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HUMAN CHROMOSOMAL STUDIES IN KUALA LUMPUR

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INTRODUCTION

THIS IS a report of 233 individuals studied during the period 1973 to 1975 for a cytogenetic evaluation of some marked congenital anomalies and mental retardation. We also attempted fibroblast cultures from spontaneous abortuses material. The study was made in order to define the extent, types and variations of chromosomal abnormalities present. Such data are useful for the purpose of genetic counselling; each individual detected as 'chromosomally abnormal' in the study is in essence helping to establish the range of 'chromosomal syndromes' prevalent in Kuala Lumpur at that time.

MATERIALS AND METHODS

Samples were provided by the Departments of Paediatrics, Obstetrics & Gynecology, University Teaching Hospital K.L.; Assunta Hospital; Institute for Medical Research/General Hospital and mentally retarded schools in Sentul and Brickfields, Kuala Lumpur. Capillary blood samples were collected for the standard microculture technique. Only in certain cases were venous blood collected and similarly cultured for 72 hours. Slides were prepared using the standard air-drying procedures. Fibroblast cultures from spontaneous abortion material were initiated following the procedure of Hyman (1968).

RESULTS AND DISCUSSION

Table 1 shows the extent of chromosome abnormalities among the cases studied. Most of our samples were predominantly newborns and children. 168 normal karyotypes were encountered, presumbly factors other than chromosomal, may be involved. Of the 65 abnormal karyotypes detected, there were 48 cases of standard tri G21+ Down's syndrome (73.85%), 3 cases of Dq/Gq translocation Down's syndrome (4.62%), 3 cases of tri D13+ Patau's syndrome (4.62%), 4 cases of tri E18+ Edwards' syndrome (6.15%) and 4 cases of X0 Turner's syndrome (6.15%). 3 balanced Dq/Gq translocation heterozygotes (2n = 45) were detected in one family.

Of a wide variety of possible chromosomal aneuploidies, in general, only three common autosomal trisomies survive birth; 47, 21+ (standard trisomy G), 47, 13+ (trisomy D) and 47, 18+ (trisomy E).

The incidence at birth of Down's syndrome in populations of European origin is in the region of 1 in 700 (Smith & Berg, 1976; Hamerton, 1971). A sufficiently comprehensive incidence survey at birth in Asian populations has yet to be reported but generally the incidence appears to vary with the age of the mother. The majority of our trisomy G cases were born to older mothers above 35 and fall into the older maternal age dependent group (Smith & Berg, 1976). It is significant that our trisomy G cases comprise at least 20% of the cases referred to us and forms about 74% of all abnormal karyotypes. Clearly, this was by far the most frequent clinically diagnosed, being confirmed cytogenetically. From what is obviously a biased sampling of abnormal cases, we can only stress that standard G trisomy Down's syndrome forms a significant proportion

Table 1: Chromosomal findings in 233 Individuals

Sample Type	Normal Karyotypes			Abnormal Karyotypes												Total
	M*	F*	Total	Down's Syndrome					Balanced Dq/Gq translocation heterozygote		Patau's Syn. Tri D13+		Edwards' Syn. Tri E18+		Turner's Syn. XO	
				tri G21+		Dq/Gq Trans.		Total								
				M	F	M	F		M	F	M	F	M	F		
I Newborns/ Children	85	63	148	24	24	2	1	51	1	1	1	2	0	4	4	64
II Adults	7	13	20	0	0	0	0	0	0	1	0	0	0	0	0	1
Total			168													65

*M denotes males, F denotes females

and is present in at least 1/3 of those surveyed in the two retarded schools.

An interesting translocation Dq/Gq Down's syndrome affected family was encountered (Fig. 1). The mother was a balanced carrier of the translocation (2n = 45). Of her five children, three were balanced heterozygote carriers and look phenotypically normal and two, a boy and a girl were translocation mongols (2n = 46). The father was not available for study. The mother's age was between 25–34 years at the birth of all her affected children and agree with a lower average age group for mothers of familial mongolism generally associated with translocation. There were no normal karyotype children. The two translocation mongol children were clinically indistinguishable from standard trisomy 21 mongols. Unfortunately, we were unable to obtain the maternal grandparents for study and are therefore unable to ascertain as to whether the translocation was sporadic in the mother or was inherited from one of her parents.

