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Population-Based Prevalence of Cancer Family History in Southeastern Iran

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Abstract

Background: Cancer family history (CFH) could be an effective non-invasive preventive tool for cancer screening. There are limited data on the prevalence of CFH.
Objectives: We aimed to estimate a robust population-based prevalence of CFH in southeastern Iran.
Methods: This study is a population-based survey. Participants were recruited in a multistage proportional-to-size cluster sampling design. A validated interview form was used, including a pedigree table and a cancer detail table. A positive CFH was defined as a verbal self-report of cancer diagnosis in at least 1 relative. The CFH prevalence was estimated according to age, gender, residential area, relatives' closeness, and cancer type. Estimated prevalence values were corrected for the sensitivity of self-reported CFH in a Monte Carlo-based sensitivity analysis.
Results: A total of 2057 interviews with a male-female ratio of 1.14: 1 were analyzed. The overall prevalence (95% uncertainty level (UL)) of CFH in at least 1 relative (first or second-degree relatives (FDR/SDR)) was 37.06 (27.50, 47.05). The prevalence (95% UL) of CFH in at least 1 female and male FDR was 12.54 (8.62, 17.25) and 11.07 (7.22, 15.34), respectively. The prevalence (95% UL) of a positive history of lung, breast, and colorectal cancers in at least 1 FDR was 2.05 (1.36, 2.90), 1.36 (0.79, 2.08), and 1.23 (0.63, 2.02), respectively.
Conclusions: The prevalence of positive CFH in FDRs is less than that of developed countries and exceeds 11.8% in the general population of southeastern Iran. CFH taking by general practitioners in routine visits is recommended as a screening tool in this population.

Keywords: Neoplasm, Family History, Prevalence, Iran

1. Background

Cancer family history (CFH) has been shown to be an important risk factor or predictor for cancer (1-4). A positive CFH is not only due to genetic susceptibility but may result from nongenetic factors (5-7). Thus, it could be used as an effective preventive medical tool for hereditary and nonhereditary cancer screening (8-10).

Despite the importance and effectiveness of using CFH, there are relatively little data on its prevalence and epidemiology, especially in developing countries (11, 12). As we know, there are only 2 population-based reports on the prevalence of CFH in Iran, and both are from studies in Tehran metropolitan area (12, 13). However, the prevalence of CFH may differ across different geographies and populations. In addition, most studies on the prevalence of CFH have defined it according to self-reports by patients or probands (9, 11, 14). However, a growing body of evidence supports the lack of sensitivity of self-reported CFH (15). It means that when patients or probands report their CFHs, they might miss some of their relatives with a cancer history, leading to an underestimation of the CFH prevalence.

Accordingly, estimating the CFH prevalence in Iran could be valuable for health policymakers to make more accurate decisions on cancer prevention and plan cost-effective cancer screening programs (9).

2. Objectives

We estimated the robust population-based prevalence of CFH in southeastern Iran. To provide more accurate estimates, corrections were made for the lack of sensitivity of the self-reported CFH.

3. Methods

3.1. Study Design

We used data from the second part of a multipart study on the familial incidence and prevalence of cancer in Kerman (16). In this part, participants were recruited in a population-based survey design. Study details have been published earlier (16, 17). In brief, a multistage proportional-to-size cluster sampling design was used to sample the Kerman district's Persian speaking, 20 to 60 years old resident population from August 2014 to February 2015 (16). For sampling, the rural and urban areas of the Kerman district were considered as 2 different strata. In each stratum, substrata were defined considering the population of each settlement. Then, clusters were defined in each substratum. These clusters had similar age and gender proportions to those of Kerman Province. Finally, the clusters were selected randomly regarding each substratum size, and two interviewers sampled within the clusters (16).

A validated interview form was used for data collection. The interview form mainly included a pedigree table and a cancer detail table. Interviewers were well-trained, adequately paid, encouraged, and supervised to ensure data quality. Interviews were gender-matched and conducted after written or verbal consent. At first, interviewees were asked to enumerate their family members and any CFHs. Then they were asked for details of the CFHs they had enumerated in the first step.

