Chapter 9

Population-based survival from breast and cervical cancer and lymphoreticular malignancies in Bangalore, India

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Introduction

Population-based cancer registration in the Bangalore urban agglomeration began in 1982 under the National Cancer Registry Programme of India, sponsored by the Indian Council of Medical Research. The registry, based at the Kidwai Memorial Institute of Oncology, covers a population of 4.5 million and an area of 191.2 km^2. Bangalore, the capital of Karnataka state in south India, is located at an altitude of 914 m above sea level, at latitude 12°58′N and longitude 77°38′E (Fig. 1). It is rapidly growing and is well known for high-technology industries, particularly computer software.

The registry has reported incidence data since 1982 in annual reports and in the reports published by the National Cancer Registry Programme. Incidence data were also published in Volumes V–VII of *Cancer Incidence in Five Continents* (Muir *et al.*, 1987; Parkin *et al.*, 1992, 1997). The registry has proved to be a valuable base for epidemiological and clinical investigations, as well as providing valid information for the Karnataka state cancer control programme.

The Coordinating Unit of the National Cancer Registry Programme, based at the Kidwai Memorial Institute of Oncology, and the Bangalore population-based cancer registry actively followed up cases of cancer in selected sites for the purposes of the survival study, once the routine registry operations concerning incident case-finding had stabilized. The survival experience of patients with breast cancer, uterine cervical cancer, Hodgkin's disease, non-Hodgkin lymphoma, multiple myeloma and leukaemia in our population are described in this report.

Figure 1. Map showing location of Bangalore

Cancer registration

Cancer registration is carried out by active case-finding carried out by 'social investigators' from the registry, who visit the various sources of data to identify incident cancer cases. The registry staff, who are university graduates in biological sciences or social sciences, have been trained or retrained in-house and in courses and workshops covering all aspects of cancer registration, organized by the National Cancer Registry Programme.

The social investigators collect information on a standard form, which is then returned to the registry for further processing. The registry has identified 30 large hospitals and 200 small hospitals as potential sources of data, and these are visited by the registry staff on a regular schedule. The Kidwai Memorial Institute of Oncology, where the registry is

