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PRINT: ISSN 0975-1270 ONLINE: ISSN 2456-6306 DOI: 10.31901/24566306.2010/02.02.05

A Case - Control Study on Risk Factors of Mental Retardation from an Urban Area of North Coastal Andhra Pradesh

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KEYWORDS Genetic Demography. Blood Groups. Mental Retardation. North Coastal Andhra Pradesh. South India

ABSTRACT A state of mental retardation may be produced by various endogenous and exogenous influences acting independently or in concern with each other. The present article attempts to describe the results of the genetic demography and blood group markers carried out in patients of mentally retarded school children of Visakhapatnam city of North Coastal Andhra Pradesh. An attempt was made to compare with those of controls. Socio – demographic variables, consumption of drugs, gestation period, nature of delivery, prenatal and postnatal histories and Rh incompatibility plays an important role in birth of a children with low IQ. Our study concludes place, menarcheal ages of mothers, paternal age, paternal smoking, gestational period, nature of delivery shows the risk of mental retardation in offsprings is significantly high.

INTRODUCTION

Mental retardation (MR) is a genetic disorder manifested in significantly below average overall intellectual functioning and deficits in adaptive behavior. Mental retardation is a particular state of functioning that begins in childhood and is characterized by decreased intelligence and adaptive skills and also is the most common developmental disorder (Bregman 1991). Mental retardation in young children is often missed by clinicians. The condition is present in 2 to 3 percent of the population, either as an isolated finding or as part of a syndrome or broader disorder (Daily et al. 2000).

Approximately 3% of the population has an intelligence quotient (IQ) of less than 70, among whom a cause for the mental retardation can be established in less than half of all cases (Flint et al. 1995). The prevalence of severe mental retardation is about 3 per 1.000 population and 30 per 1.000 for mild mental retardation (Harper 1993).

Causes of mental retardation are numerous and include genetic and environmental factors. In at least 30 to 50 percent of cases, physicians are unable to determine etiology despite thorough evaluation (Baird and Sadovnick 1985). In about one-third of all cases, the cause of mental retardation is not known. The remaining two-thirds of cases are thought to be caused by one of four factors: heredity, prenatal problems, childhood illness, and environmental factors. About 5 percent of mental retardation cases are caused by genetic factors. A number of environmental, genetic or multiple factors can cause mental retardation. It is also believed that behavioral or societal factors such as poverty, malnutrition, maternal drug and alcohol use, as well as severe stimulus deprivation can contribute to MR (McLaren and Bryson 1987). Unfortunately, in approximately 30 to 50 percent of cases, the etiology is not identified even after thorough diagnostic evaluation (Schaefer and Bodensteiner 1992; Cury et al. 1997). Some persons have a congenital malformation of the brain; others had damage to the brain at a critical period in pre- or postnatal development. Acquired causes of retardation include near drowning, traumatic brain injury and central nervous system malignancy. The most common cause of MR in industrialized nations is fetal alcohol syndrome with an incidence rate of 1 in 100 births. The second leading known cause of MR is Down syndrome, or trisomy 21, with an incidence rate of 1 in 800-1.000 births (Campbell et al. 2004). Malnutrition is a common cause of reduced intelligence in parts of the world affected by famine, such as Ethiopia (Durkin et al. 2000; Wines 2006).

Diagnosis is highly dependent on a

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comprehensive personal and family medical history, a complete physical examination and a careful developmental assessment of the child. These will guide appropriate evaluations and referrals to provide genetic counseling, resources for the family and early intervention programs for the child (Rutter 2006).

Blood groups have become striking aspect in the field of human biology. They had become very important genetic markers in the field of genetics from beginning of the century. ABO blood groups show inheritance (Vondungerne and Hirzfeld 1910). It has been regularly observed that all blood groups known till today follow a certain pattern of inheritance. Indeed blood groups have been most useful tool in human genetics and a complex genetical phenomenon is best understood with the help of blood groups.

To find out the socio-demographic effects on mental retardation and to determine is there any association between red cell antigens and mental retardation.

METHODOLOGY

The patient of mental retardation for the present study is collected by the investigation in Lebenshilfe School, area of Visakhapatnam district, from March 2008 to March 2009. The present study includes 100 already diagnosed patients of mental retardation (study group) were picked and equal number of healthy normal individuals (control group) with the same age and sex in the same geographical region. The epidemiological and demographic data was collected from the study and control groups with the help of pre designed questionnaire by following field survey.