The Ethics Committee of Kerman University of Medical Sciences approved the original study (KMU/93/50). The current study was approved by Shiraz University of Medical Sciences (code: IR.SUMS.MED.REC.1401.169).

3.2. Cancer Family History Definition and Verification

A positive CFH was defined primarily as a verbal self-report of cancer diagnosis in at least 1 relative by probands. The sensitivity of CFH reports was assessed, and the results were published (17). The details of reported cancer cases were also verified via a one-sided blind phone call with patients themselves if it was possible (if patients were alive, aware of the cancer diagnosis, and emotionally able to talk about their cancer) or the patients' next-of-kins. The reported cancer details during the phone-based interviews were considered more accurate than those reported during the face-to-face interviews, considering the closeness of the proband with the patient.

3.3. Statistical Analysis

To estimate the corrected prevalence, first, the numbers of probands with at least 1 affected relative with cancer were enumerated across different strata. It was done according to the probands' age, gender, and area of residence, as well as the kinship degree and number of affected relatives. These stratum-specific numbers, then, were multiplied by the sensitivity to the power of (-1) of self-reported CFHs according to our previous report (17). Subsequently, the corrected prevalence was estimated as the corrected number of probands with positive CFH over the number of participants in the related stratum. Estimations of the corrected prevalence and 95% uncertainty levels (ULs) were done in a Monte Carlo-based sensitivity analysis with 5000 scenarios. In each scenario, the number of probands with a positive CFH and the value of sensitivity of the self-reported CFH had a possibility to randomly change based on a Poisson and normal distribution, respectively. The iteration was continued until the statistical robustness, and stability of the estimates of bounds was achieved (5000 scenarios) (18). In addition, the prevalence of tumor-specific familial histories of cancer was estimated in a similar way, except for the enumeration of cancer cases instead of the number of probands with a positive CFH, over the total number of study participants. Based on a similar procedure, we also estimated the prevalence of tumor-specific cancer history in relatives 50 years of age or younger at the time of cancer diagnosis and related 95% ULs.

All estimates were estimated separately for first and second-degree relatives (FDR/SDR). Estimations and modeling were done using Microsoft Excel.

4. Results

A total of 2057 interviews with a male-female ratio of 1.14: 1 were analyzed (the response rate was 79%). The distribution of participants across genders, age groups, and residential areas was similar to that of the resident population in Kerman district (Table 1).

A total of 845 verifiable (via phone calls) cancer cases were reported by 663 probands (the probands reporting affected relatives in both FDR and SDR groups were counted twice). All cancer patients' mean age (at diagnosis) was 58.10 years, with an SD of 15.76 years. The mean ± SD age of patients who were reported by 20 - 29, 30 - 39, 40 - 49 and 50 - 60 years old respondents were 55.48 ± 16.44, 58.76 ± 16.10, 59.39 ± 14.11, and 63.16 ± 13.89 years old, respectively. Of all cancer cases, 239 cases were FDRs with a mean age of 54.67 ± 17.35 years, and 606 cases (mean age 59.46 ± 14.92 years) were SDRs.

The overall corrected prevalence (95% UL) of CFH in at least 1 relative was 37.06 (27.50, 47.05). The corrected

Table 1. Sampling Strata and Stratum Specific-Prevalence of Cancer Family History (n = 2057)

