



## Incidence of acute lymphoblastic leukaemia in white and coloured children in the Western Cape

P B Hesselning, P Hartley, L Zietsman, S van Lill, S Preston-Martin, G Wessels

**Objectives.** To record the age-specific incidence rate (ASIR) for diagnosed acute lymphoblastic leukaemia (ALL) in coloured and white children aged 0 - 12 years in the Western Cape (WC).

**Design.** A retrospective population-based study using the 1991 population census to calculate the mean annual childhood population and the ASIR for ALL in the 0 - 4, 5 - 9 and 10 - 12-year age groups in rural and Cape Town metropolitan areas for the period 1983 - 1999. Odds ratios were calculated using EpiInfo 2000.

**Setting.** Registry records of the paediatric cancer units at Tygerberg and Red Cross War Memorial Children's hospitals where all children with ALL in the WC were initially treated.

**Subjects.** All white and coloured children aged 0 - 12 years diagnosed as having ALL from 1983 - 1999.

**Outcome measures.** The ASIR by age and ethnic group in rural and metropolitan patients in the WC.

**Results.** The estimated annual childhood population in 1991 was 709 151 with 80.4% coloured and 19.6% white children, of whom 60% were resident in the Cape Town metropolitan area and 40% in the rural area of the WC. Of 246 children with

ALL diagnosed in the period 1983 - 1999, 144 were male and 102 female. The ASIR in coloured children aged 0 - 4 years was 17.1/10<sup>6</sup> in the rural and 30.5/10<sup>6</sup> in the metropolitan area, compared with 55.7/10<sup>6</sup> and 56.2/10<sup>6</sup> respectively in white children. In the 5 - 9-year age group the ASIR in coloured children was 10.0/10<sup>6</sup> in the rural and 16.6/10<sup>6</sup> in the metropolitan area compared with 27.6/10<sup>6</sup> and 26.7/10<sup>6</sup> respectively in white children. The 10 - 12-year age group had comparable incidence rates in both populations and geographical areas. Only one case occurred within a 20 km radius of the Koeberg nuclear reactor.

**Conclusions.** White children have an ASIR for ALL comparable to rates of diagnosis in the USA, while only half as many coloured children aged 0 - 9 years were diagnosed in both the rural and metropolitan areas. This contrast may indicate significant underdiagnosis of ALL in coloured children over the period in question. The change in health policy since 1994, which has improved access to primary health care, may improve the rate of diagnosis among coloured and black children.

*S Afr Med J* 2004; **94**: 533-536.

Acute lymphoblastic leukaemia (ALL) is the most common childhood cancer in South Africa.<sup>1</sup> Patients with ALL have an overall event-free survival probability above 75% when treated with modern chemotherapy and optimal supportive care.<sup>2</sup> A survey of children treated at all the children's cancer centres in South Africa recorded an estimated crude mean annual incidence rate of 76 new cases of cancer per million children aged below 15 years for the period 1986 - 1991.<sup>1</sup> However, this

survey had many limitations. This figure compares with an age-standardised rate (ASR) in Europe which varied between 124.9/10<sup>6</sup> and 158.7/10<sup>6</sup> in children aged below 15 years per annum respectively in the UK and Denmark for the period 1980 - 1990.<sup>3,4</sup> If South African rates are comparable to rates in the UK and Denmark, the possible implication of this survey is that only half of the children who developed cancer in South Africa during that period were diagnosed and treated.

Epidemiological surveys of acute leukaemia in what was originally the greater Cape Province (subsequently divided into the Western, Eastern and Northern Cape provinces) for the periods 1978 - 1985 and 1987 - 1991 recorded an age-specific annual rate for ALL of 20/10<sup>6</sup> in white children and 12/10<sup>6</sup> in coloured children in the 0 - 9-year age group.<sup>5,6</sup> Between 1985 and 1989 the ASR for ALL was 33.7/10<sup>6</sup> in children in the USA aged 0 - 14 years.<sup>7</sup> The ASR for ALL in children in the USA aged 0 - 18 years increased from 27.2/10<sup>6</sup> in 1975 to 34.5/10<sup>6</sup> in 1997.

