

# Profile of cancer family clustering in Jordan

S.A. Khoury<sup>1</sup> and D.F. Mas'ad<sup>2</sup>

## مرتسم التجمعات العائلية للسرطان في الأردن

سامي أيوب الخوري، ديانا فؤاد مسعد

**الخلاصة:** استقصى الباحثان التجمعات العائلية للسرطان في عينة عشوائية من المرضى المسجلين في السجل الوطني الأردني للسرطان لعام 1999، وهي السنة التي كانت فيها المعطيات أكثر استكمالاً من غيرها. وقد تم تصميم أداة خاصة وجمعت المعطيات بإجراء مقابلات شخصية. ومن بين العينة النهائية التي شملت 707 مريضاً بالسرطان كان لدى 23% منهم قصة عائلية إيجابية للسرطان، و59% منهم تجمعهم قرابة من الدرجة الأولى. ولكل حالة مستلقتة كان 1.39 من المخالطين، وكان نصفهم من أقرباء الدرجة الأولى للحالة المستلقتة و17% منهم كان لديهم سرطان في نفس الموضع التي أصيبت به الحالة المستلقتة. ويبدو أن التجمعات العائلية للسرطان في الأردن ذات أهمية من وجهة نظر الصحة العمومية، ويوصي الباحثون بمتابعة حثيثة وفورية لأعضاء العائلات التي فيها حالات سرطانية.

**ABSTRACT** This paper explores cancer family clustering in a random sample of patients registered in the Jordan National Cancer Registry for the year 1999, the most recent year that complete data were available. A special instrument was designed and data collected through personal interviews. Of the final sample of 707 cancer patients, 23% had a positive family history of cancer, 59% of which was first-degree clustering. For every proband there were 1.39 contacts. Half of them were first-degree relatives of the proband and 17% had cancer at the same site as the proband. Family clustering of cancer in Jordan appears to be of public health significance, and we recommend immediate and thorough follow-up of family members of cancer cases.

## Profil des cas familiaux de cancer en Jordanie

**RÉSUMÉ** Cet article étudie les cas familiaux de cancer dans un échantillon aléatoire de patients inscrits au registre national des cancers de Jordanie pour l'année 1999, année la plus récente pour laquelle on dispose de données complètes. Un instrument spécial a été conçu et des données ont été recueillies grâce à des entretiens personnels. Sur l'échantillon final de 707 patients cancéreux, 23 % avaient des antécédents familiaux de cancer, dont 59 % chez des parents au premier degré. À chaque cas index correspondait 1,39 sujets contacts. La moitié de ces sujets étaient des parents au premier degré du cas index et chez 17 % d'entre eux, le cancer était localisé au même endroit que ce cas index. Les cas familiaux de cancer en Jordanie semblent avoir une importance du point de vue de la santé publique et nous recommandons un suivi immédiat et approfondi des membres de la famille des personnes atteintes de cancer.

<sup>1</sup>Department of Community and Family Medicine, Faculty of Medicine, University of Jordan, Amman, Jordan (Correspondence to S.A. Khoury: prof\_samikhoury@yahoo.com).

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## Introduction

In the study of cancer family history, 3 types can be identified: hereditary, familial and sporadic [1]. Factors suggesting an inherited risk of cancer include: 3 or more affected first-degree relatives, cancer occurring in 3 generations through the paternal or maternal lineage and/or 2 first-degree relatives diagnosed at an unusually early age for adult onset cancers [1,2]. Familial clustering of cancer is defined as the tendency for the disease to occur in people who have affected relatives [3] but no features of hereditary cancer [1,4]. It is important to differentiate between the clinical sense of familial clustering as defined here and the epidemiological concept of familial aggregation as recognized by an increased risk to relatives of a person with the disease compared with relatives of a person without the disease [5].

