RESEARCH ARTICLE

Comparison of Population Based Cancer Incidence Rates among Circassians, Chechans and Arabs in Jordan (1996-2005)

Raja Mohd-Talal Fathallah[1&], Rana Dajani[2&*]

Abstract

Background: Cancer is a complex disease caused by multiple factors, both genetic and environmental. It is a major health concern worldwide, in the Middle East and in Jordan specifically and the fourth most common killer in the Middle East. Hypothesis: The relative genetic homogeneity of the Circassian and Chechan populations in Jordan results in incidences of cancer that differ from the general Jordanian population, who are mostly Arabs. Materials and Methods: National Cancer Registry data were obtained for the years 1996-2005 The Chechen and Circassian cancer cases were identified and cancer registry data were divided into three populations. Crude rates were calculated based on the number of cancer cases and estimated populations. Results: Breast cancer is the most common cancer type constituting about one third of female cancers in all three populations. Higher crude rates are observed in the Circassian and Chechen populations than in the Arab Jordanian population. The rate ratios (95%CI) in Circassians and Chechens with respect to the Arab Jordanian population are 2.1 (1.48, 2.72) and 1.81 (1.16, 2.85), respectively. Lung cancer is the most common cancer in male Arab Jordanians and Chechens with crude rates of 4.2 and 8.0 per 100,000 respectively. The male to female ratio in these two populations in respective order are 5:1 and 7:1. The lung cancer crude rate in Circassians is 6.5 per 100,000 with a male to female ratio of only 1.6:1. The colorectal cancer crude rates in Arab Jordanians and Chechens are similar at 6.2 and 6.0 per 100,000, respectively, while that in Circassians is twice as high. Conclusions: Considerable ethnic variation exists for cancer incidence rates in Jordan. The included inbred and selected populations offer an ideal situation for investigating genetic factors involved in various cancer types.

Keywords: Cancer incidence data - epidemiology trends - Circassian - Chechan - Jordan

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Introduction

Despite extensive research efforts for more than a decade, the genetic basis of common human diseases remains largely unknown. Although there have been some notable successes. Cancer is a complex disease with multiple factors both genetic and environmental. Cancer is the second most common killer after cardiovascular disease in the world today (Ferlay et al., 2010). 13% of all deaths worldwide are caused by cancer. 63% percent of cancer deaths in 2008 occurred in developing countries (Ferlay et al., 2010). The projection of new cancer cases is expected to rise from 7.6 million in 2008 to 13 million in 2030 (World Health Statistics Report, 2012). 70% of these cases by 2020 are expected to occur in developing countries (Sener and Grey, 2005). Nevertheless, developing countries have taken major steps in cancer prevention. This has been reflected in decreased colorectal and breast cancer incidence over the years. Centers for Disease Control and Preventions (CDC) reported colorectal cancer incidence rates decreased among men and women from 1999 through 2008. Breast cancer incidence rates among women decreased from 1999 through 2004, and remained at a constant level from 2004 through 2008 (http://www.cdc.gov/Features/dsCancerAnnualReport).

Cancer is a major health concern in the Middle East. Cancer is the fourth most common killer in the Middle East (Freedman, 2006) and the second cause of death in Jordan (Mortality Data in Jordan, 2008) reaching 14% of deaths (Al-Tarawneh et al., 2010). Ismail et al. (2013) showed that although the incidence of cancer in Jordan is less than most developed countries; there is an overall increase in cancer incidence in females over the years (Ismail et al., 2013). Recently, the World Health Organization predicted that the largest increase in cancer incidence in the next 15 years will be in the Middle East (http://www.emro.who.int/dsaf/dsa1002.pdf). The incidence to mortality rate ratio in the Middle East is 70% compared to 50% in the West. It is predicted that there will be a 40% increase in new cancer cases by 2020 (Rastogi et al., 2004; WHO, 2009).

The National Cancer Registry was established in 1996 in Jordan and has been a valuable resource for providing the incidence of cancer in Jordan (Ministry of Health, 2008). It is predicted that the Jordanian population will increase from 6.3 million to 7.1 million by the year 2020. The number of diagnosed Jordanian cancer cases will

*[1]Center for Diabetes, Genetics and Endocrinology, [2]Department of Biology and Biotechnology, Faculty of Science Hashemite University, Zarqa, Jordan [&]Equal contributors *For correspondence: rdajani@hu.edu.jo*

increase from 5,110 in 2008 to 7,281 in 2020. The causes of this increase are unknown however future predications should be addressed to allow for planning for cancer care and its economic impact on Jordan.

