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Familial Patterns and Biological Markers of Dyslexia

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ABSTRACT Dyslexia is one of the most common learning disability. Though dyslexia is a major educational problem, studies on biological aspects of dyslexia are very limited in India. Here we report prevalence, inheritance patterns and biological markers of dyslexia in 179 selected families from South India. Families were ascertained through probands attending special schools for dyslexic students as well as from regular schools from Karnataka state, South India. Prevalence and types of inheritance patterns were recorded. A questionnaire concerning allergies, asthma, arthritis, migraine etc. was used to assess the prevalence of immune disorders. Occurrence of chicken pox, measles, mumps, delayed milestones, birth complications, motor coordination problems, short sight and left handedness, fatty acid deficiency signs were recorded in the dyslexic probands. Among school children, prevalence of dyslexia is found to be 9.87% and in the selected families the prevalence is 28.32%. Based on the affectedness, dyslexia phenotypes were classified as severe and mild deficits. Mild deficits were better compensated than the severe deficits. Among the selected families autosomal dominant mode of inheritance was found to be more prevalent. Consanguinity plays a major role in familial aggregation of dyslexia. Allergy, migraine, delayed milestones, low level of blood cholesterol and certain fatty acid deficiency signs were found to be associated with dyslexia. Since complex array of symptoms are associated with dyslexia an integrated research approach is needed for effective diagnosis and remediation of dyslexia.

INTRODUCTION

Language is acquired naturally in a sequence of listening, speaking, reading and writing (Gayan et al. 1999). Failure in any of these processes may lead to serious problems at school, at work and in social situations. There are many types of language disabilities; the most common is developmental dyslexia, which is defined as difficulty in learning to read and spell despite adequate education, intelligence, sociocultural opportunities and without any obvious sensory deficits (Shaywitz 1998). It accounts for 80% of learning disabilities (Lerner 1989). Multiple etiologies are proposed for this complex trait and there are strong evidences for its genetic basis (Saviour and Ramachandra 2006).

Since dyslexia is a major educational problem, interest and knowledge of dyslexia is increasing in different parts of the world but no much study has been done on biological aspects of dyslexia in Indian context. In view of this, here we made an attempt to investigate the patterns of genetic transmission of dyslexia and the biological markers in 179 families of dyslexic children.

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SUBJECTS AND METHODS

Families were ascertained through probands attending special schools for dyslexic students as well as from regular schools from Karnataka state, South India. Following tests were used for the diagnosis: a) Teacher rating: Rutter's Proforma A and B (Rutter 1967) was used to get the teachers rating on children's academic performance as well as the presence of behavioral and emotional problems to eliminate those with severe behavioral/ emotional problems if they are primary causes of poor academic achievement. b) Raven's (Colored) Progressive Matrices (RCPM/ RPM) was used to ascertain that those children with poor reading/writing are not below normal in their intellectual/reasoning function (Rao and Reddy 1968). c) Graded reading and spelling tests were administered to ascertain that they were behind at least by two grade norms in reading as required by the operational definition of dyslexia. In addition to the above-mentioned criteria, school examination marks and clinical certificates

issued from institutes such as National Institute of Mental health and Neurosciences, Bangalore and All India Institute of Speech and Hearing, Mysore were used as supportive evidences. The families were asked to participate only if the probands met the above criteria. Informed consent was obtained from the parents before inclusion in the study. Information pertaining to age, medical history, sex, highest academic grade achieved, nature and severity of reading and spelling during school years (Boder 1973; Allred 1990), current reading and spelling ability or other academic difficulties of the family members were recorded.

A questionnaire concerning the presence of allergies, asthma, arthritis, migraine etc was recorded to assess the prevalence of immune disorders. Occurrence of chicken pox, measles, mumps, delayed milestones, birth complications, motor coordination problems, short sight and left handedness also were recorded to verify the association of these with dyslexia. Fatty acid deficiency signs in the probands were assessed using the scale employed by Stevens et al. (1995). This scale includes seven items excessive thirst, frequent urination, dry skin, dry hair, brittle nails, dandruff and follicular keratosis. Typing of blood was carried out on 179 dyslexic probands and control subjects. Haemoglobin estimation was carried out in 145 dyslexic children using Sahli's haemoglobinometer. Cholesterol estimation was also carried out by cholesterol oxidase-peroxidase method (Arntz 1979). Individuals who had no history of reading, spelling, or other academic difficulties were selected as control subjects.

