Need for epidemiological evidence from the developing world to know the cancer-related risk factors

ABSTRACT

The existing evidence on cancer etiology has mostly come from epidemiological studies conducted in the developed world. Now there is an urgent need to gather information on cancer risks in developing countries. Due to recent economic, demographic and health transitions, cancers are on the rise in many developing countries. Future epidemiological studies in these countries should address changing diet, level of physical activity, various environmental and occupational exposures, smoking habits and infections, relative to cancers. In many low resource settings western and conventional lifestyles can be found side by side. Therefore, epidemiological studies in such societies should determine the wide varieties of potentially dangerous exposures, examine changing patterns of related factors and should study other contributing variables as well. Apart from the advantages of such research, there are some challenges. For example, incomplete cancer and death registration, lack of documentation, only partial computerization of medical records, cultural barriers and other technical difficulties can present problems. Some strategies to meet these challenges will be discussed in this paper. There is an immediate need for more detailed epidemiological studies before these developing societies are transformed.

KEY WORDS: Cancer, neoplasm, developing countries, prevention, risk factor, cancer control

BACKGROUND

The current data in the area of cancer etiology and prognosis has been drawn from epidemiological studies conducted in the western world. Nearly one-third of these studies were conducted in either Europe or North America, so the results are representative for only a fraction of the global population. The world does not yet know about the dietary habits, lifestyle or environmental and genetic risk factors of cancer among those who live in developing countries.[1] Epidemiological studies in these countries could substantiate existing evidence, but they could also provide valuable new information that may prevent cancer.

As a result of global economic development, most developing countries are undergoing changes in the overall health status of their populations. People are living longer than before due to improved public health, better nutrition and advances in medical treatment. Even so, cancer rates are on the rise along with other health problems related to life expectancy, diagnostic facilities and aging populations. Despite the fact that incidence rates of various cancers in developing countries are lower than in the developed world, cancer is still posing a problem on the already resource-stretched economies. In many moderately wealthy countries, cancer is already one of the leading causes of death and cancer rates are projected to increase.

POTENTIAL AREAS OF RESEARCH

Tobacco is a major contributor to the cancer scourge in developing countries. Despite its well known causal effect worldwide, it is difficult to gauge the effect of tobacco in developing countries where the majority of cancer patients are smokers, but the cancer incidence is not proportional among smokers.[2] This can be attributed to various factors, such as type of tobacco, duration of smoking habit, amount of carcinogens, metabolism and genetic environmental interactions.[3] In these societies, the lack of population based data on tobacco use, the lack of systematic evidence and vested political interest in the tobacco economy further complicate research efforts to arrive at some valid conclusions. Most of the smoking models from developed countries are based on cigarette use, whereas the predominant forms of tobacco consumption in developing countries are beedis, cigars, cigarettes, chutta, dhunzi, pipe, chilum and hukka, among others. Chewing tobacco is also very popular in a mixture such as pan masala or pan chewed with salted lime, chewed with aracca nut or as snuff, mishri, gutka.
identifies etc.\textsuperscript{[4-5]} Any future epidemiological studies should address the carcinogenicity of various forms and types of tobacco ingested in the developing world.

Fat intake in developing countries has increased substantially, with East and Southeast Asian and Chinese populations among the most affected. Until now, the major dietary source of energy in developing countries has been vegetable oil, but the intake of animal fat has increased from 8% of total calories in the 1960s to 13% in the 1990s.\textsuperscript{[6]} This nutrition transition toward the animal foods in China and other developing countries may increase the risk of some cancers.\textsuperscript{[7]} At the same time, due to the lack of purchasing power and consumption attitudes, people eat less fruits and vegetables in developing countries. A recent publication of the World Health Organization attributed insufficient consumption of fruits and vegetables with 19% of the stomach, 20% of the esophagus, 12% of the lung and 2% of colorectal cancer cases worldwide.\textsuperscript{[8]} There are many dietary components used in African, Asian or Latin American cuisines which were considered as protective cancer factors. Turmeric and cumin in the Indian cuisine and black beans used in Guatemalan cuisine have been investigated for their anti-tumor properties.\textsuperscript{[1,9]}