The Jordan National Cancer Registry (NCR) is a population-based registry established in 1996 under the umbrella of the Ministry of Health when cancer became a reportable disease. The main objectives of the NCR are: to define the size of the cancer problem and the pattern of cancer occurrence in Jordan and to make cancer incidence and prevalence data available to health planners in order to plan for cancer prevention, control and management in a cost-effective way. All cancer cases diagnosed among Jordanians and non-Jordanians residing in Jordan are reported to the NCR.

In the year 2002, a field survey was designed to study the time lost in the management of cancer patients. Cancer family clustering in Jordan was included as part of this survey. When the study was designed, 1999 was the latest year in which the information pertaining to registered cancer patients was complete and accurate. Therefore that year was selected for the

study. The aim of this paper is to explore the profile of family clustering of cancer in a sample of cancer patients registered in the NCR for the year 1999.

## Methods

### Background to the Jordan NCR

Cancer reports to the Jordan NCR come from hospitals, private practitioners and pathology and haematology laboratories in both the public and private sectors, universities and the Royal Medical Services. No cancer case is registered unless the diagnosis is confirmed by a pathology report.

The NCR usually classifies registered cases by anatomical site. From among all 41 primary anatomical sites reported [6], 19 sites were selected for this survey based on the frequency of incidence, the gravity of the outcome and the need to represent all organ systems. These anatomical sites were: larynx, stomach, colon, rectum, lung, leukaemia, multiple myeloma, bone, melanoma and non-melanoma/skin, female breast, cervix, uterus, prostate, urinary bladder, brain and central nervous system, thyroid, Hodgkin and non-Hodgkin lymphoma.

### Sample

To facilitate the tracing and follow-up of patients, the survey sample was selected from the population of Jordanian nationals residing in Jordan and registered in the NCR for 1999. The number of new Jordanian cases registered in that year was 3142, yielding a crude incidence of 64 per 100 000 population for all cancers (the population of Jordan for 1999 was estimated at 4 900 000 persons).

Computer lists of patients registered by each of the 19 selected anatomical sites were obtained from the NCR. The total number of patients was 2503, representing

the sampling frame for the survey, which covered 80% of all Jordanian patients registered for that year. For each anatomical site, the number of patients to be included in the final sample was determined according to a specific ratio based on the total number of patients registered in that site. The sampling ratio varied between 1/1 for small numbers of patients and 1/5 for the larger numbers. The limited resources available to the investigators dictated this approach.

Randomization of the final sample was done in 2 steps: first the determination of a starting point on each list provided by the NCR and secondly the determination of patients to be included in the sample according to the ratio already determined. The starting point for each list (the first patient to be selected) was determined by drawing a random number between 0–9. After this initial step, selection of patients proceeded from that starting point according to the preset ratio for that anatomical site. For example: if the random number drawn was 4 and the preset ratio of the anatomical site was 1/5, the first patient to be selected to enter the sample (the starting point) would be the 4th patient on the NCR list, the second would be patient number 9, the third is patient number 14 and so on. The final sample was 707 patients or 1/3.5 of the number of Jordanian cases registered for the 19 anatomical sites selected for the survey.

### Survey instrument

For the purpose of this survey, the following terms were defined: proband—a patient with a confirmed cancer and registered in the NCR for the year 1999; contact—a member of the proband's family with cancer as reported by the proband or a close relative if deceased.

The survey team designed a special instrument to fulfil the objectives and needs of the survey. Part 1 included socio-

demographic information about the patient or proband. Part 2 included information about the disease and anatomical site. Part 3 explored the history of cancer occurrence in the family of the patient as reported by the patient or a close relative, if the patient was deceased. It included information pertaining to the family member(s) with a diagnosed cancer: age at diagnosis, sex, relationship to the patient, anatomical site of the cancer and outcome of the disease (alive or dead).

