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RESEARCH IN THE REGIONAL CANCER PROGRAMME

INTRODUCTION

The promotion and development of research activities in relation to various WHO programmes at the regional level, have received an impetus since 1975, when the decision was made to establish Regional Advisory Committees on Biomedical Research, and to involve the Regional Offices to a much greater extent in the Organization's research activities.

However, in EMRO, interest in research activities in the field of Cancer dates back to the Group Meeting convened in November 1971 in Baghdad, when experts from within and outside the Region gathered to discuss and review the problems of cancer control and research in the Region.

In early 1975 the Regional Advisory Panel on Cancer was established with the following terms of reference:

1. To assess the cancer situation in the Region and advise the Regional Director on the best way to use WHO technical and financial support to obtain higher cost/benefit results.

2. To elaborate a Regional Programme for cancer and to evaluate the development of such a programme, making the required corrections from time to time in order to adapt the programme to meet cancer realities of the Region.

3. To evaluate experience collected by Regional Reference Centres on various cancer sites and types, and to decide upon the best methods to be disseminated widely throughout the Region for cancer prevention, detection, diagnosis, treatment, rehabilitation, etc.

4. To assess the need to develop scientific and practical cancer activities in areas where a particular type of cancer situation is evident throughout the Region.

The Panel, since its inception, has continued to meet annually in different countries of the Region.

Following the recommendations of the first meeting of the Advisory Panel, the following Institutes were designated as Regional Collaborating Centres:

1. Medical Research Institute, Alexandria
   Regional Collaborating Centre for Cancer of the bladder, hypopharynx and head and neck

2. National Cancer Institute, Cairo
   Regional Collaborating Centre for Cancer of the bladder, hypopharynx and head and neck

3. Salah Azaiz Institute, Tunis
   Regional Collaborating Centre for breast and uterine cervix cancers

4. Cancer Institute, Teheran
   Regional Collaborating Centre for lymphomas and oesophageal cancer

The terms of reference of these Collaborating Centres are:

1. Research in the field of epidemiology, aetiology and pathogenesis of cancer which constituted the specific field of each RCC.

2. Elaboration of adequate preventive measures.

3 Development of early detection methods.

4. Standardization and recommendation of methods for diagnosis, treatment. rehabilitation as appropriate for the Region.

5. Training of cancer personnel at regional and inter-country level.

The activities of the Collaborating Centres are reviewed during the annual meetings of the Regional Advisory Panel.

CANCER SITUATION IN THE REGION

In order that the proposed regional research activities in the field of Cancer ca be reviewed in the correct perspective, a resumé of the Cancer situation in the Region and of the existing resources for Cancer Control and research, is given below.

Most of the available data on Cancer in this Region is based on relative frequenc obtained from hospital-based cancer registries. There are only three population-base cancer registries (Iran, Iraq and Israel), of which only one is able to produce true cancer incidence data.

Some of the common cancers in the countries of this Region are:

Skin Cancer

Skin cancer in most of the Middle East countries was found to represent between 10 and 28 per cent of all cancers. It is common not only in males, but the relative frequency in females is also high in Afghanistan, Iran, Iraq, Israel, Lebanon and the Sudan.

Until now no reliable information concerning the dose/effect relationship for ultraviolet exposure and skin cancer exists and the area of Middle East countries offe the best possibilities for such research. It is predictable that an increase in skii cancer will be observed in all countries of the area, if proper data become available in the future.

Lymphomas

These constitute another type of malignent tumour prevalent in Middle East counti Under this term are included Hodgkins as well as non-Hodgkins lymphomas (lymphosarcor reticulosarcome, etc.) and abdominal lymphoma.

Lymphomas are the second commonest type of cancer in males in Afghanistan, Iran Lebanon and the first in Iraq. Even in those countries where lymphomas are not amon the first two types, they occupy the third to fifth place (Egypt, Israel, Sudan and Tunisia). Roughly it could be said that 8-12 per cent of all malignant tumours in Middle East countries are lymphomas.

Data obtained from the Israeli Cancer Registry about those who immigrated to Israel from various parts of the world show clearly that lymphomas are more frequent in immigrants from the North African coast (Morocco, Algeria, Tunisia, Libya, Egypt) and Asia (Iran, Iraq, Yemen, Democratic Yemen) than in those coming from Europe. Except for some African countries, in no other area of the world are lymphomas so frequent as in the Middle East countries.