RESULTS

Prevalence: Of the 1,813 children screened, 52.40% were boys and 47.60% (1.1:1) were girls. Of these 14.82% of boys and 4.40% of girls were affected and prevalence of the disorder was found to be 9.87% (Table 1). The ratio of male to female probands was found to be 3.7:1, Chi-square test revealed that affectedness in males were highly significant ($p<0.05$). Age of the probands ranged from 8-17 years. Table 2 provides comprehensive data on the frequency of individuals affected with dyslexia in 179 families of probands. Out of 2200 individuals including probands from 179 families screened; about 54% and 46% were males and females respectively (1.2:1) and 623 individuals were affected with dyslexia (28.32%) wherein 58% and 42% were males and females respectively. The ratio of affected males to females in these families was found to be 1.4:1. Chi-square test reveals that there is significant difference between affected males and females ($p<0.05$).

Based on the extent of affectedness of the trait, dyslexic individuals were classified into severe dyslexics and mild dyslexics. Severe and mild dyslexics were shown two phenotypes, both reading-spelling deficit and only spelling deficit. 576 individuals had both reading and spelling deficit, of them 81.06% had severe deficits. Only 7.54% of the affected individuals have shown problems with spelling and males were more frequently affected with severe (87.88%) and mild (71.43%) spelling deficits. Individuals with spelling deficits were better compensated the

Table 1: Prevalence of dyslexia in 10 different schools of Karnataka, South India

Schools	*No. of children screened*	*Boys (%)*	*Girls (%)*	*No. of dyslexic children (%)*	*Dyslexic children*	
					Boys (%)	*Girls (%)*
A	251	130 (51.79)	121 (48.21)	23(9.16)	18(7.17)	6(2.39)
B	279	145 (51.97)	134 (48.02)	25(8.96)	16(6.81)	9(3.23)
C	291	151 (51.89)	140 (48.10)	25(8.59)	19(6.53)	6(2.06)
D	328	170 (51.83)	158 (48.17)	21(6.40)	15(4.57)	6(1.83)
E	47	43 (91.49)	4 (8.51)	35(74.47)	34(72.34)	1(2.13)
F	19	14 (73.68)	5(26.32)	5(26.32)	3(15.79)	2(14.29)
G	14	11 (78.57)	3(21.43)	4(28.57)	4(28.57)	0(00)
H	134	70(52.24)	64 (47.76)	16 (11.94)	12(8.96)	4(2.99)
I	113	52(46.02)	61 (53.98)	6(5.31)	6(5.31)	0(00)
J	337	164 (48.66)	173 (51.34)	18(5.34)	14(4.15)	4(1.19)
Total	1813	950(52.40)	863 (47.60)	179 (9.87)	141*(7.78)	38*(2. 09)

* χ^2 = 59.27; df =1; p <0.05

Table 2: Frequency of dyslexia in 179 dyslexic families

	Total (%)	*Males (%)*	*Females (%)*	*Compensation of deficits*	
				Males(%)	*Females(%)*
Individuals screened	2200	1189(54.05)	1011(45.95)	-	-
Individuals affected	623 (28.32)	360*(57.78)	263*(42.22)	63(17.5)	61(23.19)
Reading-spellingdeficit					
Severe	505(81.06)	273(54.06)	232(45.94)	28(10.26)	41(17.67)
Mild	71(11.40)	48(67.61)	23(32.39)	21(43.75)	14(60.87)
Spelling deficit					
Severe	33(5.30)	29(87.88)	4(12.12)	7(4.14)	2(50.0)
Mild	14(2.25)	10(71.43)	4(28.57)	7(70)	4(100.0)

* χ^2 = 15.10 ; df =1; p <0.05

difficulty than severe reading-spelling deficit and mild spelling deficits were better compensated than that of other deficits. It is found that 23.19% of the females were compensated the difficulties, while only 17.5% of the males compensated their difficulties (Table 2).

Inheritance Pattern: Pedigrees of 179 families revealed three types of inheritance pattern of dyslexia, viz, autosomal dominant, autosomal recessive and complex pattern (Table 3). 60% of the families have shown autosomal dominant inheritance of the defects, of them 82% of the families had dominant inheritance of reading-spelling deficit. In a few families spelling deficit was also inherited dominantly (17.59%). Autosomal recessive inheritance of reading and spelling deficits were also found however, only very few numbers of families had shown recessive inheritance. About 33% of the families, dyslexia was nonfamilial among them 56% had shown reading-spelling deficits. About 61% of the families at least one first-degree relative of proband was affected. It was found that only 16.76% of the families both parents were affected, 37.98% of the families mothers were affected and fathers were affected in 36.87% of the families. Both parents and all the sibs were affected in about 10.61% of the families. When father was affected, 32.14% of the families siblings of the probands were affected, while when mother was affected, 37.50% of the families siblings were affected. When both parents were affected, 47.61% of the families siblings were affected. Percentage of affected first-degree relatives of the probands is given in Figure1a. In 5.78% of the families only proband and their second degree relatives were affected and none of the first-degree relatives were affected.

