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Cytogenetic, Socio-economic and Biological Study of Down Syndrome Patient

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ABSTRACT Down syndrome is mainly numerical change of chromosome 21 which is found 1 per 1200 live births in India. Chromosomal analysis is necessary for primary diagnosis. Socio-economic factor may affect indirectly in case of Down syndrome patient. Previous miscarriage of mother is related with the next birth of Down syndrome baby. After screening 218 genetically abnormal cases, 45 cases were diagnosed as Down syndrome, in Genetics Department of Ramakrishna Mission Seva Pratishthan. Detailed clinical and socio-economical history and anthropometric measurement were taken from these particular patients. Maximum cases of Down syndrome are from Socio-economically deprived area. Stunting growth is found in Down syndrome cases. 75.56% mothers have previous reproductive wastage.

INTRODUCTION

Down syndrome (DS) children suffered from mental impairment and multiple malformations due to the presence of trisomy of chromosome 21. Although the phenotypical features of DS patients are variable but there are enough similar symptoms to enable the expert to suspect the diagnosis (Pediatrics 2001). Hypotonia, small brachycephalic head, epicanthic folds, upward slanting palpebral fissures, Brush field spots (not found in India), flat nasal bridge, small ears, and excessive skin at the nape of the neck, small mouth, single transverse palmer crease, protruded tongue and short fifth finger with clinodactyly etc. are some common physical features of Down syndrome. Another common feature is a wide space with a deep fissure between the first and second toe. The degree of mental impairment is severe in very rare occasions. Otherwise it varies ranging from mild to moderate. There is a possible risk of congenital heart defects, gastrointestinal atresias, Hirschsprung disease, leukemia, acquired hip dislocation, otitis media, eye disease including cataracts and severe refractive errors, hearing loss, obstructive sleep apnoea and thyroid disease. The condition of 95% children with Down syndrome is because of non-familial trisomy 21. Other 3-4% of Down syndrome persons with same phenotype characters have an unbalanced translocation between chromosome 21 and another C or G group of chromosome, especially chromosome 14. In the rest of 1-2% of persons with the Down syndrome have 2 cell lines: normal cell line and trisomy 21 cell line. It is known as mosaicism. These people may be phenotypically less severely affected than persons of first two types but their conditions are generally indistinguishable in all other aspects (Pediatrics 1994; Cohen 1996; Cooley and Graham 1991; De laCruz 1977).

Trisomy 21 is one of the commonest autosomal chromosomal abnormalities in the newborns and its occurrence is 1 in 650-1000 live births (Hook 1982). Around 25% of the DS conceptions survive to birth and the post birth data indicates greatly improved life expectancy in 80%. Frequency of trisomy 21 is 0.115 percent (range from 0.07 to 0.16 percent) (Bhasin 2005). Gardner and Sutherland (2004) estimated +21 chromosome frequencies are 0.12 percent among newborns, from non-banded data and moderate level banding data. Governmental care of this syndrome has increased in the past few years. Though implications exist for providing the proper health care in different hospitals and medical institute to Down syndrome individuals and DS pregnancy, but due to parental screening in early stage of pregnancy in some cases there seem to be a decline in the birth prevalence of DS baby. The reported occurrence

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of DS is around 1 in 1250 live births in India (Verma and Singh 1975). Karyotyping or chromosomal analysis is essential for individual case suspected to have the trisomy 21 status, so that the genetic implications may be assessed.

In this paper an attempt has been made to study the several factors like cytogenetic, socioeconomic, biological and anthropometric effects affecting Down syndrome patients.

MATERIAL AND METHODS

The data comprises cases referred to the Genetics Department of Ramakrishna Mission Seva Pratishthan from all over West Bengal (District hospitals, Health centers, Govt. Hospitals, private clinics and outdoor and indoor departments of Ramakrishna Mission Seva Pratishthan). The total number of cases referred was 212, out of which 45 were diagnosed with Down syndrome.