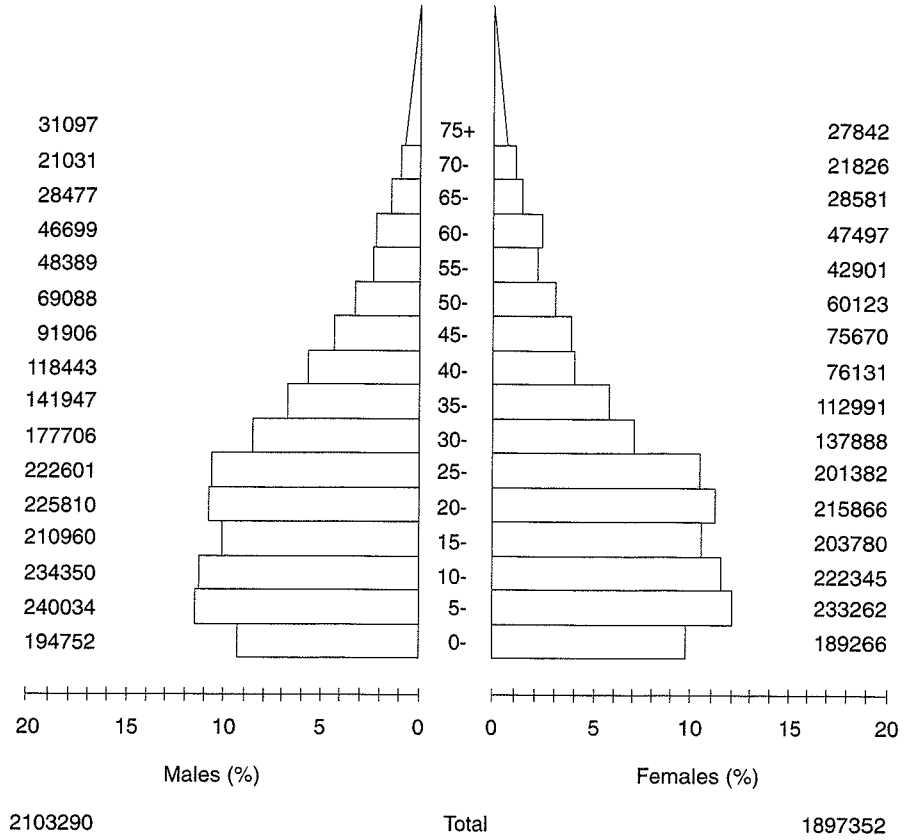

Figure 2. Average annual population of Bangalore, 1988–92

based, is the largest source of data, accounting for two-thirds of registered cases. Records of deaths from all causes are scrutinized at 14 municipal corporation units and information on cancer deaths is abstracted. By means of personal data, these are matched with the incident cancer database. Efforts are made to trace back the unmatched cases to hospital records; if this is not successful, they are registered as 'death certificate only' (DCO) cases.

Information obtained from these various sources are processed and merged together in the registry. Data are coded using the manual of the National Cancer Registry Programme (National Cancer Registry Programme, 1987). The primary site and morphology are coded using the *International Classification of Diseases for Oncology,* First Edition (ICD-O) (WHO, 1976). The data are entered into the computer and further consistency checks and analyses are carried out in the registry. Internal quality control measures are regularly carried out. The registry staff are supervised by a medical officer, who is responsible for the quality of the data. The data are reported using the *International Classification of Diseases, Ninth Revision* (ICD-9) codes (WHO, 1978). The data from the registry are reviewed annually in a review meeting of the National Cancer Registry Programme.

Cancer incidence in Bangalore

Table 1 gives the number of cases registered, average annual crude rates and age-standardized incidence rates for the period 1988–92 by sex and various cancer sites. Fig. 2 shows the age structure of the population, from which the incidence rates are calculated. The average annual crude and age-standardized incidence rates for all sites in males were 64.7 and 99.8 per 100 000 person-years; in females, they were 81.4 and 119.5 respectively.

The major cancer sites in males were the stomach (9.9%), oesophagus (8.3%), lung (7.4%), prostate (4.3%) and larynx (4.0%). Mouth and tongue cancer together accounted for 6.2% of the cases. Among females the common cancers were

Table 1. Annual cancer incidence per 100 000 person-years in Bangalore, India, 1988–92

	MALES			FEMALES		
Site	Number	Crude rate	ASR	Number	Crude rate	ASR
Lip	11	0.1	0.2	10	0.1	0.2
Tongue	228	2.2	3.5	70	0.7	1.2
Salivary gland	42	0.4	0.6	30	0.3	0.4
Mouth	188	1.8	2.8	534	5.6	8.9
Oropharynx	136	1.3	2.2	31	0.3	0.5
Nasopharynx	30	0.3	0.3	19	0.2	0.2
Hypopharynx	366	3.5	5.8	69	0.7	1.1
Oesophagus	557	5.3	8.8	501	5.3	8.5
Stomach	666	6.3	10.3	321	3.4	5.1
Colon	162	1.5	2.4	128	1.3	2.0
Rectum	212	2.0	3.1	172	1.8	2.8
Liver	185	1.8	2.7	80	0.8	1.3
Gallbladder	36	0.3	0.5	41	0.4	0.7
Pancreas	95	0.9	1.5	54	0.6	0.9
Larynx	267	2.5	4.3	37	0.4	0.6
Lung	495	4.7	8.1	103	1.1	1.7
Bone	97	0.9	1.0	81	0.9	0.9
Connective tissue	74	0.7	0.9	66	0.7	0.9
Melanoma of skin	21	0.2	0.3	14	0.1	0.2
Other skin	104	1.0	1.5	90	0.9	1.4
Breast	18	0.2	0.3	1381	14.6	21.3
Cervix uteri				1732	18.3	27.2
Corpus uteri				118	1.2	1.9
Ovary				293	3.1	4.3
Prostate	289	2.7	4.7			
Testis	50	0.5	0.5			
Penis	98	0.9	1.4			
Bladder	217	2.1	3.3	46	0.5	0.8
Kidney	78	0.7	1.2	45	0.5	0.7
Brain	262	2.5	3.1	132	1.4	1.6
Thyroid	92	0.9	1.1	233	2.5	3.2
Hodgkin's disease	122	1.2	1.3	52	0.5	0.6
Non-Hodgkin lymphoma	281	2.7	3.7	142	1.5	2.1
Multiple myeloma	43	0.4	0.7	36	0.4	0.6
Lymphoid leukaemia	103	1.0	1.1	54	0.6	0.7
Myeloid leukaemia	161	1.5	1.9	127	1.3	1.6
All sites	6808	64.7	99.8	7719	81.4	119.5
All sites except skin	6704	63.7	98.3	7629	80.4	118.1