Understanding cancer causes can be the first step towards setting prevention and early detection guidelines. Many factors can contribute to the complexity of understanding cancer which include growing proportion of elderly people, reduction in deaths due to communicable diseases, changes in lifestyle and increased exposure to cancer promoting substances. In addition to increased prevalence of tobacco use, changes in diet and decreased physical activity. Other factors are genetic which makes it difficult to distinguish between environmental and genetic factors for lack of the ability to isolate a population from another or to normalize circumstances. The National Cancer Institute has recognized the need to better define the cancer burden in racial/ethnic minorities and medically underserved populations. There are many reports that show evidence for differences in cancer rates in different ethnic populations e.g., http://www.haematologica.org/cgi/content/full/96/7/1049; http://info.cancerresearchuk.org/cancerstats/inequalities/

Studies concerning the incidence of cancer in ethnic populations in the Middle East and developing countries are sparse. Jordan presents a unique case of three ethnic populations genetically isolated living in the same geographical area and environment (Barbujani et al., 1994; Bulayeva, 2006). These three populations are: 1. Arabs; the original inhabitants, 2. the Circassians and 3. the Chechans. The Circassians and the Chechans immigrated to Jordan 140 years ago. They have since then maintained genetic isolation in the sense that there is limited intermarriage with any other ethnic group (Kailani, 2002). In their respective countries of origin they were also genetically isolated. Nasidze et al has reported high levels of genetic differentiation for both Y chromosome and mtDNA. This is due to isolation and small population sizes (Nasidze et al., 2004). The HV1 mitochondrial DNA is unique to each population (Jaradat, personal communication) and linguistically they speak two different languages. The two populations are from an ancient lineage of the human race (Barbujani et al., 1994; Bulayeva, 2006; Nasidze et al., 2004).

We looked at the incidence of various cancer types in these three populations and compared them to identify differences and similarities in an attempt to identify genetic versus environmental factors affecting certain types of cancers. We hypothesized that certain types of cancer will have unique incidences in particular ethnic populations because these populations are genetically predisposed to develop this type of cancer. Our rational is that these populations are one; genetically isolated; and two share the same environment with the other two; populations we are comparing to. This study will help in setting the stage to investigate the relevant risk factors that contribute to the development of various cancer types and encourage screening for cancer for prevention. As well as asserting the role of ethnicity in cancer genetics background for therapy.

In addition this is the first report on the rate of cancers in the Circassian and Chechan populations in Jordan and the Middle East.

Materials and Methods

Data collection

Approval from IRB committee of the Ministry of Health to access the cancer registry from 1996-2005 was obtained. Confidentiality of using registry data which includes names was handled cautiously.

Lists of family names for each population were compiled in cooperation with the Chechan and Circassian elders and local associations representing these two groups based on their records.

Cancer registry data for the Circassian and Chechan patients data using the family names for identification was filtered. The Chechan's population was estimated to be 10,000 while the Circassian's population to be 20,000. The female and male population in Circassians and Chechans were not estimated. The Jordanian total population was obtained from the Cancer Registry Report for the years 2000-2001. Upon identifying the Chechan and Circassian population by the family names, the rest of the Jordanian registry data was considered to be Arab Jordanians. Age and gender was obtained from Jordan Cancer Registry.

Statistical methods

Crude rates per 100,000 were calculated as follows; the number of new cancer diagnosed cases of each cancer type divided by the population in the specified time period multiplied by 100,000. Crude rates for each gender was not obtainable as the male and female population in Circassians and Chechens were not estimated. For crude rates' comparison of each population; Circassians and Chechens, with Arabs Jordanian, Population-to-Jordanian rate ratio (RR) for the most common types of cancer was calculated. A ratio greater than one indicates that Jordanian crude rate is less than the population's corresponding rate. 95% confidence interval (95% CI) for the rate ratio was also provided. A confidence interval which does not contain 1 (equal rates) shows that Arab Jordanian rate is significantly different from the population's rate for any particular cancer type. Confidence intervals were constructed based on the assumption that cancer counts follow a Poisson distribution. Logarithmic transformation was applied to rate ratios to obtain an approximately normal distribution. Confidence limits were back transformed to be presented in the original scale. The rate ratio's 95% confidence limits were calculated as follow: EXP [ln(RR) ± 1.96*SD(ln(RR))], where SD(ln(RR)) is the standard deviation of the logarithmic transformation of the rate ratio (ln(RR)).