Factor	n	Observed Counts		Corrected Prevalence (95% UL) [a]	
		FDRs	SDRs	FDRs	SDRs
Gender					
Male	1093	105	222	121 (11.07) (7.22, 15.34)	251 (22.95) (15.96, 30.59)
Female	963	107	229	121 (12.54) (8.62, 17.25)	259 (26.88) (18.84, 35.51)
Age group					
20 - 29	894	59	212	69 (7.71) (4.61, 11.38)	249 (27.83) (17.63, 39.06)
30 - 39	516	53	117	62 (12.09) (7.14, 18.08)	136 (26.32) (16.26, 37.24)
40 - 49	339	47	78	54 (15.84) (10.85, 21.45)	89 (26.21) (19.26, 33.87)
50 - 60	306	53	44	61 (19.84) (14.00, 26.85)	50 (16.45) (11.15, 22.33)
Residency					
Urban	1525	161	323	202 (13.22) (9.57, 17.15)	404 (26.49) (19.95, 33.47)
Rural	532	51	128	64 (11.98) (8.02, 16.74)	159 (29.94) (21.75, 39.23)
Overall	2057	212	451	242 (11.76) (9.33, 14.52)	515 (25.03) (20.28, 30.01)

Abbreviations: UL, uncertainty level; FDRs, first-degree relatives; SDRs, second-degree relatives; CFH, cancer family history
[a] Values are expressed as No. (%).

prevalence (95% UL) of CFH in at least 1 first-degree relative in females and males was 12.54 (8.62, 17.25) and 11.07 (7.22, 15.34), respectively. Despite slight variations, the prevalence of CFH was not significantly different between sampling strata (Table 1).

Of the 663 probands with a positive CFH, 140 (21.11%) reported a cancer history in at least 2 relatives, and 42 (6.3%) reported a CFH in at least 3 relatives (Table 2).

The corrected prevalence (95% UL) of a positive history of lung, breast, and colorectal cancers among FDRs was 2.05 (1.36, 2.90), 1.36 (0.79, 2.08), and 1.23 (0.63, 2.02), respectively. These were the 3 highest estimated cancer prevalence values in FDRs. However, brain (corrected prevalence = 0.78; 95% UL, 0.39, 1.25), leukemia (0.75; 0.34, 1.29), and breast (0.70; 0.33, 1.17) cancers were the most prevalent cancers in younger (age $\leq$ 50 years) FDRs (Table 3).

The highest corrected prevalence values of positive cancer history in SDRs were estimated for lung (4.82, 95% UL, 3.55 - 6.22), breast (4.09, 95% UL, 2.80 - 5.63), and stomach (3.98, 95% UL, 2.90 - 5.24) cancers, respectively. Furthermore, the most prevalent cancers in younger SDRs were breast (1.73; 1.06, 2.55), leukemia (1.04; 0.51, 1.70), and lung (1.00; 0.55, 1.53) cancers (Table 3).

There was no difference between the corrected prevalence of CFH in paternal and maternal relatives (data was not shown).

5. Discussion

Familial cancer histories are commonly used in epidemiological studies and as a clinical predictor of increased risk for cancer (8, 11, 19-21). In addition, the assessment of CFH could be an effective tool for cancer screening in high-risk groups (8, 22). We used data from a relatively large representative study to estimate the prevalence of cancer-specific family history in southeastern Iran. According to our previous work in the same population, the estimated prevalence was corrected for lack of sensitivity of probands reported CFH. Overall, the corrected prevalence of all cancer sites' family history in FDRs and SDRs was estimated to be 11.76% and 25.03% in the general population, respectively. The positive histories of the lung (2.05%), breast (1.36%), colorectal (1.23%), leukemia (1.16%), and stomach (1.11%) cancers were the first 5 common types of CFH in FDRs, respectively. Also, the 5 most prevalent CFHs among SDRs were related to lung (4.82%), breast (4.09%), stomach (3.98%), leukemia (3.00%), and colorectal (2.47%) cancers.