Detailed histories of the patients were taken on a prepared questionnaire. The data used for creation of the growth charts were age at examination (years and months), height (cm) and weight (kg). The measurements were taken following standard anthropometric technique (Martin and Saller 1957). The data for each sex were divided into different age groups. Each child contributed only one single set of data for each age group. Detailed but prudent and persistent investigations were made regarding the family and spouse income, the living status, educational status, health awareness and type and adequacy of housing.

On a personal level, particularly for the mothers, their fears, anxieties and stresses of family life were looked into. The time gaping of pregnancies, sexual practices, and use of contraceptives were noted. The past obstetric history provided valuable information regarding recurrent abortions (spontaneous abortion or induced abortion) before the birth of Down syndrome baby, exposure to drugs, harmful chemicals and increased maternal age. Clinical feature of the patient was also noted.

Cytogenetic Analysis of the Index Patients by Short Term Leukocyte Culture Method

Blood cultures were made for chromosome preparations using 4 ml sodium heparinized BD Vacutainer ™. 2 ml peripheral blood was collected from the DS patients for Phytohemaglutinin stimulated lymphocyte cultures (Moorehead et al. 1960). Slides were prepared after harvesting the blood samples. Giemsa stain was used for staining some prepared slide (Hungerford 19650). Other slides were used for G-banding method of karyotyping (Wendy 2001). Approximately 50-60 metaphase plates were studied in Zeiss microscope under oil immersion lens (100X). The karyotyping results were noted using the recommendation of International System for Human Cytogenetic Nomenclature (Mitelman 1985).

RESULTS

In our study among 45 cases, maximum numbers (42.2%) were in the age group of 1-12 months and minimum numbers (4.44%) were in 18-30 years age group (Table 1). Thus, more than 40% of DS cases were diagnosed below 1 years of age which indicates that pediatricians and other medical professionals are aware of the clinical phenotype of DS and prompt the cytogenetic confirmation. Among karyotyped cases there were 26 males and 19 females with a sex ratio of 1.37. The cytogenetic results of the analyses of 45 cases of Down syndrome are presented in Table 2. Non-disjunction of trisomy 21 and hence free trisomy 21 (Fig.1) was the most common type of abnormality detected in 93.33% (N=42) of the cases; and 3 (6.67%) showed mosaic pattern. Birth order of DS showed a higher number of first and second born. It was found that maximum number of patients (22.2%) came from south 24 parganas which is socioeconomically deprived area in West Bengal. 13.33% patients came from Bangladesh, neighboring country of India is also socio-economically not well developed (Table 3). We have significantly found that approximately 50% of DS cases came from very low income group and 17.78% of DS patient's family lie below poverty line as can be seen from Table 4. The risk for DS increased as the number of low socioeconomic factors present throughout the mother's life increased. The highest proportion of infants was among mothers with secondary education. The birth of Down syndrome was the highest among mothers with the lowest education. Growth is an important biological parameter of DS cases which shows the actual health status of the particular patient. Here percentiles of height and weight of DS children of eastern region were compared to NCHS standard. Stunting of height and wasting

