ARTICLE

The epidemiology of cystic fibrosis in the Western Cape province

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Objectives. To determine the incidence and prevalence of cystic fibrosis (CF) among populations of the Western Cape province of South Africa.

Design and subjects. Descriptive study using data from a database of CF cases and the 1996 Census.

Measures. CF births from 1987 to 1996 and known CF patients in 1996 were compared with Census birth data and population data, respectively.

Results. The very small numbers of black African CF patients precluded estimating the epidemiology in this group. The incidences of CF for coloured and white patients were 1 in 9 845 and 1 in 2 853 live births, respectively. There was under-ascertainment of cases in non-metropolitan areas. The prevalence of CF per 100 000 of the population was 2.6 and 11 for the coloured and white populations, respectively. The estimated number of persons with CF in these two groups in South Africa in 2001 was 571.

Conclusions. CF was more common in the coloured population and less common in the white population than previously estimated. Under-diagnosis occurred in non-metropolitan areas in both groups.

Cystic fibrosis (CF), an inherited disease of exocrine glands, occurs in all of South Africa's population groups.[1] In the 1980s, Hill *et al.*[2] explored the incidence and prevalence of the condition among white and coloured populations, the only groups then known to have CF. The incidence figures, based on the 12 white and 8 coloured children with CF born in the western part of the then Cape Province between 1980 and 1983, were 1:2 027 and 1:12 305 live births, respectively. It was noted that under-recognition of CF in the coloured population was likely.

In the light of the small number of incident cases and an increasing proportion of coloured CF patients attending CF services in Cape Town, a re-appraisal of the epidemiology of CF among white and coloured populations was carried out using data from the 1990s. The very small numbers of black African CF patients precluded estimating the epidemiology in this group.[3]

Methods

The number of coloured and white children born with CF in the Western Cape province in each of the years from 1987 to 1996 was determined using data on year and place of birth from a database of CF patients in the province maintained at Red Cross War Memorial Children's Hospital (RCCH) that records details of patients born since 1974.[4] Details of the database composition and maintenance are given elsewhere;[4] every effort was made to identify all persons with CF in the province. Group classification (coloured or white) was assigned as on the hospital sticker. Birth data for the province were based on the 1996 Census.[5] The number of children between the ages of 0 and 9 years were tabulated in two 5-year groups (0 - 4 and 5 - 9 years). These figures were equated with the number of live births in those 5-year periods and the overall 10-year period. It was assumed that under-5 mortality would not have altered the figures significantly as childhood mortality was relatively low in these two groups.[6] The Western Cape was divided into two parts: Cape Metropole (Western Cape province Census areas 1 - 7, i.e. Bellville, Cape, Goodwood, Kuilsrivier, Mitchell's Plain, Simonstown, Wynberg) and non-Cape Metropole (all other areas) using the Census areas.

Incidence and carrier rates for CF (with 95% confidence intervals (CIs)) were computed. The two 5-year periods were examined separately to determine if there was consistency in the incidence rates.

Prevalence rates were determined for 1996. This was a Census year, allowing accurate determination of the coloured and white populations of the Cape Metropole and other areas of the Western Cape province.[5] 1996 was also the year in which a study of transition to adult-oriented care in CF was undertaken.[7] This required the names of all adults and older adolescents with CF attending the CF clinics at Groote Schuur Hospital. This, together with the RCCH database, allowed the ascertainment of almost all patients with CF in the province and their addresses. Prevalence is reported as the number of CF cases per 100 000 of the population.

Results

The incidence and carrier rates for CF are given in Table I. The proportion of CF births in non-Cape Metropole areas was the same for the two groups (8/32 coloured; 4/24 white).

There was a significant difference in the incidence of CF between the white and coloured groups ($p < 10^{-5}$). If the Cape Metropole figures are taken as representing the true incidences of CF as suggested by Hill *et al.*,[2] the difference remained ($p < 10^{-5}$).

The prevalence rates for CF are given in Table II. One hundred and ten CF patients were known to be living in the province in 1996. Only one of these was a black African. Forty-one were coloured and 68 white.

