Original Article

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Correlation of Maternal Age with Prevalence of Chromosomal Anomalies in Patients of Anorectal Malformation

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Abstract

Introduction: Aims: To identify the Anorectal malformations patients in North Indian region and then study the karyotype of these patients to evaluate cytogenetic aberrations and then correlate it with the maternal age. **Subjects and Methods**: Forty eight patients of anorectal malformation were selected from Department of Paediatric Surgery, KGMU, UP, Lucknow. Blood samples were collected and their cytogenetic study was done in the Department of Anatomy, KGMU-U.P, Lucknow. Karyotypes obtained were further analysed. **Results:** Out of 48 children enrolled in the study, karyogram could be obtained for 45 cases (93.75%). Maternal age at the time of birth of the child was <30 years in 91.1% cases. There were only 8.9% women who were >30 years of age at the time of birth of the child. However, proportion of those with anomalies was significantly higher in >30 years age group (75%) as compared to that in <30 years age group (2.4%). **Conclusion:** Although low maternal age was found most commonly, but number of cases with chromosomal anomalies was reported more in >30 years of age, which could be due to increased risk of congenital anomalies and malformations with advanced age.

Keywords: Anorectal malformations (ARM), karyotyping, chromosomal anomalies, trisomy 21, congenital anomalies.

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Introduction

Congenital malformation and congenital birth defects include structural, functional, behavioural and metabolic disorders present at birth defects which are common among all races, cultures and socioeconomic strata. Amongthe various congenital anomalies of hindgut development, ARM is frequently encountered defect seen in paediatric surgery, with an estimated incidence of 1 in 2500 live births.[1] These include series of defects ranging from slight malposition of anus to complete anal atresia, fistulas and other complex anomalies of the hindgut and urogenital Organs.[2] The environmental or genetic risk factors for this multifactorial disorders are still largely unknown. Genetic factors play a very important role in pathogenesis of ARM. Evidence of inherited factors in favour of increased risk of ARM in relative descended from a common ancestor,[3] patients with chromosomal abnormalities having an ARM component, and genetic knock-out animal models reproduce human ARM anomalies are largely reported. Environmentalfactors are also involved in the development of ARM along with genetic factors. Due to changing social dynamics, like late marriage, the reproductive patterns of the society is changing drastically. Thus the incidence of congenital anomalies, trisomy's and syndromes has been increasing day by day in children born to a mother with advanced maternal age.[4]

Subjects and Methods

The present study was conducted in the cytogenetics laboratory of the Department of Anatomy, King George's Medical University Lucknow, UP, in collaboration with the Department of Paediatric Surgery, King George's Medical University Lucknow, UP. Ethical clearance was taken by ethical clearance board of King George's Medical University U.P, Lucknow with vide letter number 88th ECM II B- Thesis/P14. 48 patients (33 males, 15 females) of Anorectal malformation were selected randomly from the Department of Paediatric Surgery, KGMU U.P, Lucknow. A detailed history was taken from parents of the patients. Under complete aseptic conditions, 2-3ml of venous blood was collected in heparin vials from ARM patients. Further cytogenetic processing was done in Department of Anatomy and slides were prepared. Karyotyping was done and the karyotypes obtained were further analysed using CYTOVISION software. 20 metaphases were observed for every case. In case of positive findings, 40 metaphases were observed.

Results

Inthis study, majority of cases were males (n=33; 68.8%). There were 15 (31.2%) females. Sex ratio (M: F) was 2.2.

Culture was successful in 93.75% cases. 45 out of 48 samples could be successfully cultured, remaining 3 samples failed [Table 1]

Table 1: Karyogram obtained/Not obtained (n=48)

SN	Outcome	No.	%
1.	Obtained	45	93.75
2.	Not obtained	3	6.25

Maternal age at the time of birth of child was <30 years in majority (n=41; 91.1%) cases. Only4 (8.9%) women who were >30 years at the time of birth of the child. However, proportion of those with anomalies was significantly higher in >30 years age group (75%) as compared to that in <30 years age group (2.4%) (p=0.001) [Table 2].

