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CHROMOSOME ANOMALIES IN SRI LANKA : A CYTOGENETIC PROFILE

by

R. JAYASEKARA

(*Director, Human Genetics Unit, University of Colombo, Sri Lanka*)

ABSTRACT . The spectrum of chromosome anomalies detected in a population referred to the Human Genetics Unit, Faculty of Medicine, Colombo, using lymphocyte culture and Giemsa banding technique, is reported. The availability and usefulness of chromosome analysis and its direct application in the preventive and curative aspects of medicine is stressed.

Down syndrome showed a significantly high incidence, but with an unexpectedly high frequency of trisomy 21 due to non-disjunction in young parents. The possibility of the existence of other genetic or environmental factors stronger than the influence of ageing gametic cells, which might trigger off non-disjunction in young Sri Lankans, is suggested.

INTRODUCTION

Human population cytogenetics was initially a descriptive science which involved surveys of individuals to obtain data on the frequency of chromosome anomalies. Today it includes the assessment of rates of cytogenetic anomalies and their variants, their seggregation and mutation rates and also their phenotypic consequences. Newborn and adult populations, special populations like prenatal, perinatal and even mid-second trimester foetuses, as well as populations exposed to harmful and potentially harmful environmental agents have been studied (1). However, consecutive live born babies provide the most representative and unselected sample of 'normal' individuals (2). This is a record of the spectrum of cytogenetic anomalies detected at the Human Genetics Unit at the Faculty of Medicine in Colombo, during a period of three and a half years.

MATERIALS AND METHODS

All patients referred to the Unit between October 1983 and April 1987 for a possible chromosome anomaly had a sample of intravenous blood taken and a 72 hour lymphocyte culture set up (3). The chromosomes were stained using a plain Giemsa stain and a rapid Trypsin-Giemsa banding method (4). The slides were examined using a Leitz Photomicroscope, and for each patient 10 spreads were analysed. When all these spreads showed the anomaly, 15 more spreads were analysed to confirm it. In the case of a mosaic a total of 100 spreads were analysed. Of the total of 409 referrals made, 76 showed a chromosome anomaly. The anomalies were classified into broad diagnostic categories, and reclassified into cytogenetic subgroups where appropriate. For Down syndrome, additional information like the parental ages at birth of child were noted. Khi square tests were used in the statistical analysis.

RESULTS

Table 1 shows the range and frequency of chromosome anomalies detected at the Unit and the frequency of the specific cytogenetic types within each category. A simple khi square test on the three main categories Down syndrome, Turner syndrome and Klinefelter syndrome revealed that there was a highly significant excess of Down syndrome (76.3%) in this sample.

TABLE 1. Frequency of chromosome anomalies

Chromosome anomaly	No.	Percent (%)
*Down syndrome		
Trisomy 21	54	71.0
Translocation 13/21	1	1.3
Translocation 14/21	1	1.3
Trisomy mosaics	2	2.6
Sub Total	58	76.3
*Turner syndrome		
45XO	9	11.9
Mosaic (45XO/46XX)	2	2.6
Sub total	11	14.5
*Klinefelter syndrome		
47XXY	4	5.3
Mosaic (47XXY/46XY)	1	1.3
Sub total	5	6.6
Trisomy 13 (Patau syndrome)	1	1.3
Trisomy 18 (Edward syndrome)	1	1.3
Total	76	100.0

khi square 31.7 ; d.f. 2 ; $p < 0.001$

* Groups used for analysis

Table 2 shows the distribution of 54 cases of trisomy 21 Down syndrome by maternal and paternal ages at birth of the child. Trisomy 21 Down syndrome made up 93% of the total detections of the condition and were referred to the Unit for genetic counselling as their maternal and paternal ages were less than 35 years. Statistical analysis of the maternal age distribution and of the paternal age distribution did not show any particular age group of young parents to be associated with trisomy 21.

TABLE 2. Distribution of Trisomy 21 Down syndrome patients born to young parents (< 35 years) by maternal and paternal ages at birth

Age group years	Maternal n	Paternal n
20—24	18	17
25—29	19	18
30—34	17	19

(khi square — 4.5 ; d.f. 2 ; p > 0.1) (khi spuare — 4.5; d.f. 2 ; p. > 0.1)

DISCUSSION

The magnitude of human chromosome anomalies is amply reflected in studies of their incidence in large surveys of live newborns, stillbirths, spontaneous abortions and mid-trimester amniocentesis data (1). They provided evidence of numerical errors involving whole chromosomes or a widely divergent variety of structural rearrangements. About 0.56 per cent of live newborns have a chromosome anomaly (2,5) and 0.2 per cent have balanced and unbalanced structural rearrangements as reported in six surveys (2).

Down syndrome is the most frequent autosomal abnormality in liveborn infants and the commonest genetic cause of severe mental retardation, and accounts for one-third to one-fourth of all such cases in the developed countries (6). In the spectrum of cytogenetic variation seen in Down syndrome, trisomy 21 which is due to meiotic non-disjunction in gametogenesis or mitotic non-disjunction in the early zygote, has been shown to be significantly associated with increasing maternal age (7), and with increasing paternal age (8,9,10).

In this study a significantly high proportion (76.3%) of the chromosome anomalies detected were Down syndrome, Of the 58 cases, all of them born to young parents (mean parental age less than 35 years at birth of child), 54 (93%) were trisomy 21 (see Table 1). This excess of trisomy 21 over translocation in young parents was unexpected as the trisomy 21 category is well known to be associated with late parental age (> 35 years) (11). Even within this younger group, no particular paternal or maternal age group was associated with trisomy 21. This high percentage of trisomy 21 in the study is probably due to non-disjunction in young Sri Lankan parents. Further studies are needed to determine the role of factors other than age in the aetiology of Down syndrome.

Determining the cytogenetic type of Down syndrome is useful for the diagnosis of the minimally affected mosaic and in the calculation of recurrence risks for future pregnancies. The recurrence risks for future pregnancies will vary from a low 1% following the birth of a trisomy 21 baby, through 5—15% for a D/G or 21/22 balanced translocation carrier parent, to 100% in the case of a 21/21 balanced translocation carrier parent. In this study both cases of translocation Down syndrome detected were not transmitted by a carrier parent, but were new mutations in the developing zygote, a situation which carries a very low risk of recurrence.

Even though Turner syndrome was shown to be due to a 45×0 chromosome complement in 1959 (12), the diagnosis of this disorder in Sri Lanka was dependant till recently on buccal smear studies. Lymphocyte cultures and karyotyping can now confirm suspicions in a typical case, or help diagnose the condition even in a mildly affected mosaic. Despite the wide variety of cytogenetic types reported worldwide, so far only the 45×0 and the 45X0/46XX types have been detected in Sri Lankan females. It may be that the Sri Lankan female genome appears to be more resistant to certain mutations, or that other reported cytogenetic types of Turner syndrome cause minimal disability or resulted in intrauterine death. The early detection of this clinical entity could assist in the management of the condition, as anabolic steroids, low doses of oestrogens and/or human growth hormone, have been reported to be capable of improving the growth of patients with this condition (13,14,15,16). The detection of a mosaic with the presence of a 46XY cell line would be an indication for a laparotomy with a view to detecting tumoural degeneration of the gonads (17).

The Klinefelter syndrome is another disorder which can now be diagnosed accurately using lymphocyte cultures. Early diagnosis could lead to the institution of hormone therapy which has been shown to benefit patients (11).

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