Cytogenetic studies in infants with congenital malformations

Author(s): Muthukumaravel. N., Ramachandra Rao. K. and Vishnu Bhat. B.

Vol. 9, No. 1 (2005-10 - 2005-12)

Curr Pediatr Res 2005; 9 (1 & 2): 11-14

Muthukumaravel. N., Ramachandra Rao. K. and Vishnu Bhat. B*.

Cytogenetic Section, Department of Anatomy and Department of Pediatrics*, JIPMER, Pondicherry, India

Key Words: Cytogenetic studies, Karyotyping, Congenital malformations

Accepted April 02, 2005

Abstract

Chromosomal aberration leading to congenital malformations is an important cause for infant mortality. Forty five infants with congenital malformations affecting various systems were screened by photokaryotyping for evidence of cytogenetic abnormalities after taking thorough family and obstetric history. Among the cases multiple malformations suggestive of Down's Syndrome was the commonest. The association between malformations and parental consanguinity was found to be significant. Most of the babies with malformations were low birth weight babies. Chromosomal anomalies in the form of Trisomy 18 and 21 were seen in cases with multiple malformations. Avoiding consanguineous marriage may help in reducing the incidence of congenital malformations.

Introduction

Congenital malformations form an important cause of infant mortality. Although many aetiological factors have been attributed for congenital malformations, chromosomal abnormalities [1] and consanguinity in parents [2] play significant role in their occurrence. This study was undertaken to investigate the pattern of malformations, the type of cytogenetic variation in each category of malformation and to correlate the type of malformation with cytogenetic variation.

Materials and Methods

Forty five live infants with major or multiple congenital malformations referred from the Department of Pediatrics to the Department of Anatomy for Karyotyping were included in this study. Equal number of normal babies delivered in the Labour room of this Institute were taken as controls. Maternal age, Parity, Parental consanguinity, sex of baby, Birth weight, type of malformations etc. were recorded in a preplanned proforma for all infants. Using peripheral blood sample, short term lymphocyte culture [3] was done for all cases. From these cultured lymphocytes photokaryotyping was done for all cases.

Results were correlated with malformations and analysed using chi square test.

Results

Maternal age of less than 20 years or more than 25 years were significantly associated with occurrence of malformations in babies ($P<0.05$). Congenital malformations were more common among babies of consanguineous parents ($P<0.05$). 33 out of 45 cases (73.3%) had consanguinity among parents. There was no significant difference in sex distribution. Malformations were more among low birth weight babies (Table I).

Multiple malformations suggestive of Down's syndrome was the commonest among the cases investigated (28 cases out of 45). These were followed by nervous, alimentary and urogenital system anomalies. Out of 28 cases suggestive of Down's syndrome, 5 cases were cytogenetically normal, 4 cases had mosaic form of Trisomy 21, one had Trisomy 18 and remaining 18 had Pure Trisomy 21. Trisomy 18 was seen in 2 cases. One had occipital meningoencephalocoele and another had clinical features suggestive of Down's syndrome. One case with atrial and ventricular septal defects had Trisomy 21. (Table II).

Table I: Maternal and Infant factors in relation to malformations.

