Chapter 3
METHODOLOGY

The general description of methodology of the study, which is common for all objectives will include the following headings;

(i) the study design; (ii) the setting where the research work was conducted (iii) the source population, (iv) the study population; (v) the selection criteria; (vi) the sampling procedure; (vii) the sample size; (viii) the recruitment, data collection and tools and (ix) the data analysis.

3.1 Study design

Mixed study designs were followed in the conduct of the study: descriptive cross sectional study for development and validation of the tool and case control design for risk factor analysis. The research work included a theory driven, psychometric approach for developing and validating the new tool, the Childhood Autism Tool-Trivandrum (CAT-T).

3.2 Study setting

The study was conducted at Child Development Centre (CDC) Kerala, a tertiary care teaching centre in the urban limits of Thiruvananthapuram, Kerala State in Southern India. The CDC, Kerala does not have a geographical catchment area, and therefore children from different parts of the state and the neighboring state of Tamilnadu make use of the clinical services offered by CDC Kerala.
Children for the study were recruited from January 2009 to June 2010. This period of more than a year was planned to account for any seasonal variations in the enrolment of the children, who utilized the services offered at the centre. It was also planned to conduct the study for 18 months as that period would be required to recruit adequate sample size that was required as per the sample size calculation.

3.3 Target population

All children in Kerala having autism in the age group 2 – 6 years irrespective of gender, geographic area, religion formed the target population.

3.4 Source population

During the study period of 18 months, nearly 10,000 children were seen at various developmental clinics of CDC Kerala and Pediatric Neurology clinics of SAT Hospital, Medical College, Thiruvananthapuram. This population formed the source population for the different stages of this research work. Children having clinical suspicion of autism were referred to the Autism clinic of CDC Kerala for further evaluation. Therefore every child with suspected autism was considered a potential participant in the research, if he or she had fulfilled the below mentioned selection criteria.

3.5 Study population

Children (2 – 6 years) with clinical suspicion of autism referred to autism clinic of CDC, Kerala formed the study population.
3.6 Selection criteria

The children were recruited into the study from the autism clinic of CDC Kerala, only if the following inclusion and exclusion criteria were satisfied.

3.6.1 Inclusion criteria

Those children, who had impairment in the areas of communication, socialization and having restricted interest or repetitive behaviour were included, if the child was between 2 to 6 years of age. This age range was selected because of the difficulty in diagnosing autism in less than two years of age as well as the varied clinical presentations that are possible below this age. The upper limit of 6 years was taken in this study as it is important to identify a child with autism before 6 years of age in order to enable maximum effectiveness of treatment. Identifying children after 6 years although is important, from a public health perspective, it is most useful to identify children who will get maximum benefit from early intervention. This will help in reducing the burden of disability from the perspective of Government’s policy and planning.

Children were included in the study only if the primary care giver had a working knowledge of Malayalam, Hindi or English. This was essential as it was important for the rater, using different measures, in the study to interact with the child and the primary care giver.

3.6.2 Exclusion criteria

Those children were excluded from the study, if they had physical disabilities like visual impairment and hearing impairment as it was
difficult to assess the child. Also it was important to exclude these children as special sensory disabilities can result in symptoms like poor language development, poor social skills and repetitive behaviors that can mimic autism.

Those children who had any acute illnesses or on medications that would affect the assessment process were also excluded. Children whose primary care givers had known mental illnesses, clinically assessed by the rater on an earlier date were also excluded as the information given was considered unreliable. Primary care givers who were not living with the child at least for a year was also excluded as developmental history given by them may be unreliable. Finally, children whose primary care givers did not want to participate in the research program or unwilling to give informed consent were also excluded. Thus those children who satisfied the selection criteria were recruited using appropriate sampling procedure.

