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CHROMOSOMAL ABNORMALITY IN 500 REFERRED CASES IN BAHRAIN

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Objective: Study the incidence and pattern of major chromosomal abnormalities in a Bahraini population suspected of having chromosomal abnormality on the basis of physical and/or development clinical features.

Design: Cytogenetic studies were performed on five hundred patients.

Setting: Genetic Clinic, Salmaniya Medical Centre, Bahrain during the period from 1984-1991.

Main Outcome: 134 (27 %) patients had abnormal karyotype, 97 (19 %) patients had numerical abnormalities and 37 (7 %) had structural chromosomal abnormalities. The majority of patients with numerical abnormalities (66 %) were Down Syndrome or trisomy 21, 4 % were having trisomy 13, and 4 % were having trisomy 18. Cases of X chromosome abnormalities were found in 13 % of the abnormal causes, while 12 % were having abnormality of other chromosomes.

Conclusion: This study demonstrates the spectrum of chromosomal abnormality in Bahrain but not the prevalence of these abnormalities in the country as it was only performed on a small number of patients. Bahrain Med Bull 1996:18(1):

It is well known that too many or too few copies of genes can upset the normal process of development. These abnormalities result from gross imbalances in the number and action of genes. A general rule is that the greater the imbalance, the more severe is the abnormality. Some imbalance is sufficiently small to have almost no effect on development, while other larger ones are lethal and may lead to death of embryo or child at an early age[1-5].

Singh in 1977 investigated 451 referred cases suspected in South Carolina, USA of having chromosomal abnormalities due to physical and/or developmental abnormalities, and he found changes in 28.8 %. In a comparable study, Verma in 1980 investigated 357 referred cases from New York, USA and found chromosomal abnormalities in 27.2 % of these cases, while Shah in Ahmedbad in India studied 205 referred cases and reported 39.58 % (Table 1)[7-8].

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Table 1
Abnormal karyotypes in referred cases

	Summary of karyotypes		
	Year	No of cases	% of chromosomal abnormalities
Sing et al	1977	451	28.8
Shah et al	1990	144	39.58
Verma et al	1980	357	27.2
Present study	1992	500	27.0

The present study describes the frequency and the incidence of major chromosomal abnormalities in a Bahraini population suspected of having chromosomal abnormality on the basis of physical and/or developmental clinical features.

METHODS

Patients were referred to the Genetic Clinic from the Paediatric Clinic, Gynaecology Clinic and Medical Clinic, Salmaniya Medical Centre, Bahrain, during the period between 1984 - 1991. The majority of cases were suspected of having chromosomal abnormalities because of abnormal clinical features such as mental retardation, dysmorphic feature or multiple congenital abnormalities, ambiguous genitalia etc. In case of gynaecology patients, couples with foetal loss, delayed puberty and primary or secondary amenorrhoea were the basis of referrals. Blood samples were collected in heparinised bottles and sent to a JSPS Cytogenetic Laboratory, London, United Kingdom where conventional karyotyping and fragile X studies were performed as appropriate.

RESULT

Of the 500 patients investigated 134 (27 %) patients showed abnormal karyotypes and 366 (73 %) showed normal findings. Of the abnormal karyotypes there were 97 patients with numerical abnormalities and 37 patients with structural abnormalities.

Some patients had combined abnormalities of more than one chromosome. The incidence of individual chromosome abnormalities was as follows: abnormalities of chromosome 21 were seen in 86 patients, of chromosome 13 in 7 patients, of chromosome 18 in 5 patients, of sex chromosome in 19 patients, and of other chromosomes in 16 patients. The type of chromosome aberration in Down syndrome patients was as follows: 86 (97 %) patients with trisomies and 3 (3 %) with translocation.

Table 2 shows the rare structural abnormality.

Table 2
Patients with rare abnormal karyotype

No	Name	Age	Sex	Karyotype	Phenotype
1	AAA	3	F	46,XX,+21 47,XX-2122+r22	Down's syndrome features
2	AS	NB	M	47,X,-4 T(4:13) (q35:q22) MAT	Micrognathia, undescended testis polydactyly all limbs Hepatosplenomegaly
3	ZAM	8	F	46,XX Sex DEL 17P	Mental retardation, obesity brachydactyly congenital heart disease
4	EME	6	F	46,XX DEL (9) (P22 > PTER)	Mental retardation, speech defect, Synophyros, Anteverted nares
5	AAM	7	M	46,XY, DEL (21) (q1212 > PTER)	Microcephaly, growth and mental retardation, undescended testis

6	AE	7	M	46,XY, DEL (8) (q23:q24.1)	Marasmic, inguinal hernia, mental retardation, Cafe, au lait spot
7	AN	3	F	46,XX,T (6-10) (q15:q21-20)	Microcephaly, develop-mental retardation

DISCUSSION

In the present cytogenetic survey, the observed frequency of chromosomal abnormalities was the same as reported earlier by Singh in 1977 from South Carolina and by Verma in 1980 from New York, USA[7,8].

