Available online at www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2014; 6(2): 186-188

ISSN- 0975 1556

Research Article

Paternal Age Combined with Maternal Age Influences the Incidence of Down Syndrome

*Gargi Podder, Jayshree Banerjee, Madhusnata

Department of Genetics, Ramakrishna Mission Seva Pratishthan,Vivekananda Institute of Medical Sciences, 99 Sarat Bose Road, Kolkata-700026

Available online: 1st April 2014

ABSTRACT

Context: Genetic abnormalities, such as Down syndrome possess greater risk for Children born to older parents.

Aims: The influence of maternal age on Down syndrome is well established, but little is known about the genetic consequences of advanced paternal age.

Methods and Material: This study group included both Down syndrome patients and age, sex matched healthy controls.

Results: In this later maternal age group, the paternal contribution to Down syndrome was more than 50%. A paternal age effect on Down syndrome was seen in association with maternal age of 35 years and above, and it was most pronounced when the maternal age was of 40 years and above.

Conclusions: Advanced paternal age combined with maternal age influences the incidence of Down syndrome. This effect may represent a paradigm for other genetic abnormalities in children of older fathers.

Keywords: Down syndrome, Trisomy 21, Paternal age, Maternal age, Fertility.

INTRODUCTION

Down syndrome or Down's syndrome (DS) is the genetic chromosomal disorder caused by the presence of all or part of an extra 21st chromosome. This disorder is associated with major and minor difficulties in structure. Often Down syndrome is associated with some impairment of cognitive ability. The defects vary in severity, from mild to serious developmental disabilities. Trisomy 21 or Down syndrome is a common congenital abnormality affecting 1/800 to 1,000 newborns (1). Multiple investigations have been done to identify possible risk factors, of which the most common has been parental age. Older maternal age factor may play a vital role for birth of Down syndrome was described as early as 1933 (2). About 2% of recognized pregnancies of women under the age of 25 years are trisomic, this increases to 10% for women of 36 years and to 33% by the age of 42 years (3). Several studies have reported a positive association between parity and Down syndrome, although several other groups did not find an association. The interpretation of many of these studies has been hindered by certain methodological issues. Because parity is closely correlated with maternal age, and because several early studies examining the relation between parity and Down syndrome used broad (5-year) categories in controlling for maternal age. It has been suggested, there is some evidence that women of higher parity are less likely to undergo prenatal screening for Down syndrome by amniocentesis or chorionic villus sampling and therefore are less likely to choose to terminate a Down syndrome pregnancy than women of lower parity. This would result in an excess of Down syndrome live births among multiparous women, even in the absence of a true biologic association with parity. The influence of maternal age has been observed in all population studies in respect to race, geography or socioeconomic factors. Unlike maternal age, the role of paternal age on Down syndrome has not been clearly defined. Some studies suggest no influence (4,5,6) while other, smaller studies suggest a positive paternal effect (7,8). The increasing number of older couples having children has resulted in a renewed interest in determining the genetic risk to children born to these couples. We defined the parental age effect on Down syndrome and clarified whether a paternal age effect exists as a risk factor.

SUBJECTS AND METHODS

A study was conducted on all cases with the diagnosis of Down syndrome who were referred to the cytogenetics department at Ramakrishna Mission Seva Prathisthan, Kolkata, India, from April 2010 to May 2012. A total of 85 patients were included. These 85 cases were referred from different district Hospitals, Health Centers, Clinics of West Bengal, different state of eastern India and Bangladesh and also Outdoor and Indoor Department of Ramakrishna Mission Seva Pratishthan. In addition, 30 controls were recruited age, sex matched for the delivery of an unaffected child in the same year and in the same Health Institute or region.

A detailed structured questionnaire was designed which covers general information on socio-demographic, family history of mother and father of DS child, age of those parents, health and illnesses, history of women pregnancy

gargi.podder86@gmail.com

Table 1. Distribution of mothers and fathers according to their age at the time of birth of the Down syndrome child and healthy control

Age group (years)	Down syndrome child				Healthy control child			
	No. of mother	% present	No. of father	% present	No. of mother	% present	No. of father	% present
13-20	10	11.74	0	0.00	4	13.33	2	6.67
21-25	20	23.53	6	7.06	8	26.67	4	13.33
26-30	15	17.65	19	22.35	9	30.00	11	36.67
31-35	22	25.88	23	27.05	5	16.67	10	33.33
36-40	12	14.12	13	15.29	2	6.67	2	6.67
>40	6	7.06	24	28.23	2	6.67	1	3.33

together with menstrual history, general medical history etc.

The study protocol was reviewed and approved by the Ethical Committee of Ramakrishna Mission Seva Prathisthan, Kolkata, India.

RESULTS AND DISCUSSION

Approximately 4.0% of recognised pregnancies are trisomic and about 0.5% of pregnancies are trisomy 21 and 22 (9). The study of DS in 118,265 in consecutive birth defects found that 5.3% of DS mothers had two spontaneous abortions compared to 3.7% controls (7). Recognisable abnormal foetus in younger mothers' uterus is more as compared to older mothers' (7), as a result the numbers of abortions in younger mothers are higher when compared to older women. Some studies suggest that first child infants may be a high risk of DS to older women than a later born child to women of the same age (10). This is in contrast to (7) as he found that the first born infants were at a lower risk of DS than later born infants.In 1997, Schimmel et al.(11) observed, when low birth risk present in pregnant woman of low parity may be resulted from early diagnosis of DS or any other genetic abnormal fetus prenatally somewhere, then it spontaneously abort or terminated their pregnancy.