Results

Based on the Jordan Cancer Registry, there were 33366 Arab Jordanians diagnosed with cancer during the years 1996- 2005. On the other hand the total reported cancer cases in Circassians and Chechens were 216 and 102 respectively. In females, breast cancer is the most common cancer and represents about one third of female

cancer cases in the three populations ; 32%, 36% and 37% of female cancer cases in Arab Jordanians, Circassians and Chechens respectively Figure 1. Lung cancer is the most common cancer in male Arab Jordanians and Chechens constituting 10.8% and 13.2% of male cancer cases in these populations respectively Figure 1. On the other hand prostate cancer is the most common cancer in male Circassians comprising 17.5% of total male cancer cases Figure 1E. Colorectal cancer follows breast cancer in frequency making up around 8% to 10% of the three female populations Figure 1. Further details on specific cancer types are presented below.

Breast cancer

Breast cancer is the most common cancer type in the three populations, constituting 16.2%, 19.4% and 18.6% of the Arab Jordanians', Circassians' and Chechens' total cancer cases respectively Table 1. The Circassians' breast cancer crude rate (21.0 per 100,000) was twice the Arab Jordanian's rate (10.5 per 100,000) with a rate ratio (95% CI) of 2.01 (1.48, 2.72) Table 2. Similarly Chechens' breast cancer crude rate (19 per 100,000) was significantly higher than the Arab Jordanian's rate with a rate ratio (95% CI) of 1.82 (1.16, 2.85) Table 2. Infiltrating duct carcinoma is the most common histology in the three populations Table 5.

Lung cancer

Percentages of Lung cancer from the total cancer types was similar among the three population groups; which were 6.5%, 6% and 7.8% in the Arab Jordanians, Circassians and Chechens respectively Table 1. The male to female ratio was 5:1 in Arab Jordanians, 1.6:1 in Circassians and 7:1 in Chechens Table 3. Crude rate was 4.2, 6.5 and 8.0 cases per 100,000 in the Arab Jordanians, Circassians and Chechens respectively. That is, the probability of developing lung cancer in Circassians compared to Arab Jordanians was 1.54 with 95% CI= (0.89, 2.65) and Chechens' rate ratio (95% CI) was 1.89 (0.94, 3.79) Table 2. The above data showed higher probability for developing lung cancer in Circassians and Chechens compared to Arab Jordanians but it did not reach statistical significance.

Colorectal cancer

Colorectal cancer which includes colon, rectum and rectosigmoid junction, constituted 9.3%, 12.5% and 5.9% of the Arab Jordanians', Circassians' and Chechens' total cancer cases respectively Table 1. The Colorectal cancer crude rate in Circassians (13.5 per 100,000) was over twice the corresponding rate in Arab Jordanians (6.5per 100,000). The Arab Jordanian rate was twice the Circassian rate with 95% CI of (1.49, 3.18) On the other hand, the crude rate in Chechens was similar to Arab Jordanian (6.0 per 100,000) with a rate ratio (95% CI) of 0.97 (0.43, 2.16) Table 2.

Although there were more colorectal cancer cases in males compared to females in Arab Jordanian and Circassian populations, the gender difference was not large enough and the male to female ratio was almost 1:1.

Prostate cancer

The crude rate of prostate cancer among Arab Jordanians was 2.4 per 100,000, which was 4% of the total number of cancer cases Table 2. A higher, though not significantly different, crude rate was found in the Chechan population with the corresponding rate of 4.0 per 100,000 and a rate ratio (95%CI) of 1.7 (0.62, 4.43) in reference to Arab Jordanian crude rate. In Circassians, the prostate cancer crude rate was 3.7 times that of Arab Jordanians with 95% CI of (2.34, 5.94) demonstrating a significant difference between the two rates Table 2. In fact, prostate cancer constituted 8.3% of total cancer cases in Circassians which is twice the corresponding percentage in Arab Jordanians and Chechens.

Ovarian cancer

The Circassian population had a higher crude rate of ovarian cancer (3.0 per 100,000) than Arab Jordanian and Chechen populations with crude rates of 1.2 and 2.0 per 100,000 respectively. The rate ratio (95% CI) of Circassians and Chechens ovarian cancer in reference to Arab Jordanians was 2.6(1.16, 5.80) and 1.7 (0.43, 6.93) respectively Table 2. Ovarian cancer comprised 1.8%, 2.8% and 2.0% of the Arab Jordanians', Circassians' and Chechens' total cancer respectively Table 1.

