A Racial Comparison of Cleft Patients in A Clinic Population: Associated Anomalies and Recurrence Rates

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Clinical files of 22 *black* and 88 *white cleft palate* patients, under 16 years of age, were studied. Data on the distribution of *cleft types*, *associated birth defects* and *recurrence rates* were obtained for the two *racial groups* and analyzed through the use of the X^2 test. It was found that blacks had a significantly higher ($p < .005$) rate of associated birth defects when compared to whites. No significant differences were found in recurrence rates between the racial groups.

Introduction

Clefting is the result of the interruption in the fusion of the palatal shelves with the primary palatal triangle and is described as the absence of mesoderm (Graber, 1966; Patten, 1961; Stark, 1954, 1961). Clefts of the lip and palate occur as separate entities and have been classified as such (Fogh-Anderson, 1942; Stark, 1961; Graber, 1966; Fraser, 1970). The palate is defined as any structure that lies behind the incisive foramen and includes both hard and soft tissue. Development of the lip and pre-palate is completed before the development of the secondary palate. Occurrence of clefting has been described as multifactorial with a strong genetic component (Fraser, 1970).

Since the American Cleft Palate Association has classified clefts as: clefts anterior to the incisive foramen, clefts posterior to the incisive foramen, combinations, and rare clefts (Berlin, 1971), this classification will be adhered to in this study. The following abbreviations will be used: CL = cleft lip, CP = cleft palate, CLP = cleft lip and palate.

The occurrence of clefts has been shown to vary with geographic location, sex, and race. Woolf *et al.*, (1963) found that the incidence of cleft lip and palate in Utah was 1.5/1000 with the ratio of clefts 1:2:1 for CL, CLP and CP. Males had a higher incidence of cleft lip while females had a higher incidence of cleft palate. These results were for a predominantly caucasian sample. The results of a study in New York City (Conway and Wagner, 1965) demonstrated that females had a higher incidence of isolated cleft palates regardless of race, with a ratio of white to non-whites of 2:1. Fraser (1970) also found that more females had isolated cleft palates and that more males had cleft lips. In contrast to these studies, Gilmore *et al.*, (1966), in a study in Wisconsin, found that more females had cleft lip and more males had cleft palate. Racial differences were not taken into account except for incidence which was 1/960 for whites and 1/5670 for blacks.

While incidence has been shown to vary geographically and according to sex and race, variation in the association of other birth defects and recurrence rates have not been successfully demonstrated.

Clefts may occur with or without other birth defects. According to Altemus and Ferguson (1965), blacks have a higher occurrence of malformations than whites. However, Chung and Myrianthopolous (1968) found that, when polydactaly, which accounts for half of congenital malformations in blacks is removed from the analysis, the trend is reversed. Whites also showed a much higher occurrence of multiple malformations than did blacks. Many researchers have found a

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higher association of other anomalies with CP than with CLP or CL alone (Conway and Wagner, 1965; Gilmore *et al.*, 1966; Gorlin, 1971). Only one study (Chung and Myrianthopolous, 1974) has compared clefts with associated anomalies racially. It was found that the frequency of malformations associated with clefts was significantly higher among blacks than among whites. However, this was true only for minor malformations, not major anomalies. When broken down according to cleft type, sex, and race, at least 75% of the subjects in all groups except white females with CLP had associated malformations. These inflated percentages may be because neonatal deaths were included in the sample.

As to recurrence rates, which are reported only for white populations, the highest rates for recurrence were in the siblings of cleft patients, and the next highest were in the parents of cleft patients (Woolf *et al.*, 1963; Gilmore *et al.*, 1966; Fraser, 1970).

For these reasons, the racial comparison of occurrence ratios, association with other birth defects, and recurrence is the subject of this investigation.

Methods

Computerized records of all cleft patients from birth to 16 years of age in the University of Pittsburgh Cleft Palate Center were printed out. Since there were fewer blacks than whites in this age group in the clinic, the entire black sample was studied and a white sample was age-matched to it by year of birth so that the age distribution in both groups was the same. All white children born in a year in which a black child was born were retrieved from the computer printout by patient number. Then four white children were selected by use of a random numbers table for that particular year. Thus, there were 22 black children and 88 white children in the study. This approximates the presumed distribution of blacks to whites with clefts (Gorlin *et al.*, 1971). Race was predetermined and recorded from clinical files. Age matching was done only to obtain a similar age distribution for both races. There was no variation in the incidence of clefting from year to year for blacks or whites according to the records of the Pennsylvania Department of Health.

The following data were then recorded from clinical records: sex, cleft type, occurrence of other birth defects, and recurrence in first and second degree relatives.