3.7 Sampling procedure

Consecutive sampling was followed in the selection of subjects. Children referred to Autism clinic were evaluated using Childhood Autism Rating Scale (CARS), the standard reference tool. 200 children were selected for tool validation, which after assessment included 143 autistic children and 57 non-autistic children as per norms of CARS.

The 143 autistic children formed the cases for the case control study for identification of risk factors for autism. Another group of 200 normal children of the same age group consecutively recruited from
well-baby clinic of SAT hospital, Thiruvananthapuram, formed the control group.

3.7.1 Sample size for validation study

The sample size calculation for the validation part of research work was based on the convergence of two sample size calculation approaches: (i) for the initial tool development and validation we used the recommendation by Gorsuch. This literature support, suggests that for every 1 item in the tool that is being developed, there should be 5 participants for tool validation (Gorsuch, 1983); (ii) for an exploratory factor analysis, a sample size of minimum of 200 has been suggested as a fair sample (Comrey, & Lee, 1992). Thus the sample size for the validation study was calculated as 200 children (39 items x 5 participants = 195 children; round off to 200 children).

3.7.2 Sample size for risk factor study

For the risk factor study, which was aimed at identifying the risk factors associated with autism, we calculated the sample size using ‘nMaster (version 0.1)’, a software for sample size calculation developed by Christian Medical College, Vellore. Sample size calculated was 141 cases and an equal number of controls. The assumption was based on the data derived from pilot study with regard to environmental factors, contributing to risk i.e., there was a prevalence of 30% unfavourable environmental factors among the controls. (the Odds ratio required was 2.0, the power of study 80% with an alpha error of 5% for a two tailed test)
3.8 Recruitment, Data collection and Tools

200 consecutive referred cases of clinically suspected autism, who attended the Autism clinic of CDC Kerala and who met all the inclusion and exclusion criteria were recruited for the validation study. Similarly, 143 autism cases from the above mentioned 200 referred cases and 200 normal children (control group), who attended the well-baby clinic of SAT Hospital, were recruited for the risk factor study. Consent from parents was obtained before recruiting subjects for this research study.

3.8.1 Data Collection for the validation study and tools

The following are the details of the tools that were used for the validation study.

3.8.1.1 The tool for the validation study

Childhood Autism Tool – Trivandrum (CAT-T): This tool, which was developed for validation has four domains namely; social interaction, communication, behaviour and sensory integration. This tool has 39 items and can be rated on a 4-point Likert scale. It takes approximately 45 minutes using a face to face interview of the parent and if needed observation of the child. It is a measure intended to be used as a tool in primary care settings and clinics for the identification of autism. (Appendix-1)

Childhood Autism Rating Scale (CARS) (Schopler, Reichler, DeVellis, & Daly, 1980) is a 15 item behavior-rating tool designed to detect and quantify symptoms of autism as well as distinguish them from other developmental disabilities. Each item on the CARS is scored on a
Likert scale, from 1 (no signs of autism) to 4 (severe symptoms). The maximum CARS score is 60, and the cut off for a diagnosis of autism is 30. The CARS scores for this study were obtained from the trained and experienced developmental therapist’s reports. This tool was used as reference standard for the validation study. (Appendix-2)

**Vineland Social Maturity Scale (VSMS) (Doll, 1965)** was used for assessing adaptive functioning in eight areas: self-help general, self-help dressing, self-help eating, socialization, self-direction, communication, locomotion and occupation. The VSMS scores for the study were obtained from the trained and experienced developmental therapist’s reports, who was blinded to the results of CAT-T and CARS. VSMS was used for measuring the convergent validity of the new tool developed (Appendix-3).

**Denver Developmental Screening Test (DDST-II) (Frankenburg, Dodds, Archer, Shapiro, & Bresnick, 1992):** This is a screening tool used for identifying the development of children less than 6 years and has got four sub-test viz., personal social, fine motor, language and gross motor. By administering DDST the overall development of children in the above four sub-test combined or delay in individual sub-test can be measured. The DDST scores were obtained from the trained and experienced developmental therapist’s reports, who was blinded to the results of CAT-T and CARS. This result was used for measuring divergent validity (Appendix-4).

