

Study of C3 Polymorphism Among the Infants Born with Neural Tube Defects and Oro-Facial Clefts

S.K. Basu¹, S. Bhatnagar², A.K. Singla¹ and N. Makol¹

1. Department of Population Genetics and Human Development

2. Department of Planning and Evaluation

National Institute of Health and Family Welfare, New Mehrauli Road, Munirka, New Delhi 110 067, India

KEY WORDS Neural Tube Defects. Oro-Facial Clefts. Serum Proteins.

ABSTRACT Data are presented on the distribution of C₃ polymorphism in infants with neural tube defects and oro-facial clefts. The frequencies of FF and FS phenotypes were found to be higher among both the groups of congenital malformed infants as compared to their respective controls. In the total material the odd ratio was found to be 2.57 for FS phenotype which shows that infants with this phenotype have more likelihood of developing such anomalies.

INTRODUCTION

The complements are major mediators of the inflammatory immune response and play an integral role in first defense against infection. Genetic polymorphism has been observed in most of its components. Polymorphism of the third component of the complement (C₃) was first reported by Ropartz et al. (1965). The three common phenotypes of C₃ system (S, SF, F) are governed by two autosomal alleles C_{3F} and C_{3S}. In addition of these, there are present a number of rare alleles which produce variants differing slightly in their electrophoretic mobility.

The C₃ system has been studied extensively owing to its higher concentration in the serum and also because it requires a simple technique like agarose gel electrophoresis for typing it. However, the amount of information available on this system in different diseases is rather limited as yet. The diseases like rheumatic arthritis (Bronnestam, 1977), diabetes mellitus, in which data on C₃ polymorphism has been reported include hepatitis and leprosy (Schur and Austin, 1968), leprosy (Agarwal et al., 1974) and systemic lupus erythematosus and

Indian childhood cirrhosis (Shahai et al., 1974). It is therefore, the present investigation has been planned to provide on such data on neural tube defects and oro-facial defects.

MATERIAL AND METHODS

For the present work routine field visits were made to different hospitals of Delhi for collection of data on infants born with neural tube defects and oro-facial clefts. Blood samples were collected from 63 infants born with neural tube defects and from 67 infants born with oro-facial clefts. Blood samples from 130 normal age and sex matched infants collected from nurseries of pediatric departments of same hospitals acted as controls.

2-3 ml blood was collected by venipuncture from each individual in a test tube containing EDTA with which it was mixed well gently. The blood samples were centrifuged at 1,000 rpm for 10 minutes and serum was separated and stored at 4°C till typing. The separated sera were subjected to high voltage gel electrophoresis for the study of C₃ phenotypes following Teisberg (1970)

The statistical analysis has been done using Microstate Software Package while for calculating the Odd Ratio, the maximum likelihood package (Reed and Schull, 1968) has been used.

RESULTS AND DISCUSSION

The data on C₃ polymorphism in infants born with neural tube defects and infants born

Table 1: Distribution of C_3 phenotype and allele frequencies in the infants born with neural tube defects and control group

Group		Phenotypes			Allele frequencies		Chi-square (d.f. =2)
		FF	FS	SS	C_3^F	C_3^S	
Infants born with neural tube defect	No.	2 (3.17)	12 (19.05)	49 (77.78)	0.127	0.873	1.25089
Controls	No.	1 (1.59)	5 (7.94)	57 (90.47)	0.055	0.945	3.74146

Percentages are in parentheses

Table 2: Distribution of C_3 phenotype and allele frequencies in the infants born with oro-facial clefts and control group

Group		Phenotypes			Allele Frequencies		Chi-square (d.f. =2)
		FF	FS	SS	C_3^F	C_3^S	
Infants born with oro-facial clefts	No.	2 (2.99)	13 (19.40)	52 (77.61)	0.127	0.873	1.03300
Controls	No.	1 (1.49)	6 (.95)	60 (89.55)	0.597	0.940	2.74418

with oro-facial clefts have been summarized in the tables 1 and 2, respectively. The incidence of the SS phenotype was found to be little higher among the normal infants as compared to infants born with neural tube defects, while that of the FS and FF phenotypes were found to be higher among the infants born with neural tube defects as compared to controls. However, the overall differences were not statistically significant ($\chi^2=7.18$, d.f.=2, $p=0.1481$) (Table 1).

Table 2 shows that the frequencies of the FF and FS phenotype were found to be higher among the infants born with oro-facial clefts as compared to control group. The frequency of the SS phenotype however, was found to be lower among the infants with oro-facial clefts as compared to controls. However, as for the infants with neural tube defects and in infants with oro-facial defects the differences with controls were found to be statistically non significant ($\chi^2=3.484$, d.f. =2, $p=0.1752$) as compared to controls.

The odd ratio has been calculated to seek an association of FS phenotypes and congenital malformation. For this purpose the data on both the malformation were pooled and results are presented in table 3. The odd ratio was

Table 3: Odd ratio among the congenital malformed babies and control subjects

Phenotype	Infants with congenital malformation	Infants without congenital malformation	Total
With FS phenotype	25	11	36
Without FS phenotype	105	119	224
Total	130	130	260

Odd ratio = 2.57

found to be 2.57 which indicated that individuals with FS phenotype had 2.57 times more likelihood to develop these anomalies as compared to the other two phenotypes.

The association of a genetic marker with an abnormality implies a hereditary cause. However, to establish association, if any, between the complement component C_3 and infants born with neural tube defects or oro-facial clefts, further studies using larger sample sizes are required.

ACKNOWLEDGEMENT

Authors are thankful to the Indian Council of Medical Research, New Delhi for funding this study.

REFERENCES

- Agarwal, D.P., Benkmann, H.G., Goedde, H.W., Delbruck, R.D. and Rougemont, A.: Levels of serum B₂C/B₂A-globulin (3) and its polymorphism in leprosy patients and healthy controls from Ethiopia and Mali. *Humangenetik*, 21: 35 (1974).
- Bronnestam, R.: Studies of the C3 polymorphism (relationship between phenotypes and quantitative immunochemical measurements). *Hum. Hered.*, 23: 128 (1977).
- Powell, E.D.V. and Field, R.A.: Studies on salicylates and complement in diabetes. *Diabetes*, 5: 730 (1960).
- Read, T.E. and Schull, W.J.: A general maximum likelihood estimation program. *Am. J. Hum. Genet.*, 20: 579-580 (1968).
- Ropartz, C., Rivat, L., Locusse, P., Debeauy, P. and Seieinbunch, M.: Un nouveau Polymorphisme sérique humain défini par L. utilisation de globules rouges tannés et revêtus de bet I. *Proc. 10th Inter. Soc. Blood Transf., Stockholm* pp. 383-384 (1965).
- Schur, P.H. and Austin, K.T.: C3 polymorphism in North India. *Acta Anthrop.*, 8: 237-243 (1968).
- Shahai, S., Srivastava, N., Goel, B.K. and Srivastava L.M.: Distribution of (C3) phenotypes in North India: A pilot study. *Humangenetik*, 43: 97-101 (1974).
- Teisberg, P.: High voltage agarose gel electrophoresis in the study of C3 polymorphism. *Vox Sang.*, 19: 47-56 (1970).