Down syndrome forms the majority of patients in this series and its incidence in Bahrain is 0.9/1000 compared to the international incidence of 1.4/1000[1,2,7]. Again, the majority (97 %) of the Down syndrome patients were trisomy, while 3 % were translocation cases. According to different surveys, trisomies occur in 92.5 % to 95 % of the cases[1,2]. It results from non-disjunction during meiosis in one of the parents and is correlated with advanced maternal age, while cases due to translocations are not. Translocation can either appear de novo in the newborn, or be transmitted from one of the parents. It is interesting to find in this survey a three year old girl with the rare karyotype of 47, XX, +21 / 47, XX, +21, +r(22) and with clinical features of Down syndrome. Both parents are above 40, and both have normal karyotype. The child had ring chromosome 229.

Some studies suggest that the distal part of the long arm of chromosome 21, and especially the band 21q22 is responsible for the characteristic phenotype of Down's. A great variety of biochemical markers have been investigated in trisomy 21. The first gene localised with certainty was that of superoxide dismutase 1 (SOD 1). This gene has been assigned to band 21q22.1 and as a result of the trisomies gene dosage effects are observed. The enzymatic activity of SOD 1 is increased by a ratio of 3:2 in trisomy 21 and decreased by half in monosomic patients with band 21q22.1[1,3].

A patient with a mild clinical picture of Down's syndrome was found to have mosaicism (46, XX / 46, XX, +21). Mosaics are individuals with two or more genetically different cell population. They are observed in 2.7 % of cases of trisomy 21. Down's syndrome children with mosaicism are less severely retarded when compared to non mosaic trisomic cases[3].

Down's syndrome has recurred in one family who had two affected children. The mother was 21 year old and these were her first and second children. Both parents' karyotypes were repeatedly studied and found to be normal. In this family it is possible that the mother is a mosaic, although she is mentally normal, with upward slanting eyes.

Trisomy 13 was present in 4 % of the abnormal cases. The major features of trisomy 13 are microphthalmia, hare lip and polydactyly. A high proportion of these zygotes are eliminated as spontaneous abortions. All our patients died either immediately after birth or during the first year of life[10,11].

Trisomy 18 was present in 4 % of the abnormal cases. The sex ratio of patients shows an excess of females and it is lethal[3].

Turner's syndrome (XO) was identified in three girls, with gonadal dysgenesis. Embryos with karyotype 45, X are very prone to be aborted[4,5].

Sex chromosome aneuploidies were present in 3 % of our numerical abnormalities, 2 % of them had XYY, and 1 % had Klinfelter Syndrome (XXY). Non-disjunction at the first meiotic division of the mother is believed to be the chief mechanism of origin3,[10,11].

We also found cases of discrepancy between the karyotype and the sex phenotype, with cases of XY females being diagnosed in early childhood because of the ambiguity of the genitalia. One of these cases reached puberty and was married for 6 years before she was diagnosed during investigation of her infertility. Ambiguity in the appearance of the external and/or internal genitalia, with or without ambiguity in the secondary sexual characteristics can be due to a considerable number of different mechanisms.

Some of 46, XY women with pure gonadal dysgenesis are the result of the loss of the testis determining factor (TDF) on the Y chromosome. In the majority of XY women with pure gonadal dysgenesis, a female or somewhat eunuchoid habitus and normal or above normal height is found. There is primary amenorrhoea, streak gonads and infantile or sometimes relatively normal appearing external and internal female genitalia. Secondary sexual characteristics particularly breast development are poor and the oestrogen is low and gonadotrophin is high.

Familial aggregation of XY gonadal dysgenesis has been documented. Therefore the existence of an autosomal recessive gene causing gonadal dysgenesis is regarded as established[1,2,10,11].

CONCLUSION

This study shows the significantly high rate of chromosomal abnormalities found in referred population, which demonstrates the importance of cytogenetic evaluation in patients who have abnormal clinical features. It also shows that chromosomal studies are mandatory in most of mentally retarded children.

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