The age-specific incidence rates (ASIR) for ALL in the new Western Cape Province (WC) in the age categories 0 - 4, 5 - 9 and 10 - 14 years in the white and coloured population are

*Department of Paediatrics, Tygerberg Hospital, University of Stellenbosch, W Cape*

**P B Hesselning, MD**  
**S van Lill, MSc**  
**G Wessels, MD**

*Red Cross War Memorial Children's Hospital, University of Cape Town*

**P Hartley, FCP (SA) (Paed)**

*Department of Geography and Environmental Studies, University of Stellenbosch, W Cape*

**L Zietsman, PhD**

*Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, USA*

**S Preston-Martin, PhD**



unknown. This information is essential for the planning and provision of cancer treatment in this province. We are concerned that a large number of children with a potentially curable disease may not be diagnosed and hence never receive treatment. The only nuclear power plant in South Africa has been in operation at Koeberg on the rim of metropolitan Cape Town since 1975. There has been much debate in England about the possible risk of emissions from such plants inducing leukaemia and lymphoma in adjacent populations.<sup>8</sup>

There has been a large influx of black people into the WC in the past 10 years. Black parents from neighbouring provinces often send their children to relatives in Cape Town for specialist medical treatment. This migration factor made it impossible in this retrospective study to verify the residential addresses of all the black children with ALL treated at the same institutions in this period, so it was impossible to include black children in this analysis.

Children aged 0 - 12 years who developed ALL during the study period in the WC were predominantly treated at the paediatric cancer units in the two academic hospitals, viz. Tygerberg and Red Cross War Memorial Children's hospitals, and both units have kept a registry of all new cases. This common procedure made it possible to calculate the ASIR for diagnosed ALL in white and coloured children aged 0 - 4, 5 - 9 and 10 - 12 years for the period 1983 - 1999.

## Patients and methods

All coloured and white children aged 0 - 12 years with a diagnosis of ALL confirmed on a bone marrow aspirate who presented at Tygerberg Hospital and Red Cross Children's Hospital in the period 1983 - 1999 were included in the study. The residential address was noted. The 1991 national population census and magisterial district demarcation were used. 1991 was the midpoint of the study period and the 1991 population was taken as the average population for every year of the study. Patients were geographically divided as living in the Cape Town metropolitan area (combined districts of Bellville, Cape Town, Goodwood, Kuilsriver, Simonstown and Wynberg), or in a rural area (all the remaining magisterial districts) in the WC.

Patients were divided into the 0 - 4, 5 - 9 and 10 - 12-year age groups at the time of diagnosis. It was not possible to include children aged 13 and 14 years to constitute the 10 - 14-year age group because the majority of children with ALL aged 13 - 14 years were treated by adult physicians at a number of different hospitals that have not all maintained the records needed for this study.

This investigation was approved by the Ethical and Scientific Review Board of the Faculty of Health Sciences at the University of Stellenbosch.

## Statistical methods

Calculation of ASRs was performed according to the direct method, using the distribution of the World Standard Population<sup>9</sup> and the 1991 South African population census. For calculation of the ASR in the 10 - 12-year age group, the number 5 400 was used as the World Standard (E Kramarova — personal communication, International Agency for Research on Cancer (IARC), Lyon France).

The 1991 census's white and coloured populations were divided into metropolitan and rural inhabitants by grouping of census districts.

Odds ratios were calculated using Statcalc of the EpiInfo 2000 program to discern whether area (metropolitan or rural), population groups, age groups (0 - 4, 5 - 9 and 10 - 12 years), or gender were significantly related to being diagnosed with ALL.

The ASIR is the crude incidence rate recorded in a specific age group, e.g. below 1 year, 1 - 4 years, 5 - 9 years and 10 - 12 years. The ASIR is used to calculate the ASR, which is an incidence rate that has undergone statistical transformation in order to permit comparison between groups differing in some characteristics, for example age.

## Results

The total calculated annual childhood population in the WC for the reference year 1991 consisted of 709 151 (19.4% white and 80.6% coloured) children aged 0 - 12 years, with 50.4% males and 49.6% females. The metropolitan population consisted of 371 556 (21.7% white and 78.3% coloured) children, and the rural population of 337 595 (16.8% white and 83.2% coloured) children. ALL was diagnosed in 246 children during the study period, with 144 (59%) boys and 102 (41%) girls and a male/female ratio of 1.4. Sixty per cent of these children lived in the metropolitan and 40% in the rural areas. The number of new cases per year is illustrated in Fig. 1. The ASIRs for the metropolitan and rural patients and the odds

