

# CONGENITAL MALFORMATIONS, TWINNING AND ASSOCIATED VARIABLES IN A BRAZILIAN POPULATION

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*A sample of 6052 newborn children (4968 whites, 1084 Blacks) issued from parents with a generally low socioeconomic level, was studied in relation to congenital anomalies and twinning rates.*

*The observed frequency of major malformations was 1.3% and of minor defects 2.0%. The twinning rate was 1.4%. Race differences were generally nonsignificant in these variables. These results are in agreement with those obtained in some other Brazilian series, but discrepancies were also observed.*

*A total of 13% of the malformations observed proved to be familial, polydactyly being the most common anomaly encountered in this class. The frequency of malformations different from those present in the propositi is higher in their sibships than the general prevalence of defective children found among the sibs of normal babies (13% and 4% respectively).*

*Age, gestation length and exposure of the mothers to noxious agents during pregnancy were not significantly different when the parents of normal and malformed children were compared. On the other hand, as expected, the parents of twins are significantly older than those of single-born, and the gestation length was much reduced in pregnancies resulting in multiple births.*

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## INTRODUCTION

Many surveys concerning the incidence of congenital malformations at birth have been reported in the literature; however, the state of knowledge in this field is not very satisfactory because often it is impossible to compare different series due to divergence in methods of ascertainment, of sampling and of diagnostic criteria (Kennedy 1967). In Brazil, on the other hand, only four previous surveys aiming at investigating this variable are known to us (Saldanha et al. 1963, Araújo 1963, Stevenson et al. 1966, Arena 1974) and all of them were restricted to groups living in the State of São Paulo. Information if the observed malformations are sporadic or familial is absent in the vast majority of reports in the world literature, the same being true in relation to other characteristics that may influence these incidences, such as socioeconomic level of the sample, history of other malformations in the family of the *propositi*, age of the parents, gestation length and exposure of the mothers to noxious agents during pregnancy. As for twinning rates, they are also known in several populations (Susanne and Corbisier 1969, Bulmer 1970) but again there are few data for Brazil (Pedreira et al. 1959, Arena 1974) and generally the same lack of information concerning associated

variables. We therefore decided to study these parameters in the population of Porto Alegre, as a part of a more general investigation which included the study of other characteristics (Araújo and Salzano 1974, 1975).

#### MATERIAL AND METHODS

The collection of information was made at the maternities of the Hospitals Presidente Vargas and Ernesto Dornelles, located in Porto Alegre, the capital of the Brazilian State of Rio Grande do Sul. They were visited at least three times a week, the data about the newborn children being collected from the maternity records, supplemented by personal examination, interviews with the physician in charge and the mothers. The socioeconomic level of the child was evaluated by the professions of his or her parents. Additional details are given in Araújo and Salzano (1974, 1975). Whenever the physician reported an anomaly, the child would be examined by one of us (AMA), in order to assure an uniform classification of the abnormalities found. Following Marden et al. (1964) and Schull and Neel (1965) the malformations were further classified as major, if it was anticipated that they would have an adverse effect on either the function or social acceptability of the individual; or as minor, if they probably would not seriously handicap his or her carrier.

#### RESULTS

Our results concerning the incidence of congenital malformations and twinning are presented in Table 1, and compared, in Tables 2 and 3, with those from several other Brazilian series. The racial composition of our sample (82% of whites, 18% of Blacks) is only a little higher than the one obtained in the last general census of the city (1950) in which this attribute was included (14%). The difference may be due to the fact that the large majority of the children studied by us is from a low socioeconomic level (75% of the 3735 for whom we have this type of information; among the Blacks 94% of 671 came from this level).

The total frequency of malformations observed in Porto Alegre was 3.3% (Table 1); the white males showed the expected higher incidence when they were compared to the females of the same racial group (3.9% vs. 2.5%); but this sexual dimorphism was not apparent among the Blacks, may be because the sample size is small.