The data were then tabulated and statistically analyzed using chi square test.

Results

In the white group of 88 subjects, 9 had CL alone, 46 had CLP, and 33 had CP. Of the 22 subjects in the black group, none had CL alone; 11 had CLP; and 11 had CP. Because the incidence of CL was so low, for purposes of statistical analysis, CL was combined with CLP since they are thought to be the same disease entity.

When broken down according to sex, the white group contained 14 females with CL/CLP and 18 with CP. Forty-one white males had CL/CLP, and 15 had CP. In the black group, there were seven black females with CLP and one with CP. Four black males had CLP, and 10 had CP. The occurrence patterns according to sex are opposite in blacks and whites (Table 1).

With regard to occurrence of other birth defects, it was found that, for the white group, 32/88 had other anomalies and for the black group 17/22 had other anomalies. Associated defects were distributed as shown in Table 2. Chi square was used for detection of differences between black and white groups with and without other birth defects, and a value of 11.92 was obtained. This was significant at $p < .005$, with one df. Blacks had a much higher occurrence of other birth defects than had whites.

Twelve of 88 or 13.6% of the white group had known syndromes as opposed to none in the black group. These included Pierre Robin, Goldenhars, Oto-Palatal-Digital, Marfans and Lip-Pit syndromes. When Pierre-Robin was eliminated, 8% had known syndromes; 4.5 of these were inherited in a Mendelian fashion.

In the black group, 10/22, or 45% had multiple anomalies, excluding the cleft, whereas only 9% of the white group had multiple anomalies when the cleft was excluded. It should be noted that these multiple anomalies in the black group were not recognized as syndromes. Data are presented in Table 3.

For this study, recurrence is defined as the proportion of patients with first or second

TABLE 1. Distribution of clefts.

	black n = 22				*white n = 88*			
	Females	%	Males	%	Females	%	Males	%
CL	0		0		3	9.375	6	11.11
CLP	7	87.50	4	28.57	11	34.375	35	62.50
CP	1	12.50	10	71.43	18	56.25	15	26.78
T	8		14		32		56	

TABLE 2. Occurrence of associated birth defects.

	Black				*White*			
	Females	%	Males	%	Females	%	Males	%
with	6	75	11	78	14	44	18	32
without	2	25	3	22	18	56	38	68
T	8		14		32		56	

TABLE 3. Types of associated birth defects.

Type of birth defect	*black M.*	*black F.*	*white M.*	*white F.*
Congenital Heart Disease	3	1	2	5
Mental Retardation	2	2	3	3
Limb Abnormalities	2	0	0	2
Skeletal Abnormalities	1	1	2	2
Hypertelorism	3	1	0	1
Abnormal Eyes	0	0	1	0
Abnormal Ears	2	2	1	0
Mandibular & Maxillary Anomalies	1	0	5	1
Hydrocephaly	1	0	0	0
Hypotonia	0	2	0	0
Congenital Hip Dysplasia	0	0	0	4
Abnormal Breast Development	1	2	0	0
Pyloric Stenosis	0	0	1	0
Pulmonic Stenosis	0	0	0	1
Genital Anomalies	3	0	1	0
Hernia	4	2	4	0
Failure to Thrive	0	3	1	0
Known Syndromes	0	0	6	6
Multiple Anomalies	5	5	3	5

degree relatives with the same type of cleft. Data on recurrence were broken down into siblings, parents, and other relatives (see Tables 4a, b and c). A chi square was run between the racial groups, and no significant difference was found.

Discussion

The reported occurrence of clefts is distributed in a 1:2:1 ratio for CL, CLP, and CP with race not specified (Gilmore *et al.*, 1965; Fraser, 1970; Woolf *et al.*, 1963). The fact that the distribution for this study is different for both the white and black groups could result from several factors. It may reflect the distribution in the Greater Pittsburgh area, or it may reflect only the distribution of clefts in the clinic population which is in the same ratio or approximately 1:4:4 for CL, CLP and CP. It is possible that children with cleft lip only are not seen as often in the clinic because more parents elect to handle these simpler problems outside the clinic framework.

