Article is available online at http://www.webio.hu/por/2002/8/1/0062

ARTICLE

Large-Scale Pathology-Based Cancer Data – a Reflection of Population-Based Cancer Data

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Pathology-based cancer data is a high quality reflection of the patterns of cancer in the population it represents, provided the demographic details of the patients are carefully recorded. Relative frequency data is neither a replacement for population-based data nor a suggested alternative; it simply enhances the quality of population data and in very large data sets reflects the cancer patterns observed in the representative populations. Aware of the standard shortfalls of pathology-based data, the department of pathology, 'The Aga Khan University Hospital' (AKUH) standardized its data, representing 53.4% of the cancer data of Karachi Division (Pakistan) and also reflecting the cancer pattern of other provinces of Pakistan. This data was compared with 4 different population and institutional-based data sets. The findings substantiate the observation that "despite the problems of interpretation of data from pathology laboratories, they are an invaluable source of information on cancer patterns in much of the world where incidence data are unavailable". If developing countries, unable to organize National Population-Based Registry should as an alternate develop National Pathology-based Registers a well targeted and monitored, a Cancer Control Program would be possible. A good quality, large-scale pathology data with demographic details of the patient recorded can also be extended to give coverage to the population. (Pathology Oncology Research Vol 8, No 1, 62–67, 2002)

Keywords: cancer, pathology

Introduction

Pathology-based cancer data is a high quality reflection of the patterns of cancer in the population it represents, provided the demographic details of the patients are carefully recorded. Relative frequency data is neither a replacement for population-based data nor a suggested alternative; it simply enhances the quality of population data and in very large data sets reflects the cancer patterns observed in the representative populations. It also remains an invaluable source of information on cancer patterns in much of the world where incidence and mortality data are unavailable.[1.]

Received: Dec 12, 2001; *accepted:* Febr 18, 2002

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Data of cancer cases identified in pathology laboratories, if incomplete information is available gives either an over-registration of non-resident cases or a duplication of cases. The risk of associated selection bias of different hospitals and over-representation of more easily accessible sites may remain. Despite these drawbacks, if interpretations are made in the light of information on selective factors, invaluable scientific information may be derived from this data.

In the present times easily available and affordable facilities for endoscopic biopsy, fine needle aspiration biopsy, fine needle aspiration cytology and ultrasound guided biopsies have considerably diminished the deficits of cases of inaccessible tumors (e.g. lung and pancreas). Major surgical and invasive procedures like laparotomy have limited use as pure diagnostic procedures now and the high cost of radiology procedures as a diagnostic tool are also a deterrent in low resource areas as in developing countries. Increased usage of non-invasive diagnostic laboratory pro-

cedures has therefore improved the percentage of microscopic verification and the validity of incidence data.

Comparisons of frequencies between the population-based Karachi data[2,3,4] and the pathology-based AKUH cancer data for Karachi produce rather similar results. This indicates that the development of a pathology-based data for developing countries like Pakistan would be helpful to bring forth a minimum incidence rate for the country, till such a time that a proper population-based national registry is established.

National population-based registries though ideal may not be practicable in developing countries due to restrictions of finances and a lack of technical expertise. However national pathology registers can function because there are relatively few laboratories, and their records are well organized[1]. Some of the bias introduced when the material examined comes from one or two hospitals with specialized facilities can be avoided by registration of all biopsy-diagnosed cancers for an entire country[1]. Unfortunately the vast majority of hospital-based and pathology-based data in the country is recorded without establishing the residency status of the patient or without recording a retraceable address or telephone number or even the correct name. This invaluable data is therefore wasted as no conclusions can be made from the cancer data if the population from which the cases are drawn is not known. Duplication of data also cannot be avoided. In such circumstances, incidence rates cannot be calculated, but the data when presented as proportions or relative frequencies is also not representative of the population.

The population of developing countries is numerically more than developed countries, and as such the global cancer burden tilts towards the developing countries. These countries cover large geographical areas with variable environmental exposures, diverse ethnicities and genetic patterns. It is therefore ironic that most developing countries lack a well-organized cancer control program largely due to a deficiency of incidence data. A few cancers are targeted mainly a result of availability of funds in the particular field. However an effective monitoring is not possible. If the pathologists in developing countries could overcome the problem of demographic details in their data, a National pathology-based registry could be possible and a minimal incidence rate for the country or at least the major cities could be calculated. A targeted and monitored cancer-control program can thus be developed.