**Development of the new tool – Childhood Autism Tool – Trivandrum: General properties of the tool**: The tool was planned to be a discriminatory one for identification of autism among 2 to 6 year old
children and to have cut-off score value for diagnosing the condition. The tool is to be in Malayalam and English and should have satisfactory psychometric properties. It should be simple and culturally appropriate and will be made available for professionals for their clinical use for the diagnosis of autism.

### 3.8.1.2 Steps in the development of the new tool

The standard guidelines for the development of tools were adopted. The various steps followed were;

**Step 1:** *Forming the expert panel for the technical advice for developing the tool:* The developing of CAT-T, the new tool was done by a team of 12 multidisciplinary experts that included Pediatrician, Child Psychiatrist, Pediatric Neurologist, Clinical Psychologist, Special Educators, Specialist Nurses, Developmental Therapists, Epidemiologist, Sociologists, who had a mean (SD) of 22 (7.42) years of experience in working with children with developmental needs. The team had members who had developed, validated and published measures for national and international use in the past. This team offered their technical expertise in the development and validation of the CAT-T over many rounds of workshops.

**Step 2:** *Agreeing on the measure and conceptualization of construct:* To achieve a common goal, the experts participated in brainstorming sessions, clarified, identified and agreed on developing a new tool for autism based on the various existing instruments for identifying the disorder. The panel also decided what should constitute the construct of autism and why? During that process, the available
instruments of Gilliam Autism Rating Scale, Modified Checklist for Autism in Toddlers, Trivandrum Autism Behavioural Checklist, Autism Diagnostic Inventory and Autism Diagnostic Observation Schedule were also reviewed. Since all the reviewed instruments had the construct of autism represented by three symptoms clusters it was decided to use the similar construct with appropriate cultural and age amendments. As the American Psychiatric Association in its latest version of the Diagnostic and Statistical Manual (DSM-5) has conceptualized the criteria for autism as also having sensory impairment, it was decided by the expert panel to include this symptom cluster as the fourth component of the construct for the new measure. This construct with its sub construct were converted to items that would represent the clinical symptoms.

Step 3: Decision on the nature of the measure: After reaching the consensus on the construct, the expert panel decided on the overall character of the items that would best capture the construct of autism. The nature of the items was thus decided to reflect the 4-symptom clusters of autism, obtained from the primary care giver by the clinician, involving face-to-face interview using the appropriate regional language namely Malayalam. The result thus obtained by the new instrument was confirmatory in nature, with final dichotomized ‘case’ or ‘no case’ diagnosis available to the clinician depending on appropriate diagnostic threshold (Fitzpatrick, Davey, Buxton, & Jones, 1998).

Step 4: Item development:

Item generation: The item development based on the construct was done using focus group discussions (FGD) with parents of children with autism and in-depth interviews with professionals, who have
worked with children having autism. These FGDs gave rise to the items constituting the item pool. Along with this, ideas regarding the items were taken from existing screening and diagnostic tools of autism and also from literature. Two FGDs with parents were conducted and 15 in-depth interviews with professionals including Developmental Pediatricians, Psychiatrists, Pediatric Neurologists, Clinical Psychologist, Sociologists, and Speech Therapist were done. Based on the above qualitative methodology, an item pool having 82 items was prepared.

**Item selection:** From the item pool, the items were rank-ordered by the panel members, and further reduced the items using endorsement rate approach (Webb, Horton, & O’Neal, 2002). The items were discussed in detail with the panel of experts, consensus were obtained for retaining the items and finally a tool having 39 items were finalized as the first draft tool. The new tool, CAT-T, was based on;

(i) clarity (how easy they were to understand from the clinician’s perspective),

(ii) importance (how often clinicians label the item as a problem for them) and

(iii) frequency (how often the clinicians utilize the item) of endorsement.

