Original Article

Impact of Comorbidity on Three Month Follow-up Outcome of Children with ADHD in a Child Guidance Clinic: Preliminary Report

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ABSTRACT

Context: Attention deficit hyperactivity disorder (ADHD) is one of the common neurodevelopmental disorders. **Aims:** Study objective is to report impact of comorbidities on short-term outcome in children with ADHD followed in a child guidance clinic. **Settings and Design:** This was done in a child guidance clinic run jointly by the pediatric and psychiatry department at a tertiary teaching hospital. This is a 3 month prospective follow-up study to assess the outcome in ADHD children. **Materials and Methods:** Children attending pediatric department with behavioral problems or poor scholastic performance were screened for ADHD and further confirmation of diagnosis was done by semistructured interview of the child and parent. Children functional assessment and ADHD symptom profile was compared at baseline and at follow-up. We screened for and excluded those showing autistic spectrum disorder and having worse than mild mental retardation. Baseline variables were compared between improved and not improved subgroups and impact of these variables on outcome at 3-month follow-up was analyzed. **Statistical Analysis:** Descriptive statistics. **Results:** Of the 25 children completing the study, at the end of 3 months, 15 improved (not fulfilling criteria for ADHD) and 10 did not improve. Applying Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS) for diagnosis of psychiatric comorbidities, six had associated psychiatric comorbidities. This was significantly higher in those who did not improve. **Conclusions:** Presence of comorbidities at baseline was found to affect outcome at 3 month assessment in this preliminary study. Future studies with larger sample and longer follow-up are needed for finding the predictors of outcome in ADHD children in developing nations.

Key words: *Attention deficit disorder with hyperactivity, children, comorbidity, follow-up studies*

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders in children.[1] About 7% of children of school age have been reported to have ADHD.[2] Worldwide pooled prevalence of ADHD is 5.29%.[3] Prevalence of ADHD in India ranges from 1.6 to 14% in various studies.[4] ADHD is considered a lifelong condition. It is being increasingly diagnosed among preschool children. It is associated with a multitude of comorbidities and presence of comorbidities will have an impact on the therapeutic strategy chosen. Pharmacotherapy alone may be beneficial in decreasing the core symptoms of ADHD when occurs without comorbid conditions. But when comorbidities exist, it requires additional interventions.[5,6] Due to large variation in prevalence of ADHD reported in India and due to its mere population size, community-based observation studies will be a

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herculean task. In this connection, clinic based studies offer good opportunity to start such observation in children referred for their ADHD problem. Such studies will also help in improving the clinical services available and thereby indirectly reducing burden on family as well as on society at large. There is paucity of Indian studies that give data on impact of such comorbidities on the natural history and outcome of children with ADHD. This preliminary study was aimed to identify and characterize common comorbidities in children diagnosed to have ADHD in a tertiary care hospital-based setting and also investigate if these comorbidities have an impact on a short-term outcome of these children. We chose an arbitrary point of three months for follow up as this is the common period during which parents and physicians want an appraisal on whether treatment is working or not.

MATERIALS AND METHODS

The study was conducted in child guidance clinic (CGC) run in collaboration with department of psychiatry. All children below 12 years of age, presenting to the general pediatrics outpatient department with predominantly poor scholastic performance and behavioral problems referred to CGC, who have not received any kind of intervention for the same previously, were screened using the ADHD rating scale version IV (ADHD-RS-IV) for inclusion into the study.[6] If they fulfilled the inclusion and exclusion criteria for ADHD, they were recruited for the study. Study was approved by the Institute Ethics Committee and an informed consent was taken from the parents.

Children with worse than mild mental retardation, those qualifying for autistic spectrum disorder and those with associated uncontrolled medical or neurological conditions were excluded. As rough measure of their intelligence, we used Vineland Social Maturity Scale (VSMS), Indian adaptation[7] and for identifying autistic spectrum disorder we used Childhood Autism Rating scale (CARS),[8] validated for Indian children.[9] Children having VSMS score <50 (worse than mild mental retardation) or having CARS score ≥33 (suggestive of Autism) were excluded from the study.