ASR: Age-standardized incidence rate (world population)

uterine cervix (22.7%), breast (18.1%), mouth (7.0%), oesophagus (6.6%) and stomach (6.6%). The highest age-standardized incidence rate of mouth cancer and the second highest rate for oesophageal cancer in females in the world are observed in Bangalore. The male-to-female ratio of age-standardized incidence rates in Bangalore is 0.3:1 for mouth cancer and 0.97:1 for oesophageal cancer. There is a declining trend in the incidence of uterine cervical cancer (Nandakumar *et al.*, 1995a). A slow but steady increase in female breast cancer has also been observed.

Cancer-related health services

Health services in Bangalore and in the state of Karnataka are predominantly provided by the health department of the state government of Karnataka. Recently, the private and voluntary sectors have participated increasingly in the provision of secondary and tertiary care, particularly in urban areas. Secondary and tertiary medical care in Bangalore are provided by 30 large hospitals and the teaching hospitals of the five medical schools. The Kidwai Memorial Institute of Oncology is the premier comprehensive cancer centre in the state, with responsibilities for cancer control. It has good facilities

Table 2. Cases of cancer registered and data quality indices, Bangalore, India, 1982–89

Site	ICD 9	No. of cases registered	Data quality indices		Cases excluded from analysis		Cases included for survival analysis	
			% DCO	% HV	DCO	Others	No.	%
Breast	174	1514	2.4		34	119	1361	89.9
Cervix	180	2422	1.2	91.7	28	239	2155	89.0
Hodgkin's disease	201	230	1.7	96.1	4	20	206	89.6
Non-Hodgkin lymphoma	200,202	482	2.5	93.8	12	42	428	88.8
Multiple myeloma	203	100	2.0	91.0	2	1	97	97.0
Lymphatic leukaemia	204	187	2.1	95.2	4	12	171	91.4
Myeloid leukaemia	205	287	3.1	96.2	9	8	272	94.8
All leukaemia	204-8	586	5.0	91.5	29	23	534	91.1

DCO: Death certificate only; HV: Histological verification

for cancer diagnosis and therapy and provides services for 10 000 new cancer patients per year. Facilities for cancer surgery exist in several hospitals in the city; radiotherapy is provided in six hospitals besides the Kidwai Memorial Institute of Oncology. Chemotherapy is also available in several hospitals.

Prevention and early detection activities

A state cancer control programme, following the recommendations of the World Health Organization, operates in the state of Karnataka. The emphasis is on health education, aimed at tobacco control, healthy diet and early detection of cervical, breast and oral cancer. Operational research into the implementation of specific cancer control measures is a major component of the programme. The introduction of anti-tobacco health education horizontally throughout the health services, using primary health care workers, was evaluated recently and the results showed an encouraging medium-term reduction in the prevalence of the tobacco habit (Anantha *et al.*, 1995). Efforts are also under way to promote the early detection of cervical cancer, using female health workers in the primary health care sector of the health services. There are no organized screening programmes.

Survival analysis

Subjects

A total of 5334 cases were registered during the period 1982–89 for the following cancer sites/types, for which survival is described in this paper: breast (1514), uterine cervix (2422), lymphoma (712), multiple myeloma (100) and leukaemia (586) (Table 2). More than 90% of these patients had histological verification of their cancers.

The proportion of cases registered on a DCO basis ranged from 1.2% to 5.0% in different sites; a total of 109 DCO cases were excluded from the final analysis. Those without any follow-up information after diagnosis were also excluded. A total of 4781 cases (89.6% of incident cases) were thus eligible for survival analysis (Table 2).