Leukemia

The Leukemia crude rates in Circassians and Chechens (4.5 and 6.0 per 100,000) were higher than Arab Jordanians' crude rate of 3.1 per 100,000. The rate ratios

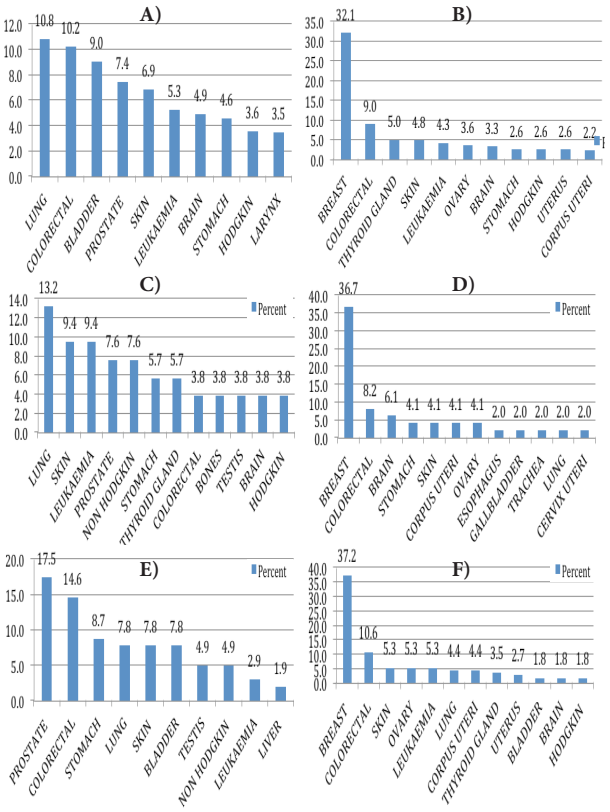

Figure 1. Top Most Common Cancers in A) Male Arab Jordanian; B) Female Arab Jordanian; C) Male Chechens; D) Female Chechens; E) Male Circassian; and F) Female Circassian in Jordan (1996-2005)