We collected the following data for each child included in the study: Demographic and clinical variables; using the unstructured initial interview. ADHD diagnosis was confirmed by using semi-structured clinical interview, Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS) for children and adolescent as per information given by the parents[10] and Clinical subtype of ADHD and severity of ADHD were assessed at baseline using the ADHD-RS scale based on DSM-IV diagnostic guidelines for ADHD.[6] K-SADS generates

Diagnostic and Statistical Manual of Mental Disorders, 4th edition(DSM-IV) based diagnosis and same instrument was used for diagnosis of other psychiatric comorbidities in the children. We assessed the functioning level of children in various domains in last 6 months prior to initial assessment; we took the worst performance as baseline Child Global Assessment Scale (CGAS) score.[11]

There was no sample size calculation and based on CGC new cases register, study intended to recruit 50 consecutive ADHD children between November 2009 and March 2011, first time diagnosed, and not receiving any treatment for the same previously. Forty-nine children who were referred to the CGC during this period were screened for ADHD using ADHD-RS. Of the 49 children, 26 met the study criteria and were recruited as subjects for the study during the stipulated time period. At the time of recruitment, sociodemographic parameters were recorded. Baseline ADHD severity and CGAS were estimated. To screen for comorbidities, K-SADS semistructured clinical interview was done in presence of the parent. Most information was sought from child and corroborated from parents and in young children who were not able to understand or not cooperative enough for interview, information regarding their behavior was sought from parents. Each child was also assessed and managed as per existing department guidelines as usual and these were independent of study assessment and its findings. A follow-up assessment was done by the investigator after end of 3 months. Subjects were reminded of the appointment over phone. At that visit, ADHD-RS was reapplied. ADHD severity score and CGAS (best performance of the child in the preceding month) were recorded. As it was a short-term follow-up study, at the end of 3 months, children were divided into improved and not improved categories. Those who did not fulfill the criteria for ADHD on the ADHD-RS based on symptom frequency in the preceding 1 month were labeled as improved. Those who remained status quo or those who worsened were labeled as not improved.

Details regarding treatment received and compliance with treatment were also noted. All information was then recorded in the database for analysis. Of the 26 subjects recruited initially, 25 completed follow-up and were included for the analysis [Figure 1].