Follow-up methods

The follow-up methods employed by the registry are described in detail elsewhere (Nandakumar, 1993; Nandakumar *et al.*, 1995a, 1995b, 1995c). They involved both active and passive measures. The incident cases were first matched with death certificates mentioning cancer or tumour as cause of death. For the unmatched cases, information was obtained by active follow-up measures involving home visits, postal enquiries, enquiries in the workplace and scrutiny of case records based on listings for clinical follow-up in hospitals. For more than 85% of cases, follow-up information was obtained by active methods: matching with death certificates yielded information on only a few cases, because not all deaths were registered and certification of the cause of death was sometimes inadequate or incorrect. In most cases, the person's vital status was established by house visits by trained social workers. The closing date of the study was 31 December 1993.

Table 3. Observed and relative survival by site and sex, Bangalore, India, 1982–89

Site	ICD 9	All ages and both sexes combined							% Survival rate at 5 years by sex					
		Number	Observed survival (OS)			Relative survival (RS)			Male			Female		
		included	1 yr	3 yr	5 yr	1 yr	3 yr	5 yr	Number	OS	RS	Number	OS	RS
Breast	174	1361	82.2	55.5	41.7	83.4	58.2	45.1				1361	41.7	45.1
Cervix	180	2155	76.4	50.5	37.6	77.5	52.8	40.4				2155	37.6	40.4
Hodgkin's disease	201	206	80.3	61.7	55.1	81.1	63.6	58.0	158	54.4	57.2	48	57.8	61.0
Non-Hodgkin lymphoma	200,202	428	59.7	42.2	31.6	60.8	44.5	34.5	289	29.5	32.4	139	36.0	38.7
Multiple myeloma	203	97	64.7	31.3	22.3	66.3	33.8	25.5	61	26.2	30.2	36	14.5	16.3
Lymphatic leukaemia	204	171	50.6	34.0	29.3	51.1	35.0	30.7	117	30.3	31.8	54	27.1	28.3
Myeloid leukaemia	205	272	52.4	30.9	20.5	52.9	31.8	21.5	145	14.2	14.9	127	27.9	29.0
All leukaemia	204-8	534	48.5	29.9	22.3	49.0	30.8	23.4	322	20.4	21.4	212	25.3	26.4

Analytical methodology (see Chapters 2, 3 and 5)

The index date for calculation of survival time was the incidence date. The survival time for each case was the time between the index date and the date of death *or* date of loss to follow up *or* 31 December 1993. Cumulative observed and relative survival probabilities were calculated using Hakulinen's method (Hakulinen, 1982; Hakulinen *et al.*, 1994). The expected survival for a group of people in the general population similar to the patient population with respect to age, sex, and calendar period of observation were calculated using the abridged life tables of the urban Indian population (Registrar General of India, 1995). Age-standardized relative survival (ASRS) was calculated for all age groups and for the age group 0–74 years by directly standardizing site-specific and age-specific relative survival to the site-specific age distributions of the estimated global incidence of major cancers in 1985 for comparison with results from other countries.

Results

The one-year, three-year, and five-year observed and relative survival rates by site are given in Table 3. The one-year relative survival rate was over 75% for cancers of the breast and uterine cervix and for Hodgkin's disease. It was less than 60% for patients with leukaemia. The five-year relative survival rates were 45.1% for breast cancer; 40.4% for cervical cancer; 58% for Hodgkin's disease; 34.5% for non-Hodgkin lymphoma; 25.5% for multiple myeloma; 30.7% for lymphatic leukaemia; and 21.5% for myeloid leukaemia.

Higher five-year relative survival rates for lymphoma and myeloid leukaemia were observed among females as compared with males; lower rates were observed in females for multiple myeloma and lymphatic leukaemia (Table 3).

Declines in relative survival were observed with advancing age in the case of cancers of the breast and cervix and non-Hodgkin lymphoma (Table 4). Fig. 3 shows the observed survival by clinical extent of disease for breast cancer. For localized breast cancer, the five-year observed survival was 56.9%; for those with regional spread it was 37.6%; and for those with distant metastasis it was 13%.