These data are compared in Table 2 with those obtained in previous surveys of Brazilian populations. These studies differ among themselves in relation to the method of investigation, and the concept of what constitutes a major or minor malformation was not uniform either. We tried to make the figures more comparable by examining the lists presented and classifying the anomalies according to our criteria. But it is not known how different the results would be if especially the minor malformations had been studied with a standardized method. The incidences obtained in Porto Alegre for the major malformations are similar to those encountered by Araújo (1963) and Stevenson et al. (1966), but different from those observed in the two other surveys listed. Whites and Blacks show practically the same values in the three series in which a race separation was made. Due to the problems already mentioned concerning the definition of what is a minor anomaly, no comparison is possible in relation to this parameter among the several surveys.

The Porto Alegre figures for multiple births (Table 1) show one triplet plus 84 twin pairs (1.4%) among 6052 newborn children. No significant difference in this incidence according to race was observed; but among the Blacks the proportion of DZ twins (estimated by Weinberg's method) is smaller than would be expected, probably due to sampling problems.

TABLE 1  
CONGENITAL MALFORMATIONS AND TWINNING IN PORTO ALEGRE

	Whites	Blacks	Total
Total births	4968	1084	6052
<i>Single births</i>			
<i>Males,</i>			
Normal	2376	527	2903
Malformed	96	20	116
%	3.9	3.7	3.8
<i>Females,</i>			
Normal	2367	500	2867
Malformed	61	20	81
%	2.5	3.8	2.7
<i>Both sexes,</i>			
Normal	4743	1027	5770
Malformed	157	40	197
%	3.2	3.7	3.3
<i>Multiple births</i>			
Male-Male	24	6	30
Male-Female	21	3	24
Female-Female	23	7	30
Female-Female-Female	—	1	1
Total	68	17	85
% MZ <sup>a</sup>	0.5	0.9	0.6
% DZ <sup>a</sup>	0.9	0.6	0.8
% MZ + DZ	1.4	1.5	1.4

<sup>a</sup> Obtained by using Weinberg's differential method.

TABLE 2  
CONGENITAL MALFORMATIONS IN FIVE BRAZILIAN SERIES

Authors	Population	Method	Race	% Malformations		No. of births
				Major	Minor	
Araújo (1963)	São Paulo, SP	Retrospective	Unknown	1.7	2.3	19,293
Saldanha et al. (1963)	São Paulo, SP	Retrospective	Whites	2.2	0.6	15,532 7,090
			Blacks	2.4	0.6	
Stevenson et al. (1966)	São Paulo, SP	Prospective	Whites	1.5	0.6 <sup>a</sup>	7,818 6,031
			Blacks	1.7		
Arena (1974)	Campinas, SP	Prospective	Unknown	3.3	10.8	2,964
Present report	Porto Alegre, RS	Prospective	Whites	1.3	1.9	4,900 1,067
			Blacks	1.4	2.3	

<sup>a</sup> No separate figures according to race are provided by the authors.

TABLE 3  
TWINNING IN SIX BRAZILIAN SERIES

	Pedreira et al. (1959)	Souza et al. (1966)	Saldanha et al. (1963)	Stevenson et al. (1966)	Arena (1974)	Present report
Population	Salvador, BA	Juiz de Fora, MG	São Paulo, SP	São Paulo, SP	Campinas, SP	Porto Alegre, RS
Total no. of births	36,873	17,203	22,226	14,634	2,998	6,052
Multiple births						
Twins, Male-Male	214	—	—	61	7	30
Male-Female	250	—	—	81	9	24
Female-Female	182	—	—	69	13	30
Total	646	207	537	211	29	84
%	1.76	1.20	2.42	1.44	0.97	1.38
% MZ <sup>a</sup>	0.40	—	—	0.33	0.37	0.59
% DZ <sup>a</sup>	1.36	—	—	1.11	0.60	0.79
Triplets, N	10	—	9	2	1	1
% <sub>ooo</sub>	2.71	—	4.05	1.37	3.30	1.65

<sup>a</sup> Obtained by using Weinberg's differential method.

$\chi^2$  for heterogeneity in the general incidence of twinning:  $\chi^2 = 112.1$ ; 5 d.f.;  $P < 0.001$ .