The data like gender distribution, age, area, religion and caste, food habits, menarcheal age of mother, parental ages, parental marriage type, gestation period, nature of delivery, consumption of drugs during pregnancy, birth order, maternal reproductive history, prenatal and post natal history, intelligent quotient, was collected both from the patients and controls. The blood samples were collected for the ABO and Rh blood typing. The gene frequencies were calculated and goodness of fit between the observed and expected phenotype frequencies are tested according to Taylor and Prior (1938).

RESULTS AND DISCUSSION

The intelligence quotient (IQ) of patients of mental retardation was observed and it is found that most of the cases were under severe mental retardation. Table 1 represents different categories of socio – demographic variables in study and control groups. It is observed from the table, more number of cases were observed under the age group 10-25 years in both study and control groups, more number of individuals were observed in urban area in both study and control groups (study group: 81% and control group: 67%). Another variable menarcheal ages of mothers of study and control groups, it is clear from that table more number of mothers are observed under the age group of 12-14 years (study group 47% and control group 63%). Age at the time of children delivery i.e. maternal ages in study and control groups, it is showing that more number of individuals (13 cases) are observed in the age group above 30 years of maternal age when compared with controls (4 cases) as it may be assumed that the advanced maternal age is one of the influencing factor of mental retardation. Where as in paternal age in study and control groups i.e. age at the time of children birth, it is indicating that, more number of individuals (16 cases) are observed above 35 years of paternal age when compared with controls (3 cases). Zhong (1992) reported effects of parent's age, birth order and mental retardation of unknown etiology. The results found that mental retardation of unknown etiology is related to the age of parents and birth order. The paternal age is the main factor while the maternal age in not a significant effect and birth order also in not a significant effect after readjusting the other factors. Compared to paternal age group of under 25. There are significant increase of relative risks of age group 30-34 and 45 above, about 1.8 and 2.7 fold increase in univariate analysis and 1.9 and 3.3 fold increase in controlling the maternal age and birth order, a chi-square test for trend of distribution of paternal age also indicates a significant dose response relationship between increasing risk with age. The significance of result and methods of analysis were discussed. Consanguineous marriage is one of the causes for mental retardation. Parental marriage type in study and control groups, it is observed from the table the consanguinity is very high (37%) in patients of mental retardation when compared to

Table 1: Distribution of cases and controls by different categories of socio-demographic variables

Variable	*Categories*	*Cases (%)*	*Controls (%)*	*Chi - Square*	*P value*
Age group of	10 – 25 years	52	63		
study and controls	25 – 40 years	48	37	1.804	0.179
Place	Rural	19	33		
	Urban	81	67	40.436	0
Menarcheal ages	10 – 11 years	21	27		
of mothers	12 – 14 years	47	63	94.069	0
	15 – 16 years	32	10		
Maternal ages of	16 – 20 years	7	7		
mothers of study and	21 – 25 years	33	41		
control group	26 – 30 years	47	48	248.848	0.207
	31 – 35 years	8	3		
	> 35 Years	5	1		
	< 20 years	6	3		
Paternal ages of	21 – 25 years	18	28		
fathers of study and	26 – 30 years	33	37		
control group	31 – 35 years	27	29	217.847	0
	36 – 40 years	11	2		
	> 41 years	5	1		
Parental marriage type	Consanguineous	37	18		
	Afinal	63	82	1.591	0.207
	Type of	UN 18.00	UN 4.00		
	Consanguinity	MBD 7.00	MBD 7.00	6.28	0.712
		FSD 12.00	FSD 7.00		
Maternal Reproductive	Abortions	4	1		
History	Still births	2	1		
	without any abortions and still births	94	98	0.13	0.998
Birth order in study	I	42	50		
and Control Group	II	42	37		
	III	15	12	9.382	0.403
	IV	1	1		

controls (18%). Socio-demographic variables such as Age Groups (χ^2 = 1.804; p = 0.179), Maternal age at the time of patient or control delivery (χ^2 = 248.848; p = .207), Parents marriage type (χ^2 = 1.591 ; p= .207), Type of consanguinity (χ^2 = 6.280 ; p = .712), Reproductive history of mother (χ^2 = .130; p = 0.998), Birth orders in study and control group (χ^2 = 9.382; p = .403) shows not significant in our study. Place (χ^2 = 40.436; p = .0001), Paternal age at the time of children delivery (χ^2 = 217.847; p = 0.0001), menarcheal ages of mothers of children (χ^2 = 94.069; p = 0.0001), variables shows high significant in the risk of mental retardation. Madhavan and Narayan (1991) reported consanguinity among parents as a cause of mental retardation in their children is debatable. If the parents are consanguineously married, the risk of mental retardation in the offspring is significantly high (χ^2=11.52; p <0.001). Among the consanguineously married families, the blood relationship of uncle-niece seems to have the highest risk of affecting the offsprings. Morton (1978) reported the risk for mental retardation in matings of normal parent's increases from 0.012 with random mating to 0.062 for first-cousin parentage but that dominance deviations are a negligible cause of family resemblance of IQ. Variable maternal reproductive history of study and control groups, it is observed from the table, more number of abortions and still births (6 cases) are in study group when compared with control group (2 cases). It may be assumed that these still births and abortions are due to consanguineous marriages or RhD incompatibility. There is a relationship between birth order and mental retardation in Zhong (2000) studies but in the present study birth order follows nearly the same trend in both study and control groups.

