

## PATTERN OF MALIGNANT TUMORS IN KERMAN PROVINCE

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### ABSTRACT

From March 1980 to March 1989 a total number of 2254 (7.6%) new malignant cases from Kerman province were diagnosed by examination of surgical specimens, blood films and bone marrow smears. The crude relative frequency of cancers was studied and compared with other areas of Iran. Gastric (11.36%) and urinary bladder (7.01%) carcinomas were significantly more common in Kerman province than other parts of Iran. Esophageal malignancy was also common in this area. No significant difference was found in the pattern of lymphomas and leukemias. Frequencies of cancer of the cervix (3.24%) and oral cavity (3.73%) were less as compared to other parts of Iran.

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### INTRODUCTION

Epidemiologic studies have shown that frequency and distribution of cancer varies enormously between population subgroups defined by such variables as race, age, sex, occupation, geographic factors and life style. Few epidemiologic studies of cancer have been reported from some parts of Iran. Review of these reports showed a significantly higher incidence of esophageal carcinoma in the northeast of Iran.<sup>1,2</sup> Carcinoma of urinary bladder was reported to be more common in Fars province<sup>3</sup> and cervical cancer was more frequent in Tehran<sup>4</sup> than other parts of Iran. Little is known about the pattern of malignant diseases in Kerman province. The present study was undertaken to show the relative frequency of malignant lesions in this region of Iran.

### MATERIAL AND METHODS

The data used in this study were collected from pathology records registered from March, 1980 to March, 1989 in the cancer registry of Kerman. All the

cases were diagnosed in two histopathology laboratories of Kerman Medical School. These laboratories were the only diagnostic centers present in this region, receiving almost all biopsy material from Kerman province. During this period, 29,602 pathological samples were referred to these laboratories and 2254 new cases of malignancy were diagnosed histologically or by examination of peripheral blood and bone marrow smears. All cases were studied and diagnosed by conventional morphologic methods. All malignant neoplasms registered were classified by anatomic site and morphological features and coded according to the coding scheme.<sup>5</sup> Some clinical information as sex, age, and site of sampling were also recorded. Cases with grossly incomplete information or repeatedly biopsied or doubly registered were carefully excluded from study materials.

### RESULTS

From March 1980, to March 1989, 29,602 samples for histopathologic and hematologic examination were referred to these laboratories. 2254 (7.61%) new cases of malignancy were diagnosed and included in this study. 254 cases were rejected on the grounds mentioned above. The overall male: female ratio of cancer was 1.39:1. The significantly high male: female ratio in

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non-sex organs were found in cancers of urinary bladder (7.32:1), adenocarcinoma of esophagus (6.75:1), lungs (5.7:1), larynx (3.75:1) and stomach (3:1). Cancers of gall bladder (male: female ratio 0.39:1), Thyroid (0.43:1), and large bowel (0.82:1) exhibited female preponderance. More than 50% of malignant cases occurred between 45 to 70 years of age, while maximum frequency of cancer was in the sixth decade of life (Fig. 1). During the age of 26-40 years, females were at slightly higher risk than males, mainly because of cancers of breast, thyroid, large bowel, cervix and biliary tract.

Overall, carcinomas were about 5 times more common than sarcomas. Indeed, most common sarcomas were malignant lymphomas (7.0%) and leukemias (6.21%). About 8.29% of cancers presented initially by metastasis; in decreasing order of frequency to lymph nodes (30.86%), liver (23.46%), serosal cavities (23.46%) and other sites (22.22%).

Crude relative frequency (CRF) of the 15 most common cancers were given in Table I. In males the first two outstanding cancers were of stomach (14.64%) and urinary bladder (10.6%) if skin cancer (18.61%) was excluded; whereas in the female, these ranked 4th and 14th respectively. Mean age for gastric adenocarcinomas was 58.5 years in males as compared to 15% in females. Peak incidence was in the sixth decade of life (49% in males and 31% in females). Mean age for bladder carcinoma was about 63 years in both sexes. More than 80% of cases occurred in 6th and 7th decade of life with peak incidence in 7th decade (50% of cases). Breast (14.85%) and cervix (7.74%) cancers ranked second and third after skin (18.23%) cancer in females.

In skin cancer, which ranked first in both sexes, basal cell carcinoma (72.1%) was the most common, followed by squamous cell carcinoma (22.22%) and malignant melanoma (4.65%). Squamous cell carcinoma

was about three times more common in males than females, with a mean age of 59 years in both sexes. Male female ratio of basal cell carcinoma was 1.16:1 and mean age was 58 years in males as compared to 60 years in females.

