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Incidence Estimation of Leukemia among Koreans*

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This study was undertaken in order to estimate the incidence of leukemia among Koreans. Medical records were studied of patients with diagnoses of either ICD-9 038 (septicemia), or 204-208 (leukemias), or 284 (aplastic anemia), or 289 (other diseases of the blood and blood-forming organs) in the claims sent in by medical care institutions throughout the country to the Korea Medical Insurance Corporation (KMIC) during the period from January 1, 1986 to December 31, 1987. These records were abstracted in order to identify and confirm new cases of leukemia among the beneficiaries of KMIC, which covers about 10% of the whole Korean population. Using these data from the KMIC, the incidence rates of leukemia among Koreans were estimated as of July 1st, 1986 to June 30, 1987. The crude incidence rate of all types of leukemia among Koreans is estimated to be 3.45 (95% CI; 0.77-9.55) and 2.29 (95% CI; 0.28-7.81) per 100,000 in males and females, respectively. The cumulative rate for the age span 0-64 is 0.25% in males and 0.18% in females, and for the age span 0-74, 0.35% in males and 0.23% in females. The adjusted rates for the standard world population are 3.90 and 2.48 per 100,000 in males and females, respectively. The relative frequencies by type are 51.5% for AML, 21.6% for ALL, 20.2% for CML, and only 1.5% for CLL. The incidence patterns of various types of leukemia, of which this is the first report in Korea, are analyzed and presented. A relatively higher incidence of AML among male children was observed (ALL: 1.39, AML: 1.73/100,000) which is one of the notable findings.

Key Words: *Leukemia, Incidence, Korean*

INTRODUCTION

The leukemias, a diverse group of malignancies that all arise from cell systems that circulate in the peripheral blood and arise in large part from bone marrow, are not a particularly common from of human cancer and comprise less than 5% of the total annual cancer incidence (IARC, 1987). Despite being uncommon, however, in recent years there has been a considerable improvement especially in diagnosis and treatment.

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This is probably due to certain practical advantages in research, e.g., readily available animal models which provide easy access for sampling of leukemic cells, along with relatively pure preparations of malignant cells for examination. Meanwhile, in spite of our recently expanded knowledge of leukemia pathogenesis, effective methods for human leukemia prevention, except for minimizing exposure to ionizing radiation and such marrow-toxic chemicals as benzene, have not yet been produced. Also, the incidence of leukemia has continuously increased since the 1950s (Cartwright & Bernard, 1987).

The incidence is relatively high in Western countries and low in Asia, Central America, and Africa. Japan, however, has recently shown a dramatic increase in the incidence of leukemia among men (IARC, 1987). The incidence patterns of the specific types of leukemia

differ widely by age and sex (Cartwright & Bernard, 1987). For instance, acute lymphocytic leukemia (ALL) occurs most frequently among children less than 15 years old. The incidence rate, especially high among 3-5 year-olds, decreases gradually after childhood and then increases again during old age. The incidence of acute myelogenous leukemia (AML) increases with age, but in Aftica, it mainly affects boys aged 5-9 years (Oladipupo Williams & Bamgboye, 1983). The incidence of chronic myelogenous leukemia (CML), meanwhile, suddenly increases after middle age and peaks in the age group of 50-60. Chronic lymphoblastic leukemia (CLL), accounting for 25-30% of all cases of leukemia affecting Caucasians, rarely afflicts Asians (Fraumei & Miller, 1967; Sweet, 1977).

In Korea, the basic statistical data on leukemia, as well as on most other cancers, are not yet available. The National Bureau of Statistics (NBS) reported that the death rate by the leukemia among Koreans in 1988 was 3.2 per 100,000 for males and 2.7 for females, but only about 40% of the death certificates (cause of death), on which the NBS report was based, were issued by medical doctors (NBS, 1988). In Addition, even though the Ministry of Health and Social Affairs (MOHSA) has operated the central cancer registry since July 1980, still the registered cases are too small and somewhat selective to be used for producing incidence statistics. According to the cases registered during the 6 years from 1982-1988, the relative frequency of malignancies of hematopoietic and reticuloendothelial systems (blood, bone marrow, and spleen) to all cancers was 4.0% in males, which was 4th in rank, and 3.4% in females, which was 8th in rank (MOHSA, 1989). The admission rate of leukemia per year among medical insurance beneficiaries was around 14.4 per 100,000 population for males and 14.1 for females in 1988 (KMIC, 1988), which has increased in recent years (in 1986, the rate was 8.1 for males and 8.5 for females). Kim JS (1988) reports that the prevalence rate of malignant neoplasms of lymphatic and hematopoietic tissue (ICD-9 200-208) is 16.3 per 100,000 in males and 14.1 in females.