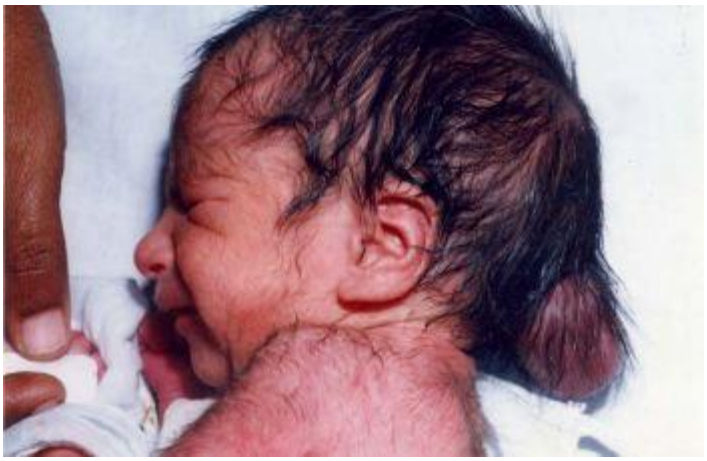
Factor	Cases		Control		p Value
	No	%	No	%	
1. Maternal age in yrs					
< 20	14	31.1	1	2.2	
21 – 25	26	57.8	34	75.6	
> 25	5	11.1	10	22.2	< 0.05
2. Parity of Mothers					
Primi	22	48.9	23	51.1	
Multi	23	51.1	22	48.9	NS
3. Parental consanguinity					
Consanguineous	33	73.3	21	46.7	
Non consanguineous	12	26.7	24	53.3	< 0.05
4. Sex distribution					
Males	25	55.6	25	55.6	
Females	20	44.4	20	44.4	NS
5. Birth Weight in Kg					
< 2	18	40.0	3	6.7	
2 to 2.5	16	35.6	18	40.0	
> 2.5	11	24.4	24	53.3	<0.05

Table II: Type of malformations and chromosomal abnormalities

Malformations	Chromosomal abnormalities	No. of Cases
1. Malformations suggestive of Down's syndrome	Pure Trisomy 21	18
	Trisomy 21/Normal Mosaicism	4
	Nil	5
	Pure Trisomy 18	1

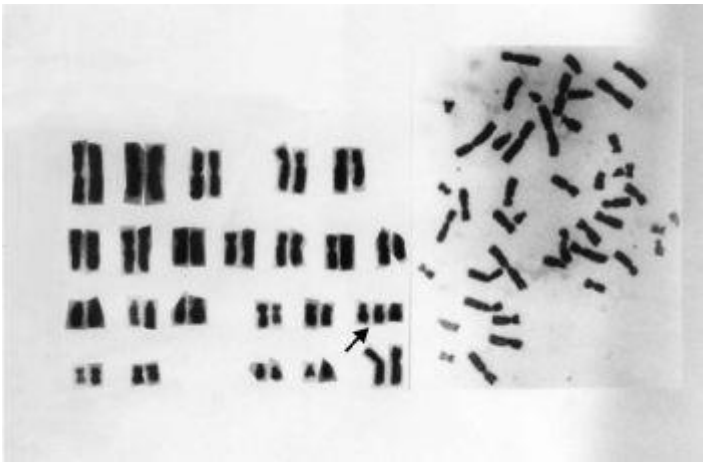
2. Major Nervous system malformations		
Occipital meningoencephalocoele	Trisomy 18	1
Lumbar meningocoele	Nil	1
Occipital meningocoele	Nil	2
Lumbar meningomyelocoele with hydrocephalus	Nil	1
3. Major Cardiovascular system malformations		
Atrial septal defect with ventricular septal defect	Trisomy 21	1
Atrial septal defect	Nil	1
4. Major Alimentary canal malformations	Nil	5
5. Major urogenital system malformations	Nil	4
6. Case with limb malformations	Nil	1

Figure 1: Baby with occipital meningoencephalocoele



(For larger image, click here)

Fig. 2: Photokaryotype of the case in Figure 1 showing Trisomy-18 with Sex Chromosomal Complement as 47 XX +18



(For larger image, click here)

Discussion

In the present series, the congenital malformations were seen more commonly among babies of mothers who were less than 20 years of age. Chinara et al [4] and Kulshrestha et al [5] had reported higher incidence of malformations in babies of mothers aged above 25 years. But Mittal and Grewal [6] reported higher incidence of malformations in mothers aged below 20 years.

In the present study, there was no significant correlation between parity of mothers and congenital malformations. Bhat et al [2] also did not find any increase in incidence of malformations with increasing partiy of the mothers.

Association between the parental consanguinity and malformations was found to be significant in the present investigation and it was in agreement with the findings of Bhat et al [2], Singh et al [7] and Agarwal et al [8]. Singh et al [7] had observed parental consanguinity among 38.4% of cases with malformations. Whereas in the present study, the incidence of consanguinity was 73.3%.