Of 179 families, 66 families of probands showed consanguineous marriage (36.87%) while among control families consanguinity was only 13.40%. Figure 1b shows percentage of consanguineous marriages among parents, grandparents, great grandparents of probands. First cousin marriage was more prevalent (50%) among parents. Univariate logistic regression was applied for consanguinity using case-control families and it revealed significant odds ratios (p=0.001). Among these consanguineous families, 62 families had shown autosomal dominant pattern of reading-spelling deficit and 4 families had shown autosomal recessive pattern of reading-spelling deficit.

Biological Markers: Figure 2a presents percent of different biological markers which were examined in probands and controls. Of the 12

Table 3: Inheritance pattern of Dyslexia among 179 dyslexic families

Type of inheritance	*No of Families (Total=179)*		*Families with Reading Spelling deficit*		*Spelling deficit*	
	*#**	*%*	*#*	*%*	*#*	*%*
Autosomal Dominant	108*	60.34	89	82.41	19	17.59
Autosomal Recessive	12*	6.70	12	100.00	-	-
Non-familial	59*	32.96	33	55.93	26	44.07

* χ^2 = 77.25 ; df =2; p <0.05

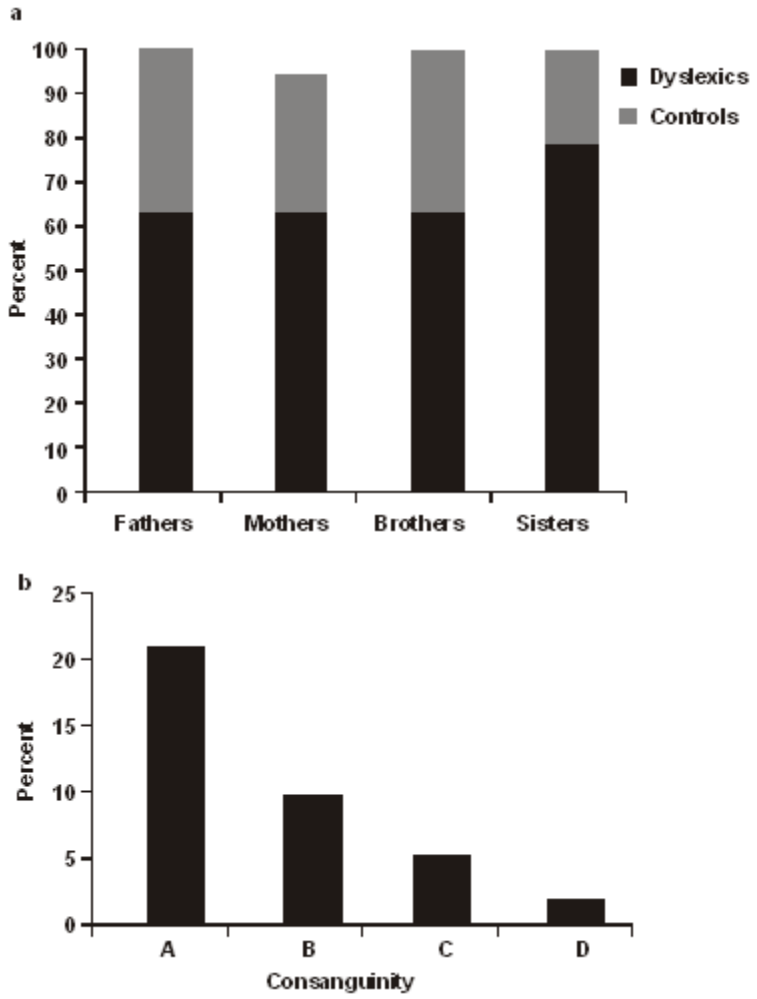

Fig. 1a. Distribution of normal and dyslexic readers among first degree relatives of dyslexic probands. Fig. 1b. Percent of consanguineous marriages among A: parents B: grandparents, C: both parents and grandparents, D: parents and great grandparents

markers observed in dyslexics, delayed milestones and allergy had higher prevalence. Significant odds ratios were obtained from univariate regression analysis for allergy, migraine, measles, asthma, birth complications, delayed milestones and left handedness, and multivariate logistic regression analysis showed significant odds ratios only for allergy, migraine and delayed milestones (Table 4). Among the seven fatty acid deficiency signs (FADS) were assessed, frequent ones found in dyslexics were presence of dry and scaly skin, dry hair and dandruff (Fig. 2b). Univariate regression analysis obtained significant odds ratios for all the FADS except frequent urination but multivariate analysis showed significant odds ratios only for dry skin (Table 4).