For rural Kangwha County, with a population of around 88,000, cancer incidence data were reported recently (Kim et al., 1990). A total of 18 cases, 12 males and 6 females, of leukemia were identified during the 5 years of 1983-1987 in that area, which is equivalent to the incidence rate of 5.5 per 100,000 in males and 2.7 in females. But these statistics could not be representative ones for Korea as a whole, because the data were based on a small number of cases and population.

A series of nationwide incidence estimation studies of cancers among Koreans has been undertaken by the authors since 1988. Some of the results, such as liver, stomach, and thyroid cancer, has been reported (Ahn et al., 1989 & 1991). This is the fourth report of the serial studies presenting the incidence patterns of leukemia among Koreans by sex, age, and type.

MATERIALS AND METHODS

The study population of this investigation were the beneficiaries of the Korea Medical Insurance Corporation (KMIC) during the period of 1986-1987 as described in the previous report (Ahn et al., 1989 & 1991).

Potential cases of leukemia were screened by sorting out all admitted cases diagnosed as leukemia (ICD-9 204-208) in the claims sent by medical care institutions throughout the nation during the 2 years from January 1, 1986 to December 31, 1987. In the claims, 3 diagnostic names at most are usually indicated per case, and to allow for possible misdiagnoses, septicemia (038), aplastic anemia (284), diseases of the white blood cells (288), and other diseases of the blood and blood-forming organs (289) were also included as potential cases. A total of 1579 patients (2416) claims were selected and listed as potential leukemia patients.

Two methods were used to abstract the medical records of each potential case: an abstractor visited each medical care institution directly, or an abstract format was mailed to be filled out by the doctors who cared for the patients. The visiting abstractors were recruited among the junior or senior medical students of Seoul National university College of Medicine and trained on how to review and abstract the medical records of each case using an abstracting format. They were then assigned to visit the hospitals or clinics, where 5 or more potential cases had been claimed. For the other institutions where 4 or fewer cases were listed, the abstract formats were mailed to be filled out and brought back by the doctors who cared for patients. Out of a total 1579 patients, 1526 (96.6%) were abstracted by visiting 74 institutions directly and mailing to 163 institutions throughout the country.

Diagnoses of leukemia were confirmed by the hematooncologist (Dr. HHKoo) by a review of the medical records abstracts. Confirmation was primarily based on whether or not a bone marrow examination (BME) had been performed. In cases without BME, the leukemia was defined as "blasts found on the peripheral blood smear (PBS) with common symptoms (fever, pallor, malaise, bone pain, etc.), signs (hepatomegaly,

splenomegaly, lymphadenopathy, etc.) and laboratory findings after excluding infection or leukemoid reaction." Specific types of leukemia could be classified only among those cases with BME.

A total of 329 patients were confirmed as leukemia, and out of these 134 cases, of which the dates of onset were between July 1, 1986 and June 30, 1987, were sorted out as newly-occurred leukemias among the 4,328,790 KMIC beneficiaries during that one year. using these data, age-, sex-, and typespecific incidence rates of leukemia among Koreans were estimated as well as crude-and age-adjusted rates. A 95% confidence interval (95% CI) of the crude rates was also estimated using Poisson distribution.

RESULTS

Distribution of leukemia cases by sex, age, and type

Out of 134 cases, 79 (60.0%) are male patients and 55 (40.0%) female.

By type, the AML topped the list with 69 cases (51.5%), followed by the ALL with 29 cases (21.6%). The CML and CLL ranked third and fourth with 27 (20.2%) and 2 (1.5%) cases, respectively. Among the 127 classifiable cases, 98 (77.2%) were acute leukemias (Table 1).