A comparison of our data with five other Brazilian series is made in Table 3. The differences among the samples for the general frequency of twinning is highly significant, the highest value (2.42) being the one obtained by Saldanha et al. (1963) and the lowest that found by Arena (1974) (0.97); the Porto Alegre incidence is somewhere in the middle of these extremes.

Table 4 shows the racial variation in the incidence of the most frequent malformations observed in Porto Alegre, which is compared with that found in two series studied in São Paulo. In six instances it was possible to test these racial differences in our material; the null hypothesis was rejected for umbilical hernia ( $\chi^2 = 7.8$ ; 1 d.f.;  $P < 0.01$ ) and, as would be expected, for polydactyly ( $\chi^2 = 22.2$ ; 1 d.f.;  $P < 0.001$ ). The latter also occurs in higher frequencies among the Blacks of São Paulo; and, in good agreement with our findings, umbilical hernia was also found to be more prevalent in persons of this ethnic group by Saldanha et al. (1963) ( $\chi^2 = 17.4$ ; 1 d.f.;  $P < 0.001$ ). As for the comparison among series, though the numbers are small, it seems that angioma and hemangioma, and umbilical hernia, are somewhat more prevalent in Porto Alegre, the opposite being true in relation to cardiopathy and hypospadias.

Data indicating if the same malformation diagnosed in the *propositi* was also found among their parents and sibs are shown in Table 5. There is an excess of familial cases among the Blacks that is entirely due, however, to polydactyly (of the 10 cases, 7 are of persons with this condition). The data concerning malformations different from those encountered in the *propositi* are given in Table 6. The frequency observed in the sibships of the latter (13%) is higher than the general prevalence of defective children found among the sibs of normal babies (4%).

TABLE 4  
 MOST FREQUENT MALFORMATIONS IN PORTO ALEGRE AND IN FOUR SERIES STUDIED IN THE STATE OF SÃO PAULO

Malformation	Present report		Araújo (1963)		Saldanha et al. (1963)		Stevenson et al. (1966)		Arena (1974)					
	Whites	Blacks	Whites + Blacks	Whites	Blacks	Whites	Blacks	Whites	Blacks	Whites + Blacks				
	n	%	n	%	n	%	n	%	n	%				
	(N = 4,900) (N = 1,067) (N = 19,293) (N = 15,532) (N = 7,090) (N = 7,818) (N = 6,031) (N = 2,964)													
Cryptorchism	23	9.3	8	14.6	—	—	41	5.1	23	6.2	—	—	21	13.9
Angioma and hemangioma	9	1.8	3	2.8	14	0.7	—	—	—	—	—	—	—	—
Hypospadias	4	1.6	—	—	61	3.2	25	3.1	13	3.5	—	—	7	4.6
Umbilical hernia	7	1.4	7	6.6	8	0.4	7	0.5	18	2.5	—	—	—	—
Talipes equinovarus	7	1.4	—	—	1	0.1	—	—	—	—	13	1.7	10	1.7
Pes planus	7	1.4	1	0.9	—	—	—	—	—	—	—	—	—	—
Melanic spot	6	1.2	—	—	—	—	—	—	—	—	—	—	—	—
Down's syndrome	5	1.0	—	—	—	—	15	1.0	3	0.4	7	0.9	4	0.7
Cardiopathy	4	0.8	—	—	31	1.6	40	2.6	14	2.0	5	0.6	4	0.7
Preauricular papilloma	4	0.8	2	1.9	—	—	1	0.1	—	—	—	—	—	—
Polydactyly	2	0.4	8	7.5	1	0.1	38	2.4	43	6.1	2	0.3	35	5.8

N = Total number of births; n = Number of children with the specific malformation.

TABLE 5  
 OCCURRENCE OF THE SAME MALFORMATION OBSERVED IN THE PROPOSITI AMONG THEIR PARENTS AND SIBS  
 (Porto Alegre)

Type of the malformation	Whites	Blacks	Total
Sporadic	94 (93)	18 (64)	112 (87)
Familial	7 (7)	10 (36)	17 (13)
Subtotal	101	28	129
Unknown	56	12	68
Total	157	40	197

Percentages in relation to the subtotal for which information was available in parenthesis. The familial malformations observed among the Whites were: achondroplasia, cleft palate, microcephaly plus several anomalies, pes planus, protruding last sacral rib, pyloric stenosis, and talipes equinovarus; among the Blacks: angioma plus hemangioma, melanoma, minor genital anomaly and polydactyly (7 cases).