In developing populations, the attitude towards leisure-related (or) recreational physical activity is different from the developed world. In traditional settings, the main physical activity comes from manual labor for males and from domestic activities for females. There is an absence of effective health awareness programs in developing countries. Various lifestyles and the dynamic nature of the workplace, both need to be examined. Above all, it is essential to study the role of physical activity as a cancer preventative in developing countries.\textsuperscript{[10]}

In emerging countries, indoor/outdoor environments and environmental exposures are different from the developed world. In these countries the cooking and heating needs are usually met by solid and biomass fuels, which are sources of carcinogenic indoor pollutants. But exposure levels will differ between these two populations, since most of the people live outdoors in low resource settings, whereas due to cold weather most of the people spend their time indoors (90% in North America) in the Western world. It is also a widely recognized fact that the risk of cancer among nonsmokers is mainly due to carcinogenic components like radon, benzene and polycyclic aromatic hydrocarbons. There is a ten-fold difference in outdoor air pollution levels of carbon dioxide and sulfur dioxide between the Third World and Western cultures. Epidemiological research has to address these mechanisms clearly before we can properly assess them in terms of risk factors in developing countries.\textsuperscript{[10]}

The types of occupations and their related exposures are different in developing and developed economies. In emerging economies, we usually find a wide range of traditional occupations such as farming or plantation work, along with more modern industrial jobs in manufacturing and service sectors. Work places exhibit both adequate and inadequate safety measures. Research approaches here need to evaluate the health risks arising from modern industrial exposures compared to traditional occupations. So far, not much attention has been paid in the developing world to the pool of agriculture workers and those working in other disorganized sectors. Epidemiologists are interested in studying the causal relation between cancers and exposures to extreme weather conditions, prolonged exposure to sunlight, proximity to chemical and fertilizer poisons and potential mechanical hazards.\textsuperscript{[11]} The relation between cancers and various primary industry exposures is also not very well known in developing countries.

There are many underprivileged countries using hazardous materials that were phased out in developed countries a few decades ago. For example, asbestos is generally used for construction of houses and warehouses and some countries are still using leaded fuel. The chemical compositions used in textile dyes and materials used in rubber, bakery and other related industries are sometimes entirely different from those used in developed countries. Understanding their potential role in terms of cancer risk is vital for epidemiology.

Infections play a different role as risk factors in developing and developed worlds. About one-fifth of total cancers in low-income countries are due to infection compared with just one-in-ten cancers in developed countries.\textsuperscript{[12]} The difference is clearly seen among incidence rates of liver cancer in the western and developing world as the occurrence of this tumor is mainly attributable to hepatitis B and C viruses and exposure to aflatoxin. In Gambia, hepatocellular carcinomas in males is attributable to hepatitis B (57%), whereas hepatitis C contributes significantly (20%) among females.\textsuperscript{[13,14]} On the other hand, these infections only account for 7.7% of liver tumors in the United States.\textsuperscript{[15]} HIV-defining cancers are under investigation in Africa and the existing evidence suggests that HIV-infected patients are most likely to develop Hodgkin’s lymphomas, cervical carcinomas and other anogenital neoplasms (invasive cancer and CIS), leiomyosarcoma and conjunctival squamous cell carcinoma etc.\textsuperscript{[16,17]} The relation between human papilloma viruses and cancer has been clearly established from studies in developing countries.\textsuperscript{[18,19]} Recently, preventative vaccines have been developed; now public health experts are conducting research to answer certain questions such as: Who should receive these vaccinations (women, boys or girls) and how can they be distributed at a reasonable price in developing countries where the need is highest? However, the relation between the hepatitis B/C virus, simian virus 40 (SV40) and Epstein-Barr virus and cancers needs detailed investigation in developing countries.

**STRENGTHS**

Studies in developing countries can provide unique opportunities to test the etiology of cancers and contribute to a better understanding of related mechanisms. People living in...
these countries are affected by different environmental exposures, diet and lifestyles. Their socio-economic backgrounds are quite different from the majority of people in the western world. There is a wide range of differences in demographic related factors; mainly the status of women, work participation, family size, parity, preferences for male offspring, autonomy, access to the health care systems, all of which play a vital role in influencing the outcome. Once diagnosed with cancer, it is very interesting to study the prognosis and survival patterns of patients in developing countries, since diagnostic, treatment and case-management protocols are very different there, compared to developed countries.