The distribution of cleft types according to sex for the white group is consistent with other studies (Woolf *et al.*, 1963; Conway and Wag-

TABLE 4a. Frequency in siblings.

	black				*white*			
	Females	%	Males	%	Females	%	Males	%
yes	1	12.5	1	7	0	0	2	3.7
no	7	87.5	13	93	30	100	52	96.3
T	8		14		30		54	

TABLE 4b. Frequency in parents

	black				*white*			
	Females	%	Males	%	Females	%	Males	%
yes	0	0	1	7	2	6.25	5	9.25
no	8	100	13	93	28		49	90.75
T	8		14		30		54	

TABLE 4c. Frequency in other relatives.

	black				*white*			
	Females	%	Males	%	Females	%	Males	%
yes	0	0	0	0	3	10	10	18.5
no	8	100	14	100	27	90	44	81.5
T	8		14		30		54	

ner, 1965; and Fraser, 1970). The distribution of clefts in the black group is consistent with that reported in one study, with more black males having cleft palate and more black females having cleft lip and palate (Gorlin, 1971).

With regard to other birth defects, it was found that almost all of the black children had associated midline defects. One possible explanation for this is that, since incidence is much lower in blacks, clefting may not be seen very often unless it is associated with other anomalies. Almost all of the defects seen are in tissue derived from mesoderm. This suggests that clefts, as well as other midline defects, may occur much earlier in development, during the differentiation and proliferation of the mesodermal germ layer. This would be consistent with the findings of Bersu *et al.* (1976) and Vij *et al.*, (1971). The isolated occurrences may be due to random environmental factors.

The white group may be exhibiting more than one type of occurrence. Several had known syndromes (Gorlin, 1971), and others exhibited isolated clefts perhaps because of random environmental factors. The occurrence of clefts from mesodermal insufficiency is the subject of our continuing research.

The proportion of blacks with recurrence in siblings appears clinically to be higher than the proportion of whites with recurrence in siblings. However, in this study, there was no significant difference between the racial groups. A study is now in progress utilizing a larger sample, a more detailed family history, and pedigree analysis in order to learn more about recurrence.

Because this investigation was a pilot study, no direct conclusions should be drawn from it. However, it is important in pointing to trends which may have an impact on counseling parents of children with clefts.

References

Altemus, L. A., and Ferguson, A. D., Comparison of incidence of birth defects in Negro and white children, *Pediatrics 3b*, 56–61, 1965.

Berlin, A. S., Classification of cleft lip and palate. In: *Communicative Disorders Related to Cleft Lip and Palate*, ed. Bzoch, K. Boston: Little, Brown and Co., 1971, 14–28.

Bersu, E. T.; Petersen, J. C.; Charboneau, W. J.; and Opitz, J. M., Studies of malformation syndromes of Man XXXX1A: Anatomical studies in Hanhart—Syndrome—A pathogenic hypothesis, *J. Ped.*, *122*, 1–

17, 1976.

Chung, C. S., and Myrianthopolous, N. C., Racial and prenatal factors in major congenital malformations, *Am. J. Hu. Gen.*, *20*, 144, 1968.

Chung, C. S., and Myrianthopolous, N. C., Birth defects, *Orig. Art. Series*, *X*, *11*, 1974.

Conway, H., and Wagner, K. J., Incidence of clefts in New York City, *Cleft Palate J.*, *30*, 286–290, 1965.

Fogh Anderson, P., *Inheritance of Cleft Lip and Palate.* Copenhagen: Busck, 1942.

Fraser, F. C., Genetics of cleft lip and palate, *Am. J. Hu. Gen.*, *22*, 336–352, 1970.

Gilmore, S., and Hofman, S., Clefts in Wisconsin: Incidence and related factors, *Cleft Palate J*, *3*, 186–199, 1966.

Gorlin, R. J.; Cervenka, J.; and Pruzansky, S., Facial clefting and its syndromes, *Birth Defects Orig. Art. Series*, *7*, *7*, 1971.

Graber, T. M., Cranio-facial and dental development, In: *Human Development*, ed. Falkner F. Philadelphia: W. B. Saunders, 1966, 510–511.

Patten, B. M., Normal development of the facial region, In: *Congenital Anomalies of the Face and Associated Structures*, ed. Pruzansky S. Springfield, Ill.: Charles C Thomas, 1961, 84–91.

Stark, R., Pathenogenesis of hare lip and palate. *Plast. Reconstr. Surg.*, *13*, 20, 1954.

Stark, R., Cleft lip and Palate, In: *Congenital Anomalies of the Face and Associated Structures*, ed. Pruzansky S. Springfield, Ill.: Charles C Thomas, 1961, 6–83.

Woolf, C. M.; Woolf, R. M.; and Broadbend, J. R., A genetic study of cleft lip and palate in Utah, *Am. J. Hu. Gen.*, *2*, 209, 1965.

Vij, S., and Kanagasuntheram, R., Cleft palate and associated anomalies in a 30 mm. C.R. length human embryo, *Cleft Palate J*, *18*, 409–414, 1971.