A particular type of gastro-intestinal lymphoma with production of an abnormal immunoglobulin has been described. This type of lymphoma was later found in other countries around the Mediterranean as well as in South Africa, the Far East, etc., and was called Mediterranean lymphoma or immunoproliferative small intestinal lymphoma (IPSID).

Bladder Cancer

This is another frequently seen cancer in the Middle East, where schistosomiasis is widespread - the Nile Valley as well as the Tigris and Euphrates valleys seem to be the main areas involved, although schistosomiasis is known in some parts of the Middle East (Saudi Arabia, Democratic Yemen, Yemen, Iraq, Iran, etc.). Bladder cancer is a very interesting subject for the Middle East countries, being until now the only human cancer in which a parasite has an aetiological role.

In countries outside this Region bladder cancer does not constitute more than 7 per cent of all malignant tumours, while data from Cancer Registries in Cairo and Alexandria show that it accounts for 15 to 38 per cent of cancer in males and 4 - 11 per cent in females. In Iraq, where at least 1 million schistosomiasis cases must exist, there is also a high frequency of bladder cancer in males and females of up to 14 per cent. In the Sudan this observation is not seen due to misleading reporting (all urinary cancers which are perhaps mainly bladder). In Isral and Lebanon bladder cancer is also within the first ten most frequent cancers. Data obtained from the Israeli Cancer Registry show that immigrants from Morocco, Algeria, Tunisia, Libya and Egypt have twice the frequency for bladder cancer as that encountered in Israeli-born with Asian-born immigrants (Iraq, Iran, Yemen) being situated between the two above-quoted categories.

Oesophageal cancer

This is another type of cancer particularly widespread in Eastern Mediterranean countries. It constitutes 14 - 15 per cent of all malignancies in males and 6 - 9 in females in Iran. Although no proper data have been published, oesophageal cancer is also encountered in Saudi Arabia, the two Yemens and Afghanistan. In high incidence areas, the age-adjusted figures reach 140 for males and 130 for females per 100 000 population. The high frequency of oesophageal cancer is noted in North East of Iran with an incidence rate of 210 per 100 000 population in males and 185 per 100 000 population in females. The factors which may play a role in the aetiology of this disease in Iran may be due to the following: tobacco, Nass, alcohol, opium, sukhteh (burnt residue of opium), tea, riboflavin deficiency, Epstein-Ban virus or histo-compatibility antigen.

In the high risk area, an asymptomatic chronic oesophagitis was noted and is probably a preneoplastic lesion.

Oral Cancer

It has a high incidence especially in Pakistan, in the Karachi area more than 21 per cent of cancers in males and 18 per cent in females consist of cancer of the oral cavity. In terms of incidence this represents approximately 25 cases per 100 000 inhabitants. Premalignant oral lesions such as leukoplakia, severe dysplasia, etc. were found in 705 per 100 000 inhabitants. Apart from Karachi, oral cancer was reported also in Jamshoro, Multan and Lahore with a frequency between 10 and 20 per cent in males as well as in females. Other countries from the Middle East where oral cancer is reported are: Sudan (5.7 per cent in males, 3.2 per cent in females) and Egypt, Afghanistan, Iran, Lebanon and Tunisia.

The main explanation of the high frequency of oral carcinoma in Middle East countries could be related to chewing and smoking habits.

In the Sudan the use of Trombac (local tobacco) mixed with Atroon (mixture of sodium carbonate and bicarbonate and other chemiclas) placed under the tongue or lip has also been incriminated.

No epidemiological data are available concerning the effect of chewing bethel, khat or other similar vegetable products which are common in other Eastern Mediterranear countries.

Nasopharyngeal carcinoma

This has a higher frequency in Tunisia (11.5 per cent in males, 5.0 per cent in females) but is also found in Egypt, Iraq, Lebanon, Pakistan and the Sudan. As with this disease in the Chinese population, the hypothesis of EB virus is now under verification, together with the idea of a special susceptibility of local populations to this type of tumour.

Bone tumours

Mainly osteosarcoma - have a high frequency in Pakistan (5.2 per cent in males, 3.4 per cent in females) reaching in some provinces even a higher percentage (Peshawar: 8.9 per cent in males, 5.6 per cent in females - Multan: 6.7 per cent in males, 5.5 per cent in females, etc.). Similar figures are found in Afghanistan. No explanation could at present be offered for this observation.