Down's syndrome due to Dq/Gq Robertsonian translocation involving chromosomes of the D and G groups were first described by Polani *et al.* (1960), familial transmission was later described in a similar case by Penrose *et al.* (1960). Theoretically, in the absence of selection, equal numbers of normal, carriers and Down's syndrome individuals can be expected in offsprings of both male and female heterozygous carriers. Hamerton (1970, 1971) in pooled family data estimated in maternal transmission, a 10% chance of an infant with Down's syndrome being produced. With the father as a heterozygous carrier however, there is a marked decrease in the risk of producing an affected child (about 5%) and there appears to be more heterozygous carriers produced. Hamerton suggested that this difference could be due to selection against unbalanced sperms or a different segregation pattern with a possibly higher adjacent segregation in oogenesis compared to spermatogenesis or a differential lethality of unbalanced zygotes.

The practical importance of such a translocation family is to caution and explain to potential parents about the risks involved. In the present family studied the mother was warned against having further children and was told that her three phenotypically normal carrier children are all potentially able to transmit the translocation to future genera-

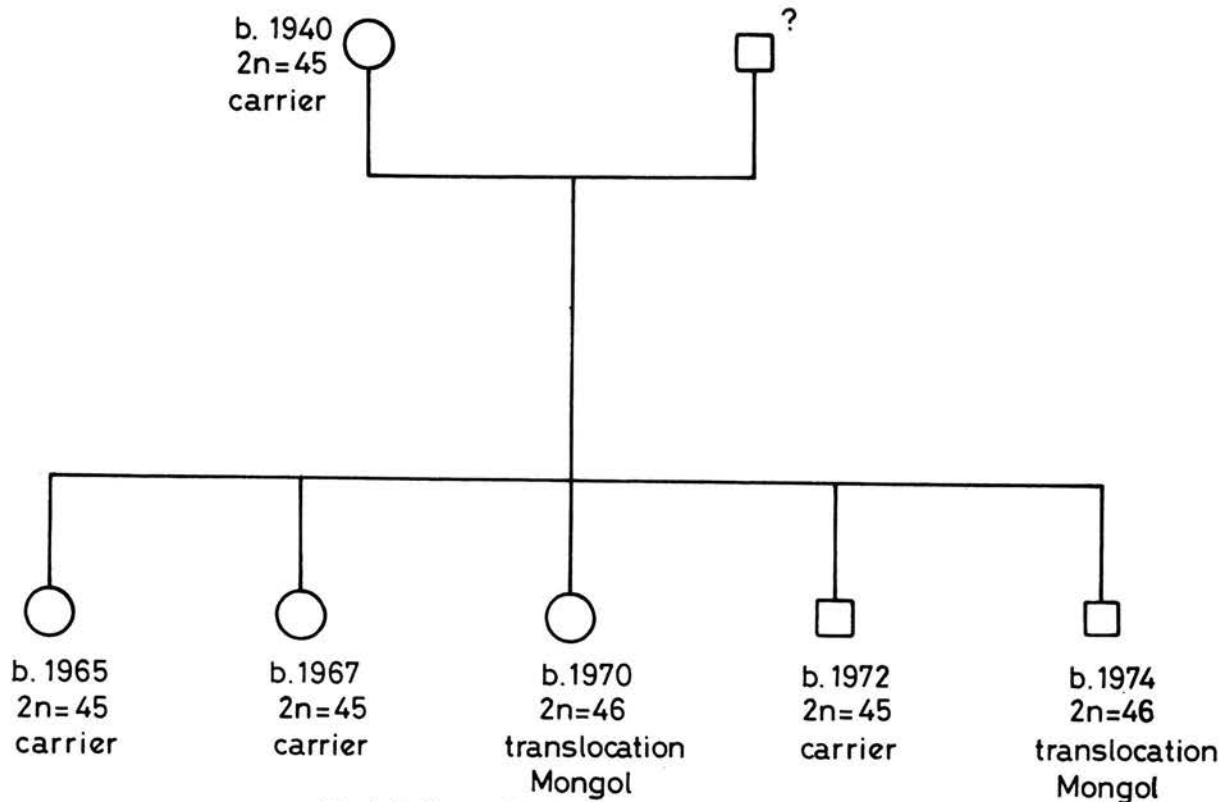

Fig. 1 Pedigree of Dq/Gq translocation affected family

tions. A single Dq/Gq index patient was also found but no follow up family study was available.

In our Down's syndrome samples, there appears to be equal numbers affected in both sexes and no sex bias is to be expected.

3 trisomy D13+ cases were karyotyped (Patau's syndrome) and no Dq/Gq translocations were observed (Table 1). Incidence at birth is about 1 per 5000 births (Hamerton, 1971). The syndrome first described by Patau *et al.* (1960) as very severe congenital malformations incompatible with prolonged life. The 3 cases studied did not survive long after birth. Like trisomy E18+ Edwards' syndrome, with severe congenital abnormalities, a failure to thrive and a short life expectation is to be expected. Incidence figures of trisomy E18+ described by Edwards (1960) are quite similar to Patau's syndrome. We detected 4 trisomy E18+ females. There seems to be a maternal age effect like Patau's syndrome but less pronounced than Down's syndrome. More females with trisomy E18+ have been reported and this is due to a greater male fatality rate in the first few weeks of life (Weber, 1967). Maternal age dependend nondisjunction primarily accounts for these standard D, E and G trisomies.