Aware of the standard shortfalls of pathology-based data, the Department of Pathology, 'The Aga Khan University Hospital' (AKUH), tried to overcome the difficulties, which diminish the importance of laboratory data by improving the registration of demographic details during 1996 to 1997. Data 1998 onwards was of demographically standardized quality and highly reflective of the representative population.

Methods

The data of 'The Aga Khan University' Pathology Department, diagnosed on the basis of histopathology, fine needle aspiration cytology, fine needle aspiration biopsy and hematology during a 2-year period (1st January 1998 to 31st December 1999) was reviewed and studied.

The demographic details of the registered pathology data were precise and complete. Items such as age, sex, name, address, telephone numbers and nature of surgery were well recorded at the reception counter. A single medical registration number was given to each in-patient and different specimens of the patient given separate sub-identification numbers and data updated. All cancer cases, both the in-patient and the outpatients were also given a specific cancer registration number and information updated with subsequent visits. It was thus possible to recognize duplicate examinations of the same patient. This required a well-trained staff available at all the 31 collection points of this University lab, throughout the country and also of the registration staff at the main lab. Awareness of the legal and academic requirements of accuracy of demographic data was a part of the training of the collection staff. Validity checks and random retrace of cases was conducted for follow-up and for confirmation of the information recorded.

Internal and external quality checks were used for diagnostic pathology as well as the pathology-based cancer data. External quality assurances for diagnostic pathology were maintained by the College of American Pathologists (CAP) surveys. Internal quality control and standardization of the diagnosed data was maintained by using prompt and adequate fixation, grossing as per standard protocol and using histochemical stains, immunohistochemical techniques and biological markers as and when required. ISO 9002 certified the clinical pathology lab in 1999. Consensus diagnosis of all doubtful cases at the daily departmental consultation conferences improved the quality of diagnosed data. Assistance and technical help of Armed Forces Institute of Pathology (AFIP) Washington DC was taken for confirmation of challenging cases. Immunohistochemistry was used for malignancies, which necessitated cellular typing and sub-typing.

Computerized and manual validity checks for the cancer data were also performed as per recommendations of International Agency for Research on Cancer (IARC) and International Association of Cancer Registries (IACR).[5,6] This involved factors influencing comparability i.e. classification and coding. The data are classified using the International Classification of Diseases-Oncology (ICD-O2)[7] and computerized using a customized version of Canreg-3. This software includes facilities for detecting duplicate registrations of the same cancer and for performing checks on the validity of the entered data. The data was re-

checked with the help of the AKUH laboratory database using SNOMED[8] coding and the Canreg-3 database of the Karachi Cancer Registry. The variables that were recorded were the hospital patient-number date of incidence, name, age, sex, address, topography, morphology, grading and staging. The data was analyzed with the help of analytical software EPI-Info incorporated into Canreg-3 and SPSS database. Incidence tables were made using the International Classification of Diseases 10th Revision (ICD-10).[9]

Thus standardized, the AKUH pathology data was compared with 4 data sets. The AKUH data for Karachi division was compared with the population-based data of the same population in the same time frame. The AKUH data for Karachi South (sample population of Pakistan) was similarly compared with the population-based data of Karachi South. All 4 data sets were also compared with the only other data set of Karachi, the JPMC data of 1979-1983 and the contemporary data of another city in Pakistan, Quetta in Baluchistan. The last comparison was essential to highlight differences in the cancer patterns in different geographical regions of the country.

Rresults

During a 2-year period between 1st January 1998 to 31st December 1999, the department of Pathology, The Aga Khan University Hospital (AKUH) dealt with 76 296 cases. 14.9 % of the total cases were cancers. The residency status of the cancers in Sindh Province was - Karachi