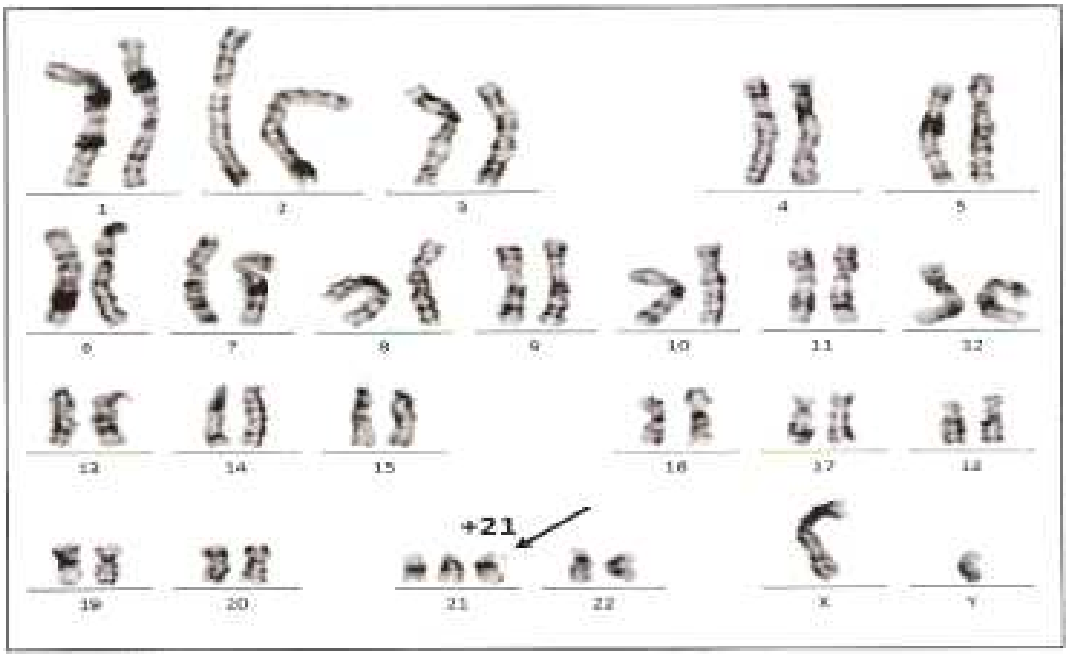

Fig. 1. GTG banded karyogram of a male individual with pure trisomy 21

was apparent in the study group, especially in the age group of 1-12 months. But overweight of children was not found in other age group (Table 5). Previous birth wastage of mother is another important prevalence risk factor of DS cases. Out of 45 cases 34 mothers (75.56%) had a reproductive wastage, out of which 18 mothers had spontaneous abortion, 13 had induced abortion and 3 mothers had still born baby.

Table 1: Distribution of Down syndrome patients according to sex and age

Age Group	*No. of male*	*No of female*	*Total no of cases*	*%*
Up to 1 month	7	2	9	20.0
1-12 months	9	10	19	42.2
1-4 years	4	4	8	17.78
5-9 years	1	2	3	6.67
10-18 years	4	0	4	8.89
18-30 years	1	1	2	4.44
Total	26	19	45	100

DISCUSSION

In the present study 212 cases were referred from different districts of West Bengal and other states of India and Bangladesh with various genetic disorders. Out of these 212 cases, 45 DS cases were identified.

Table 2: Cytogenetic study of Down syndrome patients

Age group	*Mosaic down*		*Trisomy 21*	
	No. of cases	*% of cases*	*No. of cases*	*% of cases*
Up to 1 month	1	2.22%	8	17.77%
1-12 months	1	2.22%	18	40%
1-4 years	-	-	8	17.77%
5-9 years	1	2.22%	2	4.44%
10-18 years	-	-	4	8.89%
18-30 years	-	-	2	4.44%
Total	3	6.67%	42	93.33%

Table 3: Distribution of Down syndrome patients according to their place of origin

Origin of the patient	*No. of cases*	*%*
Kolkata	3	6.67
Howrah	5	11.1
North24 parganas	2	4.44
South 24 parganas	10	22.2
Nadia	2	4.44
Burdwan	3	6.67
Medinipur	7	15.56
Birbhum	1	2.22
Murshidabad	2	4.44
Bihar	3	6.67
Assam	1	6.67
Bangladesh	1	13.33

Table 4: Distribution of Down syndrome patients according to their Economic Condition Of the family

Economic Condition Of the family							
Very poor <1000/- per month		*Poor1000-5000/- per month*		*Middle Class 5000-15000/- per month*		*Affluent >15000/- per month*	
No. of cases	*%*	*No. of cases*	*%*	*No. of cases*	*%*	*No. of cases*	*%*
8	17.78	22	48.9	10	22.22	5	11.11

Ninety-five percent individuals with Down syndrome have extra chromosome 21 (Fig.2) and 4% of DS people, have translocation between chromosome 21 and another acrocentric chromosome (Mikkelsen 1977; Thuline and Pueschel 1982). On other hand 1-4% mosaic Down syndrome was found (Mikkelsen 1977; Lovering and Percy 2007). In this study it was found 93.33% have trisomy 21 and 6.67% have mosaicism. Not a single case of chromosomal translocation was observed.