Fig. 1 shows the distribution of leukemia cases by type and age group in the male and female. In the male, the AML occupied a large part in each of the 3 age groups (50% for under 15 years old, 57% for 15-49 years old, and 64% for 50 years old and over). But in the female children the ALL is the major one (70%), and in the other age groups of the female the AML is prominent (55% and 64%, respectively).

Annual incidence rates of all types of leukemia among Koreans

The crude incidence rates of leukemia among Koreans as of 1985 are estimated to be 3.45 (95% CI; 4.28-2.71) per 100,000 in males and 2.29 (95% CI; 2.96-1.71) in females. So approximately 1160 new cases developed in Korea during the year 1985 (Table 2).

The age-adjusted rate for the world standard population stood at 3.90 for males, 2.48 for females, and 3.15 for both sexes.

The cumulative rate for the age span 0-64 was 0.22% (male: 0.25, female: 0.18%), and the rate for 0-74 was 0.28% (male: 0.35% female: 0.23%).

The age specific incidence rates of all types of leukemia fluctuated until the 40s, and then increased with the peak incidence occurring at age group 65-69 years in both sexes as 14.7 per 100,000 for male and 8.1 for female (Table 2 and Fig. 2).

Annual incidence rates of leukemias by type

Acute Myelogenous Leukemia (AML): The crude incidence rate of AML among Koreans is 1.44/100,000 people per year as of 1985 (95% CI; 1.82-1.10). For the male, it is 1.86 (95% CI; 2.49-1.32) and 1.09 (95% CI; 1.57-0.70) for the female. The age-adjusted rate is 1.62 (2.12 for males, 1.19 for females). In the male, the 0-4 years age group shows a relatively high incidence rate, and then the rates slightly attenuate until 15 years of age, when they gradually increase afterward with age. In the case of the female, the overall rate increases with age (Table 3 & Fig. 2).

Acute Lymphoblastic Leukemia (ALL): The crude incidence rate of ALL among Koreans is 0.80/100,000 per year as of 1985 in males (95% CI; 1.22-0.47) 0.63 (95% CI; 1.01-0.34) in females, and 0.71 (95% CI; 0.98-0.48) for both sexes. The age-adjusted rate is 0.75 in total (0.83 in males, 0.68 in females). The incidence curve of ALL by age shows a wide "V"-spaped pattern in both sexes: high early in life and declining and low in the middle-age groups, and

Table 1. Distribution of leukemia cases occurring during the period of July 1, 1986-June 30, 1987 among Korea Medical Insurance Corporation beneficiaries by type and sex

Type	Male		Female		Total	
	No.	%	No.	%	No.	%
AML	43	54.4	26	47.3	69	51.5
ALL	16	20.3	13	23.6	29	21.6
CML	16	20.3	11	20.0	27	20.2
CLL	2	2.5	—	—	2	1.5
Unclassified	2	2.5	5	9.1	7	5.2
Total	79	100.0	55	100.0	134	100.0