Table 1. Number of New Cases by Primary Site

ICD O	Primary Site	All N (%)	Arab Jordanians N (%)	Circassians N (%)	Chechens N (%)
All		33684	33366	216	102
C00-C14	Lip, oral cavity and pharynx lip	319 (0.95%)	318 (0.95%)	1 (0.46%)	
C10	Oropharynx	7 (0.02%)	7 (0.02%)		
C11	Nasopharynx	284 (0.84%)	283 (0.85%)	1 (0.46%)	
C12	Pyriform Sinus	6 (0.02%)	6 (0.02%)		
C13	Hypopharynx	13 (0.04%)	13 (0.04%)		
C14	Other and Ill-defined sites in lip, oral cavity and pharynx	9 (0.03%)	9 (0.03%)		
C15-C26	Digestive organs	5968 (17.7%)	5912 (17.7%)	42 (19.4%)	14 (13.7%)
C15	Esophagus	228 (0.68%)	227 (0.68%)		1 (0.98%)
C16	Stomach	1217 (3.61%)	1202 (3.60%)	10 (4.63%)	5 (4.90%)
C17	Small intestine	157 (0.47%)	156 (0.47%)		1 (0.98%)
C18	Colon	2041 (6.06%)	2018 (6.05%)	20 (9.26%)	3 (2.94%)
C19	Rectosigmoid junction	323 (0.96%)	318 (0.95%)	5 (2.31%)	
C20	Rectum	781 (2.32%)	776 (2.33%)	2 (0.93%)	3 (2.94%)
C21	Anus and anal canal	90 (0.27%)	90 (0.27%)		
C22	Liver and intrahepatic bile ducts	445 (1.32%)	443 (1.33%)	2 (0.93%)	
C23	Gallbladder	266 (0.79%)	264 (0.79%)	1 (0.46%)	1 (0.98%)
C25	Pancreas	326 (0.97%)	325 (0.97%)	1 (0.46%)	
C26	Other and Ill-defined digestive organs	94 (0.28%)	93 (0.28%)	1 (0.46%)	
C30-C39	Respiratory system and intrathoracic organs	3137 (9.31%)	3107 (9.31%)	18 (8.33%)	12 (11.8%)
C30	Nasal cavity and middle ear	50 (0.15%)	50 (0.15%)		
C31	Accessory sinuses	54 (0.16%)	53 (0.16%)	1 (0.46%)	
C32	Larynx	650 (1.93%)	646 (1.94%)	3 (1.39%)	1 (0.98%)
C33	Trachea	13 (0.04%)	12 (0.04%)		1 (0.98%)
C34	Bronchus and lung	2207 (6.55%)	2186 (6.55%)	13 (6.02%)	8 (7.84%)
C37	Thymus	38 (0.11%)	37 (0.11%)	1 (0.46%)	
C38	Heart, mediastinum, and pleura	113 (0.34%)	112 (0.34%)		1 (0.98%)
C39	Other and ill-defined sites within respiratory system and intrathoracic organs	12 (0.04%)	11 (0.03%)		1 (0.98%)
C40-C41	Bones, joints and articular cartilage	492 (1.46%)	487 (1.46%)	3 (1.39%)	2 (1.96%)
C44	Skin	1977 (5.87%)	1956 (5.86%)	14 (6.48%)	7 (6.86%)
C47	Peripheral nerves and autonomic nervous system	27 (0.08%)	27 (0.08%)		
C48	Retroperitoneum and peritoneum	99 (0.29%)	98 (0.29%)		1 (0.98%)
C49	Connective, subcutaneous and other soft tissues*	375 (1.11%)	374 (1.12%)	1 (0.46%)	
C50	Breast (Excludes Skin Of Breast C44.5)	5465 (16.2%)	5404 (16.2%)	42 (19.4%)	19 (18.6%)
C51-C58	Female genital organs	1851 (5.50%)	1828 (5.48%)	17 (7.87%)	6 (5.88%)
C51	Vulva	48 (0.14%)	48 (0.14%)		
C52	Vagina	23 (0.07%)	23 (0.07%)		
C53	Cervix uteri	342 (1.02%)	339 (1.02%)	2 (0.93%)	1 (0.98%)
C54	Corpus uteri	377 (1.12%)	370 (1.11%)	5 (2.31%)	2 (1.96%)
C55	Uterus, nos	427 (1.27%)	423 (1.27%)	3 (1.39%)	1 (0.98%)
C56	Ovary	606 (1.80%)	598 (1.79%)	6 (2.78%)	2 (1.96%)
C57	Other and unspecified female genital organs	21 (0.06%)	20 (0.06%)	1 (0.46%)	
C58	Placenta	7 (0.02%)	7 (0.02%)		
C60-C63	Male genital organs	1621 (4.81%)	1592 (4.77%)	23 (10.6%)	6 (5.88%)
C60	Penis	19 (0.06%)	19 (0.06%)		
C61	Prostate Gland	1269 (3.77%)	1247 (3.74%)	18 (8.33%)	4 (3.92%)
C62	Testis	323 (0.96%)	316 (0.95%)	5 (2.31%)	2 (1.96%)
C63	Other and unspecified male genital organs	10 (0.03%)	10 (0.03%)		
C64-C68	Urinary tract	2475 (7.35%)	2459 (7.37%)	12 (5.56%)	4 (3.92%)
C64	Kidney	692 (2.05%)	688 (2.06%)	2 (0.93%)	2 (1.96%)
C65	Renal pelvis	15 (0.04%)	15 (0.04%)		
C66	Ureter	13 (0.04%)	13 (0.04%)		
C67	Bladder	1747 (5.19%)	1735 (5.20%)	10 (4.63%)	2 (1.96%)
C68	Other and unspecified urinary organs	8 (0.02%)	8 (0.02%)		
C69-C72	Eye, brain and other parts of central nervous system	1618 (4.80%)	1607 (4.82%)	5 (2.31%)	6 (5.88%)
C69	Eye and adnexa	155 (0.46%)	154 (0.46%)		1 (0.98%)
C70	Meninges	24 (0.07%)	24 (0.07%)		
C71	Brain	1391 (4.13%)	1383 (4.14%)	3 (1.39%)	5 (4.90%)
C72	Spinal cord, cranial nerves, and other parts of central nervous system	48 (0.14%)	46 (0.14%)	2 (0.93%)	
C73-C75	Thyroid and other endocrine glands	1215 (3.61%)	1205 (3.61%)	6 (2.78%)	4 (3.92%)
C73	Thyroid gland	1111 (3.30%)	1103 (3.31%)	4 (1.85%)	4 (3.92%)
C74	Adrenal gland	78 (0.23%)	76 (0.23%)	2 (0.93%)	
C75	Other endocrine glands and related structures	26 (0.08%)	26 (0.08%)		
C76	Other and Ill-defined sites	1277 (3.79%)	1265 (3.79%)	7 (3.24%)	5 (4.90%)
C81	Hodgkin lymphoma	1032 (3.06%)	1026 (3.07%)	3 (1.39%)	3 (2.94%)
C82-C85	Non Hodgkin lymphoma	800 (2.38%)	790 (2.37%)	5 (2.31%)	5 (4.90%)
	Lymph nodes*	723 (2.15%)	720 (2.16%)	3 (1.39%)	
C90	Multiple myeloma	507 (1.51%)	505 (1.51%)	1 (0.46%)	1 (0.98%)
C91-C95	Leukaemia	1604 (4.76%)	1589 (4.76%)	9 (4.17%)	6 (5.88%)
C99	Hematopoietic disease	936 (2.78%)	933 (2.80%)	2 (0.93%)	1 (0.98%)