Among dyslexics, A (34.64%) was the most common blood group followed by O (34.08%) and B while O (40.78%) was the most common blood group among controls followed by B (24.02%) and A (20.67%). Univariate and multivariate regression was done to know specific relationship between dyslexia and ABO

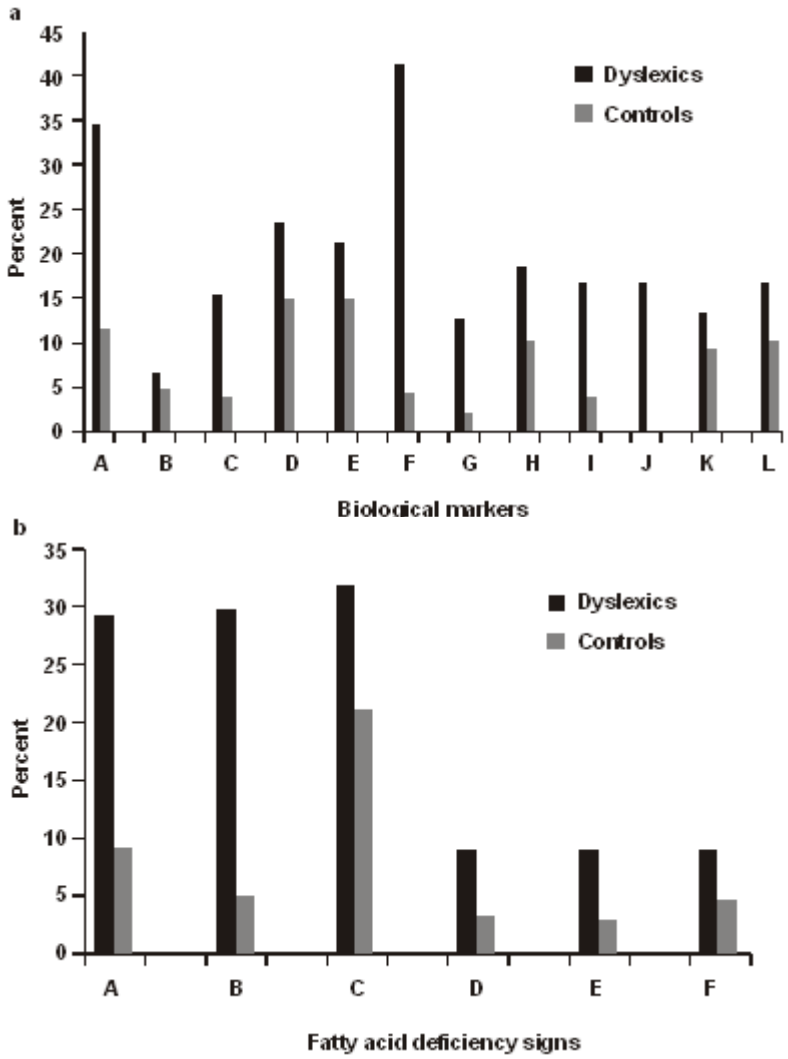

Fig. 2a. Percentage of biological markers observed among 179 dyslexics and control group. A=allergy, B=arthritis, C=asthma, D=birth complications, E=Chickenpox, F=delayed milestones, G=Left-handedness, H=measles, l=migraine, J=motor coordination, K=mumps, L=myopia
Fig. 2b. Percentage of fatty acid deficiency signs observed among 179 dyslexics and control group. A=dry scaly skin, B=dry hair, C=dandruff, D=brittle nails, E=polydipsia, F=polyuria

blood group. Univariate analysis revealed significant odds ratios only for A+ blood group (p =0.020) but multivariate analysis did not show significant odds ratio for any of the blood group (data not shown). Hemoglobin level was also estimated in 108 male dyslexic children and mean hemoglobin level was found to be 12.43+/- 0.22 and in 38 female dyslexic children it was 11.87+/- 0.32. While controls showed mean Hb level of 14.8+/- 0.18 in males and 13.2+/- 0.27 in females. Serum cholesterol level was also estimated in 100 dyslexic children and it was found that only 17% of dyslexic children had normal amount of cholesterol in the serum (Fig. 3).

