ORIGINAL ARTICLE

Cytogenetics and Genetic Counseling of Patients in North India

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Abstract

This brief write-up is with reference to our 1-year (May 2003- May 2004) experience at the Department of Molecular Biology and Immunology at Indraprastha Apollo Hospitals, New Delhi. Cytogenetics of 60 patients with amenorrhoea, recurrent abortions, infertility, monosomy X, chromosome mosaics, pseudohermaphoditism and Downs syndrome was carried out. The importance of chromosome studies followed by genetic counseling is stressed in this present paper.

Key Words

Chromosomal disorders, Genetic counseling

Introduction

Recent advances in cytogenetic techniques made a valuable contribution toward the practice of modern medicine. The introduction of the banding techniques into cytogenetics has been regarded as a significant step in the identification of chromosomal anomalies which gave insight to many of the problems of health.

Repetitive spontaneous first trimester miscarriage as well as second and third trimester in utero fetal death are considered as recurrent pregnancy losses. They represent 1% of all pregnancies (1). Chromosomal abnormalities affect at least 7.5% of all conceptions. Most of these abnormalities are spontaneously aborted and the frequency in live births is about 0.6% (2). Three to four percent of all births are associated with a major congenital malformation, mental retardation, or genetic disorder, a rate that doubles by 7-8 years of age, with later-appearing or later-diagnosed genetic disorders (3).

Centers for genetic counseling are important sources of information about the frequencies of chromosomal disorders, with such data allowing a more detailed analysis of these disorders (4). In addition, these centers allow us to determine the types or profiles of individuals who seek genetic counseling (such profiles tend to vary among developed and developing countries), and also to establish the pattern and extent of chromosomal variability in distinct human populations (5).

Although chromosomal disorders are among the most important causes of childhood mortality in India, diagnosis of such disorders has not received much attention. We at the Molecular biology and Immunology Lab at Indraprastha Apollo Hospitals, New Delhi, have made a beginning recently in this direction.

Material and Methods

After taking an informed consent, 60 patients (in the age range of 28-39 years) attending Genetic Services at Molecular biology and Immunology lab at Indraprastha Apollo Hospitals, New Delhi from 2003 to 2004 were included in the present study. Detailed information like: age, duration of work, health history, family history, diet, social habits, medication taken in the last 3 months and reproductive history was collected in a well designed proforma from the patients. Chromosomal analysis was performed on heparinized whole blood samples from these patients using standard protocols (6). The karyotypes were interpreted using the recommendation of International System for Human Cytogenetic Nomenclature (7). A

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minimum of 30 mitotic cells was examined for numerical and structural abnormalities and 5 karyotypes were prepared per patient.

Results

Of the 60 patients, abnormal chromosomes were found in 10 (16.6%) of the cases, with numerical abnormalities; the remaining 50 patients had normal karyotypes. Among the 10 abnormal karyotypes, most were autosomal alterations except for 3, which were sex chromosomal alterations. Among the autosomal chromosomal alterations, 3 children showed trisomy 21 (Down's syndrome). In another 3 patients with missed abortions, the cytogenetics analysis was carried out on products of conception (POCs), which showed monosomy, 9, 14 and trisomy 20. An 8-year-old phenotypically male child with female genitilia on cytogenetic analysis showed 46,XX kayotype. 3 more patients, (18-26year-old females) were mosaics and showed 45,XO karyotype (Turners syndrome). Their phenotype included short stature and primary amenorrhea.