Table 1. **Relative frequency data (males)**

Site	*AKUH* K.D.***	*Karachi Division*	*AKUH K.S.****	*Karachi South*	*Karachi (JPMC)*****	*AKUH Quetta*
	1998-1999	1998-99	1995-99	1995-99	1973-88	1998-1999
Oral Cavity C00-08	10.2	10.5	11.3	12.2	12.7	**4.1**
Pharynx C09-14	3.3	3.9	4.1	5.5	**17.0**	0.9
Esophagus C15	3.2	3.6	3.6	4.0	**6.9**	15.0
Stomach C16	3.5	2.8	4.0	3.0	**1.9**	7.4
Small intestine C17	0.4	0.3	0.4	0.7	0.1	0.2
Colo-rectum C18-21	4.7	4.5	4.8	4.1	2.0	5.2
Liver C22	3.3	2.6	3.6	2.9	3.7	**7.5**
Gallbladder etc. C23-24	1.0	1.0	0.8	0.8	0.3	1.3
Pancreas C25	0.5	0.5	0.9	0.6	0.3	0.4
Nose, sinuses etc. C30-31	0.3	0.4	0.2	0.2	0.7	0.2
Larynx C32	4.5	5.0	5.3	5.8	5.2	**1.3**
Bronchus, lung C33-38	9.8	10.8	9.6	11.6	**16.5**	3.2
Bone C40-41	2.2	1.6	2.2	1.8	2.1	2.4
Connective tissue C47-49	2.2	1.9	2.4	2.4	1.5	3.1
Mesothelioma C45	0.1	0.1	0.1	0.1	0.0	0.0
Melanoma of skin C43	0.3	0.3	0.3	0.3	0.2	0.2
Other skin C44	3.9	3.4	3.5	3.2	3.5	**5.7**
Breast C50	0.3	0.7	0.2	0.6	0.3	0.7
Prostate C61	4.0	4.0	4.2	4.0	**1.1**	4.2
Testis C62	1.0	1.1	0.9	0.9	1.8	2.0
Penis C60	0.1	0.1	0.1	0.1	0.0	0.0
Other male genital C63	0.1	0.0	0.0	0.0	0.1	0.0
Bladder C67	4.4	4.5	5.2	5.4	3.0	4.2
Kidney etc. C64-66;68	1.3	1.4	1.2	1.2	1.3	2.4
Eye C69	0.4	0.4	0.4	0.3	0.8	0.5
Brain, nervous system C70-72	3.2	3.3	2.8	3.1	**1.7**	3.0
Thyroid C73	0.8	0.7	1.2	0.9	0.7	**1.4**
Other endocrine C74-75	0.1	0.1	0.2	0.2	0.3	0.2
Hodgkin's disease C81	1.6	1.9	1.8	2.5	2.4	2.7
NHL* C82-85;96	6.8	5.6	4.8	4.8	3.4	**8.8**
Multiple myeloma C88-90	0.9	1.8	1.0	0.9	**2.1**	0.5
Leukemia C91-95	5.2	4.5	3.7	4.0	**1.1**	1.7
Other & unspecified	16.4	16.7	15.2	11.9	5.3	9.6

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(71.5%), Hyderabad (6.5%), Sindh except Karachi and Hyderabad (2.7%), Punjab Province (7.4%), Baluchistan Province - Quetta 10.2% and North West Frontier Province (1.8%). A total of 11.6% of the malignancies had been verified on the basis of cytology, 84.4% histologically and the rest on the basis of hematology.

The Aga Khan University Hospital (AKUH) cancer frequency data of the Karachi Division when calculated showed that 52.2% were males and 47.8% were females. The relative frequency of the five commonest cancers in males was: cancer of the lung (ICD-10 categories C33-C34) (9.5%) followed by oral cavity (ICD-10 categories C00-C06)(9.1), lymphomas (non-Hodgkin's lymphoma ICD-10 categories C82-C85; C96 & Hodgkin's disease ICD-10 categories C81) (8.4%), leukemia (ICD-10 categories C91-C92; C95)(5.2%) and colo-rectum (ICD-10 categories C18-C21)(4.7%). These accounted for 36.9% of all malignancies in males, in this data set.

The relative frequency of cancers in females was: cancer of the breast (ICD-10 categories C50) (34.3%), the most frequently recorded malignancy, followed by oral cavity (ICD-10 categories C00-C06) (7.1%), ovary (ICD-10 categories C56) (4.0%), lymphoma (ICD-10 categories C81-C85; C96) (4.6%) and colo-rectum (ICD-10 categories C18-C21) (3.5%). These accounted for 53.5% of all malignancies in females, in this data set.

The frequency data of Quetta in the province of Baluchistan as recorded by the AKUH pickup points there shows a distinct pattern. The commonest cancer in males was cancer of the esophagus (ICD-10 categories C15) (15%) followed by lymphomas (non-Hodgkin's lymphoma ICD-10 categories C82-C85; C96 & Hodgkin's