While doing item selection, endorsement rate of 75% was taken as the criteria for inclusion in the tool.

**Step 5: Item wording and sequencing:** The items generated used simple language, avoided jargons, avoided double barreled questions, double negatives, leading questions, loaded words and use of presuming questions. All items used a maximum of 20 words to enable easy reading
(McColl, Jacoby, Thomas, et. al., 2001). Those items which were difficult for clinicians to follow, had ambiguous examples taking into account the prevalent social practices and norms were deleted. Finally, these items were sequenced into the 4 respective symptom domains; (i) Social interaction, (ii) Communication, (iii). Behaviour and (iv). Sensory integration.

**Step 6: Formatting, Endorsement and Scoring pattern:** The endorsement pattern used 4 point Likert scale system to best capture the observation by the clinician. The 4-points in the Likert scorings were 0:Never, 1:Sometimes, 2: Often, 3: Always. These endorsement choices were given to the clinician in tick boxes (Boynton, & Greenhalgh, 2004). Equal weightage was given for all items. The draft tool having 39 items were prepared considering the appearance, layout, print details such as font and type as well as instructions based on the recommendations to minimize the variability in diagnosis (McColl, Jacoby, Thomas, et. al., 2001).

**Step 7: Translation and back translation:** In the translation-back translation process that followed, the items were translated forward (from Malayalam to English) and backward (from English to Malayalam) by two teams with at least two independent, bilingual translators each, to achieve the proximity between the source and target versions. During the translation procedures conceptual, content, semantic, operational and functional, equivalents of the items were maintained. Finally, resolution of problematic items was based on the opinion of the third independent person for removal of the items when warranted (Leplege, Verdier, 1995).
Step 8: **Pre-testing:** The 39 item draft tool was pre-tested by peer review, expert review and respondents review.

(i) **Peer review:** The tool was given for comments to 10 doctors, who were involved with treating children including autistic for obtaining their opinion regarding the feasibility, readability, style, formatting and clarity of language as part of peer review.

(ii) **Expert review:** The tool was also given to 10 experts and consultants, who were actually clinicians and subject experts in the field like; developmental pediatricians, psychiatrists, clinical psychologists, speech theropists, as part of expert review for their comments regarding the feasibility, readability, style, formatting and clarity of language.

(iii) **Respondent review:** The items in the tool were also shared to 10 parents of autistic children, who were referred to Autism clinic of CDC, as part of respondents review.

This process ensured the face and content validity of the newly developed tool.

Step 9: **Pilot study:** A pilot study was done on a representative sample of 20 children to assess the comprehensibility of the tool and the anticipated logistic issues in the final administration of the tool. Minor refinements in the tool was done after the pilot study. Thus a draft tool having 39 items was developed for further validation, which was named as Childhood Autism Tool – Trivandrum (CAT-T) (Appendix-1)

Step 10: **Final Administration of the tool on study sample:** The 39 item draft tool was administered on the sample population of 200 children. The psychometric properties of the tool was measured during the process.
3.8.1.3 Validation of the newly developed tool

Data collection for the validation of the tool was also done simultaneously, along with the final administration of the 39 item tool.

All the 200 children with suspected impairment in social development, language development and abnormal behavior were examined clinically for the diagnosis of autism, using the CARS by the investigator and the presence or absence of autism was confirmed. Another rater who was blinded to the CARS diagnosis independently administered the Childhood Autism Tool – Trivandrum (CAT-T), the new tool for validation. This assessment protocol was followed to minimize the rater bias. All assessments were done in an environment that was standardized and thus similar for all children recruited for the study. If the child was unwell or uncooperative for the testing, the child was invited to come again for another session. This assessment was based on a face-to-face interview with the mother and by observing the behaviour and development of the child. The assessment of a child took about 45 minutes to complete. Separate proforma having details of all 200 children with regard to CARS and CAT-T scores were maintained. The details of CAT-T and CARS are enclosed as Appendix-1 & 2 respectively.