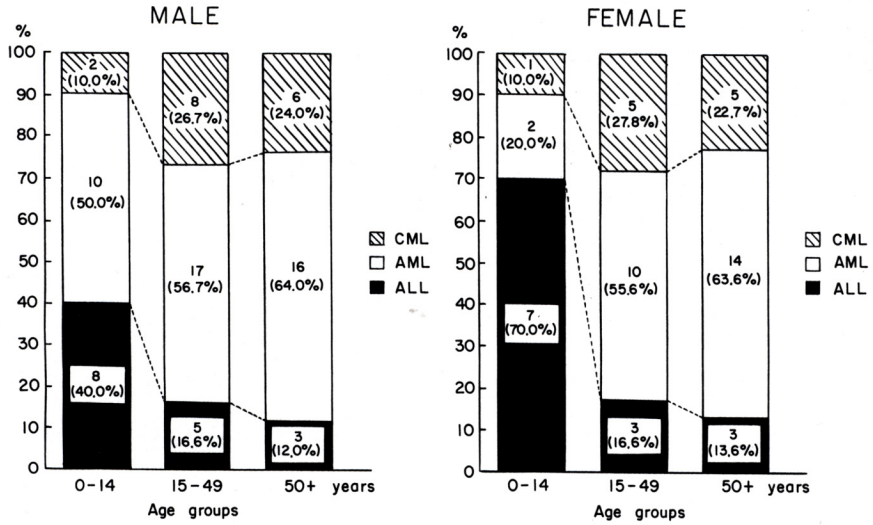

Fig. 1. Percent distribution of leukemia cases occuring during the period of July 1, 1986-June 30, 1987 among KMIC beneficiaries by type and age group

Table 2. Ago-specific annual incidence rate of all types of leukemia among Koreans by sex, 1986-1987

unit: per 100,000 population

Age group (year)	Male	Female	Total
0 – 4	4.02	1.91	3.02
0 – 4	4.02	1.91	3.02
5 – 9	3.57	1.09	2.37
10 – 14	2.96	2.64	2.80
15 – 19	2.04	0.53	1.31
20 – 24	2.20	1.03	1.59
25 – 29	2.80	0.85	1.78
30 – 34	4.05	2.88	3.46
35 – 39	2.32	3.00	2.66
40 – 44	3.26	2.50	2.88
45 – 49	2.27	1.42	1.83
50 – 54	4.54	8.12	6.35
55 – 59	5.27	2.97	4.08
60 – 64	10.41 (0.25%)*	7.80 (0.18%)*	9.02 (0.22%)*
65 – 69	14.66	8.05	10.93
70 +	4.96 (0.35%)**	0.89 (0.23%)**	2.31 (0.28%)**
Total crude:	3.45***	2.29***	2.86***
adjusted:	3.90	2.48	3.15

*: cumulated rate for the age span 0 – 64

**: cumulated rate for the age span 0 – 74

***:95% CI are 4.28 – 2.71 for male, 2.96 – 1.71 for female, and 3.40 – 2.36 for total. The estimated number of new cases of leukemia per year among Koreans is 699 (867 – 549) males and 462 (597 – 345) females as of 1985

NOTE: Crude rate for the Korean population as of 1985 age adjusted rate for the world population