Tabulation of the results related to age of the parents, gestation length, and exposure of the mothers to noxious agents during pregnancy yielded non-significant differences among normal and malformed children. On the other hand, as expected, the parents of twins, especially those of male-female pairs, are significantly older than those of single-born, and the gestation length was much reduced in pregnancies involving twins. Detailed tables concerning these variables are available on request.

TABLE 6  
 OCCURRENCE IN THE SIBSHIPS OF ANOMALIES DIFFERENT FROM THOSE PRESENT IN THE PROPOSITI  
 (Porto Alegre)

Condition of the sibships	Normal children		Malformed children	
	N	%	N	%
With malformed persons	150	4	13	13
Without malformed persons	3367	96	90	87
Subtotal	3517	—	103	—
Information not available	410	—	29	—
Total	3927	—	132	—

Since we had to eliminate for this tabulation sibships of one, significantly decreasing the number of Black families, no separation according to race was made.

## DISCUSSION

Any investigator of the epidemiology of congenital malformations knows the difficulty of obtaining comparable figures when different samples are confronted. This is especially true in intercountry comparisons, but even within a country significant differences may appear due to diversity in the way the studies were conducted. In the specific case of Brazil, it is hard to believe that the discrepancies found in the incidence of major malformations observed among samples obtained in the same State (São Paulo) by different researchers are biologically « real ». The distinct methods of study employed (prospective or retrospective), as well as divergent diagnostic criteria and sampling problems may be more likely explanations for the differences. This is especially true when specific malformations are compared (see, for instance, the aberrant figure obtained for polydactyly by Saldanha et al. 1963, among white subjects). We agree with Kennedy (1967) and several other authors, who stressed the need for a better standardization of these studies.

Diagnostic problems disappear when the incidence of twinning is compared. In this case the variation observed among the different Brazilian samples, even when the study by Saldanha et al. (1963) (who showed a very high value) is not considered, is statistically significant ( $\chi^2 = 32.1$ ; 4 d.f.;  $P < 0.001$ ). There is a difference even between the prevalences observed in Porto Alegre and Campinas, obtained with very similar methods of study (1.38% vs. 0.97%;  $z = 2.6$ ;  $P < 0.01$ ). Variation in the racial composition of the samples, as well as in the age of the mothers under study, may explain these discrepancies.

Most of the comparisons made between Blacks and whites in Porto Alegre yielded non-significant differences (incidence of congenital malformations, percentage of major and minor defects, twinning rates). Besides the dissimilarity, observed also in many other studies, on the prevalence of polydactyly, the only other significant variation found was the one related to the frequency of umbilical hernia; and in this case, environmental factors may have played a role (the higher value was observed among the Blacks, who have lower standards of living).

We observed an increased prevalence of malformations different from those present in the *propositi* in the sibships of malformed babies, compared with that found in sibships of normal newborn children. There are conflicting reports in the literature concerning this matter (see, e.g., Neel 1958, Niswander and Adams 1968). Two explanations can be given for the positive findings: (a) a general increased liability to congenital defects in these sibships (that could be due either to genetic or environmental factors); or (b) a tendency among the parents of malformed children to examine in more detail their previous reproductive histories, giving more attention including to the occurrence of minor defects. Our data do not permit a decision about which of these hypotheses is more likely for the explanation of our results.

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## RIASSUNTO

*Malformazioni Congenite, Gemellarità e Altre Variabili in una Popolazione Brasiliana*

È stato studiato, in relazione alle anomalie congenite ed alla frequenza di gemellarità, un campione di 6052 neonati (4968 bianchi, 1084 negri) di genitori con un livello socio-economico generalmente basso.