Brief description of instruments/scales used:
- DSM-IV-TR:[12] Is a manual of mental disorders produced by American Psychiatric Association (APA). It gives criteria and guidelines for making psychiatric diagnosis in all age groups.
- ADHD-RS-IV:[6] ADHD-RS is based on DSM-IV based criteria for diagnosing ADHD. It contains list of commonly occurring ADHD symptoms categorized
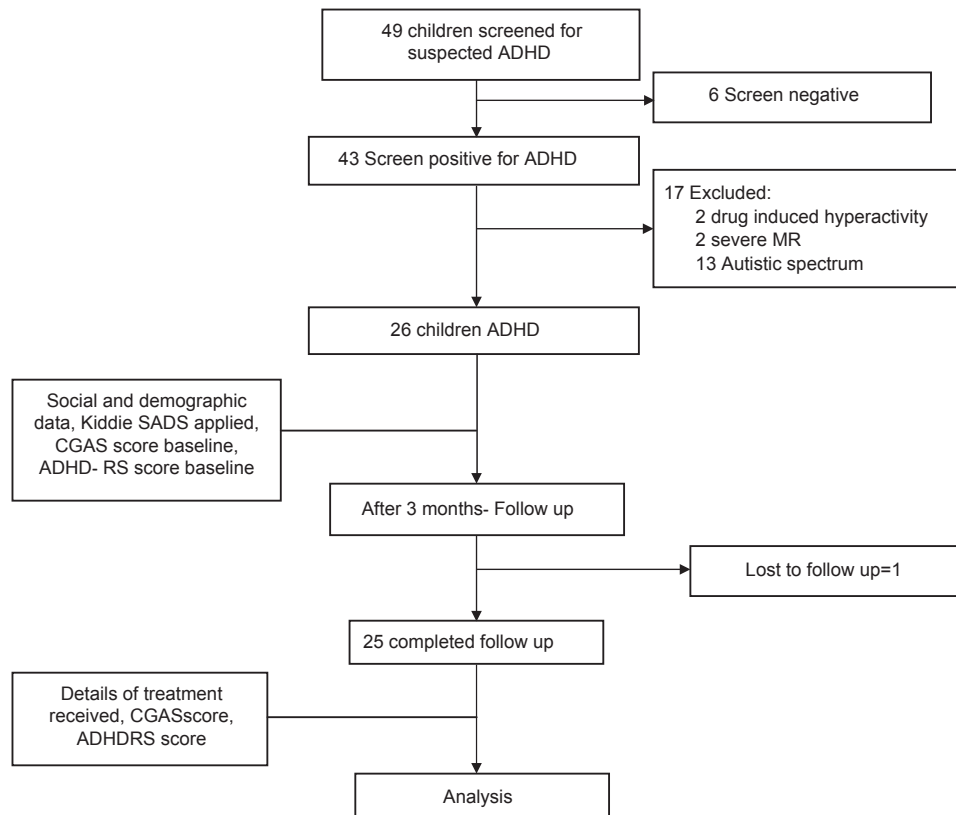
Figure 1: Flow chart of study participants

into symptoms of inattention and symptoms of hyperactivity-impulsivity. All items are rated on a 4-point Likert Scale (0-3) based on frequency of symptoms over past 6 month period. Total score was used as ADHD severity score in this study.

- VSMS Indian adaptation:[7] Social quotient (SQ) shows high correlation (0.80) with intelligence. VSMS can be used for the age group of 0-15 years. Child chronological age is matched with the level of social tasks he/she is capable of doing so as to arrive at mental age. This was used for assessing social quotient of the child. This was considered rough estimate of level of intelligence of the child.
- K-SADS Present and Lifetime version (K-SADS-PL) for School-Age Children:[10] Semistructured interview using K-SADS is helpful in diagnosing different DSM-IV psychiatric conditions. There are different versions. The present study used the K-SADS-PL. It has strong content validity and includes detailed probes useful in eliciting clinically meaningful information. In cases of speech delay, uncooperative nature or small children, the parent was interviewed regarding child's symptoms. A preliminary study has shown that K-SADS-PL can also be used in preschoolers with good reliability.[13]
- CGAS:[11] This is an adaptation of global assessment of functioning in adults. It gives an estimate of child's level of functioning irrespective of primary

diagnosis or treatment. It is rated on a scale of 1-100, divided into intervals of 10 units. Lowest score means poor functioning and higher the score better the global functioning of child.

- The Childhood Autism Rating Scale (CARS):[8] It is a 15-item behavior-rating scale designed to detect and quantify symptoms of autism as well as to 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 33. Any child scoring 33 or above was considered as having autistic traits. Diagnostic accuracy, reliability, and validity of using the CARS in Indian children have been established already.[9]

RESULTS

Three chief complaints for which medical attention was sought were: Overactive/disruptive nature in 12 children; poor scholastic performance in eight children; and speech delay in five children. Among males, commonest presenting complaint was being overactive/disruptive nature seen in ten children. Among females, most common presenting complaint was poor scholastic performance seen in three children.