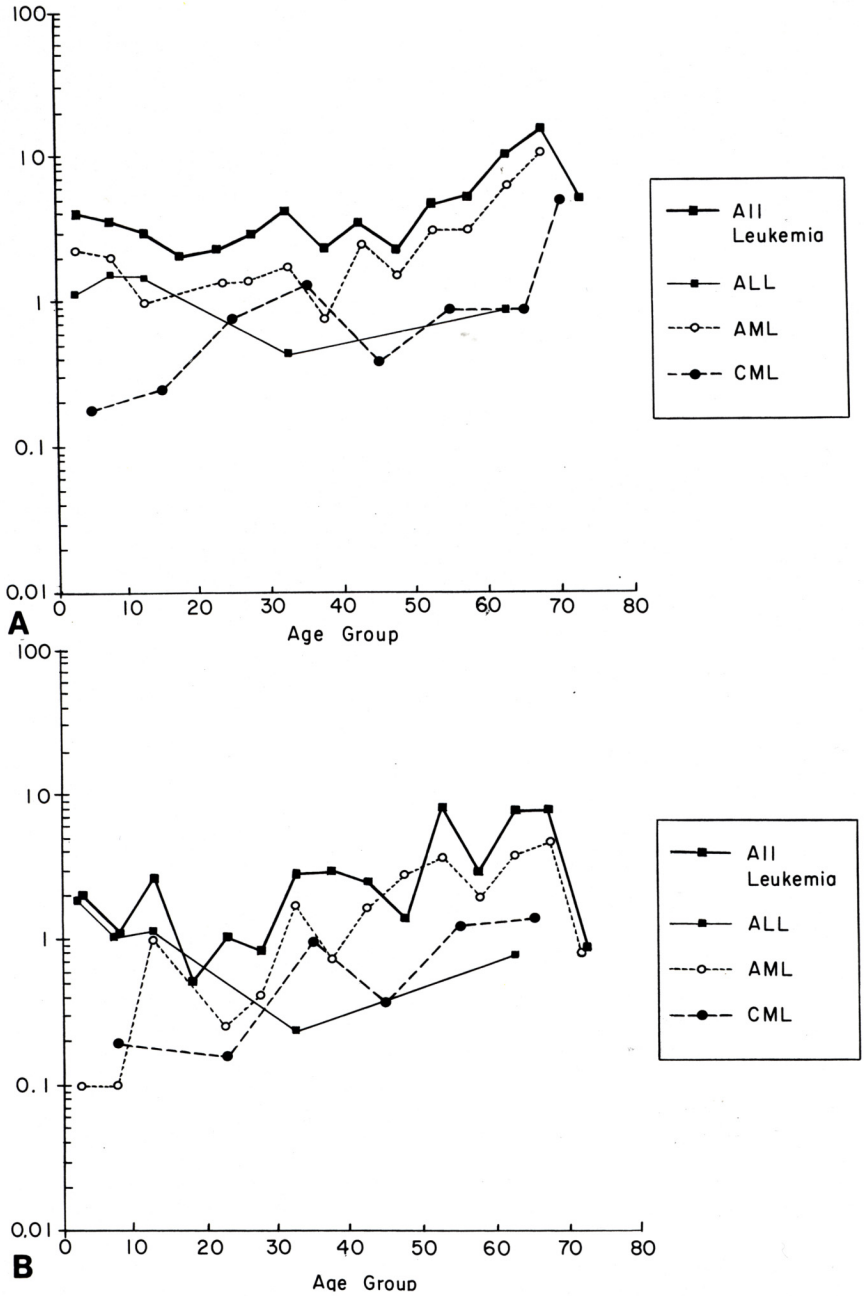

Fig. 2a. Age-specific annual incidence rate of leukemia among Koreans by type and sex (Male)
Fig. 2b. Age-specific annual incidence rate of leukemia among Koreans by type and sex (Female)

increasing and high again in the older age group (Table 3 & Fig. 2.)

Chronic Myelocytic leukemia (CML): The crude incidence rate of CML among Koreans is 0.55/100,000 people per year as of 1985 (95% CI; 0.79-0.35). In the male it is 0.65 (95% CI; 1.04-0.35) and 0.46 (95% CI; 0.78-0.22) in the female. The age-adjusted rates are 0.75 and 0.46 in males and females, respectively. For both sexes, the age patterns of CML incidence show the bimodality. The incidence rates for

Table 3. Age-specific annual incidence rate of leukemia among Koreans by type and sex, 1986-1987

Age group	Male			Female			Total		
	AML	ALL	CML	AML	ALL	CML	AML	ALL	CML
0 – 9	2.30	1.15	0.57	—	1.91	—	1.21	1.51	0.30
4 – 9	2.04	1.53	—	—	1.09	—	1.05	1.32	—
10 – 14	0.99	1.48	0.49	1.06	1.06	0.53	1.02	1.27	0.51
15 – 19	2.04	—	—	—	—	0.53	1.04	—	0.26
20 – 24	0.55	1.65	—	0.51	0.51	—	0.53	1.06	—
25 – 29	1.40	—	1.40	0.42	—	—	0.89	—	0.67
30 – 34	1.73	—	2.31	1.73	0.58	0.58	1.73	0.29	1.44
35 – 39	0.77	0.77	—	0.75	0.75	1.50	0.76	0.76	0.76
40 – 44	2.44	0.81	—	1.67	—	0.83	2.06	0.41	0.41
45 – 49	1.51	—	0.76	2.81	—	—	1.47	—	0.37
50 – 54	3.02	—	0.76	3.69	1.48	2.22	3.36	0.75	1.49
55 – 59	3.16	—	1.05	1.98	—	—	2.55	—	0.51
60 – 64	5.95	4.46	—	3.90	1.30	2.60	4.86	2.77	1.39
65 – 69	10.47	—	2.09	4.83	—	—	7.28	—	0.91
70 +	—	—	4.96	0.89	—	—	0.58	—	1.73
Total 1)*	1.86	0.80	0.65	1.09	0.63	0.46	1.44	0.71	0.55
2)**	2.12	0.83	0.75	1.19	0.68	0.49	1.62	0.75	0.58

*: crude rate for Korean population as of 1985

**: age-adjusted rate for the world population

NOTE: The cumulative rates for the age span 0 – 64 are 0.14%, 0.06%, and 0.04% for AML, ALL, and CML, respectively, in males and 0.09%, 0.04%, and 0.04% in females.