Table 2: Correlation of maternal age with prevalence of chromosomal anomalies

SN	Age of mother	Total (n=45)	With anomalies (n=4)*	Without anomalies (n=41)*
1.	≤30 Years	41 (91.1%)	1 (2.4%)	40 (97.6%)
2.	>30 Years	4 (8.9%)	3 (75.0%)	1 (25.0%)

p=0.001 (Fisher exact test); *Percentages have been calculated for row total

The main chromosomal anomaly found to be associated was Trisomy 21 in patients with advanced maternal age. Trisomy 21 was reported in 6.7% (3 cases out of 45 cases). Among those 3 cases, 2 cases were males whereas one was a female. One case (2.2%) of turner syndrome was reported in age less than 30 years [Table 3 & Figure 1]

Table 3: Incidence of Trisomy 21 in karyogram obtained

SN	Outcome	No.	%
1.	Normal karyotypes	41	91.1
2.	trisomy 21	3	6.7

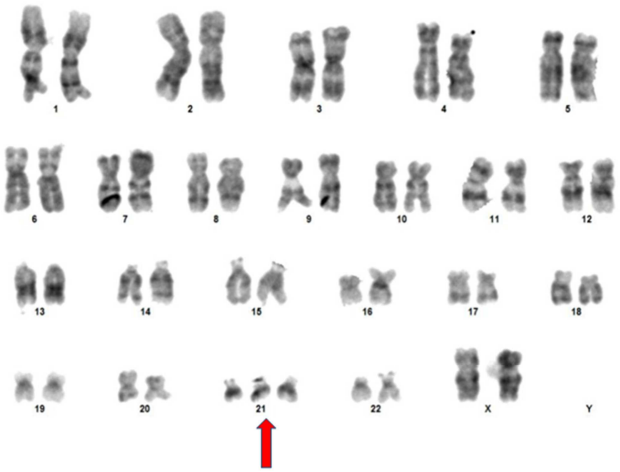

Figure 1: karyogram of trisomy 21 female.

Discussion

Various problems such as chromosomal anomalies, twin pregnancy are found to be associated with advanced maternal age. It is widely recognised that older maternal age is strongly associated with chromosomal birth defects such as trisomy's 13,18, 21.[5] Severalstudies have also observed an association between older maternal age and non-chromosomal birth defects such as neural tube defect, cleft lip or palate etc.[6] According to some studies the risk for non-chromosomal birth defects with older maternal age is negligible compared to the risk for chromosomal birth defects.[7] Anorectal malformations consist of a wide spectrum of diseases, affecting both males and females, and involve the distal anus and rectum as well as the urinary and genital tracts. ARM includes malformations ranging fromminor and easily treated defects, with an excellent functional prognosis, to those that are complex, difficult to manage, are often associated with other anomalies, and have a poor functional prognosis. Anorectal malformations if associated with various chromosomal aberrations resulting in various syndromes could be responsible for poor prognosis, especially in neonatal life. Individualenvironmental or genetic risk factors are still largely unknown in etiopathogenesis of anorectal malformation. In order to maintain urinary and faecal continence, these anomalies require surgical management in neonatal period itself. About 20-80% of patients with ARM have one or multiple associated anomalies. Complex urogenital, cardiac, and other system anomalies had an adverse impact on the survival of such patients.[8,9] Currently available data on relationship between the presence of chromosomal anomalies in ARM patients and maternal age are inconsistent. In particular very little is known on impact of maternal age as a risk factor.

Threone et al. (2013) studied 335 patients of ARM, among which 214 patients (64 %) were diagnosed in the ZAR group and 121(36%) in the Italian group. Of note is the statistical difference between the two groups in the maternal age (p = 0001). Average maternal age in ZAR group and Italian group was, respectively, 28 and 34 years (p = 0.0001).[10] Ciongradi et al. (2016) did retrospective analysis of 146 patients with ARM in which mothers age ranged from 16 to 42 years old, with a mean age of 21.3 ± 2.3 years old.[11] In the present study age of mothers ranged from 19 to 36 years with a mean age of 25.04±4.10 years. Maternal age at the time of birth of the child was <30 years in majority (n=41; 91.1%) cases. There were only 4 (8.9%) women who were >30 years at the time of birth of the child. However, proportion of those with anomalies was significantly higher in >30 (75%) as compared to that in <30 years age group (2.4%) (p=0.001). As observed, in our study low maternal age was found most commonly, but the cases with anomalies were reported more in maternal age >30 years. The findings in our study could be due to the fact that there is increased risk of congenital anomalies and malformations in children born to mothers with advanced age.

Conclusion

Although low maternal age was found most commonly, but number of cases with chromosomal anomalies was reported more in >30 years of age, which could be due to increased risk of congenital anomalies and malformations with advanced age. Thus further more studies need to be carried out to establishclear and significant relationships between maternal age and prevalence of chromosomal anomalies, if any.

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