Socio-economic status has been earlier established as a risk factor (Khoshnood et al. 2004). According to Bhasin (2005) parental social status is evaluated from the status of the father and it is interesting that fathers of boys had enlarged Y. Socio-economic factors include education, income, and family occupation. Low birth weight and prenatal, neonatal and post neonatal mortality are some adverse prenatal and infant outcomes as these are the major known risk factors (Vrijheid et al. 1999). Surprisingly little literature exists specifically examining the socio-economical inequalities in the prevalence of the chromosomal aberration. The researchers have found that a significant proportion (approximately 50%) of DS cases originated form very low income group of which 15% lie below the poverty line and 33% mothers had only elementary education (Table 6). Bulk of the patients came from interior of south 24 Parganas which is one of the socio-economically deprived areas of West Bengal. This data is comparable with the study of Scottish children (Murdoch 1982) where they found prevalence of DS among lower social classes or residents of more socio-economically deprived areas. Mother's level of education was most highly associated with their knowledge of whether or not they had been screened (Khoshnood et al. 2004). If mothers are well educated they are concerned about prenatal screening. The current findings explained that, socio economic differentials may effect to the prevalence of DS but further follow-up studies will be required in the large scale of population.

Table 5: Distribution of Down syndrome patients according to their standing height and weight

Age group	*Category*	*< 5th percentile*		*5th-10th percentile*		*10th-25th percentile*		*25th-50th percentile*		*50th-75th percentile*		*> 75th percentile*	
		No of cases	*%*	*No of cases*	*%*	*No of cases*	*%*	*No of cases*	*%*	*No of cases*	*%*	*No of cases*	*%*
Upto 1 month	Height	4	9.76	2	4.88	0	0	2	4.88	0	0	1	2.44
	Weight	2	4.44	3	6.67	1	2.22	1	2.22	1	2.22	1	2.22
1-12 months	Height	7	17.1	0	0	2	4.88	3	7.32	3	7.32	0	0
	Weight	10	22.2	2	4.44	4	8.89	2	4.44	1	2.22	0	0
1-4 years	Height	5	12.19	1	2.44	2	4.88	1	2.22	0	0	0	0
	Weight	3	6.67	4	8.89	1	2.22	0	0	0	0	0	0
5-9 years	Height	2	4.88	0	0	0	0	0	0	0	0	0	0
	Weight	1	2.22	1	2.22	1	2.22	0	0	0	0	0	0
10-18 years	Height	3	7.32	0	0	0	0	1	2.22	0	0	0	0
	Weight	1	2.22	1	2.22	0	0	1	2.22	1	2.22	0	0
18-30 years	Height	2	4.88	0	0	0	0	0	0	0	0	0	0
	Weight	2	4.44	0	0	0	0	0	0	0	0	0	0

Table 6: Distribution of Down syndrome patients according to their Education of mother

Education of mother									
Illiterate		*Elementary education*		*Primary education*		*High School*		*College*	
No. of cases	*%*	*No. of cases*	*%*	*No. of cases*	*%*	*No. of cases*	*%*	*No. of cases*	*%*
8	17.78	15	33.33	11	24.44	6	13.33	5	11.11