Table 2 explains frequency of drugs consumption during gestation period among study and control groups. It is inferred from the table, more number of alcoholics and smokers are observed in study group (44 cases) when compared with the control group (33 cases). Users of *guthka* and *khaini* are observed in less frequency (1 case in each) in study group. Whereas they are completely absent in control group. In this table paternal alcoholics (χ^2=2.51;

p <0.113) shows the risk of mental retardation in offsprings is significantly high. Paternal smoking (χ^2=0.250; p <0.617), user of maternal smoking (χ^2=1.01; p <0.316), user of paternal *guthaka* (χ^2=1.01; p <0.316), users of paternal *khainis* (χ^2=1.01; p <0.316), users of maternal *khainis* (χ^2=1.01; p <0.316) shows non-significant result in our study. According to Roeleveld et al. (1992), paternal smoking and maternal consumption of alcohol are related to higher incidence of mental retardation in offspring. Exposure to poisons like lead or mercury may also affect mental ability (Aicardi 1998; Daily et al. 2000).

Table 3 represents gestation period and nature of delivery in study and control groups. It is clear from the table all controls have full term babies when compared to study group. The delivery is very complicated in the mothers of the study group, even though they are in normal condition. More number of individuals is observed in full term (94 cases) and only 6 cases of premature births occur in study group whereas in controls all cases are full term births. Gestational period (χ^2=6.19; p <0.013), nature of delivery (χ^2=21.6; p <0.0001) shows the risk of mental retardation in offsprings is significantly high. Complications of prematurity, especially in extremely low-birth-weight infants, or postnatal exposure to lead can also cause mental retardation (Piecuch et al. 1997).

Table 4 describes the distribution of prenatal and postnatal histories in patients of mental retardation. It is clear from the table 25 cases (25%) are having prenatal history and 92 cases (92%) are having post natal history. Mental disability can result when the fetus does not develop inside the mother properly. Moreover, prenatal causes include congenital infections such as cytomegalovirus, toxoplasmosis, herpes, syphilis, rubella and human immunodeficiency virus; prolonged maternal fever in the first trimester; exposure to anticonvulsants or alcohol; and untreated maternal phenylketonuria (PKU) (Stromme and Hagberg 2007). Diseases like whooping cough, measles, or meningitis can cause mental disability if medical care is delayed or inadequate. Exposure to poisons like lead or mercury may also affect mental ability (Aicardi 1998; Daily et al. 2000). Perinatal causes involve late pregnancy (compli-

Table 2: Frequency of drugs consumption during gestation period among study and control groups

Nature of drug addiction	*Drug addiction during birth of baby (Paternal)*				*Drug addiction during birth of baby (maternal)*			
	Study group %	*Control group %*	χ^2	*p value*	*Study group %*	*Control group %*	χ^2	*p value*
Alcohol	19.00	11.00	2.51	0.113	-	-	-	-
Smoking	25.00	22.00	0.250	0.617	1.00	-	1.01	0.316
Guthka	1.00	-	1.01	0.316	-	-	-	-
Khaini	1.00	-	1.01	0.316	1.00	-	1.01	0.316

Table 3: Gestation period and nature of delivery in study and control groups

Variable	*Categories*	*Cases (%)*	*Controls (%)*	χ^2	*p value*
Gestational period	Full term	94.00	100.00	6.19	0.013
	Premature	6.00	-		
Nature of Delivery	Normal	86.00	71.00	21.6	0.0001
	Forceps	9.00	3.00		
	Caesarean	4.00	26.00		
	Kept in incubator	1.00	-		

Table 4: Distribution of prenatal and postnatal histories in mentally retarded cases

Prenatal	*Number*	*Percent*	*Postnatal*	*Number*	*Percent*
Consumption of Drugs for aborting fetus	4	4.00	Congenital jaundice	13	13.00
Consumption of Drugs for fever and jaundice	2	2.00	Congenital smallpox/chicken pox	6	6.00
Did not have monthly Cheque up	8	8.00	Jaundice	7	7.00
Accidents	4	4.00	Epilepsy	23	23.00
Stress and mental strain	7	7.00	Delayed birth cry	31	31.00
			Birth cry absent	12	12.00
Total	25	25.00		92	92.00

