

RESEARCH LETTER

TABLE I: PERFORMANCE OF THE STUDY QUESTIONNAIRE AGAINST CONNERS' RATING SCALES

		<i>Conners' rating scales</i>	
		<i>positive</i>	<i>negative</i>
*Parents' Questionnaire	+	28	16
	-	8	448
#Teachers' Questionnaire	+	10	5
	-	2	83

+: positive or -: negative for ADHD; Cohen's Kappa 0.67* and 0.77#

To conclude, ADHD is an important behavior problem in adolescents. DSM-IV based questionnaire, which is simple to administer and score, can be a useful screening tool in resource-limited settings.

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REFERENCES

1. Willoughby MT. Developmental course of ADHD symptomatology during the transition from childhood to adolescence: a review with recommendations. *J Child*

Psychol Psychiatry. 2003;44:88-106.

2. Biederman J, Faraone SV, Taylor A, Sienna M, Williamson S, Fine C. Diagnostic continuity between child and adolescent ADHD: findings from a longitudinal clinical sample. *J Am Acad Child Adolesc Psychiatry.* 1998;37:305-13.
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 4th edition. Washington (DC): APA Press; 2000.
4. Conners CK. *Manual for Conners Rating Scale.* North Tomananda, New York: Multi health system; 1989.
5. Raven JC, Court JH, Raven J. *Standard Progressive Matrices.* London: H K Lewis and Co. Ltd; 1977.
6. Scahill L, Schwab-Stone M. Epidemiology of ADHD in school-age children. *Child Adolesc Psychiatr Clin N Am.* 2000;9:541-55.
7. Pineda D, Ardilla A, Rosselli M, Arias BE, Henao GC, Gomez LF, *et al.* Prevalence of Attention deficit hyperactivity disorder symptoms in 4-17 year old children in the general population. *J Abnorm Child Psychol.* 1999;27:455-62.
8. Rohde LA, Biederman J, Busnello EA, Zimmermann H, Schmitz M, Martins S, *et al.* ADHD in a school sample of Brazilian adolescents: a study of prevalence, comorbid conditions, and impairments: *J Am Acad Child Adolesc Psychiatry.* 1999;38:716-22
9. Bard DE, Wolraich ML, Neas B, Doffing M, Beck L. The psychometric properties of the Vanderbilt attention-deficit hyperactivity disorder diagnostic parent rating scale in a community population. *J Dev Behav Pediatr.* 2013;34:72-82.

Chimeric Fusion Karyotypes in Childhood B-cell Acute Lymphoblastic Leukemia

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Cytogenetics study using combination of conventional cytogenetics and fluorescent insitu hybridization was carried out in 171 pediatric acute lymphoblastic leukemia patients subgrouped to B-ALL ($n=126$) and T-ALL ($n=45$) by bone marrow morphology and immunophenotype. The chromosomal aberration frequency in B-ALL and T-ALL was 79% and 71%, respectively. TEL/AML1 translocation was detected in 28% of patients.

Keywords: *Complex chromosomal change, FISH, Giemsa banded karyotype, Translocations.*

The most common type of childhood leukemia is acute lymphoblastic leukemia (ALL), which has a B-cell precursor phenotype. The main subtypes of ALL involve multiple genetic alterations including point mutations and deletions, and are also characterized by gross chromosomal changes such as translocations, which are likely to cause illegitimate recombination or juxtaposition of normally separated genes. In leukemias, an in-frame fusion gene is often created, generating a hybrid protein with altered properties. More than 200 genes are known to be involved in translocations in leukemias [1]. Multiplex reverse transcriptase polymerase-chain-reaction (RT-PCR)

based study for few chimeric transcripts in both adult and pediatric ALL from Northern India has recently been reported [2].