TABLE I. INCIDENCE AND CARRIER RATES FOR CYSTIC FIBROSIS IN THE WESTERN CAPE PROVINCE

	Periods					
	1992 - 1996		1987 - 1991		1987-1996	
	Coloured	White	Coloured	White	Total coloured	Total white
Non-Cape Metropole areas						
Number of births	114 089	17 273	113 989	21 839	228 078	39 112
CF births	8	2	0	2	8	4
Incidence	1:14 261	1:8 637		1:10 920	1:28 510	1:9 778
95% CI					1:16 835 - 1:92 593	1:4 950*
Carrier rate	1:60	1:46		1:52	1:84	1:49
95% CI					1:65-1:152	1:35*
Cape Metropole areas						
Number of births	114 754	27 251	121 524	29 815	236 278	57 066
CF births	10	11	14	9	24	20
Incidence	1:11 475	1:2 477	1:8 680	1:3 313	1:9 845	1:2 853
95% CI					1:7 042 - 1:16 420	1:1 984 - 1:5 076
Carrier rate	1:54	1:25	1:47	1:29	1:50	1:27
95% CI					1:42 - 1:64	1:22-1:36
Western Cape province						
Number of births	228 843	44 524	235 513	51 654	464356	96178
CF births	18	13	14	11	32	24
Incidence	1:13 461	1:3 710	1:16 822	1:4 695	1:14511	1:4007
95% CI					1:22 222 - 1: 10 775	1:2 865 - 1:6 667
Carrier rate	1:58	1:30	1:65	1:34	1:60	1:32
95% CI					1:52-1:75	1:27-1:41

*Only lower CI calculable.
CF = cystic fibrosis; CI = confidence interval.

TABLE II. PREVALENCE OF CYSTIC FIBROSIS IN THE WESTERN CAPE PROVINCE IN 1996

	Population group		
	Coloured	White	Total population
Non-Cape Metropole areas			
Population	1 016 443	331 247	1 347 690
CF patients	12	14	26
Prevalence rate/ 100 000	1.2	4.2	1.9
Cape Metropole areas			
Population	1 129 668	490 303	1 619 971
CF patients	29	54	83
Prevalence rate/ 100 000	2.6	11	5.0

CF = cystic fibrosis.

Discussion

This study presents a revision of the CF epidemiology among the coloured and white populations of the Western Cape province. The figures are based on a longer period and a larger number of incident cases than the original study.[2] They are based on a database of cases that went up to 2006. The great majority of CF cases among the groups under study would have been diagnosed by the age of 7 years, increasing the validity of the incidence figures for a period that ended 10 years before.

Birth incidence figures may be influenced by a number of factors. This study uses clinical identification rather than any form of screening. Newborn and couple screening (except where there is a family history of CF) does not occur in this area. Any systematic under-ascertainment of clinical cases would have distorted the figures. This is particularly possible in the coloured group, where infant death even in diagnosed cases of CF has been a problem.[8] In both groups, cases diagnosed in adults would not be reflected in the incidence figures, but this has not been a common phenomenon in the Western Cape province.

The study confirms the difference in the incidence of CF between the coloured and white population groups first shown by Hill *et al.*,[2] It also shows an apparently lower incidence of CF in non-Cape Metropole areas. There is no biological explanation for the difference in incidence as the urban and rural populations in these two groups largely come from the same stock so, as suggested by Hill *et al.*,[2] under-ascertainment is the most reasonable explanation for this. The true incidences of CF are likely to approximate to those found in the Cape Metropole.

The incidence figures were similar to but not the same as those from the early 1980s.[2] The incidence in the coloured population

CF was more common in the coloured population and less common in the white population than previously estimated.

TABLE III. EXPECTED NUMBERS OF COLOURED AND WHITE PERSONS WITH CYSTIC FIBROSIS IN SOUTH AFRICA IN 2001

	Coloured		White		Total
	Population	Persons with CF	Population	Persons with CF	Persons with CF
Eastern Cape	478 807	12	304 506	33	45
Free State	83 193	2	238 791	26	28
Gauteng	337 974	8	1 758 398	193	201
KwaZulu-Natal	141 887	4	483 448	53	57
Limpopo	10 163	0	126 276	14	14
Mpumalanga	22 158	1	203 244	22	23
Northern Cape	424 389	11	102 043	11	22
North West	56 969	1	244 035	27	28
Western Cape	2 438 976	61 (95% CI: 46 - 76)	832 901	92 (95% CI: 75 - 113)	153 (95% CI: 129 -177)
Total	3 994 516	100 (95% CI: 80 - 119)	4 293 642	471 (95% CI: 429 - 515)	271 (95% CI: 523 - 617)

was 16% lower in the earlier study. More confidence can be placed in the new figure of 1:9 845 live births as the greatly reduced 95% CI indicates (Table I). The equivalent 95% CI in the earlier study was 1:7 246 to 1:40 000. For the white population, CF would appear to have been less common that the earlier figures suggested. The lower limit of the 95% CI for the 1987 - 1996 incidence was almost the same as the incidence of 1:2 027 given by Hill *et al.*,[2] These new rates have implications for counselling for CF risk in these groups.