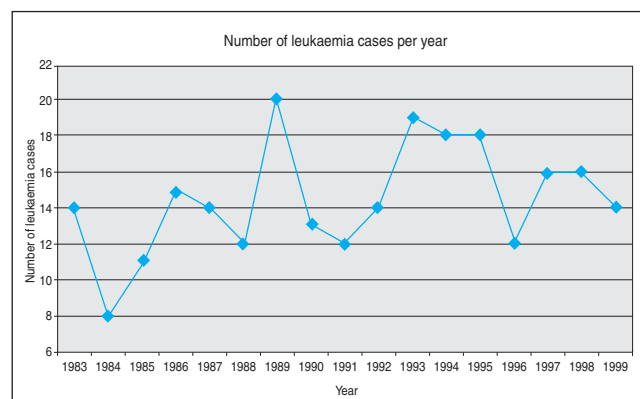


Fig. 1. Number of leukaemia cases per year in the Western Cape, South Africa (1983 - 1999).



Table I. Age-standardised incidence rates (ASIRs) for ALL in the Cape Town metropolitan area

Age group (years)	Coloured children		White children		Odds ratio White/coloured	p-value
	Number	Rate/10 <sup>6</sup>	Number	Rate/10 <sup>6</sup>		
0 - 4	58	30.5	28	56.2	1.84 (1.14 - 2.95)	0.007
5 - 9	33	16.6	15	26.7	1.60 (0.83 - 3.05)	0.126
10 - 12	10	9.4	3	9.7	1.02 (0.22 - 4.0)	0.975
Total	101	20.4	46	33.5		

Table II. Age-standardised incidence rates (ASIR) for ALL in Western Cape rural areas

Age group (years)	Coloured children		White children		Odds ratio White/coloured	p-value
	Number	Rate	Number	Rate		
0 - 4	32	17.1	19	55.7	3.26 (1.78 - 5.93)	< 0.000
5 - 9	19	10.0	11	27.6	2.75 (1.23 - 6.08)	0.005
10 - 12	15	14.9	3	13.4	0.89 (0.21 - 3.27)	0.858
Total	66	13.8	33	41.3		

ratio for white children compared with coloured children to be diagnosed, are given in Tables I and II.

The ASIR in white children in the 0 - 4 and 5 - 9-year age categories is approximately double that of coloured children in both the metropolitan and rural areas. In the small group of patients aged 10 - 12 years, however, the ASIR was similar for white and coloured children in the metropolitan and rural areas. The odds ratio for diagnosis in metropolitan white children in the 0 - 4-year age group compared with coloured children was 1.84 (95% CI: 1.14 - 2.95,  $p < 0.007$ ). The nuclear reactor at Koeberg in the WC started to produce electricity in 1984. Only one case of leukaemia was recorded within a 20 km radius of Koeberg during the 17-year study period.

## Discussion

The ASIR in white children in the WC was higher than the rates previously recorded in the larger old Cape Province, and is comparable with rates for the 0 - 4 and 5 - 9-year age groups in Western Europe.<sup>3,4</sup> Coloured children aged 0 - 9 years have a lower ASIR than white children in both the metropolitan and rural areas. This difference is more pronounced in rural patients. The rate of diagnosis in coloured urban children was far higher than that for coloured rural children. The ASIR for ALL in North American children aged 10, 11 and 12 years was 21, 19 and 17 per million respectively for the period 1984 - 1994.<sup>7</sup> The ASIR in our patients aged 10 - 12 years was lower than that of North American children but similar for both ethnic groups. It is difficult to explain the lower ASIR in rural coloured children solely on the basis of poor accessibility to health services in the rural areas because the lower ASIR in

coloured children was also present in the metropolitan area. According to the 1996 national population census the average monthly income per person (10% sample) was R637.21 for the coloured and R2 679.93 for the white populations. In the same census it was found that when comparing coloured and white adults, 11% versus 4% had had no schooling, 8% versus 27% had completed secondary school and 4% versus 24% had completed tertiary education respectively. A socio-economic analysis of the families of 81 coloured newly diagnosed children with cancer admitted to Tygerberg Hospital from 1989 to 1993 revealed that 17% of parents were totally illiterate, more than 50% were totally dependent on public transport, and 35% of rural families earned less than the equivalent of under US\$150 per month.<sup>10</sup> Health services at primary, secondary and tertiary level in the public sector were available free of charge to poor people in this period. One could speculate that poor parental education and poor socio-economic status may have contributed to less than effective utilisation of available resources. Another possible factor may be the failure of health workers at primary health care level to suspect leukaemia when a child presents with bruising, lymphadenopathy or splenomegaly, or to refer the child for investigation. This inference suggests an educational challenge, because childhood cancer is a rare disease, and has to be envisaged as a potential diagnosis amid a very high local incidence of infectious diseases such as tuberculosis and HIV/AIDS in young children. Poor families will mostly use a state primary health care facility when a child is not well while more affluent families will primarily consult a private physician. The fact that an internationally comparable ALL rate was recorded in white children, however, suggests that the necessary medical and



diagnostic skills are indeed available in this province to diagnose all children with ALL.