The cumulative rates for the age span 0-74 are 0.19%, 0.06%, and 0.07% for AML, ALL, and CML, respectively, in males, and 0.12%, 0.04%, and 0.04% in females.

both males and females increase with age until 40 years old, and then slightly decline, in the 50s, then increase again thereafter with the second peak occurring in the old age group.

DISCUSSION

The incidence data of leukemia, as with other cancers, are usually obtained from population-based cancer registries (Brincker, 1982), but they may suffer from deficiencies regarding the completeness of reporting, as well as diversity in the diagnosis and classification of the various type leukemias. Thus, uncertainties remain regarding the age-and sex-specific incidence statistics by type of leukemia, although the age and sex-specific data of all types combined are fairly well-documented.

The case-finding procedures used in this study are basically the same as those of registration as described in the previous report (Ahn et al., 1989 & 1991). As for the leukemias, however, these procedures have the strength of being able to classify with uniformity the various types in a large part (94.8%) of the cases. Also, nearly all the medical records (96.6%) of the potential cases were abstracted and the distribution of leukemia cases by age, sex, and type of leukemia in the statistical studies on leukemia in Korea which had been conducted through the hospital series by the Korean hematological Society (Hong et al., 1967 & Hahn et al., 1987) is similar to this study, which gives a high credence to the data collected.

The use and validity of the KMIC population as a source for the estimation of national level incidence has been discussed already in the previous reports (Ahn et al, 1989 & 1991), which led that the KMIC population studied is sufficient and undeviated sample to estimate the incidence.

The worldwide incidence rates of leukemias by

region (Muir et al., 1987) are as follow: Among males, the Maori tribe of New Zealand shows the highest rate of 10.9 per 100,000 people. A comparable figure for most European nations is 8-10/100,000. Latin American countries show a relatively low incidence rate, as compared with that of Europe. Brazil, for instance, records 6.2. The rate is even lower in Shanghai, China, and Osaka, Japan, which record 5.4 and 5.3, respectively. The incidence rate among Koreans is one of the lowest in the world, similar to that of Bombay, India. Among females, the incidence rate is lower than that of males. Most European countries record 6-7/100,000 and Brazil shows 4.1. Both Shanghai and Osaka record 3.6, and Bombay shows 2.6, compared with 2.5 in Korea (Fig. 3).

In Western countries, the age-specific incidence rate of all types of leukemia increases with age, and more than 50% of all cases occur in people over 50 years of age (Cartwright & Bernard, 1987). Especially those over 75 years of age show a remarkable increase in the incidence rate. This increase can be partly explained by improved diagnostic practice and the increased availability of medical care (Lund & Lio, 1983). However, the possiblity that the increase may be partly due to an increase of environmental risks should be considered (Hansen et al., 1983). This study shows that the incidence rate is high among children and decreases thereafter until it makes a turnaround in the age group of 30-34 years, and then makes a dramatic increase in the 50-years-and-over age group.

Most Western countries report that 60% of all leukemic cases are acute and 40% are chronic (Jandle, 1987). In this study, however, 73.1% of all the cases were acute and the remaining, 21.7%, were chronic, which shows a high percentage of acute leukemia among Koreans compared with Western European countries.

The age pattern of AML incidence in this study is similar to that of other countries. In male children, the level of icidence of AML is higher than that of ALL, which is a different figure from those of other countries.