Our estimates are less than the previous estimates from developed countries (14, 20). For instance, Kumerow et al. (14) reported a CFH prevalence of 35.6% (34.8%, 36.4%) in all cancer sites in FDRs compared with our estimate of 11.76% (9.33, 14.52). Also, Mitchell et al. (20) reported a CFH prevalence of 9.4% (5.8, 14.9) for colorectal cancer among FDRs, while our estimated prevalence was 1.23% (0.63, 2.02). This lower prevalence may be due to a higher prevalence of CFH in developed countries. A lower cancer incidence in Iran, especially in the south (23-25), could be

Table 2. Prevalence of Cancer Family History in Southeastern Iran (2015) According to Degree and Number of Affected Relatives (n = 2057)

At Least No. of Affected Relatives	Observed Counts		Corrected Prevalence (95% UL)	
	FDRs	SDRs	FDRs	SDRs
1	212	451	11.76 (9.33, 14.52)	25.03 (20.28, 30.01)
2	23	117	1.27 (0.74, 1.89)	6.49 (4.99, 8.20)
3	4	38	0.23 (0.04, 0.48)	2.11 (1.41, 2.92)

Abbreviations: UL, uncertainty level; FDRs, first-degree relatives; SDRs, second-degree relatives; CFH, cancer family history

Table 3. Corrected Prevalence of Cancer Family History in Southeastern Iran (2015) According to Tumor Sites [a]

Tumor Site	All Ages				Ages ≤ 50 Years			
	FDRs		SDRs		FDRs		SDRs	
	n	P (%) (95% UL)	n	P (%) (95% UL)	n	P (%) (95% UL)	n	P (%) (95% UL)
Lung	42	2.05 (1.36, 2.90)	99	4.82 (3.55, 6.22)	9	0.44 (0.16, 0.80)	21	1.00 (0.55, 1.53)
Stomach	23	1.11 (0.63, 1.68)	82	3.98 (2.90, 5.24)	5	0.22 (0.05, 0.47)	17	0.83 (0.43, 1.33)
Breast	28	1.36 (0.79, 2.08)	84	4.09 (2.80, 5.63)	14	0.70 (0.33, 1.17)	36	1.73 (1.06, 2.55)
Prostate	22	1.06 (0.59, 1.62)	50	2.45 (1.66, 3.35)	0	0	2	0.11 (0.00, 0.29)
Leukemia	24	1.16 (0.61, 1.87)	62	3.00 (1.80, 4.42)	15	0.75 (0.34, 1.29)	21	1.04 (0.51, 1.70)
Liver	17	0.83 (0.42, 1.33)	43	2.11 (1.42, 2.95)	6	0.28 (0.06, 0.55)	10	0.5 (0.20, 0.88)
Colorectal	25	1.23 (0.63, 2.02)	51	2.47 (1.41, 3.75)	5	0.24 (0.05, 0.53)	18	0.88 (0.40, 1.50)
Brain	22	1.05 (0.59, 1.62)	42	2.05 (1.36, 2.84)	16	0.78 (0.39, 1.25)	18	0.88 (0.47, 1.40)
Uterine	15	0.73 (0.33, 1.23)	23	1.10 (0.59, 1.72)	10	0.49 (0.18, 0.89)	7	0.36 (0.11, 071)
Larynx	7	0.36 (0.11, 071)	44	2.13 (1.31, 3.10)	0	0	10	0.49 (0.17, 0.89)
Bladder	13	0.61 (0.25, 1.07)	9	0.43 (0.14, 0.79)	2	0.12 (0.00, 0.32)	2	0.12 (0.00, 0.32)
Bone marrow	9	0.43 (0.14, 0.79)	17	0.85 (0.41, 1.38)	4	0.18 (0.00, 0.42)	5	0.24 (0.05, 0.52)
Other	29	1.41 (0.81, 2.14)	49	2.37 (1.56, 3.37)	15	0.73 (0.33, 1.23)	24	1.21 (0.61, 2.00)
Unknown	6	0.30 (0.06, 0.61)	57	2.79 (1.83, 3.95)	5	0.24 (0.05, 0.53)	23	1.09 (0.60, 1.73)

Abbreviations: P, prevalence; UL, uncertainty level; FDRs, first-degree relatives; SDRs, second-degree relatives; CFH, cancer family history
[a] The total number of cases in this table is more than 845 since the cases with multiple primary and/or metastatic cancers were counted more than once.

another reason. It might also be partly due to the lower sensitivity of verbal family history assessment compared with the data provided by the familial cancer registry or high-quality data linkage procedures used in studies in developed countries. As we reported in our previous work, verbal family history taking may suffer from serious false-negative rates for several tumor sites (17).