To ensure the accuracy of the family relationship, a detailed relationship list was attached to the instrument. This list included: father, mother, paternal and maternal grandparents, male and female siblings, children (male and female), paternal and maternal uncles and aunts, male and female paternal and maternal cousins, male and female nephews and nieces, husband and wife, grandchildren and cousins once-removed who were the offspring of a cousin of the proband.

For the purpose of this paper, 3 types of cancer family clustering were defined [7]. For probands with more than one relative with cancer, family clustering was classified as first-degree if at least one first-degree relative was reported with cancer regardless of the relationship of other affected relatives; second-degree if second- and third-degree relatives were reported with cancer and third-degree if only third-degree relatives were reported with cancer. However, a single isolated third-degree relative reported with cancer was not considered as family clustering.

Relationship in a family history included the following relatives to the proband [2]: first-degree relatives—children, brothers, sisters and parents; second-degree relatives—paternal and maternal grandparents, aunts, uncles, nieces and nephews and grandchildren; third-degree relatives—male and female paternal and maternal cousins.

Paternal and maternal great aunts and uncles were included if that individual had had cancer and/or one of his/her first-degree relatives had been affected with cancer.

### Data collection

Ethical approval for the survey was secured from the Department of Statistics, Ministry of Health and Ministry of Interior before data collection was started.

Two qualified and experienced fieldworkers were thoroughly trained. The instrument was field-tested, feedback was discussed with the workers and solutions to encountered problems were formulated. After this field test, the instrument was finalized. Data collection was from 1 May 2002 to 30 August 2003.

The NCR provided patients' addresses as received from the reporting sources. Only 47% ( $n = 336$ ) of the sample had correct names and telephone numbers. These constraints were managed through a complete telephone directory, which was used to contact individuals with the same family surname. A close relationship within extended families was helpful for locating patients, alive or deceased. After all means were exhausted, 534 patients (75.5%) of the sample ( $n = 707$ ) were located and their forms completed. This was the final survey sample on which all results were based.

Before starting the actual interviews, the fieldworkers informed patients or their close relatives of the nature and purpose of the survey and verbal consent was obtained. Only 4 patients out of 707 refused to be interviewed. The survey team reviewed each instrument for completeness and accuracy. If an instrument was found to be incomplete or inaccurate, it was returned to the field for the necessary corrections. The project team coded each instrument according to a coding manual.

### Data analysis

Data analysis was performed at the computer centre of the University of Jordan using *Statistical analysis system (SAS)* package, version 7.2.

This paper is confined to the results derived from the analysis of the third part of the survey about cancer family clustering. Only cases with a positive family history were included. A complete report of the original survey and all its instruments are available on request [8].

### Results

**Table 1** shows the distribution of the study sample by site of malignancy in the proband and family history of cancer. There were 124 probands (23.3%) with a positive family history, 374 (70.0%) with a negative history and 36 (6.7%) who did not know their family history.

**Table 2** shows the distribution of probands with positive family history of cancer ( $n = 124$ ) by site of malignancy and type of reported family clustering. It is worth noting that 73 probands (58.9%) had first-degree family clustering, 33 (26.6%) second-degree and 18 (14.5%) third-degree.

**Table 3** shows the distribution of probands with positive family history of cancer by site of malignancy and number of family members reported with cancer (contacts). The number of total contacts was 172 cases. This table also shows the ratio of contacts to proband, ranked in descending order from 1.8/1 to 1.0/1. The average contacts/proband ratio was 1.39/1. Leukemia and cancer of the bone had the highest contact/proband ratio, while cancer of the stomach, cancer of the urinary bladder and non-Hodgkin lymphoma had the lowest