We have 4 XO, Turner's syndrome cases, the other chief sex chromosome aneuploidy, XXY, Klinefelter's syndrome was absent. It has been estimated that there's an incidence rate of 1 in 2500 female births with Turner's syndrome, (Maclean *et al.,* 1964, Mikamo, 1968) and has been frequently observed in abortuses (Carr, 1965; 1972). Maternal age is not increased.

An attempt was made to culture fibroblast cells from spontaneous abortuses material. Unfortunately, most of the specimens collected were products of conception, mainly placental tissue too macerated for culture. 8 foetuses (fit for culture) arrived in the laboratory. There were 5 successful cultures, however two mishaps at the final stage or removing the monolayer of cells from the glass surface resulted in the cells lost. Out of the three typable karyotypes, two were normal and one was an XO/XX mosaic. The usually accepted explanation for XO/XX mosaicism is loss of an X chromosome during cleavage in the early embryo. The frequency of chromosomally abnormal abortuses is about 20% (Hamerton, 1971) with the most frequent type of abnormality being trisomy, followed by triploidy, 45 XO aneuploidy is the most common single type found.

The above study gives an insight to the extent and variation of 'chromosomal syndromes' present in Kuala Lumpur at the time. The importance of coordination in such work is to be stressed. It is hoped that the above study would lay the groundwork for future such studies locally.

SUMMARY

233 individuals were analysed for a cytogenetic evaluation of some marked congenital abomalies and mental retardation. 65 abnormal karyotypes were detected. These include 48 cases of standard trisomy G21+ Down's syndrome, 3 cases of Dq/Gq translocation Down's syndrome, 3 cases of trisomy D13+ Patau's syndrome, 4 cases of trisomy E18+ Edwards' syndrome and 4 cases of XO, Turner's syndrome, 3 phenotypically normal, balanced Dq/Gq translocation heterozygotes were observed in one family. An attempt to initiate fibroblast cultures from spontaneous abortuses material provided 3 successful karyotypes, 2 normal and an XO/XX mosaic. This study provides us with an insight to the extent of 'chromosomal syndromes' present and is an useful groundwork for future such studies locally.

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