The most common tumours in other parts of the world which have a peculiar distribution in some Middle East countries:

1. Breast cancer - comments are based only on available figures on relative frequency and therefore could be subject to some bias. Eastern Mediterranean countries could be divided into three main categories in respect to breast cancer frequency in females:

(a) High frequency: Breast cancer is the first cancer site in females in Egypt, Israel, Pakistan, Sudan and Tunisia, accounting for 20 per cent and more of all cancers. A similar situation is found in many other countries such as Canada (22.5 per cent), New York State (23.4 per cent); England (23.7 per cent), Sweden (23.8 per cent), Denmark (19.8 per cent). Mention should be made of a particular form of inflammatory breast cancer which seems to be very common in Tunisia.

(b) Medium frequency. Breast cancer being the first or second most frequent malignant tumour in females with 15 to 19 per cent, as in Afghanistan, Iraq and Lebanon. A similar situation is found in Iceland, Finland, Nigeria, etc.

(c) Low frequency: Less than 14 per cent, breast cancer being in the third position - Iran (situation similar to Yugoslavia, Japan, etc.).

2 Cervical uterine cancer - three tendencies could be seen:

(a) High frequency. 20 per cent and over - cervical cancer being the first localization in females as in Lebanon (38 per cent) and Iran (21.1). Ethiopia has also a high frequency of cervical cancer, Uganda (26.2 per cent), South Africa (41.9 per cent), Chile (30.3 per cent), Colombia (35.0 per cent), Singapore (26.8 per cent). In Tunisia its frequency is 18.4 per cent and is in the second place.

(b) Relatively low frequency: Cervical cancer being between 6-12 per cent and having a position lower than the third localization among malignant tumours. Such a situation is encountered in Egypt, Iraq and Pakistan. Similar data were obtained from Canada, New York State, England, Finland, Iceland and Sweden.

(c) Very low frequency: Less than 3 per cent as in Israel and Afghanistan. Such a situation was not found in the group of countries which were investigated in this respect.

3. Lung cancer - is not very common in Middle East countries. Frequencies between 4.0 and 10.5 per cent were recorded in Iran, Tunisia, Pakistan and Israel, and its place being from third to seventh in the countries. In other Middle East countries, lung cancer does not appear among the first two localizations of malignant tumours.

Since smoking habits are increasing very rapidly, a rapid change in lung cancer trends in the future is expected.

4. Liver cancer - this has a relatively high frequency in Pakistan, Sudan and Iran. Aetiologically it is related to hepatitis B. Virus in Pakistan and to contamination with aflatoxin in the Sudan.

RESOURCES FOR CANCER CONTROL AND RESEARCH ACTIVITIES

National Cancer Institutes providing comprehensive services and some research facilities exist only in three countries of the Region. Departments of Radiotherapy are present in twelve countries where they carry the main burden of looking after cancer patients. Medical Oncology departments, outside comprehensive Cance Institutes are present in only 5-6 countries in the Region.

In the remaining eight countries of the Region, where there are no departments of Radiotherapy or special Cancer units/centres, cancer patients are being treated by surgery and/or chemotherapy, prescribed by a physician without any special training.

Cancer research is mostly clinical and based on accumulation and analysis of records of cancer cases. Some epidemiological studies of descriptive nature have been carried out in the recent years. Cancer epidemiologists and experts in other fields of cancer research are hardly available in this Region.

It is worth noting that national cancer control plans have not been formulated in most countries of the Region. This undoubtedly reflects the inappropriate attention being given to Cancer as a health problem.

No estimates can be made, however crude, of funds available for Cancer Research in the various countries of the Region. However, in view of the limited resources available for medical research in general, the funds allocated for research in Cance would appear to be negligible.

PROPOSED RESEARCH ACTIVITIES

Objectives

The research component of the Regional Cancer Programme should have the followi objectives:

a) to improve the existing knowledge and understanding of theCancer problem and of the associated causal factors in the Member States of the Region,

b) to assist in the formulation of National Cancer Control Programmes for preventi detection and treatment of common cancers,

c) to facilitate and improve the teaching and practice of Oncology.

PLAN OF ACTION

The research activities can be dealt below under four main topics:

1. Cancer causation
2. Cancer prevention and detection
3. Cancer management
4. Fundamental cancer research

1. Cancer causation

1.1 Cancer epidemiology

Considering the paucity of valid data on the cancer situation in the Region, ar the meagre resources available for research in Cancer, it is proposed that planning and implementation of well designed epidemiological studies should receive considera emphasis.