Figs. 4 and 5 show the observed survival for cervical cancer patients by clinical extent of disease and by the different stages identified by the International Federation of Gynaecologists and Obstetricians (FIGO). The five-year observed survival rates were 49.5% for localized, 36.5% for regional and 19.3% for distant-spread categories of cervical cancer. The five-year observed survival rates for the various FIGO stages were as follows: stage I: 66%; stage II: 47.4%; stage III: 33.1%; stage IV: 6.2%; stage not categorized: 41.2% (Fig. 5).

Discussion

The relative survival rates experienced by our population for the cancer sites included in the study are rather low. The poor five-year survival in the case of breast and cervical cancers in our population is not surprising, since more than two-thirds of breast cancer patients, and four-fifths of cervical cancer patients for whom details of clinical extent of disease were available, presented at the time of diagnosis with non-localized cancers. The fact that one-quarter

Table 4. Site-specific and age-specific number of cases by age group, five-year relative survival and ASRS, Bangalore, India, 1982–89

Site	ICD 9	Number of cases by age group						% Relative survival (RS) at 5 years						RS	ASRS%	
		≤34	35–44	45–54	55–64	65–74	75+	≤34	35–44	45–54	55–64	65–74	75+		All ages	0–74
Breast	174	151	344	387	280	143	56	49.5	50.1	44.3	44.1	36.3	25.6	45.1	40.4	44.1
Cervix	180	163	495	697	506	233	61	46.1	46.1	41.6	35.7	31.0	27.8	40.4	38.4	39.9
Hodgkin's disease	201	108	30	33	23	9	3	69.4	47.7	43.5	33.0	80.1	0.0	58.0	54.8	59
Non-Hodgkin lymphoma	200,202	164	48	73	73	49	21	42.1	35.0	37.1	28.2	20.3	0.0	34.5	25.4	32.8
Multiple myeloma	203	2	12	24	32	22	5	50.7	34.1	30.9	20.0	16.5	33.9	25.5	32.0	31.5
Lymphatic leukaemia	204	122	9	11	16	12	1	29.8	28.3	38.6	63.1	0.0	0.0	30.7	24.8	30.8
Myeloid leukaemia	205	129	42	53	34	12	2	13.2	28.6	36.4	22.3	22.6	0.0	21.5	16.6	20.6
All leukaemia	204-8	301	57	80	60	29	7	21.1	24.4	31.4	33.2	9.4	0.0	23.4	18.2	22.6

ASR: Age-standardized relative survival

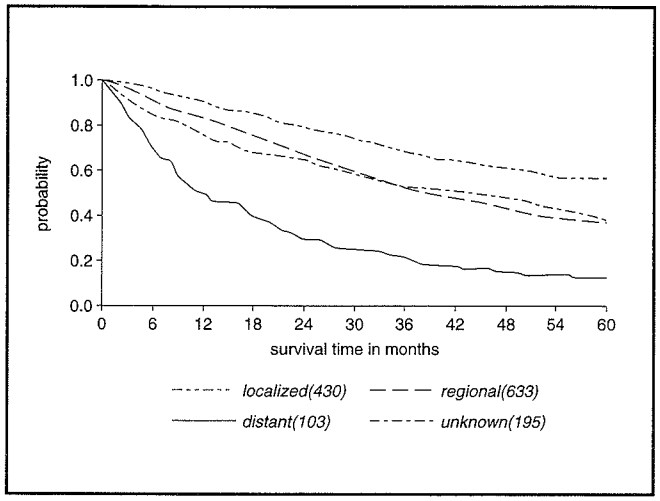

Figure 3. Survival from breast cancer by clinical extent of disease in Bangalore, India

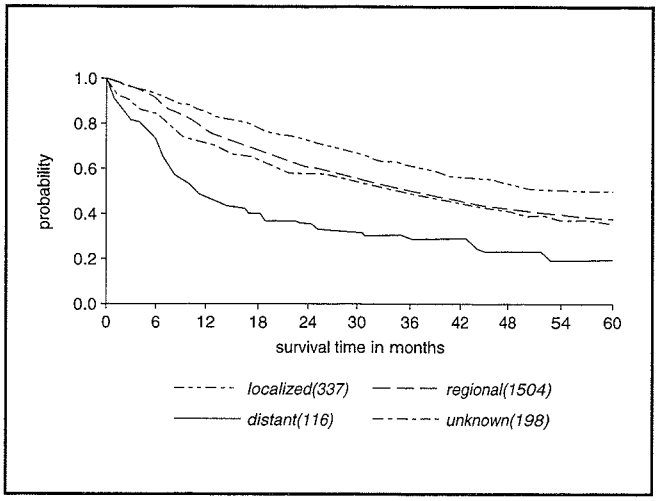

Figure 4. Survival from cervical cancer by clinical extent of disease in Bangalore, India