To a sub-set of 109 children, Denver Developmental Screening Test (DDST), was administered in order to find out the divergent validity by a developmental therapist, who was blinded to the diagnosis of the child and results of CARS. DDST is a tool used for identifying developmental delay among children less than 6 years. It has four domains including fine motor and gross motor development of children.
Hence DDST was selected for finding out the divergent validity of CAT-T, since DDST measures constructs dissimilar to those of autism.

In order to measure the convergent validity 97 children were administered the tool the Vineland Social Maturity Scale (VSMS) by a developmental therapist, who was blinded to the diagnosis of the child and results of CARS. VSMS is a tool for identifying social development of children and in autistic children social development is one of the domains, which will be defective. Hence VSMS was selected for finding out the convergent validity of CAT-T, since it measures constructs similar to those of autism.

Test-retest and inter-observer reliability was done using intra-class correlation statistic. Internal consistency reliability was measured using Cronbach’s alpha coefficient. Validity and factor analysis and item reduction were done to construct to final tool.

3.8.2 Data collection for the risk factor study and tools

The methodological details of setting, study population, selection criteria, sampling and sample size calculation have already been presented under the subsection of General methodology that is common to all phases of this research study. Only the specific methodological details in relation to risk factor study are mentioned here.

3.8.2.1 Selection criteria for autism cases

143 autistic children (2 – 6 years) identified using the standard reference tool Childhood Autism Rating Scale (CARS) from among the
200 children selected for tool validation were used for the risk factor study.

3.8.2.2 Selection criteria for control cases

Another group of consecutively recruited 200 normal children (2 – 6 years) of the same age group from the well-baby clinic of SAT hospital, Medical College, Thiruvananthapuram, formed the cases for control group of the study.

3.8.2.3 Risk factor – exposure variables

The following are the risk factor exposure variable studied in this research.

<table>
<thead>
<tr>
<th>Risk Factor – Domains</th>
<th>Exposure Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sociodemographic Risk factors</td>
<td>Age, gender, religion, caste, place of residence, type of family, number of members in the family, marital status of mother, education of mother, education of father, occupation of mother, occupation of father, monthly per capita income, consanguinity,</td>
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<tr>
<td>(Detailed interview schedule in Appendix-5)</td>
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<tr>
<td>Antenatal Risk factors</td>
<td>Blood group of child, blood group of mother, blood group of father, age of mother at child birth, age of father at child birth, birth order of child, type of delivery, low fetal movements, miscarriage symptoms, excessive fetal movements, low fetal movements, low lying placenta, antenatal uterine bleeding, low amniotic fluid, gestational diabetes, hypertension, respiratory infection/asthma, vaginal</td>
</tr>
<tr>
<td>(Detailed interview schedule in Appendix-5)</td>
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infection, urinary tract infection, hypothyroidism, epilepsy, chickenpox, rubella, infertility treatment, antenatal antibiotics use, tooth filling, excessive mental stress, prolonged labour (>16 hours), sudden delivery, induced delivery, fetal distress, cord around the neck, breech presentation.

Natal and Neonatal Risk factors
(Detailed interview schedule in Appendix-5)

Gestational age of child, delayed cry, birth injury, neonatal nursery admission, umbilical infection, neonatal jaundice, hypoglycemia, seizures, immunization, birth weight, present – weight, height and head circumference

Possible Genetic & Family related Risk factors
(Detailed interview schedule in Appendix-5)

Family history of autism, ADHD, Learning disorder, mental retardation, cerebral palsy, vision impairment, hearing impairment, speech and language disorder, epilepsy, other neuromuscular disorders, family h/o congenital malformations, family h/o psychiatric disorder

Environmental Risk factors – Early Child Rearing Practices
(Detailed interview schedule in Appendix-5)

Details of primary care giver, child taking for outings, visiting relatives with child, relatives vising the home of the child, child playing with children of his or her age group, family members telling stories or singing songs for the child, family members playing or interacting with the child, child watching TV, child attending daycare centre or nursery school, marital harmony of parents, duration of breast feeding.
3.8.2.4 The tool for the risk factor study

The tool for the risk factor analysis was an interview schedule specially designed to collect the factors that possibly predict the risk or protection given by different factors occurring before and after delivery and during infancy and toddler period. The proforma specifically prepared was based on the consensus arrived in the expert committee meetings specifically convened for this purpose.