The white population of South Africa, though having some admixture from other groups, is largely descended from European Caucasoids. Most of these antecedents were from the northern countries of Europe. Dodge *et al.*, in a thorough multicentre attempt to count every CF patient in the UK, found an incidence of 1 in 2 415 live births.[9] This figure is encompassed by the 95% CI for white CF births in Cape Town. An incidence of 1 in 3 200 has been proposed for France based on three sites of neonatal screening.[10] South Africa's white Afrikaner population, particularly in the Western Cape province, is partly made up of descendants of French Huguenots who migrated to South Africa in the 17th century. This incidence is also compatible with that among South African whites. The Netherlands is the origin of a significant proportion of the Afrikaner population of South Africa. Recent data using the ΔF508 mutation in 11 654 blood donors has suggested that the CF carrier frequency there is 1 in 32 (95% CI 1 in 28 to 1 in 36), lower than the quoted European average of 1 in 25.[11] The South African incidence found in this Cape Town study lies between the two and the 95% CI spans both. It would therefore seem that the South African incidence and carrier rates for CF for the white population correlate with those of the countries from which this population is largely derived, and are not as high as Hill *et al.* suggested.[2] There is therefore no sign of genetic drift or heterozygote advantage or disadvantage for this disease in South Africa.

Higher rural mortality may be a factor in the higher CF prevalence in urban areas.

If the Cape Metropole area incidences are applied to the non-Cape Metropole areas and if full case ascertainment in the Cape Metropole is assumed, 4 - 5 coloured and 3 - 4 white babies with CF (7 - 9 babies in all) were born each year in the province in the period under review. Comparison with the ascertained cases shown in Table I suggests that annually between 2 and 4 cases of CF were missed outside Cape Town.

Prevalence rates for CF depend on the number of cases diagnosed and their survival. There was a 3.4-fold difference in the incidence of CF between the white and coloured groups, but the difference in prevalence of CF was greater: over 4-fold higher in the white group than in the coloured group. Higher early mortality in the coloured group, as demonstrated in a study of the prognosis of CF in the Western Cape province,[7] is likely to explain this greater difference. Inward migration by relatively affluent white CF patients is another potential explanation for this phenomenon, though such migration is likely to have been matched by emigration in the volatile early 1990s.

For both groups, CF prevalence was about 2.5 times lower in rural than urban areas. This urban/rural difference in prevalence rates probably reflects the under-ascertainment demonstrated by the incidence data, but higher rural mortality may also be a factor.

The prevalence data make it possible to estimate the number of persons with CF from the coloured and white groups in South Africa. Population data from the 2001 Census[12] suggest that there would have been 100 coloured and 471 white persons with CF in the country in 2001 (Table III). Table III shows that 61 (95% CI 46 - 76) coloured CF patients would be expected in the Western Cape province. Thirty-nine cases were known, suggesting that, even in 2001, CF was being missed in this group, presumably largely in non-Cape Metropole areas.

Professor Michele Ramsay and the late Professor John Ireland are acknowledged for their helpful advice.

References

1. Goldman A, Graf C, Ramsay M, Leisegang F, Westwood ATR. Molecular diagnosis of cystic fibrosis in South African populations. *S Afr Med J* 2003; 93: 518-519.
2. Hill ID, MacDonald WB, Bowie MD, Ireland JD. Cystic fibrosis in Cape Town. *S Afr Med J* 1988; 73: 147-149.
3. Westwood T, Brown R. Cystic fibrosis in black patients: Western Cape experiences. *S Afr Med J* 2006; 96: 288-289.

4. Westwood ATR. Cystic fibrosis in the Western Cape province: Clinical and epidemiological aspects. Chapter 2. MD thesis, University of Cape Town, 2005.
5. Community profiles. Census 1996 CD ROMs. Pretoria: Statistics SA, 1998.
6. *South African Health and Demographic Survey*. Pretoria: Department of Health, 1998.
7. Westwood ATR, Henley LD, Willcox P. The transition from paediatric to adult care for persons with cystic fibrosis: patient and parent perspectives. *J Paediatr Child Health* 1999; 35: 442-445.
8. Westwood ATR. The prognosis of cystic fibrosis in the Western Cape region of South Africa. *J Paediatr Child Health* 1996; 32: 323-326.
9. Dodge JA, Morison S, Lewis PA, *et al*. Incidence, population, and survival of cystic fibrosis in the UK, 1968-95. UK Cystic Fibrosis Survey Management Committee. *Arch Dis Child* 1997; 77: 493-496.
10. Farriaux JP, Dorche C, Travert G. La mucoviscidose: quelle incidence? *Arch Fr Pediatr* 1993; 50: 540-541.
11. de Vries HG, Collee JM, de Walle HE, *et al*. Prevalence of delta F508 cystic fibrosis carriers in The Netherlands: logistic regression on sex, age, region of residence and number of offspring. *Hum Genet* 1996; 99: 74-79.
12. *Statistics South Africa Census 2001: Census in Brief*. Pretoria: Statistics South Africa, 2003.