The studies planned in developing countries are mostly evidence-based, hence cost-effective. They are expected to adopt tested methodologies and research techniques, thus these studies may provide more accurate data and save a lot of time. The unit cost per research is almost three to four times less than the current expense in developed countries. This is due to low employment costs for skilled people, low cost of data entry/analyses and low-institutional costs. Since most of the societies in developing countries are open, ethical restrictions and permission for any research involving humans may not be as much of an obstacle as they are today in the western world. In many countries, governments are looking for collaborative research agreements in the field of epidemiology; hence, it is easy to get their cooperation throughout the implementation of research protocol. It also provides an opportunity for technological transfer and the development of local talent. It is advisable to both developing and developed countries to seek help from international agencies like the World Health Organization when considering complicated issues such as ethics. Above all, most of the funding agencies are now showing interest in international (or) global (or) multi-center research approaches, as opposed to samples consisting only of a single community. So epidemiologists should take advantage of this new policy, which above all helps to improve international relations and also gives medical research a human face.

WEAKNESSES

It is not that easy to conduct research in different settings where the capacity for cancer research is in an impulsive stage. Cancer registries (or) surveillance systems provide knowledge about important cancers in a country or population. For instance, cancer registration in Asia, Africa and Latin America is restricted to urban populations. The vast majority of rural/ town populations are not covered as they are in other national surveillance systems. For example, in a vast country like India, with over 1.1 billion population, registration is mainly from 14 population-based cancer registries. Coverage by these registries is about 7% (20% Urban and 1% Rural), whereas surveillance epidemiology and end results cover 26% of the US population in 2001.[21] The problems involved in collecting and analyzing cancer registry data in developing countries have been summarized; lack of basic health care, lack of stable population, lack of trained personnel, poor follow-up, as well as poor availability of census estimates and data processing facilities.[22] However, setting up, establishing and maintaining new registries throughout the country would involve enormous cost. In general, over 70% of cancers have a microscopic diagnosis (IARC-CISs) and so a simple network of pathology departments located at medical colleges and major cancer hospitals, may be developed to estimate the nationwide cancer burden. This form of cancer mapping research has produced good results in a vast country like India.[23]

The accuracy and validity of death registrations is vital for epidemiological research, in order to verify the final results, determine survival rates, evaluate the interventions and monitor trends over time. Although vital registration systems are available in many developing countries, a good percentage of cases still go unregistered and only a fraction of them are medically certified. In many rural communities they are either non-existent or unreliable. But new registration techniques and methods, for example a verbal autopsy based on interviewing relatives about complaints, symptoms, signs, duration and treatment details of illness prior to death may be helpful for future researchers.[24]

In developing countries, as opposed to developed countries, partial computerization of medical records, vital statistics and lack of a unique identification (ID) number for each individual, may pose problems for record-linkage studies. In such cases, the major challenge is to develop probabilistic matching algorithms using non-Latin phonetics, local names and other identifiers. All prospective studies may encounter changing disease patterns, disease outbreaks, rapid urbanization and loss of follow-up procedures.

So investigators who are interested in epidemiological research should develop the relevant infrastructure. The key issue is to identify a collaborative institute to collect the best quality data (or) biological specimens possible, an institution that has the capacity to process and store the data and specimens. Data collection in rural areas is a major task; most rural people are manual day laborers in agricultural settings, so an interviewer never finds them at home during office hours. Obtaining consent from illiterate subjects is another challenge. Collecting biological samples is a very sensitive issue in rural communities, thus helping them to understand the purpose of our research is a time consuming process. Biological specimens that are transported to processing centers, without proper transportation and storage or under unfavorable temperatures is another major challenge.[1]

Planning strategies is very complex in terms of international research; obviously you have more problems to deal with involving your host and with other collaborating institutions. The obstacles created by regulatory authorities sometime frustrate a researcher to the extent that the study is cancelled.
or delayed. The researcher is often responsible to governing bodies, along with steering committees from both institutions. Adhering to financial regulations and securing permissions may require extensive crisis management skills in advance, before even implementing the research plan.

