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Down Syndrome in Hyderabad (India) and It's Vicinity

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INTRODUCTION

Since Down syndrome (DS) was confirmed as an autosomal trisomy in 1959, several researches have attempted to explore the cause of non-disjunction of chromosome 21. Delayed fertilization might be an important factor in the conception of trisomies (German 1968). Increased acrocentric chromosome association frequency was also implicated to play a role in non-disjunction (Gould et al., 1981; Rao et al., 1998). The presence of an autosomal recessive gene that could be made homozygous through parental consanguinity was earlier suggested (Alfi et al., 1980). Other factors such as physical, biological and chemical mutagens have also been found to cause non-disjunction (Vogel and Motulsky, 1986). The small number of published epidemiologic studies of DS have examined paternal occupation as a risk factor. In this study, we attempted to identify other risk factors such as living environment, socio economic status in the birth of DS.

SUBJECTS AND METHODS

During a five year period (1991-1995), 115 DS cases were consequently referred to the Institute of Genetics, Hospital for Genetic Diseases Osmania University, Hyderabad for cytogenetic confirmation. The parental history was recorded in the case sheet. The details regarding age, sex, birth order of the child, parental age reproductive history, consanguinity, living environment, occupation income etc. were recorded. The normal children births in DS families were also recorded.

Blood samples from all the subjects and parents were taken for Karyotyping. Whole blood cultures set up according to a modified method of Moorhead et al (1960), were harvested after arresting at metaphase by adding colchicine and chromosome preparations thus obtained were stained for G-bands according to Seabright (1971). At least 30 well spread and banded metaphases were analyzed visually and 5 were microphotographed for karyotyping. Statistical evaluation was done with χ^2 for significance of frequencies.

RESULTS AND DISCUSSION

The cytogenetic data on the one hundred and fifteen subjects with DS is presented in table 1. Pure trisomy 21 was detected in 90.43% of the subjects studied. Mosaic trisomy 21 was detected in 4.35% of the subjects screened, whereas 5.22% were identified to have translocation trisomy 21. The frequencies of these chromosome abnormalities is almost similar irrespective of the ethnic or racial backgrounds (Giraud and Mattei, 1975; Stoll et al., 1990; Verma et al., 1991). Chromosomal analysis of the parents including translocation trisomies revealed normal karyotypes. Review of literature suggests that the incidence of DS is parental age dependent and the maternal age has been incriminated more often than paternal age with the etiology of DS (Hook and Fabia, 1978; Stene et al., 1981). In the present study, 73% of DS children were born to mothers < 30 years of age and 65% to fathers above 30 years of age. The mean maternal age calculated as 25.4 ± 6.37 and mean paternal age was 33.0 ± 6.67 years (Table 2). We observed a reduction in mean maternal age compared to earlier study (29.54 + 6.4) from Hyderabad India (Isaac et al., 1985). The fall in mean maternal age presumably may be due to environmental pollution (Owens et al., 1983, Mikkelsen 1988). The DS incidence was prevalent in 20 – 30 years of age group in mothers, and in fathers it was between 25 – 39 years. It falls within the younger parental age group. In this contest it should be mentioned that this is the major fertility period of women in India.

Table 3 shows the DS births in different living environment, occupation and economic status. We calculated both DS children and normal children births in DS families. Significantly high frequency ($p<0.05$) of DS births found to

Table 1: Type of chromosome abnormalities in 115 subjects with DS

S.No.	Type of chromosome abnormality	No.	%
1.	Trisomy 21		
	47, XY, +21	54	
	47, XX, +21	50	90.43
2.	Mosaic trisomy 21		
	46, XY/ 47, XY, +21	3	
	46, XX/ 47, XX, +21	2	4.35
3.	Translocation trisomy 21		
	46, XY, t (14;21)	4	
	46, XY, t (21;21)	2	5.22

Table 2: Distribution of parental age of DS

S.No.	Age group	Maternal		Paternal	
		No.	%	No.	%
1.	15 - 19	7	6.09	-	
2.	20 - 24	41	35.65	13	11.30
3.	25 - 29	36	31.30	27	23.48
4.	30 - 34	16	13.91	34	29.57
5.	35 - 39	9	7.83	26	22.61
6.	> 40	6	5.22	15	13.04
	Total	115		115	
	Mean±SD	25.40+6.37		33.0+6.67	

occurred in urban area when compared to normal children and, rural area affected and normal children. The difference in DS births and normal children in DS families was not observed in industrial area, different parental occupations and income groups. The income of the parents of DS ranged from $\leq$ 2000 p.m. (low income group), $\geq$ 2000 p.m. (high income group). Birth order of DS in relation to sibship size and family income is analyzed in Table 4. Significantly ($p<0.05$) high frequency of first born found to be affected in lower income group compared to other birth order. However, the difference in the DS births was not observed among high or low income group. In case of large families last born was found to be affected.