Such studies will provide data on cancer incidence, mortality, morbidity, distribution according to age, sex, geographical areas, race, associated causative and other relevant factors. In addition, this data will be of great use in the planning of National Cancer Control Programmes.

WHO, with the help and cooperation of Regional Collaborating Centres, Cancer Institutes and Cancer Departments, can help in planning and implementing epidemiological studies on the most common cancers in the Region.

It is suggested that during the coming 3-4 years the following epidemiological studies be sponsored:

- Epidemiological aspects of uterine cervix carcinoma in Tunisia and the Sudan,
- Epidemiological aspects of inflammatory breast cancer in Tunisia,
- Epidemiological aspects of human lymphomas in Iran,
- Epidemiological aspects of oral and liver cancers in Pakistan.

If required WHO would be prepared to provide technical collaboration through consultant services for preparing protocols for these studies.

1.2 Cancer registries

Cancer registried yield valuable data. Some countries in the Region in recent years have established hospital-based cancer registries. The Organization will be collaborating with national authorities and cancer experts to extend the coverage of existing Cancer Registries and to establish them in those Cancer Centres where they do not exist.

It is also proposed to promote the development of population-based Registries in selected countries, preferably in conjunction with an ongoing population-based health related programme (in order to optimize resources).

To facilitate the implementation of the above proposals, it is planned to organize a Course in Cancer Registry, a meeting on Cancer Statistics, and to sponsor 2-3 National Training Courses on Cancer Registries, during the next 3-4 years.

2. Cancer prevention and detection

To reduce the mortality and morbidity in some types of cancer, promotion and development of research in the prevention and early detection are required.

The following research studies are proposed:

- early detection of breast cancer in general population in Tunisia and Sudan (a comparative study),
- early detection of uterine cervix in Tunisia, Pakistan,

- screening for the pre-symptomatic detection of bronchogenic carcinoma of the lungs in cigarette smokers in Egypt and Kuwait,
- study of premalignant condition of the oral cavity cancer in chewing and smoking tobacco in Pakistan by cytology,
- early detection of bladder carcinoma by cytology and biochemistry in Egypt (a comparative study).

2.3 Environmental carcinogenesis

To alleviate the danger of occupational cancer in industrial and petroleum export countries, WHO is essentially involved in promoting research in occupational cancer with the help of the health authorities of the country concerned, e.g.: cancer of the bladder in Egypt is due to chemical compounds, skin and lung cancer in Kuwait is due to sunlight and asbestosis, colon and lung cancer among carpet-makers in Iran and oral carcinoma in Pakistan, due to chewing tobacco or smoking.

The following subjects are proposed for consideration:

a. Occupational nasal cancers: nasal cancer morbidity and mortality in hardwood workers.

b. Occupational cutaneous cancers: carcinogenic mineral oil effects in metal machine industry (spinocellular epithelioma, particularly in the scrotal region).

c. Liver cancers: comparison between aflatoxin consuming and non-consuming workers exposed to similar levels of potential occupational liver carcinogens.

d. Environmental lung cancer: relationship between lung cancer mortality and morbidity vs smoke or total polynuclear hydrocarbons or 3.4 benzpyrene in the atmosphere.

3. Cancer management

Suitable protocols should be developed for diagnostic staging, treatment and rehabilitation of the most common cancer in the Region.

As the aim of the cancer control programme is to reduce the mortality and morbidity of cancer and to assure the best treatment for cancer patients, it is propo that in the countries where a special cancer is prevalent, a national coordinating bo be organized for the coordination of a unique method of treatment throughout the country.

WHO can provide consultants to the health authorities of such countries for cooperation with the coordinating body. The cancers prevalent in the following countries are proposed to be included in this project:

- Egypt: bladder cancer
- Pakistan: oral and liver cancers
- Tunisia and Iran: carcinoma of uterine cervix
- Sudan: breast and bladder cancers

One of the major problems encountered in the management of cancer patients is a high rate of drop-outs, and where attempts have been made to ensure follow-up at required intervals, they have not been very successful.

Sociological studies are needed to determine factors which deter follow-up, and for formulating and testing of innovative measures for overcoming these factors and ensuring compliance for follow-up.

4. Fundamental cancer research

Research under this heading and covering subjects such as environmental carcinogenesis, experimental oncology, immunogenetics, cell biology, etc., is not considered as priority for WHO's collaboration with Member States during the near foreseeable future.