The same interview schedule was used for cases and for controls (Pink color proforma (Appendix-5) for cases and Green color proforma (Appendix-5) for controls. Sociodemographic risk factors, antenatal risk factors, natal & neonatal risk factors, genetic and family related risk factors, environmental risk factors with special reference to early child rearing practices were the various domains of risk studied with regard to the research on risk factors for autism.

The primary respondent was the mother and if mother was not available data were collected from immediate care giver. The other baseline characteristics of the child and parents were also noted. This was done by the investigator for both cases and controls. These data were analyzed to find out the risk factors for autism.

3.9 Data analysis

Data were entered in Excel format and was analyzed using the software the Statistical Package for the Social Sciences (SPSS – version 19.0). A significance level of 0.05 and 2-tailed tests were used in the analysis and interpretation results.
3.9.1 Data analysis for tool development

The following analytical procedures were adopted as part of the development and validation of the new tool.

Reliability analysis: Reliability of the tool, which is an attribute of consistency was measured in terms of the following three measures – test-retest reliability, inter-observer reliability and internal consistency reliability.

a) Test-retest reliability was estimated to know the stability of the tool over time using intraclass correlation coefficient (ICC) statistics. For calculating the test-retest reliability the 39 item tool was administered a second time on 10 subjects during the final administration of the tool at two weeks of interval by the same investigator, who was blinded to the score obtained during the previous examination.

b) Inter-observer reliability: The CAT-T was administered and scored among 10 children by two independent examiners on the same day and the scores were correlated to see the agreement. Intraclass correlation coefficient statistic was used to find out inter-observer reliability.

c) Internal consistency reliability was done to know whether all items in the CAT-T are closely related to the construct of autism or to the appropriate sub-construct. It was estimated using Cronbach’s alpha coefficient. Internal consistency was repeated with the final tool having 24 items.
**Validity analysis:** The validity analysis of the tool was measured in terms of face and content validity, construct validity, convergent & divergent validity, and criterion validity. All these validation procedure ensure the psychometric properties of the tool.

**Face and Content validity** assessment was made during the different stages of the development of the tool. Peer review, respondent review and expert reviews ensured the face and content validity of the tool.

**Construct validity:** The construct validity of the final new tool (CAT-T) was evaluated using the standard factor analysis techniques, which is a multivariate statistical approach used in psychology, education and health. Among the two classes of factor analysis, exploratory factor analysis (EFA) was used and it was done by Statistical Package for the Social Sciences (version 19.0)

**Factor analysis and Item Reduction:** The 39 items of the tool were subjected to factor analysis and finally a tool having 24 items was developed (CAT-T). The four steps of EFA protocol was followed, and is detailed below;

**Step.1: Suitability for factor analysis:** It was analysed whether the sample size of 200 children was adequate for factor analysis by Kaiser-Meyer-Olkin (KMO) measure and Bartlett’s Test of Sphericity to find out the suitability for factor analysis.

**Step.2: Extraction of factors:** Among the various ways to extract factors, the Principal Component Analysis (PCA) was used to extract the
factors. Communalities of more than 0.4 were taken as a criterion for retaining the items.

**Step 3:** Criteria for determining factor extraction and retaining or deletion of items in the tool: For data reduction and for retaining or deletion of items of the final tool from the existing 39 items the following principles were used.