Table 4: Univariate and multivariate logistic regression analysis for markers

Variables	*Univariate*		*Multivariate*	
	Odds ratio (95.0% C.I)	*p value*	*Odds ratio (95.0% C.I)*	*P value*
Birth complications	1.780(1.044; 3.036)	0.034*	1.410(0.689; 2.884)	0.347
Delayed milestones	15.064(6.983; 32.498)	0.001*	12.287(5.204; 29.015)	0.0001*
Short sight	1.801(0.964; 3.366)	0.065	1.255(0.525; 2.996)	0.610
Left-handedness	6.450(2.183; 19.061)	0.001*	3.160(0.816; 12.237)	0.096
Immune Disorders				
1) Allergy	3.987(2.301; 6.907)	0.001*	3.312(1.500; 7.312)	0.003*
2) Asthma	4.556(1.935; 10.731)	0.001*	1.395(0.418; 4.651)	0.588
3) Arthritis	1.357(0.557; 3.306)	0.501	2.138(0.707; 6.461)	0.178
4) Migraine	4.947(2.112; 11.591)	0.001*	5.614(1.958; 16.099)	0.001*
Infectious Diseases				
Measles	2.097(1.135; 3.875)	0.018*	1.495(0.625; 3.577)	0.366
Mumps	1.476(0.763; 2.853)	0.247	1.029(0.385; 2.751)	0.955
Chickenpox	1.517(0.881; 2.614)	0.133	0.898(0.399; 1.885)	0.720
Fatty Acid Deficiency Signs				
1) Dry skin	10.336(4.547; 23.491)	0.001*	7.630(1.351; 42.908)	0.021*
2) Dull hair	7.945(3.779; 19.707)	0.001*	2.419(0.506; 11.573)	0.269
3) Dandruff	1.734(1.076:2.792)	0.024*	0.588(0.263; 1.314)	0.196
4) Brittle nails	2.412(0.967; 6.014)	0.059	2.348(0.261; 21.127)	0.447
5) Excessive thirst	3.652(1.317; 10.126)	0.013*	0.439(0.044; 4.328)	0.480
6) Frequent urination	2.068(0.874; 5.013	0.097	0.974(0.126; 7.523)	0.980

*Significant

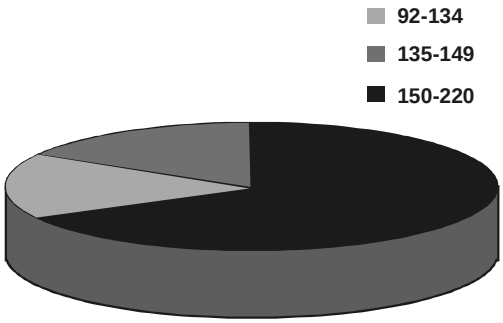

Fig. 3: Percentage of dyslexics showing amount of serum cholesterol levels.

DISCUSSION

Developmental dyslexia is a heterogeneous condition and many studies suggest neuro-physiological basis for dyslexia and the underlying cause is attributed to genetic factors (Ellis 1985; Saviour and Ramachandra 2006). Hallgren (1950) conducted genetic analysis on dyslexic children and found that 88% of these children had at least one first degree relative with same reading problems and the inheritance was found to be autosomal dominant mode. Later different researchers have reported autosomal dominant inheritance of dyslexia (Zahalkova et al. 1972; Pennington et al. 1991; Saviour and Ramachandra 2005). In the present study, 67% of the families have shown familial nature of dyslexia and 60% of pedigrees had affected individuals in each generations suggesting features of dominant trait and about 7% of the pedigrees showed autosomal recessive mode of inheritance. This could be due to genetic heterogeneity, reduced penetrance and oligogenic inheritance (Fisher and DeFries 2002). However, about 33% of the families it was nonfamilial which could be due to extrinsic factors: prenatal (birth injury), or postnatal (infections, injuries etc.). Most of the probands (71%) from nonfamilial families had a history of significant prenatal or medical complications. This clearly suggests that prenatal or postnatal risk factors play an important role in nonfamilial forms of dyslexia, but not in familial types. The observation suggests that detailed neuropsychological comparisons of nonfamilial and familial cases of dyslexia might identify qualitative differences in their profiles of functional differences.

The risk of dyslexia in a child increases from

4-13 times if one of the parents has the trait. Affected sibs are severely impaired in families with an affected father than affected mother suggesting sex-dependent penetrance (Hallgren 1950; Pennington et al. 1991). In the present study, when father is affected, only 21.87% sibs are affected but when mother is affected, 35.29% of the sibs are affected suggesting no effects of sex dependent penetrance. It is also found that sibs in families with two affected parents were at greater risk, and affected sibs in these families were severely impaired than sibs in families with one affected parent. The rate of affectedness in first-degree relatives is around 30-70% (Schulte-Korne et al. 1996). In the present study, majority of the families (61%), at least one first-degree relative was affected. The findings suggest that additive genetic effects may play an important modifying role in familial dyslexia pedigrees and dyslexia is not randomly distributed in the population, but tends to run in families.