The assumption that the ASIR for coloured and white children should be identical may also be incorrect. In the USA the Surveillance, Epidemiology and End Results (SEER) programme<sup>11</sup> rates analysis for the period 1973 - 1998 in children with ALL aged 0 - 19 years showed that the ASR for all children was 28/10<sup>6</sup>, with a rate of 27/10<sup>6</sup> in whites, 15/10<sup>6</sup> in blacks and 43/10<sup>6</sup> in Hispanics.

However if we assume that there are no genetic or environmental reasons to explain this observed difference, more than half the coloured children with ALL in the WC are not diagnosed. Only one case of ALL occurred within a 20 km radius of Koeberg nuclear reactor during 17 years, and there is no evidence from continuous monitoring that this reactor to date has exposed the public to harmful emissions. We have documented a very low ASIR of ALL in coloured children in the WC, and have no data for black children. A prospective long-term provincial and national childhood cancer registry is the only valid method to answer these questions. In the meantime two issues should be addressed. Firstly, the chance of being diagnosed at a primary health care service, which is the first visit point for most coloured and black children, should be improved by nurse training and incorporation of the recognition of early signs of cancer in the integrated management of childhood illness (IMCI) training programmes. Secondly, the Ministry of Health should note these findings, support a national childhood cancer registry and utilise

registry data to plan and provide appropriate services for the diagnosis and treatment of childhood cancer.

The authors received financial assistance from the Yvette Naude Research Fund. Dr Preston-Martin's involvement in this project was supported by grant number 1FO6TW02352 from the Fogarty International Centre.

#### References

1. Cockcroft RL. SACCSG-Cancer Registry Report 1987-1993. In: Hesselting PB, Wessels G, eds. *Proceedings of the First Continental Meeting of the International Society of Paediatric Oncology in Africa 1994*. Stellenbosch: Stellenbosch University Press, 1995: 14-16.
2. Gustafsson G, Lie SO. Acute leukaemias. In: Youte PA, Kalifa C, Barret A, eds. *Cancer in Children, Clinical Management*. Oxford University Press, 1998: 107-108.
3. Sharp L, Gould A, Harris V, et al. Scottish Cancer Registry 1981-1990. In: Parkin DM, Kramarova E, Draper GJ, et al., eds. *International Incidence of Childhood Cancer*. Lyon: IARC Scientific Publications, 1999: 369-371.
4. Storm H, Lecker S, Manders T. Danish Cancer Registry 1983-1991. In: Parkin DM, Kramarova E, Draper GJ, et al., eds. *International Incidence of Childhood Cancer*. Lyon: IARC Scientific Publications 1999: 253-255.
5. Sayer GM, Rip MR, Jacobs P, et al. Epidemiology of acute leukaemia in the Cape Province of South Africa. *Leuk Res* 1992; **16**: 961-966.
6. Hartley PS, Karabus CD, Werner ID, Wessels G, Stones DK. Incidence of childhood cancer in the Eastern, Western and Northern Cape Provinces of South Africa (abstract). *Medical and Pediatric Oncology* 2000; **35**: 282.
7. Smith MA, Gloeckler Ries LA. Childhood cancer: Incidence, survival and mortality. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 4th ed. Philadelphia: Lippincott Williams and Wilkins, 2002: 1-12.
8. Gardner MJ, Snee MP, Hall AJ, et al. Results of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria. *BMJ* 1990; **300**: 423-429.
9. Dos Santos Silva I. *Cancer Epidemiology: Principles and Methods*. Lyon: International Agency for Research on Cancer, 1999.
10. Louw H. The socio-economic status of children with cancer treated in Tygerberg Hospital and other factors influencing discharge. In: Hesselting PB, Wessels G, eds. *Proceedings of the First Continental Meeting of the International Society of Paediatric Oncology in Africa 1994*. Stellenbosch: Stellenbosch University Press, 1995: 99-101.
11. McNeil DE, Cote TR, Clegg L, Mauer A. Seer update of incidence and trends in pediatric malignancies: Acute lymphoblastic leukaemia. *Med Pediatr Oncol* 2002; **39**: 554-557.