Table 1. Demgraphic Details of Samples

Chromosomal anomalies analyzed	Sex	Age Range (Years/weeks)	No of patients	Type of the sample	Place / Region
Trisomy 21, (47, XY)	Male	1-4 yrs	2	Peripheral Blood	Dist: Dehradun and Kasipur State: Uttranchal
Trisomy 21, (47, XX)	Female	1 yr	1	Peripheral Blood	Dist: Tehrigarwal, State: Uttaranchal
Monsomy 9 (45,XX, Del 9)	Female	38 yrs (5 weeks of pregnancy)	1	Products of conception (POC)	Dist: Paurigarwal State: Uttaranchal
Monsomy 14 (45,XX, Del 14)	Female	36 yrs (3 weeks of pregnancy)	1	Products of conception (POC)	Dist: Shrinagar State: Uttaranchal
Monsomy 20 (45,XY, Del 14)	Male	38 yrs (4 weeks of pregnancy)	1	Products of conception (POC)	Dist:Bageshwar State Uttaranchal
Pseudohermaphrodistism (46, XX)	Phenotypically Male child with female genetilia	8 yrs	1	Products of conception (POC)	Dist: Alamora State: Uttaranchal
Turners syndrome (45, XO)	Female	18- 26 yrs	3	Peripheral Blood	Dist: Raikhet, Nanithal and Kasipur State Uttaranchal
Normal female, 46,XX	Female	1-8 yrs	28	Peripheral Blood	Dist:Faridabad, Gurgav, Hisar, Riwadi, Mahendragad, Rohtak, Bhivani, Jaajer, Sonipat, Panipat, Umbala, Karnal, Sirsa, Kurkshetra, Yamunanagar, Kaithal State Haryana New Delhi
Normal female, 46,XX	Female	23-30 yrs 4-8 weeks of pregnancy	12	Abortus material	Dist: Palampur, Solan State Himachal pradesh District Bulandshar, Rampur, Bareily, Pratapgad, Ghaziabad, Meerut, Muzaffornagar State Uttar Pradesh, New Delhi.
Normal Male 46, XY	Male	4-9 yrs	10	Peripheral blood	Dist: Somasipur, Patna, Madhwani State Bihar Delhi.

Discussion

Chromosomal anomalies are known to be the single most common cause of spontaneous abortion. Historically, 50% of spontaneously expelled abortuses have been thought to be chromosomally abnormal (8). In a live birth, chromosomal imbalance generally produces

some phenotypic effect, most often congenital anomalies and mental retardation (9). In the recent years cytogenetics is gaining ground in the clinical set-up in order to investigate the anomalies.

In the present study cytogenetic analysis was performed along with other investigations and the risks of recurrence of these abnormalities were analyzed. There could be many reasons responsible for such numerical abnormalities and one such was that these patients were in the age group of 36-38 years, which was an indication of advanced maternal age. As the age advances the possibilities of non-disjunction increases due to the result of segregation errors during cell division. After diagnosis of a numerical chromosomal anomaly, couples were counseled about the 1% risk for recurrence of a numerical anomaly. The parents were also counseled for prenatal diagnosis of the fetus in future pregnancies. The patients who were cytogenetically normal were subjected to other investigations to rule out anatomic anomalies, endocrine/hormonal abnormalities, and others. In the present study wherever, there were indications of cytogenetic confirmation such as, Down syndrome, Turners and couples with recurrent abortions genetic counseling was given to them and recurrence risk was also explained. Prenatal diagnosis was indicated whenever there was a chromosomal anomaly in the parent. Only major chromosomal abnormality i.e, sex chromosomal mosaicism, addition and deletion of chromosome was taken as abnormality causing abortions and the couple were counseled accordingly. In the present study the karyotype information provided a foundation for a regional cytogenetic data library designed to the families who required this service especially in case of POCs it gave some direction for further treatment. Further, karyotyping was also useful in the clinical follow-up of some disorders associated with conditions like Down's syndrome. For example Down syndrome is associated with susceptibility to acute leukemia, duodenal stenosis, and Alzheimer's disease (10). From the above results it proves clearly that cytogenetic analysis helps in taking prevention measures at an early stage, to minimize suffering at a later date.

Conclusion

Cytogenetic techniques using Giemsa banding are very important for the correct identification of a variety of syndromes. The information obtained by such techniques provides basis for determining the risks of recurrence and for deciding clinical treatment and genetic counseling. Although somewhat expensive, the accuracy of clinical diagnosis could be improved using fluorescence in situ hybridization and other complementary molecular approaches.

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