Reading and spelling difficulties compensate to an extent in certain individuals with age (Pennington et al. 1991) and compensation rate is 20% and it was reported that most of the female dyslexics compensate the difficulties than males (Pennington et al. 1986). In the present study 19.90% of the adults were compensated the difficulties and females compensated better than males. Different studies suggest that prevalence of dyslexia varies from 0.98% to 20% of the population (Zahalkova et al. 1972; Shaywitz et al. 1998; Paulesu et al. 2001). In the present study the prevalence of dyslexia among school children was found to be 9.87% and prevalence in 179 affected families was found to be 28.32%. All most all the studies reported so far agree that males are more frequently affected than females and majority of the samples involves males (Hallgren 1950; Critchley 1970; DeFries 1989; Pennington et al. 1991). Like most previous studies, we have found that in clinically ascertained samples of dyslexic probands, male probands outnumbered females in the ratio 3.7:1 and the sex ratios of affected relatives were considerably closer to unity (0.97:1). Among the probands 78.77% were males and among the affected relatives only 49.32% were males. Also, among both sibs and parents of the probands, more males than females were affected, 37.13% of both fathers and brothers, in contrast to 25.98% of the sisters and mothers. However, analysis of family pedigrees failed to support a sex-linked mode of inheritance. The higher frequency of affected males may be due to sex-controlled inheritance, or sex-limited inheritance (Zahalkova et al. 1972).

Zahalkova et al. (1972) found that consanguinity doesn't have any influence on dyslexia and none of the earlier studies have reported the association of consanguinity and dyslexia. This may be due to occurrence of less number of consanguineous marriages in the western world. However, in South India consanguineous marriages are very common (Verma and Bijarnia 2002) and in the present study, about 36.87% of the families are with consanguineous marriages, which could have influenced high prevalence of dyslexia in these families. Univariate logistic regression analysis revealed significant odds ratio (2.940) for consanguinity. It is noteworthy that none of the consanguineous families showed non-familial cases of dyslexia and it can be deduced that consanguinity is a risk factor for dyslexia.

Autoimmune disorders are commonly found in dyslexic individuals (Geschwind and Behan 1982; Galaburda 1997; Stein 2001). In the present study, 34.63% of the dyslexics showed incidence of allergic conditions. Both univariate and multivariate analysis showed significant odds ratios suggesting association of allergy with dyslexia. Different allergens were found to be dust, pollen, cotton, milk products, coco products, certain kind of drugs, citrus fruits, papaya, certain soaps, egg, fried food, coffee, coconut oil, mud, certain vegetables like ladies finger, drumstick, tomato, ridge guard, radish etc. Different individuals were specific to these allergens but not to all. Other immune disorders were found to be less prevalent compared to allergy however, univariate analysis showed significant odds ratios for migraine, asthma, measles and occurrence of migraine was also significant at multivariate analysis. There are reports of association of left-handedness and dyslexia (Geschwind and Behan 1982; Tonnessen et al. 1993). Here we found only 23 out of 179 dyslexic probands showed left-handedness and none of them had ambidexterity and univariate logistic regression analysis obtained significant odd ratio but multivariate analysis failed to obtain significant odds ratio. Dyslexics who suffered from measles, mumps and chickenpox had fatty acid deficiency signs, this may be due to the increased susceptibility to infection because of fatty acid deficiency (Horrobin et al. 1995). There

are also studies suggesting associations between impairments in motor coordination and dyslexia (Nicolson et al. 2001; Bishop 2002). Present study also found some of the dyslexics having problems with motor coordination however, no significant association was found with this condition. It is generally agreed that accomplishing milestones are delayed in dyslexics (Saviour and Ramachandra 2005). In the present study, 41.34% of the dyslexic children had delayed milestones and both univariate and multivariate logistic regression showed significant odds ratios in the occurrence of delayed milestones in dyslexics.