Mikkelsen et al. (1976), Nordensen et al. (1979) and Uchida et al. (1973) reported high frequency of DS in urban areas as observed in the present study. The increased frequency of DS in women below 35 years of age has been noticed in industrial and densely populated areas. Most of the research has focused on maternal exposures, with little attention having been paid to the possible role of paternal environmental factors in the etiology of DS, although in the

Table 3: DS births in different living environment and economic status

S. No.	Socio-economic status	DS births		Normal childrens	
		No.	%	No.	%
1	Area				
	Urban	78	62.40*	47	37.6
	Rural	37	23.87	118	76.13
2	Locality				
	Industrial	13	32.5	27	67.5
	Other area	102	42.5	138	57.5
3	Occupation				
	Agriculture	8	57.14	6	42.86
	Industry	5	62.50	3	37.50
	Others (clerks, Business, drivers, Carpenters, etc,)	102	39.53	156	60.47
4	Economic status				
	Low income group < Rs 2000 p. m.	44	43.14	58	56.86
	High income group > Rs 2000 p. m.	71	39.89	107	60.11

* As compared with the normal children $p< 0.05$, χ^2, 2X2 contingency test

Table 4: Birth order of DS in relation to sibship size and family income

Birth order	Low income group				High income group			
	DS		Normal children		DS		Normal	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
1	19	(43.18)*	3	(5.17)	26	(36.62)	9	(8.41)
2	10	(22.73)	11	(18.97)	27	(38.02)	29	(27.10)
3	7	(15.91)	13	(22.42)	9	(12.68)	22	(20.56)
4	3	(6.82)	6	(10.34)	4	(5.63)	16	(14.95)
5	1	(2.27)	4	(6.90)	1	(1.41)	4	(3.74)
6	3	(6.82)	15	(25.86)	1	(1.41)	5	(4.67)
7	1	(2.27)	6	(10.34)	1	(1.41)	6	(5.62)
8	-	-	-	-	1	(1.41)	7	(6.54)
9	-	-	-	-	1	(1.41)	9	(8.41)
Total	44	(43.14)	58	(56.86)	71	(39.89)	107	(60.11)

*As compared with other birth order (both normal and affected) $p<0.05$, χ^2, 2x2 contingency test

majority of cases the extra chromosome 21 is maternal origin, approximately 20% of errors are of paternal origin (Antonarakis, 1991). Bond and Chandley (1983) demonstrated that chemicals and other factors such as radiation induce non-disjunction during spermatogenesis. In addition to direct effect on the fathers, the mother may be exposed to variety of agents brought home from the fathers work place (Knishkovy and Baker, 1986). Hales et al., (1986) have reported that the maternal exposure through paternal

transmission of work place toxins seminal fluid, which has been shown to occur for some chemicals. A high number of DS children were detected among glass and ceramic workers, armed forces (OPCS 1982). A case control study during 1945 – 1968, did not find an association between paternal occupation group and DS (Cohen et al., 1977). Several other studies (Erickson et al., 1984; Jenerich and Bracken, 1986) also reported DS births to fathers with different occupation, however they did not provide many leads with regard to the risk posed by paternal occupation . Among other factors, the socio economic status presumed to play important role in the birth of DS. In case of large family size, last born found to be affected, this may be due to poor nutritional status in mothers. Such increased risk due to socio economic status has not been reported in the literature.

The scope of the study in living environment, occupation and economic status of parents of DS is to focus on their impact on the prevalence of DS. In recent years a fall in the mean maternal age of DS children has been observed. This fall has been thought as a consequence of environmental pollution. Ninety percent of the population used to be rural in the past but in the recent years the trend has got changed in India and migration from rural to urban areas has become imperative for livelihood and other reasons. Consequently urbanization of the population has become more effective, aprops there has been change in the occupation and living conditions and needs of life confront with the nutrition, health and hygiene and shows their effect on the future progeny. However exploration of the affect of living environment occupation, economic status of parents of DS in the present study could not provide a concrete evidence as the sample size was small but shall add to the existing data knowledge and in the days to come it may aid to pin point the effect of environmental and socio economic status on the etiology of DS.

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KEY WORDS Down Syndrome. Parental Age. Non-disjunction. Living Environment. Economic Status.

ABSTRACT We have studied the effect of living environment, occupation, and income in parents who gave birth to Down syndrome (DS) children. A significantly ($p < 0.05$) high frequency of parents of DS found to live in urban area. In case of occupation and income no significant difference was observed. However, when the birth order and the income of the parents analyzed, significantly high number of first born found to be affected in low income group. Our present observations suggest that the living environment and economic status plays a important role in the non-disjunction of chromosome 21, as resulting in the birth of DS offsprings.

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