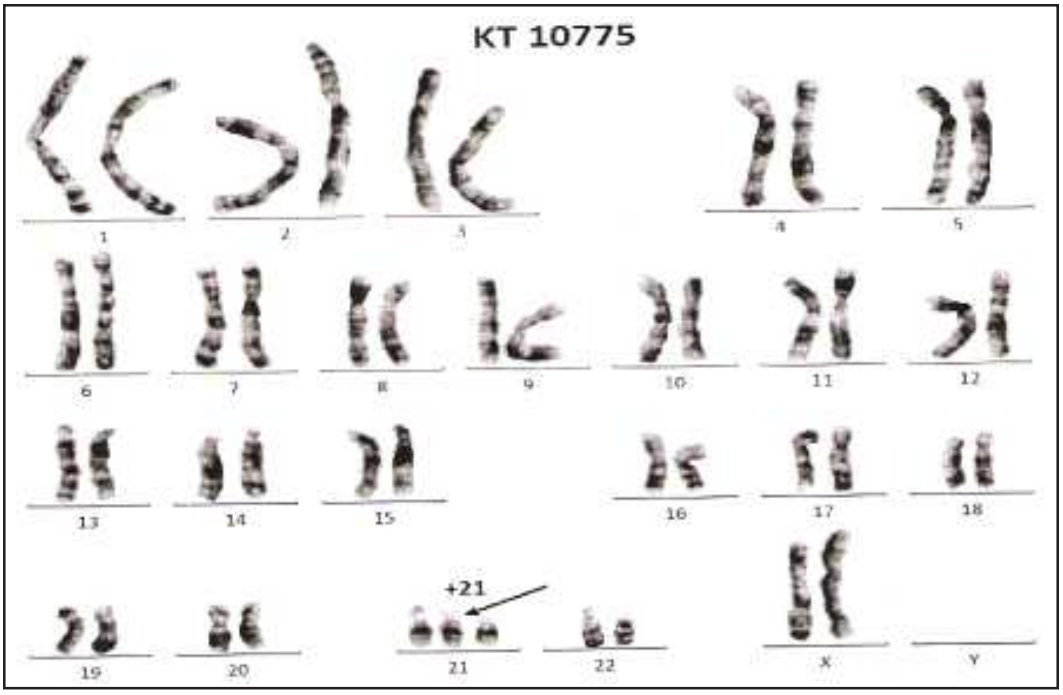

Fig. 2. GTG banded karyogram of a female individual with pure trisomy 21

Growth is an excellent indicator of health status of an individual as well as at population level. This is evident from several defunct organ systems in DS. The common feature of DS is short stature (Cronk 1978; Cronk 1989) which is due to growth retardation associated with increased age (Cronk et al. 1988). Congenital heart disease (Cronk 1989; Greenwood and Nadas 1976), sleep related upper airway obstruction (Stebbens et al. 1991), coeliac disease (Jansson and Johansson 1995; Csizmadia et al. 2000), thyroid hormone deficiency (Karlsson et al. 1998; Sharav et al. 1988), and nutritional inadequacy caused by feeding problems (Chilvers 1997) etc. are various cause of poor growth of DS patients. In the present study stunting of height and wasting was found in maximum age group.

One in one-fifty pregnancies are associated with trisomy 21 as estimated in a study, but over three quarters are miscarried (Sherman et al. 1994). In a study using data from the National Down Syndrome Cytogenetic Register (1989–96) maintained at the Wolfson Institute of Preventive Medicine, together with data on the spontaneous loss of Down syndrome pregnancies (estimated from differences in prevalence at chorionic villus sampling, amniocentesis, and birth) it is known that between 1989 and 1996, there were about 43% spontaneous loss of Down syndrome fetuses between 10 weeks' gestation and birth (Morris. in press). Also, the spontaneous loss (including stillbirths) between 16 weeks' gestation and birth was 23%. Paternal age and trisomy among spontaneous abortions and concluded that neither on statistical nor biological grounds do the data provide compelling evidence of paternal age effects on the trisomies found among spontaneous abortions, or on chromosomally normal losses (Bhasin 2005).

In our study we found that out of 45 cases, 34 mothers (75.56%) had a reproductive wastage (Table 7). Out of which 18 mothers had spontaneous abortion, 13 had induced abortion and 3 mothers had still born baby before the birth of DS baby which is a very significant finding.

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Table 7: Distribution of mothers having birth wastage before the birth of the Down syndrome child

Age group (years)	*No. of mother*	*Birth wastage*				
		Abortion		*Still births*	*Total*	*%*
		Sponta-neous	*Induced*			
13-20	5	3	1	0	4	8.89
21-25	11	5	3	0	8	17.78
26-30	13	4	4	2	10	22.22
31-35	9	2	4	1	7	15.56
36-40	5	2	1	0	3	6.67
>40	2	2	0	0	2	4.44
Total	45	18	13	3	34	75.56

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