We carried this study using conventional cytogenetics (GTG-banding) and fluorescence-in-situ hybridization (FISH) in 171 children aged between 2 years to 15.5 years diagnosed as ALL over 4 years. Of these 126 had B-ALL and 45 patients had T-ALL (B:T ALL ratio of 2.9:1). These patients had standard karyotype and FISH-analysis for common translocations e.g BCR/ABL (9;22), TEL/AML1 (12;21), E2A/PBX (1;19), MLL/AF4 (4;11). Rare translocations through FISH-based analysis were investigated whenever required. Karyotype/FISH analysis were successful in 114 (93%) of B-ALL (90 abnormal and 24 normal karyotypes). In 45 children with T-ALL, chromosomal analysis revealed normal karyotype in 12 patients by Giemsa banded karyotype/FISH, 30 patients had karyotypic abnormalities, and in 3 patients we failed to get chromosome preparations. Chimeric fusion karyotype of B-ALL is presented in **Table I**.

In our series of 126 children with B-ALL, we did not find any patient with MLL/AF4 (4;11) translocation probably because we did not have any infantile ALL, who usually carry this mutation. Proportion of TEL/AML1 translocation was higher in our patients compared to 16% in the series reported by Bhatia, *et al.* [2] and 0-9 yrs by other researchers from India [3-6]. Older series used Giemsa banded karyotype for investigation of TEL/AML1 which could miss the diagnosis due to smaller size of the translocated area. However, even when more sensitive RT-PCR was used, some series reported low prevalence of this transcript. Most of these studies did not combine Giemsa banded karyotype, FISH and RT-PCR to increase their yield of TEL-AML1 mutation. The combination of cytogenetics and RT-PCR is essential to increase the detection rate of fusion genes. Out of 25 TEL/AML1 translocations, 9 (36%) had hyperdiploidy as additional abnormality. Hyperdiploidy was also seen in BCR/ABL positive patients. Translocation (12;20) with hyperdiploidy was picked up in one patient and another had t(8;14) with duplication of chromosome number.

TABLE I CHIMERIC FUSION KARYOTYPES IN B-ALL (N=31)

Translocations	N (%)
TEL/AML1t(12;21)	25 (27.8)
BCR/ABL t(9;22)	2 (2.2)
E2A/PBX t(1;19)	2 (2.2)
c-myc/IgH t(8;14)	1 (1.1)
t (12;20)	1 (1.1)
Total	31 (31.4)

Though there could be regional and population-based differences in TEL/AML1 and other transcripts in pediatric ALL patients. Some of the differences could be related to the selected technique to detect these; multiple techniques should be used for picking up additional genetic abnormalities.

REFERENCES

1. Greaves MF, Wiemels J. Origins of chromosome translocations in childhood leukemia. *Nat Rev Cancer.* 2003;3:639-49.
2. Bhatia P, Binota J, Verma N, Bansal D, Trehan A, Marwaha RK, *et al.* Incidence of common chimeric fusion transcripts in B-cell acute lymphoblastic leukemia: An Indian perspective. *Acta Haematol.* 2012;128:17-9.
3. Inamdar N, Kumar SA, Banavali SD, Advani S, Magrath I, Bhatia K. Comparative incidence of rearrangements of TEL/AML1 & ALL 1 genes in pediatrics precursor B- acute lymphoblastic leukemias in India. *Int J Oncol.* 1998; 13:1319-22.
4. Sazawal S, Bhatia K, Gutierrez M, Saxsena R, Arya LS, Bhargava M. Paucity of TEL-AML1 translocation by multiplex RT-PCR, in B lineage acute lymphoblastic leukemia (ALL) in Indian patients. *Am J Hematol.* 2004;76:80-2.
5. Hill A, Short MA, Varghese C, Kusumakumary P, Kumari P, Morgan GJ. The t(12;21) is underrepresented in childhood B-lineage acute lymphoblastic leukemia in Kerala, South India. *Haematologica.* 2005;90:414-6.
6. Siraj AK, Kamath S, Guttierrz MI, Banavali S, Timpson G, Sazawal S *et al.* Frequencies of the major sub groups of precursor B cell acute lymphoblastic leukemia in Indian children differ from West. *Leukemia.* 2003;17:1192-5.