Fatty acids, as components of phospholipids, are important structural elements of biological membranes. They can also influence cell signaling in a variety of other ways (Richardson and Ross 2000). There is mounting evidence for abnorma-lities of fatty acid and membrane phospholipids metabolism in dyslexia (MacDonnel et al. 2000; Richardson et al. 2000). Studies have shown that severe fatty acid deficiencies lead to physical signs including excessive thirst, frequent urination and very dry, scaly skin as well as behavioral abnormalities (Stordy 1995). In the present study, all the 179 children were assessed for FADS and substantial proportion of dyslexic children had FAD, however, all the FAD signs not present in single individual. Most of the FADS were showed significant odds ratios in univariate analysis but multivariate analysis obtained significance only for dry and scaly skin. All dyslexic children who exhibited FAD signs had severe reading and spelling deficits. These results indicate that clinical signs indicative of fatty acid deficiency are common in dyslexia and this observation accord well with the earlier studies. As reported by earlier studies (Zahalkova et al. 1972) present study also found no association of ABO blood group and dyslexia. Hutchinson (1997) conducted a study on anemia and school achievement in school children and it was found that lower scores of spelling and reading in children with anemia. There are reports of influence of haemoglobin and serum ferritin on cognitive function in school children (Sungthong et al. 2002). In the present study, hemoglobin levels of dyslexic children showed low level of Hb in both males and females, however it was not significant. Cholesterol is a vital constituent of cell membranes and it is important for membrane stability and function (Zubay 1998). It was reported that decreased amount of total plasma cholesterol in people with visual subtype of dyslexia (Robinson et al. 2002). In the present study, estimates of cholesterol in 100 dyslexics showed that in most of the children serum cholesterol was below normal levels. In the human brain cholesterol is a significant component with most of this cholesterol being found within myelin (Snipes and Suter 1997). It is thought that the highly myelinated magnocells, believed to be deficient in dyslexia, may be prone to cellular malnutrition during disease due to their relatively high metabolic requirements. All the above results from the study suggest that a complex array changes are associated with dyslexia. Since dyslexia is a complex disorder multidisciplinary approach is important in developing precise and early diagnostic methods which could allow timely intervention for appropriate treatment and therapy for children with dyslexia.

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REFERENCES

Allred RA 1990. Gender differences in spelling achievement in grades 1 through 6. *Journal of educational research*, 83:187-93.

Arntz HR 1979. Diagnostik der hyperlipoproteinnamien. *Lab Med*, 3: 177

Bishop DVM 2002. Cerebellar abnormalities in developmental dyslexia: cause, correlate, or consequence? *Cortex*, 38: 491–98.

Boder E 1973. Developmental dyslexia: a diagnostic approach based on three atypical reading-spelling patterns. *Dev Med Child Neurol*, 15: 663-87.

Critchley M 1970. *The dyslexic child*. London: William Heinemann medical books Limited.

DeFries JC 1989. Gender ratios in reading disabled children and their affected relatives: a commentary. *Journal of learning disabilities*, 22: 544-45.

Ellis AW 1985. The cognitive neurophysiology of developmental (and acquired) dyslexia: A critical survey. *Cognitive Neuropsychol*, 26:169-205.

Fisher SE, DeFries JC 2002. Developmental Dyslexia: Genetic Dissection of a complex cognitive trait. *Nature reviews/Neuroscience*, 3: 767-80.

Galaburda AM 1997. Neurobiology of developmental dyslexia: Results of a ten year research program.

Learning Disabilities: A Multidisiplinary Journal, 8: 45-50.

Gayan J, Smith SD, Cherny SS, Cardon LR, Fulker DW, Brower AM, Olson RK, Pennington BF, DeFries JC 1999. Quantitative trait locus for specific language and reading deficits on chromosome 6p. *Am J Hum Genet*, 64: 157-64.

Geschwind N, Behan P 1982. Left-handedness: association with immune disorder, migraine, and developmental learning disorder. *Proc Natl Acad Sci USA*, 79: 5097–100.

Hallgren B 1950. Specific dyslexia ('congenital word blindness'): a clinical and genetic study. *Acta Psychiatr Neurol Scand*, 65: 1-287.

Horrobin DF, Glen ALM, Hudson CJ 1995. Possible relevance of phosphoipid abnormalities and genetic interactions in psychiatric disorders: the relationship between dyslexia and schizophrenia. *Med Hypotheses*, 45: 605-913.

Hutchinson SE 1997. Nutrition, anemia, geohelminth infection and school achievement in rural Jamica primary school children. *Eur J Clin Nutr*, 51: 729-35.

Lerner JW 1989. Educational interventions in learning disabilities. *J Am Acad Child Adolesc Psychiatry*, 28: 326-31.

MacDonnell LEF, Skinner FK, Ward PE, Glen AIM, Glen ACA, MacDonald DJ, Boyle RM, Horrobin DF 2000. Increased levels of cytosolic phospholipase A2 in dyslexics. *Prostagladins Leukotrienes and Essential Fatty Acids*, 63: 37-39.