The mean age of the study group at presentation was 5.5 years (standard deviation (SD)=2.12). Eleven children were in the preschool age group (age less than 5). Males constituted 76% of the sample (male: female=3:1). Hyperactive Impulsive subtype was seen in eight and inattentive subtype was seen in seven, while ADHD combined subtype was seen in ten children [Table 1]. Among males, most common subtype of ADHD at presentation was hyperactive-impulsive followed by combined subtype. Among females, common subtypes were inattentive and combined subtypes. Mean CGAS score at baseline for the entire group was 64.76 (SD=4.48). CGAS score at baseline was lowest for hyperactive-inattentive subgroup (62.75, SD=4.37) [Table 2]. Of the 25 subjects recruited, only three had VSMS score of 50-69 qualifying for mild mental retardation and six had associated language disorder. Three subjects had associated hypothyroidism

needing hormone replacement. Four children had history of febrile seizures, while three children had comorbid seizure disorder which was under control. Average number of comorbidities detected in routine CGC clinic assessment at baseline per subject was 1.52 (SD=0.87).

Applying K-SADS for screening and diagnosis of psychiatric comorbidities, six had associated psychiatric comorbidities. Of the 25 children who completed the study, at the end of 3 months, 15 improved and ten did not improve [Table 3]. No psychiatric comorbidities could be detected in improved subgroup on applying K-SADS. But comparison of number of comorbidities that were identified only based on clinical suspicion, showed that there was no significant difference between the two groups. Comparison of ADHD severity scores at baseline and at 3 months of follow-up for entire group showed a statistically significant decrease in score ($P<0.005$). There was a statistically significant decrease in ADHD severity scores for all subtypes of ADHD. Comparison of CGAS scores at baseline and at 3 months of follow-up for the entire group showed an improvement in score ($P<0.005$). Subgroup of children who had not improved on follow-up, also showed a decrease in ADHD severity score and increase in CGAS score; but they were not statistically significant. Of the 25 subjects in study, 17 were started on pharmacotherapy and behavioral therapy and remaining eight received behavioral therapy only. These interventions were not controlled or modified for the study purpose.

Analysis was made to find out if any of the baseline variables could be used for predicting the outcome at 3 month follow-up. Five variables were considered

Table 1: Various baseline parameters for the group

Parameter	*n*/Mean±SD
Gender (Male)	19
ADHD-subtypes	
Hyperactive-impulsive	8
Inattentive	7
Combined	10
Age at consultation (years)	
Range (2.5-11)	5.50±2.12
VSMS Indian adaptation	
Range (60-110)	87.40±14.54
CGAS at baseline	
Range (58-75)	64.76±4.48

ADHD – Attention deficit hyperactivity disorder; SD – Standard deviation; VSMS – Vineland social maturity scale; CGAS – Child global assessment scale

Table 2: Comparison of various parameters between ADHD subtypes at baseline

	Hyperactive subtype (*n*=8)	Inattentive subtype (*n*=7)	Combined subtype (*n*=10)	Significance by ANOVA
Age at presentation in years (mean±SD)	4.25±1.07	6.00±2.06	6.15±2.50	0.13
VSMS score (mean±SD)	95.50±10.64	85.00±8.13	82.60±18.53	0.15
CGAS baseline score (mean±SD)	62.75±4.37	64.43±3.51	66.60±4.81	0.19

ADHD – Attention deficit hyperactivity disorder; ANOVA – Analysis of variance; SD – Standard deviation; VSMS – Vineland social maturity scale; CGAS – Child global assessment scale

Table 3: *T*-test comparison of baseline parameters between improved and not improved subgroups (assuming equal variances)

Parameter	Group	Mean	Levene's test	*P* value	SE difference	95% CI
Age at presentation (years)	Not improved	6.65	0.283	0.023	0.789	0.284-3.549
	Improved	4.73				
VSMS	Not improved	92.70	0.395	0.14	5.78	−3.12-20.78
	Improved	83.87				
CGAS	Not improved	66.60	0.456	0.094	1.76	−0.57-6.7
	Improved	63.53				
Total no of comorbidities found by K-SADS	Not improved	1.00	0.000	0.001	0.27	0.44-1.56
	Improved	0.00				