The most common solid tumors in pediatric age group in decreasing order of frequency were malignant lymphomas (48.7%), bone (17.1%), renal (9.2%), genital tumor (7.9%), neuroblastoma (5.3%) and others (11.8%).

## DISCUSSION

In spite of inherent limitations of data based on only pathological material, nevertheless certain important differences in the pattern of cancer, difficult to ignore, emerge from such epidemiologic studies. Indeed we have missed a considerable number of deep-seated neoplasms because of inadequate medical autopsy facilities. Incidence of specific cancers varies considerably in different age groups, comparison of CRF between different studies is likely to be very skewed if these studies have very different population age distributions. Thus cancers which are more common in childhood will have an exaggerated CRF in young population. With available non-age standardized data, comparison with other studies will be limited to cancers whose CRF differ unmistakably by large ratio. Because of these reasons we have compared our results mainly with reports from Iran, though recent studies on cancer epidemiology are not available.

Indeed most skin cancers are of relatively trivial nature but accounted for the maximum number of cases (18.45%) in this region as in other parts of Iran.<sup>3,4</sup> Basal cell carcinoma was the most common skin cancer in Kerman province (72.1%) and in Southern Iran (58.8%)<sup>3</sup> in contrast to Tehran (28.1%)<sup>4</sup>, where

Table I. Crude Relative Frequency and Rank Order Of Most Common Cancers In Kerman Province

RO	Both sexes		Males		Females	
	Description	CRF%	Description	CRF%	Description	CRF%
1.	Skin	18.45	Skin	18.61	Skin	18.23
2.	Stomach	11.36	Stomach	14.64	Breast	14.85
3.	Bladder	7.01	Bladder	10.60	Cervix	7.74
4.	Malignant lymphoma	7.00	Malignant lymphoma	8.16	Stomach	6.78
5.	Esophagus	6.21	Esophagus	7.78	Malig. Lymphoma	5.30
6.	Breast	6.21	Leukemia	6.79	Colorectal	5.30
7.	Leukemia	6.21	Oral Cavity	3.90	Leukemia	5.20
8.	Colorectal	4.04	Larynx	3.43	Esophagus	4.03
9.	Oral Cavity	3.73	Prostate	3.28	Oral Cavity	3.50
10.	Cervix	3.24	Colorectal	3.13	Thyroid	3.18
11.	Larynx	2.53	Lungs	3.05	Ovary	2.96
12.	Lungs	2.08	Testis	1.68	Endometrium	2.65
13.	Thyroid	1.91	Soft tissue	1.52	Bones	2.33
14.	Prostate	1.91	Bones	1.45	Bladder	2.01
15.	Bones	1.81	Liver	1.37	Gall bladder	1.90

RO: Rank Order; CRF: Crude Relative Frequency.

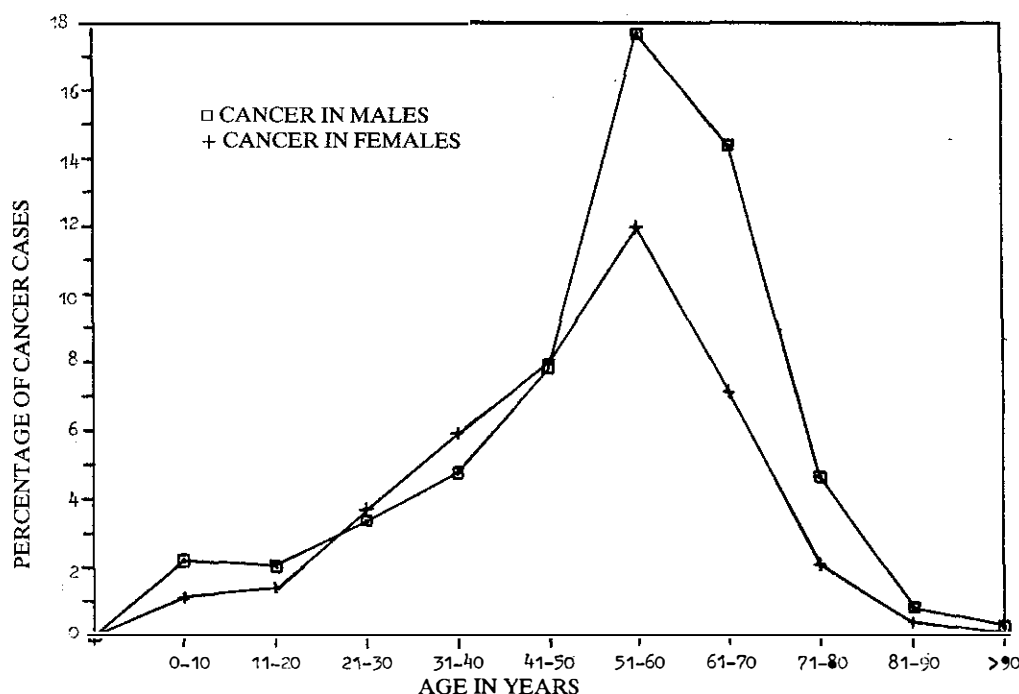


Fig. 1. Age and sex distribution of cancer in Kerman province.