**STRATEGIES**

In the 20th century cancer has gotten the better of humanity in the industrialized world, evidenced by the emergence of the disease as a leading cause of death from 1900. In the 21st century, it threatens to decimate civilization in developing countries. In the collective fight against cancer, there is much research needed, both in basic and applied domains across the globe.

The fundamental prerequisite in epidemiological research is a high quality cancer surveillance system. This program should able to provide statistical and methodological data resources that allow more authoritative interpretation of patterns and trends. As we expand the scope of surveillance systems, new tools must be developed to connect all other data sources with cancer surveillance resources. Additional data collection from cancer patients needs to be supported to advance our knowledge of the outcome of treatments and quality-of-life assessments. To fill the gaps in the data, to evaluate the interventions, to estimate population trends, research will be required to expand statistical methods and modeling so that they provide quantitative estimates.

Cancer control strategies must be based on interventions that are firmly grounded on scientific evidence, especially the findings that result from epidemiological and surveillance research. The epidemiological research should recognize human behavior as a major determinant in the successful control of cancer. Clearly it should accept the importance of social and cultural influences of cancer control in developing countries. A dramatic reduction is needed in tobacco use, especially among adults and youth to reduce the burden of tobacco-related cancers; hence, strengthening tobacco control research is essential to cancer research. It is also imperative to develop healthy and practical dietary guidelines and make sure that this information reaches everyone. Health-care programs must be integrated to effectively disseminate comprehensive health education information, concerning the risk of prolonged exposure to sunlight, the danger of infection, the benefits of regular physical activity and the importance of genetic testing.

The promotion of low cost screening strategies to detect cancers of the cervix, breast and oral cancer is also essential. The disproportionate degree of cancer in illiterate and underprivileged segments of a population and the detrimental affect of social inequality on cancer outcomes must be understood.

 Authorities in developing countries must try to improve the system of death and cancer registration and governments in general should invest more money in the public health infrastructure. Integration of cancer control research along with developmental research has been successful in many low resource settings. We need partnerships to put effective research in place; an enterprise that should involve many collaborators, including central and local agencies, voluntary organizations, cancer foundations, medical colleges, medical societies and medical professionals. Scientists in biomedical research fields from both developed and developing countries must effectively interact with applied scientists, within the public health model, if we want to see cancer on the run.

**CONCLUSION**

Some developing countries have now evolved into middle-income countries and are making significant contributions towards epidemiological research aimed at a better understanding of etiology and prognosis. In some countries the public health infrastructure is indeed developing very rapidly. The last decade has seen particular emphasis on international collaborations in epidemiology. In certain countries, progress is taking place with respect to women work participation, nutritional levels, social status and education levels. Nevertheless, globalization has industrialized many developing nations to the point where the attendant use of motorized vehicles has usurped traditional physical activities and increased levels of pollution. This issue must be addressed. In this context, development related cancers like prostate, lung, breast and colon-rectum are growing. Hence, there is an urgency to conduct detailed epidemiological studies in developing countries before these societies are transformed into western-like environments. Otherwise we may miss an unique opportunity to understand the factors that could prevent many cancers in the world.

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Announcement

Dr. J. C. Patel Birth Centenary Celebration Committee

The year 2008 is the Birth Centenary Year of Dr. J. C. Patel. Some of his students/admirers felt that it would be a good idea to celebrate this Centenary Year by organizing CMEs, Orations/Lectures, Conferences, etc. during the year. He was associated with many professional bodies, which meet regularly every year; during these annual meetings/conferences, a lecture/symposium, etc can be organized as a part of Centenary celebrations. We would like to form a Dr. J. C. Patel Birth Centenary Celebrations Committee. All his past students/admirers are invited to join the committee (without any financial commitment). Kindly communicate your name, designation, postal address, telephone number and E-mail ID to Dr. B. C. Mehta at Flat 504, Prachi Society, Juhu-Versova Link Road, Andheri (W), Mumbai 400 053 (drmehta.bc@gmail.com).