What is noteworthy about the age-specific distribution of ALL is that the incidence rate is high among children 3-5 years of age. An especially high rate among 3-5 year-olds was also observed in Britain during the 1920s and among American whites after the 1940s (Court Brown & Doll, 1961). The phenomenon also occurred among American blacks in the early 1960s (Fraumeni & Miller, 1967; Ogordis et al., 1981) and among the Japanese (Kawashima et al., 1980). More recently, Malasia also reported the same phenomenon (Sinniah & Peng, 1981), but such age-peak can't be observed in African blacks (Edington & Hendrickse, 1973; Amsel & Nabembezi, 1974; Fleming, 1985). The age-peak reflects an exposure to industrialized environment, and the fact that whites are more vulnerable than blacks indicates that socio-economic factors are involved (Neglia & Robinson, 1988). This study reveals that the incidence rate is slightly high in the 0-4 year age group and relatively evenly distributed. Moreover,

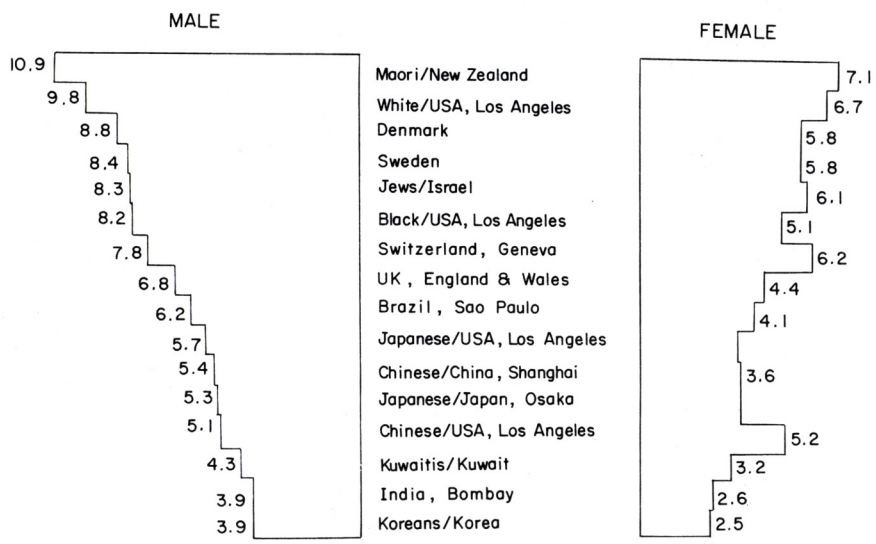

Fig. 3. Comparison of age-standardized incidence rate of leukemia by race /region

unlike the report that shows males are more susceptible to the disease (Birch et al., 1980), the sex ratio in this study is merely at 1.14:1. In the case of AML, the incidence rate increases in proportion to age, both for Korea and other countries. However, this study shows that incidence rate of AML is higher than that of ALL in male children. The reason could not be discovered in this study, so further study and research is required.

In the case of CML, the incidence rate peaks among people in their 40s in the West, and it is increasingly evident among old people (Cutler et al., 1967). According to this study, however, men 30-34 years of age and over 70 years of age and women 50-54 and 60-64 years of age show a high incidence rate. On the whole, 3 peaks are made in the age groups of 30-34, 50-54 and over 70 years. Unlike the West, where people over 40 years of age are the most susceptible to CML, Koreans, both males and females, experience a unique pattern of 2 peaks: in the age group of 30-34 years and over 70 years old for the male, and 50-54 and 60-64 years old for the female.

Numerous reports have been made on the trends of leukemia incidence, but the method of selecting the population to be studied and conducting the studies differ from country to country and from researcher to researcher. For instance, there are some reports that the incidence rate is continuously increasing (Linos et al., 1978; Geary et al., 1979; Brandt et al., 1979; kempt et al., 1980; Gordis et al., 1981). Other reports say that there is a dcreasing tendency (Fraumeni & Miller, 1967; Pratt, 1985). There are also reports that the incidence rate is stabilizing (Devesa & Silverman, 1978; Pollack & Horm, 1980; Plednak, 1986). All the existing domestic reports are based on the treatment data obtained from the hospital series, so the study should continue in order to predict future trends for Korea. In the industrialized Western societies, people are receiving more exposure to radiation and chemicals. The environmental change has caused an increase in AML (Brandt et al., 1978; Mitelman et al., 1978). In this respect, the incidence rate of AML is also expected to increase in Korea.

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