Per le malformazioni principali è stata riscontrata una frequenza di 1,3%; per quelle minori, di 2,0%. La frequenza di gemelli è risultata dell'1,4%. Le differenze razziali sono risultate in generale non significative. Questi risultati concordano con quelli ottenuti in altri campioni della popolazione brasiliana, ma sono anche state riscontrate discordanze.

Il 13% delle malformazioni osservate è risultato essere a carattere familiare; in questo gruppo l'anomalia più frequentemente riscontrata è la polidattilia. La frequenza di malformazioni diverse da quelle presenti nei candidati è più elevata nelle loro fratrie rispetto alla frequenza generale di bambini malformati riscontrata nelle fratrie di bambini normali (13% contro 4%).

L'età, il periodo di gestazione e l'esposizione della madre ad agenti nocivi durante la gravidanza non sono risultati significativamente diversi nei genitori di bambini malformati rispetto ai genitori di bambini normali. D'altra parte, come previsto, i genitori di gemelli sono significativamente più anziani dei genitori dei mononati, e il periodo di gestazione risulta più breve nelle gravidanze multiple.

## RÉSUMÉ

*Malformations Congénitales, Gémellarité et Autres Variables dans une Population Brésilienne*

Dans le cadre des anomalies congénitales et de la fréquence de gémellarité, un échantillon de 6052 nouveaux-nés (4968 blancs, 1084 noirs), provenant de parents de niveau socio-économique généralement bas, a été étudié.

Pour les malformations principales, l'on a observé une fréquence de 1,3%; pour les malformations mineures, de 2,0%. La fréquence de jumeaux était de 1,4%. Les différences raciales se sont généralement avérées non significatives. Ces résultats concordent avec ceux obtenus chez d'autres échantillons de la population brésilienne, mais certaines discordances ont pu être observées.

Dans 13% des cas, les malformations étaient de caractère familial; dans ce groupe, l'anomalie la plus fréquente est la polydactylie. La fréquence de malformations différentes de celles présentes chez les candidats est plus



élevée dans leurs fratries par rapport à la fréquence générale d'enfants malformés trouvée dans les fratries d'enfants normaux (13% contre 4%).

L'âge, la période de grossesse et l'exposition des mères à des agents nocifs lors de la grossesse n'ont souligné aucun résultat expressément différent entre les parents d'enfants malformés et les parents d'enfants normaux. D'autre part, ainsi que prévu, les parents de jumeaux sont remarquablement plus âgés que les parents de non-jumeaux, et la période de grossesse s'avère être beaucoup plus brève lors des grossesses multiples.

## ZUSAMMENFASSUNG

### *Angeborene Missbildungen, Zwillingsgeburten und andere Variablen bei einer brasilianischen Bevölkerung*

Eine Reihe von 6052 Neugeborenen (4968 weisse und 1084 schwarze) aus allgemein schlechten sozialen und wirtschaftlichen Verhältnissen stammend, wurden auf Anomalien und Zwillingsgeburten untersucht.

Dabei betrug das Vorkommen von grösseren Missbildungen 1,3%, von kleineren Missbildungen 2,0% und von Zwillingsgeburten 1,4%, ohne wesentliche Unterschiede zwischen den beiden Rassen. Diese Ergebnisse stimmen mit denen anderer Untersuchungen bei der brasilianischen Bevölkerung überein, wenn sich auch einige Abweichungen zeigen.

Aus der beobachteten Missbildungen 13% sind familiär bedingt, wobei die Polydaktilie am häufigsten ist. Andere Missbildungen als die bei den Versuchskindern festgestellten treten bei den Geschwistern derselben häufiger auf (13%) als bei den Geschwistern normaler Kinder (4%).

Was Alter der Eltern, Schwangerschaftsdauer und schädliche Einflüsse während der Schwangerschaft betrifft, ergaben sich keine wesentlichen Unterschiede zwischen den Eltern der missgebildeten und denen der normalen Neugeborenen. Andererseits sind die Eltern der Zwillinge, wie vorauszusehen, wesentlich älter als die der Einlinge und die Schwangerschaftsdauer ist erheblich kürzer bei den Mehrlingsgeburten.