VSMS – Vineland social maturity scale; CGAS – Child global assessment scale; SE – Standard error; CI – Confidence interval; K-SADS – Kiddie-Schedule for affective disorders and Schizophrenia

for the analysis: Baseline ADHD severity score, baseline CGAS, total number of clinically diagnosed comorbidities associated at diagnosis, total number of psychiatric comorbidities diagnosed by using K-SADS at baseline, and status of pharmacotherapy. Backward logistic regression was used. None of the variables considered could be identified as a predictor of this short-term outcome.

DISCUSSION

The study was conducted in a tertiary care hospital in India, in an outpatient clinic based setting. It was done in a naturalistic observational design with a follow-up of 3 months. We recruited 26 subjects of which 25 completed follow-up and were included for analysis.

Of the 25 children in study group, 24 children had comorbidities either medical or psychiatric. Eleven children had medical comorbidities of which seven had seizure predisposition (four febrile seizures and three epilepsy). Previous studies have reported occurrence of seizures in select ADHD populations between 2 and 7%, a very much lower prevalence.[14,15]

We also applied a semistructured interview, K-SADS, to all subjects for diagnosis of comorbidities. Six subjects had at least one comorbid psychiatric condition at baseline on applying K-SADS. Commonest comorbidities diagnosed by using K-SADS were oppositional defiant disorder (ODD) in four subjects and enuresis in three subjects. Other comorbid conditions diagnosed using K-SADS were: Tic disorder, encopresis, and separation anxiety disorder. None of the children in this study had associated depression. This was unlike a previous study in ADHD children where K-SADS was used, found considerable number of depressive and anxiety disorders (nearly 50% each), followed by diagnosis of ODD and conduct disorder (CD)(~41%).[16] But that study was done in adolescent age group which may be the reason for difference in findings.

Out of the 25 subjects followed-up, 15 improved and ten did not improve. Improved group differed from not improved mainly in these aspects: Being younger in age at presentation (4.73 in improved compared to 6.65 in not improved, $P=0.023$) and having lesser number of psychiatric comorbidities at baseline as assessed by K-SADS ($P=0.001$) [Table 3]. However, these two groups did not differ on age of onset of ADHD symptoms, subtype distribution, baseline VSMS score, baseline CGAS, and number of clinically diagnosed psychiatric comorbidities.

For functional outcome at follow-up, best functioning in the preceding 1 month on CGAS was used. Comparing the two for entire group, there was a significant improvement in functioning level ($P<0.005$). The subgroup that was labeled not improved based on ADHD-RS did not improve even in terms of global functioning (CGAS baseline 66.6 compared to CGAS follow-up 67.3, $P=0.3$). Hence, it can be interpreted that there is a good correlation between outcome on ADHD rating scale and functional outcome as assessed by CGAS. This is in contrast to the existing studies. One follow-up study from Europe concluded correlation between ADHD-RS-IV and measures of functional impairment were low.[17]

Although we have attempted use of valid scales that are nationally and internationally accepted, there are certain limitations. VSMS developmental quotient was used as a surrogate index of intelligence quotient (IQ). Apart from having small sample size, considerable percentage of subjects belonged to preschool age group. Many scales including K-SADS are not validated for preschool age group children. So, the results need to be interpreted with this caveat. 'Improved or not improved' status was defined by us for this study purpose, we do not know its clinical significance yet. We did not reassess the comorbidities on follow-up visit.

To conclude, there is clear case for assessment of comorbidity at baseline for any child presenting with ADHD symptoms and association between comorbidity and poor outcome in short-term. Use of standard schedules decreases false-positive comorbidities. Future studies need to be done using age specific questionnaire for preschool children and questionnaire for children with speech delay. Also natural history of comorbid conditions in preschool children and the impact of early treatment on them need to be studied.

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