, Deshpande SN. Assessment of Severity of Autism Using the Indian Scale for Assessment of Autism. Indian J Psychol Med. 2015:37;169-74.
15. Perumal V, Lekhra OP. Measurement of behavioural characteristics of children with autism spectrum disorders using Indian Scale for Assessment of Autism (ISAA). IJMRME 2017;3:37-45.
16. Alpern GD. Developmental Profile 3 (DP-3). Los Angeles, CA: Western Psychological Services; 2007.
17. Sparrow SS, Cicchetti VD, Balla AD. Vineland ™ II, Vineland Adaptive Behavior Scales, 2nd ed. Bloomington: Psychcorp, Pearson Inc.; 2005.
18. American Psychiatry Association. Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Arlington, VA: American Psychiatric Publishers; 2013.
19. Schopler E, ME Van Bourgondien, Wellman GJ, Love SR. The Childhood Autism Rating Scale, 2nd ed.Torrance, CA: Western Psychological Services, Inc; 2010.



***Web Fig.*1**. *Receiver Operating Characteristic (ROC) curves displaying discriminatory power of ISAA in relation to the expert evaluation (a) in 2-3 year old children, (b) in 3-5 year old, and (c) in 2-5 year old children.*