squamous cell carcinoma was most common (36.5%).

Interestingly, incidence of gastrointestinal malignancies was significantly higher in Kerman province (21.6%) than Fars province (11.54)<sup>3</sup> and Tehran (8.99%).<sup>4</sup> In this region, gastric cancer stood first rather than esophageal cancer as in Fars<sup>3</sup>, among the gastrointestinal malignancies in contrast to north of Iran and Tehran.<sup>2,4</sup> Gastric cancer, which was second most common (11.36%) among all cancers in Kerman province, was significantly less frequent in Southern Iran (5.52%)<sup>3</sup> and Tehran (2.56%)<sup>4</sup>. Significance of this difference is difficult to explain. Recently improved diagnostic facilities could be one factor. Exact prevalence of precursor lesions of gastric cancer such as atrophic gastritis, intestinal metaplasia of gastric mucosa and pernicious anemia were not known in this region. Similarly esophageal cancer was more common (6.21%) in Kerman region than Southern Iran (2.3%)<sup>3</sup> and Tehran (3.06%)<sup>4</sup> but less frequent than northeast of Iran.<sup>1,2</sup> In our study, 68% of esophageal carcinomas were of squamous cell type and the remaining 32% were adenocarcinoma, in contrast to other reports.<sup>6,7</sup> Our cases of adenocarcinoma of esophagus showed very high preponderance in males (6.75 times) as compared to squamous cell carcinoma of esophagus (1.87 times), while Caspian littoral provinces of Iran showed female preponderance in esophageal carcinoma.<sup>1</sup> Considering the rarity of primary adenocarcinoma of esophagus<sup>7</sup>, most of which arise from Barrett's esophagus<sup>8</sup> combined with the site of the lesion, many esophageal adenocarcinomas in this study might be extensions of gastric adenocarcinomas to the

lower esophagus. If this were true then the incidence of gastric cancer would be even higher in this region. Among the various pathogenetic factors suggested for gastroesophageal carcinomas,<sup>9,10</sup> salted and pickled food, nitrosamines or nitrosamides derived from an interaction between high nitrate-containing food and water and dietary amines, specific nutritional deficiencies along with opium consumption, high soil salinity and low rainfall might be relevant in this region. A further detailed study is needed to ascertain the exact role of such factors in gastroesophageal cancers in this region.

Cancer of large bowel accounted for about 4% of cancers (M:F ratio 0.8:1) in Kerman province. This pattern was more or less the same as in other parts of Iran,<sup>3,4</sup> though no details were mentioned in these reports. In comparison with western countries, colorectal cancer occurred in a younger age group in this region. Some investigators believe that colorectal malignancy in older age is mainly related to environmental and dietary factors whereas in younger age groups there is a genetic predisposition.<sup>11</sup> In this respect, most of our cases should have genetic predisposition, because about 50% of our cases were under 40 years of age in females as compared to 24% in males. If this age limit was increased to 50 years, then it comes to 66.6% and 48% respectively and no multiple polyps were found. Whether our cases belong to Hereditary Nonpolyposis Colorectal Cancer (HNPCC) subset of large bowel cancer,<sup>12</sup> is not yet clear because no detailed family history was available.

Carcinoma of urinary bladder was much more com-

mon in this region as compared to other parts of Iran.<sup>3,4</sup> In the present study it accounted for 10.6% of total cancer cases in males as compared to 2.7% from Tehran<sup>4</sup> and 5.1% from Fars province.<sup>3</sup> In females, bladder cancer comprised 2.1% in Kerman as compared to 0.7% and 0.8% in Tehran and Fars province respectively. We also found highly significant male preponderance (7.3 times) in cases of bladder cancer, as in Fars province (9 times).<sup>13</sup> Opium addiction mostly in men is also a notorious problem of Kerman province as in Fars, and opium has been considered as a potential urinary bladder carcinogen in men.<sup>14</sup> Pyrolysis of opium and its alkaloid has been shown to contain pro-mutagens, too.<sup>15</sup> As biogenesis of carcinoma of bladder, as in other organs, is a complex multistage phenomenon, possible interaction of other suggested factors<sup>16</sup> such as smoking, dye stuffs used in carpet industry in this region, exposure to dust or fumes, diet with high nitrates and nitrites and inflammation of bladder should be investigated. Considering the very high incidence of bladder cancer in this region, a routine screening program by urinary cytology in high risk population can be effective in detecting the asymptomatic patients at earlier stages.<sup>17</sup>

