

Numerical Chromosomal Abnormalities in the Malformed Newborns of Goa

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ABSTRACT Several cytogenetic surveys of consecutive births were undertaken at a global level to establish the incidence of aneuploidy and structural chromosomal rearrangements in the human population. A considerable variation in the frequency of chromosomal abnormalities is observed in these studies. The present study was undertaken to examine the incidence of congenital malformations and to record the frequency of numerical chromosomal abnormalities associated with the congenital malformations in Goa. This study revealed an incidence of 19.4/1000 live births. Chromosomal abnormalities were observed in 24.1% of the congenitally malformed newborns, involving 12.7% of numerical abnormalities and 11.4% of structural abnormalities. In most of the cases with numerical abnormalities, the maternal age is advanced (>30 years). It is thus evident that many congenital malformations have genetic etiology. A chromosomal study of each and every child with congenital malformation is recommended in all the pediatric sections of the hospitals for the proper management of such cases.

INTRODUCTION

From the early period of civilization, till date, there has been a constant interest in the causes and meaning of human malformations. Many explanations for human malformations have been suggested over centuries, including supernatural forces. Recent interest has focused on the interplay between genetic and environmental factors acting during the period of embryogenesis. Chromosomal abnormalities are now known to account for a large proportion of spontaneous pregnancy loss and childhood disabilities. Several cytogenetic surveys of consecutive births were undertaken (Nielsen et al. 1975; Hook and Hamerton 1977; Ferrari et al. 1982; Borovik et al. 1989) to establish the incidence of aneuploidy and structural chromosomal rearrangements in the human population. Studies on selected populations of newborns were reported (Bochkov et al. 1974; van Regemorter et al. 1984; Farhud et al. 1986; Stoll et al. 1986; Borovik et al. 1989). However, these studies show a considerable variation in the frequencies of chromosomal abnormalities.

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Few reports are available on the incidence of congenital malformations (CMs) in different parts of India (Anand et al. 1988; Chaturvedi and Banerji 1993). Incidence of 1.6% and 3.6% were reported from hospital based studies from Lucknow by Agarwal (1991) and from Ludhiana by Verma et al. (1991), respectively. Kulshrestha et al. (1983) reported an incidence of 3.4% of congenital malformations among 2409 births based on the survey conducted in a stable community in 15 villages in Haryana. A hospital based study on the role of lethal congenital malformations in perinatal deaths in Trivandrum, Kerala (Suguna et al. 1990) showed an incidence of 0.36% of lethal congenital malformations. In a preliminary hospital based retrospective study of the incidence of malformations in the neonates born during 1997-1998 in the neonatal unit of Goa Medical College, Goa, an incidence of 4.7% of CMs was observed (Shyama 2003). Reports on the frequency of chromosomal abnormalities associated with congenital abnormalities in India are very few and we have absolutely no data available from Goa. Therefore, the present study was undertaken to examine the incidence of CMs and to record the frequency of numerical chromosomal abnormalities associated with them.

PATIENTS AND METHODS

The present study is on clinically identifiable

congenital malformations in all consecutive births from 1999 to 2001 in the Goa Medical College (GMC) of Bambolim, Goa, the only tertiary medical care center of the state. Samples of peripheral blood were collected from the patients with congenital malformations for cytogenetic studies. Lymphocytes were cultured and processed to obtain well spread metaphases as per the modified technique of Moorhead et al. (1960). These chromosome spreads were processed to obtain G-bands and were analyzed for numerical and structural abnormalities.

RESULTS

During the period of study 8551 consecutive births were examined for malformations. Of these, 166 newborns had one or more congenital malformations giving an incidence of 19.4/1000 births. The cytogenetic examination of these malformed newborns revealed chromosomal abnormalities in 24.1% (40/166). Structural chromosomal abnormalities are recorded in 11.4% (19/166). Numerical abnormalities are observed in 12.7% (21/166) of the cases. Amongst the numerical abnormalities thirteen cases are

trisomy 21, three are trisomy 18, two are monosomy X, one is trisomy 13 and two are multiple mosaics (Table 1). The frequency of trisomy 21 is 7.83%, trisomy 18 is 1.81%, trisomy 13 is 0.6% and monosomy X is 1.20%.

Considering the total population of live births surveyed, the incidence of chromosomal abnormalities is 4.7/1000 births (rate: 1/213) of which incidence of structural chromosomal abnormalities is 2.22/1000 births (rate: 1/450) and that of numerical abnormalities is 2.46/1000 births (rate: 1/407). The incidence of trisomy 21, trisomy 18, trisomy 13 and monosomy X are 1.52/1000, 0.35/1000, 0.12/1000 and 0.23/1000 births, respectively. The frequencies of these abnormalities are recorded and compared with other studies in Table 2.

Mosaic cell lines are observed in some cases. These included two cases of Down's syndrome (46,XX / 47,XX+21) and one case of Turner's syndrome (46,XX / 45,XO). Unusual case of mosaic with different cell lines are observed in two identical twins born to parents with no consanguinity. They had a chromosome constitution with 4 cell lines of 46,XX / 41,XX / 77,XXX / 51,XX, and seen in both the twins. Both had ambiguous genitalia, with rudimentary ears, ear pits and pronounced hypertelorism (Fig. 1).