In the current study, a comparison was made among the different age groups of the mothers and fathers of patients and healthy control (Table no. 1).In age group of 21to 25 years and 26to 30 years percentage of healthy control's mothers is greater than DS patient's mother. But in other hand, higher age group like 36-40 years and >40years percentage of DS patient's mother is high. In age group of 21to 25 years and 26 to 30 years percentage of healthy control's fathers is greater than DS patient's father. But in other hand, higher age group like 36-40 years and >40years percentage of DS patient's father is high. This indicates that DS families are with more parity as they start conception at a younger age as compared to controls family and the DS child is mostly not the first infant, in contrast to Alfi's (10) observation.

This novel finding of a combination of maternal and paternal age influencing Down syndrome can be explained in 2 ways. The first explanation is that there are contributions of sperm of father to the trisomy 21.Sartorelli et al studied a small population of men and reported a higher frequency of sperm chromosome abnormalities in older men (12). While it has been estimated that the extra chromosome is of paternal origin 5% to 20% of the time (13), it is possible that older men may contribute the extra chromosome more frequently. To our knowledge studies regarding the sperm contribution related to paternal age are not currently available. The second explanation is that the mechanism controlling spontaneous abortion changes and becomes less efficient with increasing maternal age. That is, with increasing age the mechanisms in the mother that identify and spontaneously abort a chromosomally abnormal fetus may falter. It has been demonstrated that the relative survival of abnormal fetuses compared with normal fetuses increases with increasing maternal age (8). Our results are most likely explained by a combination of these 2 mechanisms.

The fertility rate is higher in DS families as compared to controls. This can be explained by the higher age of the DS mothers. But another explanation for the increased fertility in DS child could be that they have a higher rate of miscarriages, and as they are prone to have a DS infant also, if it correlated to a high early miscarriage due to chromosomal abnormality. This suggests that there might be an exogenous or endogenous factor which affects the rate of abortions and prevents the loss of fetus in high risk regions in general for both DS families and controls families, as well as mainly or specifically for DS families in a high risk region.

CONCLUSION

Considering that the population of parents is older and higher age of father affect is significant and should be addressed during counseling. Younger couples who preparing for the issue must be aware that advanced age of parents may not only result in increasing problem with fertility for the parents but that children born to old aged parents may be at high risk for different type of genetic abnormalities like Down syndrome. Lastly, the adverse effect of advanced paternal age on Down syndrome may beresponsible for other congenital genetic malformation in children of older parents especially father that must be addressed in future studies.

ACKNOWLEDGEMENT

This study was financially supported by the grants from Vivekananda Institute of Medical Sciences, Kolkata and DST. West Bengal. We are grateful to the Secretary, Ramakrishna Mission Seva Pratisthan, Vivekananda Institute of Medical Sciences, Kolkata for the necessary permission to carry out this study. We are also thankful to Mr. Monoj Bera for technical assistance.

Source(s) of support: Vivekananda Institute of Medical Sciences

REFERENCES

1. Cunningham FG, MacDonald PC, Gant NF, Leveno KJ, Gilstrap CC, Hankins GDV, et al. Williams Obstetrics, 21st ed. New York: McGraw-Hill 2001; 35:944.
2. Penrose LS. The relative effect of paternal age and maternal age in mongolism. J Genet 1993; 27**:**219.
3. Hassold T, Sherman S. Down Syndrome: Genetic recombination and the origin of the extra chromosome 21. Clinical Genetics2000; 57: 95-100.
4. Erickson JD. Down syndrome, paternal age, maternal age and birth order. Ann Hum Genet 1978; 41**:**289.
5. Hook EB, Cross PK, Lamson SH, Regal RR, Baird PA, Uh SH. Paternal age and Down syndrome in British Columbia. Am J Hum Genet1981; 33:123.
6. Hook EB. Issues in analysis of data on paternal age and 47, 21: implications for genetic counseling for Down syndrome. Hum Genet 1987; 77:303.
7. Stene J, Stene E, Stengel-Rutkowski S,Murken JD. Paternal age and Down's syndrome: data from prenatal diagnoses (DFG). Hum Genet 1981; 59(2):119-124.
8. Stene E, Stene J,Stengel-Rutkowski S. A reanalysis of the New York State prenatal diagnosis data on Down's syndrome and paternal age effects. Hum Genet 1987; 77:299.
9. Hassold TJ, Jacobs PA. Trisomy in man. Annu Rev Genet 1984; 18:69-97.
10. Alfi OS, Chang R, et al. Evidence for genetic control of nondisjunction in man. Am J Hum Genet1980; 32(4):477-83.
11. Schimmel MS, Eidelman AI, Zadka P, Kornbluth E, Hammerman C. Increased parity and risk of trisomy 21: review of 37 110 live births [with commentary by R Lilford]. BMJ 1997; 314:720-721.
12. Sartorelli EM, Mazzucatto LF, de Pina-Neto JM. Effect of paternal age on human sperm chromosomes. FertilSteril 2001; 76:1119.
13. Jyothy A, Kumar KS, Mallikarjuna GN, BabuRao V, Uma Devi B, Sujatha M, et al. Parental age and the origin of extra chromosome 21 in Down syndrome. J Hum Genet 2001; 46**:**347.