(a) Kaiser Criteria (Eigen value more than 1): Eigen value more than 1 was retained as a factor as per the Kaiser criteria. An Eigen value represents the amount of information captured by a factor.

(b) Scree test: The graphical representation extracted from SPSS data was used for getting information for retaining the number of factors for the final tool.

(c) Cumulative percent of variance extracted: It was decided that the retained factors should account for at least 60% of the variance, which is the accepted value for tool development in specialty subject like humanities.

**Step 4:** Varimax rotation for better interpretation: Varimax rotation was done on the extracted and retained factors in order to help in better interpretation and for labelling the factors. A factor loading above 0.4 was taken as the cutoff point for identifying items and for deleting or retaining the items. It was decided that there should be at least 2 items in a factor. Factors were named in order to communicate to others regarding the substantive nature of the factor and to understand its meaning.
Convergent validity, divergent validity and criterion validity of the final tool having 24 items was estimated.

**Convergent validity:** The convergent validity was measured by Pearson correlation coefficient. To measure this validity two tools were used – CARS and Vineland Social Maturity Scale (VSMS). The new tool, CAT-T and CARS were administered to all 200 children. To a subset of 97 children Vineland Social Maturity Scale (VSMS) was administered, which is a tool useful for measuring social development of children.

**Divergent validity:** was measured by Pearson correlation coefficient. To measure this validity Denver Developmental Screening Test (DDST), which is a tool used for assessing the development of children less than 6 year olds was used. The tool has four sub-test domains including fine motor and gross motor development. Pearson correlation coefficient of CAT-T with DDST (total) and CAT-T with sub-test of gross motor development (which is not a finding required for diagnosing autism) was measured.

**Criterion validity:** This validity was done to evaluate the diagnostic accuracy of the CAT-T, with reference to the standard tool for diagnosing autism using the following statistical tests.

**Sensitivity:** *Probability that a test result will be positive when the disease is present (true positive rate, expressed as a percentage).*

**Specificity:** *Probability that a test result will be negative when the disease is not present (true negative rate, expressed as a percentage).*

**Positive predictive value (PPV):** *Probability that the disease is present when the test is positive (expressed as a percentage).*
Negative predictive value (NPV): probability that the disease is not present when the test is negative (expressed as a percentage).

Positive likelihood ratio, Negative likelihood ratio and Diagnostic accuracy.

Receiver Operating Characteristic (ROC) analysis: ROC curve was used for calculating the sensitivity, specificity of the new tool at every possible cut-off point and plotting sensitivity against 1-specificity. The area under curve (AUC) provides the measure of overall performance of the tool.

3.9.2 Data analysis for risk factor study

The analyses were carried out at three levels for identifying the risk factors.

The descriptive analysis was used to describe the salient characteristic of the study population. The comparison between cases and controls was done using Chi-square test. Unadjusted analyses were performed for all predictive factors against the dependent variables (CARS based diagnosis of autism) using univariate regression analysis.

All variables which were found to be significant on univariate analysis were put in a multivariate (logistic) regression analysis. A final model with significant risk factors predicting the outcome was derived.
3.10 Ethical Considerations

The study was approved by the Institutional Ethics Committee of Child Development Centre. The investigator discussed regarding the details of the study to the parents and informed consent (Appendix-6) was obtained before data collection.

The families were approached by the investigator and the primary-care giver was explained about research work, the potential benefits to children with autism and the possible risks that were involved, like the ‘diagnostic labeling stigma’. The doubts of the primary-care giver were always clarified and the right to drop out from the research at any time was given and was discussed with the primary-care giver. It was also assured that in case the child drops out of the study, it will not in any way compromise the management of the child in this hospital. All data collected were available for use only to the primary investigator and the statistical team. All data identifying the child were masked with reversible anonymisation. The process of referring the child identified as autism or other neurodevelopmental disorders for enrollment in the intervention programs of the centre was deemed appropriate.