Table 1: Numerical chromosomal abnormalities in the Congenitally malformed new-borns of Goa

Numerical abnormality	No. of cases	Frequency (%)	Incidence/1000 births	Rate
Trisomy 21	13/166	7.83	1.52	1/658
Trisomy 13	01/166	0.60	0.12	1/8333
Trisomy 18	03/166	1.81	0.35	1/2857
Monosomy X	02/166	1.20	0.23	1/4348
Multiple mosaic	02/166	-	-	-
Total	21/166	12.7	2.46	1/407

DISCUSSION

Comparison of the incidence of 1.9% of congenital malformations observed in the newborns of Goa during 1999–2001 in the present study with that of Shyama (2003) (4.7%) indicates that there is a considerable reduction in the occurrence of malformations in the newborns over a period of time, since 1998. The reasons

Table 2: Comparison of the rate of numerical chromosomal abnormalities in the present study with other studies

Reference	Births	Trisomy 21		Trisomy 18		Trisomy 13		Monosomy X	
		No.	Rate	No.	Rate	No.	Rate	No.	Rate
Bochkov et al. 1974	31,888	-	-	2	1/15,944	2	1/15,944	1	1/31,888
Van Regemorter et al. 1984	10,000	17	1/476	4	1/2,500	-	-	1	1/10,000
Stoll et al. 1986	39,924	41	1/971	8	1/4,990	8	1/4,990	6	1/6,654
Farhud et al. 1986	13,037	16	1/813	1	1/13,037	1	1/13,037	-	-
Borovik et al. 1989	73,192	99	1/741	13	1/6,099	3	1/24,397	3	1/24,397
Present study	8,551	13	1/658	3	1/2,857	1	1/8,333	2	1/4,348



Fig. 1. The twin siblings with ambiguous genitalia, rudimentary ears, ear pits and pronounced hypertelorism

may be various, including a higher standard of living.

The present incidence of 1.9% of congenital malformations in the newborns of Goa is almost in agreement with similar reports from hospital based studies in different parts of the country where Mittal and Greawal (1969), Hemarajani et al. (1971), Tiberwala (1974) and Ramakrishna (1976), reported incidences of 2.0%, 2.1%, 1.8% and 1.9%, from Kanpur, Jaipur Bombay and Madras, respectively. However, the incidence in Goa is considerably lower compared to the reports from other parts of the country namely the incidences of 3.0% reported by 3.4% recorded by Ghosh and Bali (1963) in Delhi and 3.6% reported by Saifullah and Pathak (1963) from Chandigarh and 30% reported by Verma et al. (1991) from Ludhiana.

Newborns with congenital malformations exhibited chromosomal abnormalities in 24.1% of the cases. All the newborns with malformations were subjected to cytogenetic analysis in the present study, unlike several other studies where cytogenetic analysis was carried out only in suspected cases of chromosomal abnormalities or of multiple congenital abnormalities of unknown cause. These include reports of children referred for cytogenetic examination for multiple congenital anomalies excluding Down syndrome, with frequencies of chromosomal abnormalities ranging from 11.9% to 27.6% (Winter et al. 1980; Verma and Dosik 1980; Mehes and Bajn'oczky 1981; Coco and Penchaszadeh 1982; Billerbeck 1986). Many of these reports lack the data on the total number of births screened and are not always on newborn infants. Other

studies on congenital malformations in the newborn infants including the stillbirths and the malformed fetuses, report the number of cases with chromosomal abnormalities but do not have the data on the number of infants referred for cytogenetic examination (van Regemorter et al. 1984; Farhud et al. 1986; Stoll et al. 1986).

Results of the present study can be compared to the study of Bochkov et al. (1974) and Borovik et al. (1989) where they found abnormal chromosome constitution, excluding Down syndrome in 13.65% cases and 28.4% respectively. However, the higher value of 28.4% reported by Borovik et al. (1989) may be because of the use of modern techniques for cytogenetic analysis, in contrast to our study wherein we used only conventional techniques.

Various frequencies of trisomy 21 have been reported. van Regmorter et al. (1984) recorded an incidence of 1/476, Farhud et al. (1986) observed it to be 1/813 and Borovik et al. (1989) reported it to be 1/741. In the present study we report the incidence of 1/658. The rate reported by Stoll et al. (1986) is slightly lower (1/971) as compared to the present study (Table 2). The high rate in the present study may be attributed to the advanced maternal age in most of the cases.

The high rate of trisomy 18 (1/2857) observed in the present study is comparable to the rates reported by van Regmorter et al. (1984) (1/2500). However, this is much higher than many of the other reports from various parts of the globe.

The rate of trisomy 13 in the present study is 1/8333 and is lower than the rate of 1/4990 reported by Stoll et al. (1986), but higher than the rate of 1/15,944 reported by Bochkov et al. (1974), 1/13,037 reported by Farhud et al. (1986) and 1/24,397 recorded by Borovik et al. (1989).

Monosomy X is seen in 1/4348 births in the present study and is almost similar to Stoll et al. 1986 (1/6654), but higher than the rates of Bochkov et al. (1974) (1/31,888); van Regemorter et al. (1984) (1/10,000) and Borovik et al. (1989) (1/24,397).

The high rate of trisomies 21, 18 and 13 and the monosomy X in the present study can be attributed to the advanced maternal age. The maternal age was above 30 in 76.9% (10/13) of trisomy 21, 66.7% (2/3) of trisomy 18, 100% of trisomy 13 (1/1) and 100% of monosomy X (2/2). This shows a genetic predisposition of the ova to nondisjunction with increased maternal age. Therefore, it can be postulated that advanced

maternal age may be leading to the rise in the chromosomal abnormalities such as trisomy 13, 18, 21 and monosomy X on account of non-disjunction in gametes.

From this study it can be concluded that since many congenital malformations have a genetic cause, chromosomal studies should be undertaken for every child with congenital malformations, in the pediatric sections of all the hospitals for the proper management of the cases.

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