Table 2. **Relative Frequency Data (Females)**

Site	*AKUH* K.D.***	*Karachi Division*	*AKUH K.S.****	*Karachi South*	*Karachi (JPMC)*****	*AKUH Quetta*
	1998-1999	1998-99	1995-99	1995-99	1973-88	1998-1999
Oral Cavity C00-08	7.7	8.1	7.1	8.7	**15.2**	5.1
Pharynx C09-14	1.3	1.6	1.6	1.8	**8.3**	2.9
Esophagus C15	2.9	3.1	2.4	3.4	**8.3**	20.4
Stomach C16	1.2	1.2	2.0	1.8	1.1	**2.1**
Small intestine C17	0.3	0.3	0.2	0.1	0.2	0.2
Colo-rectum C18-21	3.5	3.0	3.0	2.7	1.6	3.9
Liver C22	1.7	1.5	1.8	1.8	3.3	3.0
Gallbladder etc. C23-24	2.8	3.6	2.1	2.5	2.1	3.0
Pancreas C25	0.4	0.5	0.2	0.3	0.3	0.7
Nose, sinuses etc. C30-31	0.4	0.3	0.2	0.2	0.7	0.2
Larynx C32	0.8	0.8	0.7	0.8	1.6	0.2
Bronchus, lung C33-38	1.6	1.4	1.5	1.6	**2.1**	0.0
Bone C40-41	1.5	1.2	1.4	1.2	1.5	1.4
Connective tissue C47-49	1.4	1.3	1.4	1.5	1.0	**3.9**
Melanoma of skin C43	0.2	0.1	0.2	0.3	0.2	0.5
Other skin C44	2.7	2.4	3.1	2.6	2.7	**4.4**
Breast C50	34.3	32.0	36.4	33.4	21.7	**13.0**
Uterus C54-55	2.5	2.3	3.1	2.8	2.4	2.3
Cervix uteri C53	2.3	3.7	2.1	3.8	**8.0**	2.5
Placenta C58	0.2	0.3	0.1	0.4	0.0	0.7
Ovary C56	4.0	3.8	5.0	5.6	4.5	4.4
Bladder C67	0.8	1.1	1.1	1.5	1.0	**2.3**
Kidney etc. C64-66;68	0.5	0.8	0.5	0.6	0.7	**2.1**
Eye C69	0.3	0.3	0.3	0.3	0.7	0.2
Brain, nervous system C70-72	1.8	1.8	1.8	1.9	1.0	0.7
Thyroid C73	2.1	2.1	3.0	2.6	1.1	2.8
Other endocrine C74-75	0.1	0.1	0.1	0.1	0.3	0.0
Hodgkin's disease C81	0.8	0.7	0.5	0.6	0.9	1.4
NHL* C82-85;96	3.8	3.1	3.3	2.7	1.7	**5.8**
Multiple myeloma C88-90	0.3	0.4	0.4	0.4	0.2	0.0
Leukemia C91-95	2.9	2.9	2.8	3.2	0.9	0.7
Other & Unspecified	12.9	14.2	10.6	8.8	4.7	9.2

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disease ICD-10 categories C81)(11.5%), oral cavity (ICD-10 categories C00-C06)(9.1%), leukemia (ICD-10 categories C91-C92; C95)(5.2%) and colo-rectum (ICD-10 categories C18-C21)(4.7%). These accounted for 45.5% of all malignancies in the males, in this data set.

The relative frequency of cancers in females in Quetta was cancer of the esophagus (ICD-10 categories C15) (20.4%); breast (ICD-10 categories C50) (13%); lymphoma (non-Hodgkin's lymphoma ICD-10 categories C82-C85; C96 & Hodgkin's disease ICD-10 categories C81)(7.2%); oral cavity (ICD-10 categories C00-C08) (5.1%), ovary (ICD-10 categories C56) (4.4%), and skin (ICD-10 categories C44) (4.4%). These accounted for 54.5% of all malignancies in the females, in this data set.

Grading of cancers was possible in the cases diagnosed on the basis of histopathology. Not many cases diagnosed on the basis of cytology and fine needle aspiration were graded. Grade 1 cancers comprised 14.1% of the cancers whereas grade 2 and 3 cancers were 26.4 and 16.4% respectively. 2.1% of the cancers were anaplastic. It was not possible to grade 41.0% of the cancers chiefly the cytology-verified cases.

Staging of the cancers was possible only in 40% of the total cases. The vast majority of the cases had presented with an advanced stage of malignancy and were diagnosed with regional metastases or with metastases to distant sites. Only 14.5% of the cases were diagnosed with a localized disease.

Discussion

It is an acceptable fact that 'information on the frequency of different types of cancers obtained from the registers or databases of selected medical institutions, represent only a proportion of all those occurring in the population. It is a biased sample in terms of tumor type, sex, age, socio-economic group, etc, depending on the nature of the institution(s) and the treatment facilities available. Conclusions drawn from such databases about the true frequency of different cancers may therefore be wrong and the data must always be interpreted in the light of information on selective factors that may be operating'[1].