Nicolson RI, Fawcett AJ, Dean P 2001. Developmental dyslexia: the cerebellar hypothesis. *Trends Neurosci*, 24: 508–11.

Paulesu E, Démonet JF, Fazio F, McCrory E, Chanoine V, Brunswick N, Cappa SF, Cossu G, Habib M, Frith CD, Frith U 2001. Dyslexia: Cultural Diversity and Biological Unity. *Science*, 291: 2165-2167.

Pennington BF, McCabe LL, Smith SD, Lefly Dl, Kimberling WJ, Lubs HA 1986. Spelling errors in adults with a form of familial dyslexia. *Child Development*, 57: 1001-1013.

Pennington BF, Gilger J, Pauls D, Smith SS, Smith SD, DeFries JC 1991. Evidence for a major gene transmission of developmental dyslexia. *Journal of the American Medical Association*, 18: 1527-1534.

Rao SN, Reddy IKK 1968 Indian norms of Revan's A, AB, B form. *Journal of Psychological Studies* 13: 2.

Richardson AJ, Calvin CM, Clisby C, Schoenheimer DR, Montgomery P, Hall JA, Talcott JB, Hebb G, Westwood E, Stein JF 2000. Fatty acid deficiency signs predict the severity of reading and related problems in dyslexic children. *Prostagladins Leukotrienes and Essential Fatty Acids*, 63: 69-74.

Richardson AJ, Ross MA 2000. Fatty acid metabolism in neurodevelopmental disorder: a new perspective on associations between attention-deficit hyperactivity disorder, dyslexia, dyspraxia and the autistic spectrum. *Protagladins, Leukotrienes and Essential Fatty Acids*, 63: 1-9.

Robinson GL, Sparkes DL, Roberts DK, Dunstan H, McGregor NR, Conway RNF 2002. Biochemical anomalies in people with a visual subtype of dyslexia. *International Dyslexia Association, 53rd Annual Conference*, Atlanta, Georgia.

Rutter M 1967. Children's behavior questionnaire for completion by teachers; preliminary findings. *Journal of Child Psychology and Psychiatry*, 8: 1-11.

Saviour P and NB Ramachandra 2005. Modes of genetic transmission of dyslexia in south Indian families. *Indian Journal of Human Genetics*, 11(3):135-140

Saviour P, Ramachandra NB 2006. Biological basis of dyslexia: a maturing perspective. *Current Science*, 90: 168-75.

Schulte-Korne G, Deimel W, Muller K, Guten brunner C, Remschmidt H 1996. Familial aggregation of spelling disability. *J Chil Psychol Psychiatry*, 37: 817-22.

Shaywitz, SE 1998. Dyslexia. *N Engl J Med*, 338: 307-12.

Shaywitz SE, Shaywitz BA, Pugh KR, Fulbright RK, Constable RT, Mencl WE 1998. Functional disruption in the organization of the brain for reading in Dyslexia. *Proc Natl Acad Sci USA*, 95: 2636-41.

Snipes GJ, Suter U 1997. *Cholesterol: Its Functions and Metabolism in Biology and Medicine*. New York: Plenum Press.

Stein JF 2001 The magnocellular theory of developmental dyslexia. *Dyslexia*, 7: 12-36.

Stevens LJ, Zentall SS, Deck JL, Abate ML, Watkins BA, Lipp SR, Burgess JR 1995. Essential fatty acid metabolism in boys with attention-deficit hyperactivity disorder. *American Journal of Clinical Nutrition*, 62: 761-768.

Stordy BJ 1995. Benefit of docosahexonic acid supplements to dark adaptation in dyslexia. *Lancet*, 346: 385.

Sungtong R, MoSuwan L, Chongsuvivatwong V 2002. Effects of haemoglobin and serum ferritin on cognitive function in school children. *Asia Pacific Journal of Clinical Nutrition*, 11: 117-122.

Tonnessen FE, A. Lokken A, Hoien T, Lundberg I 1993. Dyslexia, left-handedness, and immune disorders. *Arch Neurol*, 50: 411-416.

Verma IC, Bijarnia S 2002. The Burden of Genetic disorders in Indian and a framework for Community Control. *Community Genetics*, 5: 192-196.

Zahalkova M, Vrzal V, Kloboukova E. 1972. Genetical investigations in Dyslexia. *J Med Genet*, 9: 48-51.

Zubay GL 1998. *Biochemistry*. Duduque, I. A: Web publishers.