The comparison of our results with the previous studies from Iran is inconclusive (12, 13). Moghimi-Dehkordi et al. (12), in a study from Tehran, reported a total CFH prevalence of 26.1% compared with our estimate of 37.06% (27.50, 47.05). They also reported a prevalence of CFH for all tumor sites in FDRs, relatively similar to our study (12.2%), while they observed a prevalence among SDRs that is less than our estimates (15.3%). Also, in another study from Tehran, Moghimi-Dehkordi et al. (13) reported that the CFH prevalence was 1.29% and 1.76% in FDRs and SDRs, respectively, for colorectal cancer. These prevalence values are almost similar to our results regarding our estimates' ULs. Both of these studies were conducted in Tehran, which, according to the cancer registry report, generally has a higher cancer incidence than Kerman (25). However, the reason for our study's higher prevalence values of CFH (especially among SDRs) may be that our estimates were corrected for cancer visibility (17).

In line with Mai et al. (11), we found a relatively similar prevalence of CFH between different age groups, genders, and areas of residence, except for slight variations. This finding is inconsistent with Moghimi-Dehkordi et al. (12), reporting that females had more CFHs. Kumerow et al. (14) and Ramsey et al. (9) also observed more CFH reports from females and older probands. However, we believe that the prevalence of CFH in the general population is

not different between males and females. Considering 1 proband, we believe that cancer incidence in his/her relatives is not the result of their gender. In addition, an increase in CFH with probands' age may be possibly due to the higher age of their relatives. However, an explanation for the different prevalence values of CFH across population strata could be the varying sensitivity of self-reported CFHs in different subpopulations (17, 26).

According to our study results, the prevalence of positive cancer history in younger FDRs was more than 5% in the population. In addition, the study results showed that around 8% of participants had at least 2 affected relatives with cancer. From a clinical point of view, the proportion of the population with affected younger FDRs or more than 1 affected relative with cancer is considered high risk, and more invasive screening procedures should be recommended to this group (27-29). Additionally, the study results revealed that the prevalence of positive cancer history of younger SDRs was around 10% in the population. In a more conservative approach, these individuals with affected younger SDRs could also be considered high risk. Therefore, a more detailed cancer risk assessment may be beneficial in terms of cancer prevention or early detection for them (28).

One limitation of our study is the lower estimated prevalence of CFH among FDRs compared with SDRs. Such a difference should not exist in the general population since any FDR of an individual could be someone else's SDR. Therefore, being an FDR or SDR would not determine the cancer prevalence. This difference may be due to the lower total number of FDRs than SDRs regarding our method. Therefore, any possible biases in the less populated group of FDRs could have changed the estimated results enormously compared with SDRs. Another reason for this observation could be that probands may have found reporting their FDRs' cancer more burdensome than their SDRs.

Despite the correction for cancer visibility in the familial network, the effects of recall and refusal biases could not be ruled out in our study. However, based on previous studies, we believe that these effects could be considered ignorable in our setting (30, 31).

5.1. Conclusions

The robust prevalence of having at least a positive CFH in FDRs and SDRs was more than 10% and 20% of the general population of southeastern Iran, respectively. Although these values may seem relatively low, they are remarkable from a public health point of view. Therefore, mass education to encourage this population to participate in cancer screening programs and taking CFH by general practitioners in routine visits may be useful to reduce the cancer burden in southeastern Iran.

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Footnotes

Authors' Contribution: Study concept and design: H. M. and B. K.; analysis and interpretation of data: B. K. and M. B.; drafting of the manuscript: B. K.; critical revision of the manuscript for important intellectual content: A. H., H. M., and J. O.; statistical analysis: H. M.

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Data Reproducibility: The datasets used and analyzed during the current study are available from the corresponding author on request. The data are not publicly available due to privacy or ethical restrictions.

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