Table 5: Phenotype and allete frequencies of blood groups among patient and control groups

System	*Phenotype*	*Patient group*		*Control group*	
		Observed	*Expected*	*Observed*	*Expected*
ABO	A	20	43.40	21	42.78
	B	30	20.40	29	21.55
	O	42	30.60	41	29.82
	AB	8	5.60	9	5.85
	Total	100	100.00	100	100.00
		χ^2 = 1.0173 (0.30>P>0.20)		χ^2 = 1.9938 (0.20>P>0.10)	
Rh	D	94	94.00	96	96.00
	d	6	6.00	4	4.00
	Total	100	100.00	100	100.00
	Allele	*Patient group*		*Control group*	
ABO	*A*	0.1399		0.148	
	B	0.2013		0.198	
	O	0.6588		0.654	
	Total	1.0000		1.000	
Rh	*D*	0.7551		0.800	
	d	0.2449		0.200	
	Total	1.0000		1.000	

cations of pregnancy, diseases in mother such us heart and kidney disease and diabetes and placental dysfunction), during delivery (labour) (severe prematurity, very low birth weight, birth asphyxia, difficult and/or complicated delivery and birth trauma), neonatal (first 4 weeks of life) (septicaemia, severe jaundice, hypoglycemia) (Kolevzon et al. 2007). Postnatal problems include infancy and childhood. It is involved brain infections such as tuberculosis, Japanese encephalitis, and bacterial meningitis. As well as head injury, chronic lead exposure, severe and prolonged malnutrition and gross under stimulation (Leonard and Wen 2002; Zoghbi 2003).

In the absence of curative therapy, and with treatment difficult and only partially successful, prevention plays a particularly important role in mental retardation. Research conducted during the past 40 years has identified new causes of mental retardation, new means of early diagnosis, and new ways of prevention. Prenatal diagnosis, newborn screening, dietary supplementation or restriction, hormone replacement, vaccination, and immunotherapy are just some of the techniques that have been applied to prevent mental retardation. Together, these interventions have slightly reduced the overall prevalence of mental retardation, and in some instances have nearly eliminated specific causes. Much remains to be done, including developing better means of early intervention for socio cultural mental retardation and convincing society of the value of investment in such approaches. In addition to these approaches, the research frontiers today are neurobiology, earlier prenatal diagnosis, fetal therapy, gene therapy, and reducing premature birth. The potential of these investigations makes the frontier of prevention research in mental retardation.

Table 5 showing the distribution of ABO blood groups among study and control groups. The *O* allete records the highest frequency in both the groups (study group: 0.6588 and control group: 0.6540) followed by *B* and *A* alleles . The chi-square test for heterogeneity was found to be non-significant (χ^2 = 0.1120 d.f. =3; 0.99 < P) with respect to ABO system.

In Rh (D) system Rh negative phenotypes are in lowest frequency among both groups (study group: 6% and control group: 4% ;). Considering gene frequencies the *D* gene record the highest frequency in both groups (study group: 0.7551 and control group: 0.8000). The inter group chi-square test shows non significant differences (χ^2 = 0.4210 d.f. =2; 0.70>p>0.50) with respect to Rh system.

CONCLUSION

It may be concluded that the most of the cases are under severe mental retardation. More number of individuals is observed above 30 years

of maternal age. Consanguinity is very high in mental retardation patients when compare with controls. More number of alcoholics and smokers were observed in study group when compared with control group. Paternal smoking and maternal consumption of alcohol are related to higher incidence of mental retardation in offspring. Chi–square tests for place, menarchial ages of mothers, paternal age, paternal smoking, and gestational period nature of delivery shows the risk of mental retardation in offsprings is significantly high. Recent studies have implicated the habit of smoking in prenatal condition increasing the risk of mental retardation. Use of alcohol or drugs by the pregnant mother can cause mental retardation. More number of abortions and still births are observed in study group it may be due to consanguineous marriages or Rh incompatibility. Mentally retarded cases are having pre and post natal histories.

NOTE

Based on the intelligence levels mental retardation classified into four types. 1) Mild mental retardation (IQ scores in-between 50 – 70). 2) Moderate Mental retardation (I Q scores in-between 40 – 54). 3) Severe Mental retardation (IQ scores in-between 25 – 39). 4) Profound Mental retardation (IQ scores in-between < 25).

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