Bhat et al [2] had recorded higher incidence of malformations among male babies in a ratio of 1.5:1. Although there were more male babies with malformations in the present study, the difference was not statistically significant.

Regarding the birth weight and malformations, there was a statistically significant association in the occurrence of malformations in babies below 2000 gms. This is in agreement with earlier study of Bhat et al [2].

According to many standard literatures, either atrial or ventricular septal defects occur in Down's syndrome babies [1]. In our series, in a case of Down's syndrome (Trisomy 21), atrial septal defect with ventricular septal defect was observed.

In our series, 5 cases with malformations suggestive of Trisomy 21 showed normal chromosomal complement and another case with malformations suggestive of Trisomy 21 had pure Trisomy 18 on Karyotyping. The above mentioned cases might have had familial, geographical or racial dysmorphism which usually mislead clinicians. So whenever clinical features of malformations are not typical in children, cytogenetic studies should be done to confirm the diagnosis before counselling of parents. This could avoid unnecessary psychological stress in parents. Also preparing universally accepted and standardized check lists of clinical features and anthropometry for different chromosomal syndromes might help the clinicians in their diagnosis. 16q deletion syndrome [9] and D-E translocations [10] were suggested as causes for meningoencephalocoele. But in our series, an infant with meningoencephalocoele had Trisomy 18 which is a numerical aberration of chromosome. (Figures 1 and 2).

In our series, all cases with alimentary canal, urogenital system and limb malformations and majority of cases with nervous and cardiovascular system malformations had no chromosomal aberrations on Karyotyping. These are the ideal cases which have to be subjected to further investigative procedures such as Flourescent in situ hybridization

(Fish) using specific probes, gene mapping etc. These would bring out the structural aberrations of chromosomes, gene disorders etc. which might be associated with each type of these malformations.

In conclusion, it could be said that consanguinity plays a significant role in the aetiology of malformations. Chromosomal anomalies were seen in cases with multisystem involvements in the form of Trisomy 18 and 21. Hence one should discourage consanguineous marriages. Babies with a major or multiple malformations should undergo karyotyping so that genetic counselling would be more meaningful.

References

1. Fauci, Braunwald, Isselbacher, Wilson, Martin, Kasper, Hauser, Longo: Harrison's principles of Internal Medicine, 15th edn. Vol.1, McGraw-Hill Medical Publishing Division, New York, USA. 2001; PP 1331-1333.
2. Bhat BV, Babu L: Congenital malformations at birth – A prospective study from South India. Indian J Pediatr 1998; 65: 873-881
3. Arikaki DT, Sparkes RS: Microtechnique for culturing leucocytes from whole blood. cytogenetics 1963; 2:57-60.
4. Chinara PK, Singh S. East – West differentials in congenital malformations in India. Indian J Pediatr 1982; 49: 325-329.
5. Kulshrestha R, Nath LM, Upadhyaya P: congenital malformations in live born infants in a rural community. Indian Pediatr 1983; 20: 45- 49
6. Mittal VK, Grewal RS: Congenital malformations in neonates. Indian J Pediatr 1969; 36: 356- 365.
7. Singh M, Jawadi MH, Arya LS, Fatima: Congenital malformations at birth among live born infants in Afghanistan - A Prospective study. Indian J Pediatr 1982; 49: 331-335
8. Agarwal SS, Singh U, Singh PS: Prevalence and Spectrum of congenital malformations in a prospective study at a teaching hospital. Indian J Med Res 1991; 94: 413- 419.
9. Naritomi K, Shiroma N, Izumikawa Y, Sameshima K, Ohdo S, Hirayama K: 16q21 is critical for 16q deletion syndrome. Clin Genet 1988; 33: 372- 375.
10. Kabarity A, Lejeune J, Puschel E, schade H: D-E- translocation in meningoencephalocoele, microcephaly and pseudoanencephaly. Dtsch Med Wochenschr 1972; 97: 2009-2011.

Correspondence:
Professor Vishnu Bhat. B
Department of Pediatrics
JIPMER
Pondicherry 605 006
India