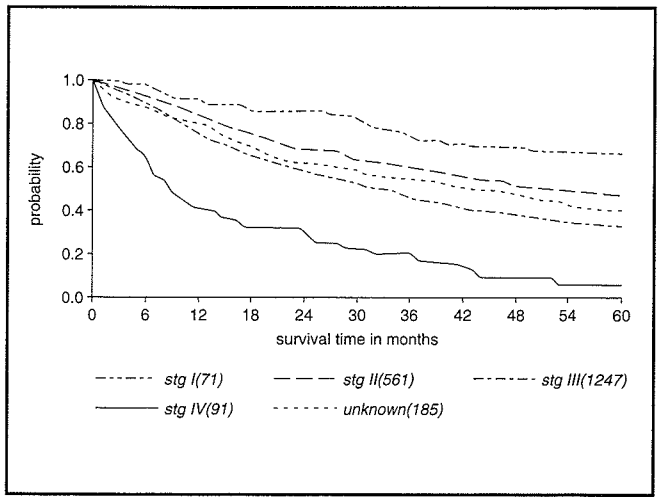

Figure 5. Survival from cervical cancer by stage of disease in Bangalore, India

of cancer patients either do not take up or do not complete their prescribed treatment at the Kidwai Memorial Institute of Oncology, the major cancer centre in the state, indicates that a good proportion of patients do not comply with treatment. This further explains the poor outcomes observed.

The age-standardized relative survival rates in our breast and cervical cancer patients (Table 4) are in the lower range of survival reported from developing countries (Sankaranarayanan *et al.*, 1996). The five-year relative survival for breast cancer observed in Bangalore is slightly lower than that reported from Madras, India (Gajalakshmi *et al.*, 1997) and from Khon Kaen, Thailand (Sriamporn *et al.*, 1995); that for cervical cancer in our population is lower than that reported from Khon Kaen, Thailand. The overall survival experience in both these sites in our population was far inferior to that in the population-based cancer registries

belonging to the Surveillance Epidemiology End Results (SEER) programme of the National Cancer Institute, USA (Kosary *et al.*, 1995) and many cancer registries in Europe (Berrino *et al.*, 1995). Although there was a clear downward trend with advancing disease in both these sites, five-year survival in our localized patients was far lower than the experience reported from the SEER programme (Kosary *et al.*, 1995). Although some stage misclassifications might have accounted for the differences to some extent, the fact remains that outcomes could be further improved by changes in treatment-related factors.

Our results for Hodgkin's disease, non-Hodgkin lymphoma and leukaemia are comparable with those reported from the USA for the period 1967–73 (Axtell *et al.*, 1976). The figure for multiple myeloma is comparable with the survival reported from the SEER registries for the period 1974–86 (Ries *et al.*, 1990). Advances in treatment, particularly in the form of combination chemotherapy, have improved the outcome from these neoplasms over the last two decades. Our results for non-Hodgkin lymphoma and leukaemia are comparable with that reported from Khon Kaen, Thailand, for the period 1985–92 (Sriamporn *et al.*, 1995). The various difficulties involved in implementing such aggressive therapies in developing-country settings have led to a poor survival rate. The possibility that these neoplasms may have a different biology and natural history in developing countries cannot be entirely excluded.

The results are educative and provide valuable leads for improving outcome from these cancers. Early diagnosis and providing adequate therapy are fundamental in improving survival outcome from breast and cervical cancers. However, the vast potential for prevention in the case of cervical cancer as a means of reducing mortality and suffering from this major illness of women in developing countries should not be overlooked. Improvements in pathological categorization of lymphoreticular malignancies and adequate therapy are the main way of improving survival from lymphoreticular malignancies. Educating the public as well as reorienting the professionals involved in prevention and therapy are equally important.

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