The cancer data of the Aga Khan University Hospital (AKUH), pathology department represents 53.4% of the cancer data of Karachi Division [population 9,802,134; males 5,261,712 (52.6%) and females 4,540,422 (47.4%), census 1998][10]. It also reflects the cancer pattern of other cities of Sindh province and the other provinces of the country especially Baluchistan. Interpreted with care this data brings forth the similarities and differences between different data series contemporary and over time. Comparisons of frequencies between the two sexes and between the population-based and pathology-based data produce rather similar results. As the population from which the cases were drawn was known, an attempt was made to calculate incidence rates and the data was also presented as proportions or relative frequencies.

The comparison of the AKUH cancer data for Karachi, with the data of Karachi South (KS) and the cancer data of Karachi Division (KD) brings to light certain facts of contemporary pathology-based data. The KS data is the sample population of the city with a mixed ethnicity pattern. The data of the KD is more representative of the sub-continent of India as the predominant ethnicity is Mohajirs, migrants from India. Both the data sets show a different incidence and frequency pattern. The AKUH pathology data for both KS and KD reflects the different patterns of both the respective population-based data sets. These comparisons were however made possible only with the use of standard formats for presenting all the data as advised by International Agency for research on Cancer (IARC).[5,6]

Unlike other pathology-based data, the AKUH data shows no deficit of cases of tumors formerly considered inaccessible e.g. pancreas and brain, probably an indication of advancing diagnostic medical technologies. A slight deficit of lung cancer is visible, as not all the cases of lung cancer are necessarily biopsied, however the difference is marginal. As both peripheral blood and bone marrow examinations are used for the diagnosis of hematological malignancies, all within the same department, no deficits of the corresponding malignancies was evident. On the contrary leukemia, was over-represented in the AKUH data. Easily accessible sites like skin cancer show a uniform representation in all data sets. There is no excess in the number of cases of skin tumors in the laboratory-based data as compared with population-based data. Bone and soft tissue tumors are marginally over-represented. A slight preponderance of lymphomas is seen, which is indicative of an internationally accepted over representation of easily accessible sites in pathology based-data and the pattern of a referral center for lymphomas. The same is true with hematological data as evidenced by the high leukemia.

Some care is needed in the interpretation of pathology-based data, especially when making comparisons between institutional and population-based data and different data series or over time. The only other published data set for Karachi was the JPMC/PMRC series largely based on radiotherapy data. This data set shows a clear selection bias of a radiotherapy center. Comparisons with this data bring forth the trends in cancer in a population with a non-existent cancer control program. Some under-representation of tumor sites may be an indicator of lack of endoscopic biopsies in the 1979-1983 era, which produced a deficit of cases of inaccessible tumors (e.g., of the lung and pancreas).

The cancer data from Quetta as collected by the AKUH pick-up points on location gives a glimpse of cancer pat-

tern in the Baluchistan province, quite distinct from the cancer pattern of Karachi. The preponderance of esophageal cancers in both the male and female is unlike the patterns seen in Karachi and may be an indicator of environmental carcinogens, of probable dietary type, acting equally on both the males and females. This is substantiated by higher rates of stomach and liver cancers in both sexes. The rates for non-Hodgkin's lymphoma are also much higher than in Karachi. The higher rates for tobacco-related cancers in Karachi are indicative of a similarity of tobacco-habits in the Mohajir (Indian immigrant) population in Karachi and the Indian region.[11-16] The cancer data of Quetta reflects the difference in ethnicity, genetic and environmental differences in the Northwest region of Pakistan.

Conclusion

The comparison of the AKUH pathology data with 4 different data sets substantiates the observation that 'despite the problems of interpretation of data from pathology laboratories, they are an invaluable source of information on cancer patterns in much of the world where incidence data are unavailable'.

The data when interpreted in the light of information on selective factors shows a slight preponderance of lymphomas, an internationally accepted over representation of easily accessible sites in pathology based-data and the pattern of a referral center for lymphomas. The same is true with hematological data, as evidenced by the high leukemias. Nonetheless, this vast data set yields very useful insights about the relative importance of different cancers, their precise classification, sub-classification, grading, and staging. It also gives insight to the different cancer patterns in various geographical regions of the country. It is therefore the right time to use this pathology data as a base for a National Pathology Registry.

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