Almost all reports from Iran indicate a uniform pattern of lymphomas, 8.46% from Tehran,<sup>4</sup> 7.6% from southern Iran<sup>3</sup> and 7.0% from Kerman province.<sup>18</sup> Incidence of lymphoma is much higher in this region of the world (Iran, Saudi Arabia, Iraq, and Lebanon) as compared to other parts of the world.<sup>19</sup> In contrast to western countries the ratio between high and low-grade non-Hodgkin's lymphoma was reversed in Iran. Although some explanations were discussed by Tabrizchee, et al.<sup>18</sup> but reasons for this significant difference are not yet completely understood.

The present study also confirms the unquestionable fact that breast cancer was the most common malignancy (excluding skin) in females. In the present study, it accounted for 14.85% of total cancer cases in females as compared to 13.4% from Tehran<sup>4</sup> and 13.9% from Fars province.<sup>3</sup> Mean age for breast cancer in Kerman province was 50 years with maximum risk between 35-65 years (more than 85% of cases) and peak incidence in the 5th decade of life. By far, most of the breast carcinomas were of the infiltrating duct variety. Most of the cases of breast cancer presented in late stages, which stressed the need of an effective motivation program for women for breast self-examination as in western countries to detect it at the earliest possible stage.

Cancer of the cervix was the second most common malignant lesion in females (excluding skin). It accounted for 7.74% of total cancer cases in females. Mean age was 53.5 years with peak incidence in 6th decade of life (more than 55% of total cases). Earlier

reports from other parts of Iran showed very high CFR of cervical cancer (11%) in Fars province<sup>3</sup> and 22% from Tehran.<sup>4</sup> The present study demonstrated a significant difference in the incidence of cancer of the cervix, though it still remained the third most common cancer in females. Improved genital hygiene, relatively older age of marriage and lesser number of pregnancies combined with widely used screening programs and better medical facilities might be responsible for this fortune.

Leukemia accounted for 6.21% of total malignant cases with male-female ratio of 1.8:1 in the present study. Acute leukemias were about nine times more common than chronic leukemias. Acute lymphoblastic leukemia occurred about 76% in children and acute myeloblastic leukemia 75% in adults. Very low CRF of leukemias (0.29%) in Habibi's report from Tehran<sup>4</sup> is understandable because that material was mostly collected from histopathologic laboratories only. Epidemiologic data of leukemia from Fars province (5.03%)<sup>3</sup> correspond with ours.

Crude relative frequency of cancer of oral cavity revealed significant variation in different parts of Iran. It accounted in Kerman province for 3.7%, Fars province, 6.1% and Tehran, 9.35%.<sup>4</sup> In all series, the lip was the most common site followed by oral mucosa. Etiologic agents like tobacco and betel nut chewing, thought to be responsible for oral cancer in Iran's eastern neighbour the Indian subcontinent, notorious for oral cancer, are not prevalent in this country.

Differences in frequencies of malignancies of deep-seated organs such as lungs (2.08%) and brain (0.87%) in our series, as compared to reports from Fars province (lung 4.25%; brain 2.73%)<sup>3</sup> and Tehran (lung 3.48%; brain 2.33%), can be explained on the grounds of inadequate medical and autopsy facilities at our center and more number of referred cases in the above study material. We found the most common solid tumors in the pediatric age group in decreasing order of frequency were lymphoma, bone, renal and genital tumors and neuroblastoma. Haghighi, et al. reported tumors of lymph node, bone, eye, brain and kidney in decreasing order of frequency from Fars province.<sup>21</sup>

The present study clearly demonstrated that gastrointestinal malignancies were most common in this region of Iran. A further detailed study on gastrointestinal cancers, especially to find out risk factors should be conducted. We also suggest periodic endoscopic check-up and other screening tests in high risk population to detect such malignancies at earlier stages. Considering the very high incidence of bladder carcinoma and advanced stages of breast cancer in females, screening programs for high risk population is also recommended. Protection of skin against direct sunshine is also advisable to prevent skin cancers.

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