**Table 1 Distribution of the study sample by site of malignancy in the proband and reported family history of cancer**

Site of malignancy in proband	Family history of cancer						Total No.
	Positive		Negative		Don't know		
	No.	%	No.	%	No.	%	
Colon	14	43.8	14	43.8	4	12.5	32
Uterus	9	37.5	13	54.2	2	8.3	24
Larynx	8	34.8	15	65.2	0	0.0	23
Hodgkin lymphoma	8	33.3	14	58.3	2	8.3	24
Breast (female)	19	26.8	47	66.2	5	7.0	71
Urinary bladder	6	25.0	17	70.8	1	4.2	24
Leukaemia	10	24.4	29	70.7	2	4.9	41
Prostate	7	24.1	19	65.5	3	10.3	29
Non-Hodgkin lymphoma	6	24.0	18	72.0	1	4.0	25
Brain and CNS	7	23.3	21	70.0	2	6.7	30
Non-melanoma/skin	4	22.2	13	72.2	1	5.6	18
Lung	7	20.0	26	74.3	2	5.7	35
Multiple myeloma	3	16.7	13	72.2	2	11.1	18
Bone	5	14.7	28	82.4	1	2.9	34
Thyroid	4	12.9	24	77.4	3	9.7	31
Cervix	2	11.8	11	64.7	4	23.5	17
Stomach	3	9.4	28	87.5	1	3.1	32
Rectum	2	9.1	20	90.9	0	0.0	22
Melanoma/skin	0	0.0	4	100.0	0	0.0	4
Total	124	23.3	374	70.0	36	6.7	534

CNS = central nervous system.

ratios. Breast cancer, which had the highest number of probands, had 1.37 contacts to 1 proband. Cancer of the colon, the second largest number of probands had a contacts/proband ratio of 1.71/1.

Overall, 85 (49.4%) of all family contacts were first-degree relatives to the proband, 54 (31.4%) second-degree and 33 (19.2%) third-degree. There were 29 contacts (16.9%) reported with cancer at the same site as that of the probands' and 143 (83.1%) with cancer in other sites.

## Discussion

The purpose of this population-based study was to explore the profile of cancer family clustering in Jordan. According to our data, a proband had a 23% chance of having a positive family clustering of cancer. Almost 59% of this family clustering belonged to the first-degree type, 27% to the second-degree type and 15% to the third-degree type. Furthermore, for every proband with a positive family history there were 1.39 con-

**Table 2 Distribution of probands with positive family history of cancer by site of malignancy and type of reported family clustering (n = 124)**

Site of malignancy in proband	Type of family clustering						Total No.
	First degree		Second degree		Third degree		
	No.	%	No.	%	No.	%	
Cervix	2	100.0	0	0.0	0	0.0	2
Urinary bladder	5	83.3	1	16.7	0	0.0	6
Uterus	7	77.8	0	0.0	2	22.2	9
Larynx	6	75.0	0	0.0	2	25.0	8
Non-Hodgkin lymphoma	4	66.7	1	16.7	1	16.7	6
Stomach	2	66.7	1	33.3	0	0.0	3
Multiple myeloma	2	66.7	1	33.3	0	0.0	3
Colon	9	64.3	4	28.6	1	7.1	14
Hodgkin lymphoma	5	62.5	2	25.0	1	12.5	8
Prostate	4	57.1	1	14.3	2	28.6	7
Brain and CNS	4	57.1	3	42.9	0	0.0	7
Breast	10	52.6	7	36.8	2	10.5	19
Thyroid	2	50.0	2	50.0	0	0.0	4
Rectum	1	50.0	1	50.0	0	0.0	2
Leukaemia	5	50.0	2	20.0	3	30.0	10
Non-melanoma/skin	2	50.0	1	25.0	1	25.0	4
Bone	2	40.0	2	40.0	1	20.0	5
Lung	1	14.3	4	57.1	2	28.6	7
Total	73	58.9	33	26.6	18	14.5	124

CNS = central nervous system.

tacts. Almost half of the contacts showed a first-degree family relationship to the proband, 31% a second-degree and 19% third-degree. There were 17% of contacts reported with cancer at the same site as that of the probands' and 83% at other anatomical sites.

Family clustering was based on the history reported by the patient or a close relative. No DNA, environmental or behavioural factors were assessed. Self-reported family history of cancer frequently suffers from inaccuracies [3,4,9]. Individuals often have incomplete or inaccurate information about cancer history in their family. The

most important reasons are loss of contact with relatives, small family size or death(s) at an early age from unrelated conditions [2].

It is important to note also that cancer in Jordan remains a social stigma, which may prevent people from revealing the presence of a cancer case in their family. This may explain the frequent inaccuracies in names, addresses and telephone numbers encountered in the reporting of cancer cases. However, the validity of the collected data on family history of cancer in Jordan is secured by a traditional and effective extended family support system, which becomes operative in cases of disease and

**Table 3 Distribution of probands by site of malignancy and number of family members reported with cancer (contacts) and ratio of contacts/proband**

Site of malignancy in proband	No. of probands	No. of contacts	Ratio contact/proband
Leukaemia	10	18	1.80/1
Bone	5	9	1.80/1
Colon	14	24	1.71/1
Larynx	8	12	1.50/1
Non-melanoma/skin	4	6	1.50/1
Rectum	2	3	1.50/1
Cervix	2	3	1.50/1
Prostate	7	10	1.43/1
Breast	19	26	1.37/1
Multiple myeloma	3	4	1.33/1
Lung	7	9	1.29/1
Thyroid	4	5	1.25/1
Uterus	9	11	1.22/1
Brain and CNS	7	8	1.14/1
Hodgkin lymphoma	8	9	1.13/1
Stomach	3	3	1.00/1
Urinary bladder	6	6	1.00/1
Non-Hodgkin lymphoma	6	6	1.00/1
Total	124	172	1.39/1

CNS = central nervous system.

death. This system is further enforced by the high rate of consanguineous marriages in Jordan [10].

A review of the available literature did not reveal a similar population-based study. Most of the studies we reviewed dealt with cancer aggregation in close relatives based on genetic information and DNA testing [1], which were not performed in this survey. This fact does not allow any valid comparison with any other study of family clustering of cancer but it might pave the way for further studies in similar societies, especially in the Arab world.

This survey demonstrated the contacts/proband ratios by site of malignancy and in the total sample. These ratios should be confirmed and supported by further in-depth studies using genetic information and DNA testing. Furthermore, the number of probands in all anatomical sites was not large enough to allow for meaningful conclusions to be drawn. A larger sample, probably including all cases registered in the NCR for that year, should be investigated.

Cancer causation is likely to be multifactorial, involving genetic, behavioural and lifestyle factors, environmental exposure

and a gene–environment interaction [11]. Clustering of cancer can be generated by shared genetic material, behavioural patterns and/or exposure to environmental factors or it can occur by chance [3].

Cancer studies can estimate risk of cancer for siblings and parent–offspring pairs but cannot distinguish between genetic and non-genetic causes of clustering of cancer [12]. Therefore, use of the expression “familial” disease without a precise definition, especially when used to refer to “hereditary” disease should be discouraged [13].

## Conclusion and recommendations

The average contacts/proband ratio of 1.39/1 shown in this study suggests that family

clustering of cancer in Jordan is of public health significance. We recommend an immediate in-depth follow-up of contacts as soon as a proband is registered. A special outreach unit should be established at the NCR to carry out this task and to facilitate early detection and prevention and control of cancer.

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***Cancer control: knowledge into action. WHO guide for effective programmes: diagnosis and treatment***

The World Health Organization estimates that 7.6 million people died of cancer in 2005 and 84 million people will die in the next 10 years if action is not taken. More than 70% of all cancer deaths occur in low- and middle-income countries, where resources available for prevention, diagnosis and treatment of cancer are limited or nonexistent.

Yet cancer is to a large extent avoidable. Over 40% of all cancers can be prevented. Some of the most common cancers are curable if detected early and treated. Even with late cancer, the suffering of patients can be relieved with good palliative care.

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