*Includes adipose tissue, aponeuroses, artery, blood vessel, bursa, connective tissue, fascia, fatty tissue, fibrous tissue, ligament, lymphatic, muscle, skeletal muscle, subcutaneous tissue, synovia, tendon

Table 2. Rates and Rate Ratios by Type of Cancer

Cancer	Circassians				Chechens		
	Rate			95% CI	Rate		95% CI
	Arab Jordanian	Circassians	Ratio		Chechens	Ratio	
Colorectal	6.19	13.5	2.18	(1.49, 3.18)	6	0.97	(0.43, 2.16)
Lung	4.23	6.5	1.54	(0.89, 2.65)	8	1.89	(0.94, 3.79)
Breast	10.50	21	2.01	(1.48, 2.72)	19	1.82	(1.16, 2.85)
Cervix Uteri	0.66	1	1.53	(0.38, 6.12)	1	1.53	(0.21, 10.86)
Ovary	1.16	3	2.59	(1.16, 5.80)	2	1.73	(0.43, 6.93)
Prostate	2.41	9	3.73	(2.34, 5.94)	4	1.66	(0.62, 4.43)
Bladder	3.36	5	1.49	(0.80, 2.77)	2	0.6	(0.15, 2.38)
Brain	2.68	1.5	0.56	(0.18, 1.74)	5	1.87	(0.78, 4.50)
Thyroid Gland	2.13	2	0.94	(0.35, 2.50)	4	1.87	(0.70, 5.00)
Hodgkin's Lymphoma	1.98	1.5	0.76	(0.24, 2.35)	3	1.51	(0.49, 4.69)
Non Hodgkin's Lymphoma	1.53	2.5	1.64	(0.68, 3.94)	5	3.27	(1.36, 7.88)
Leukemia	3.07	4.5	1.46	(0.76, 2.82)	6	1.95	(0.88, 4.35)

*Based on estimating the Circassian population to be 20,000 and the Chechan population to be about 10,000 and Jordan Cancer Registry data 1996-2005; Rate Ratio=Rate of indicated cancer type of the specified population/corresponding rate in Arab Jordanians

Table 3. Distribution of Number of Cases by Gender Colorectal, Lung and Bladder Cancer

Cancer Type	Arab Jordanian		Circassians		Chechens	
	Male	Female	Male	Female	Male	Female
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Colorectal	1721(53.7)	1481(46.3)	15(55.6)	12(44.4)	2(33.3)	4(66.7)
Lung	1823(83.4)	363(16.6)	8(61.5)	5(38.5)	7(87.5)	1(12.5)
Bladder	1515(87.3)	220(12.7)	8(80.0)	2(20.0)	1(50.0)	1(50.0)

*Jordan Cancer Registry data 1996-2008

Table 4. Distribution of Number of Cases by Gender Colorectal, Lung and Bladder Cancer

Cancer type	Arab Jordanian		Circassians		Chechens	
	Adult	Pediatric	Adult	Pediatric	Adult	Pediatric
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Bone Cancer	1141(71.0)	466(29.0)	5 (100)		2 (33.3)	4(66.7)
Lymphoma						
Hodgkin's	885(86.3)	141(13.7)	3 (100)		1 (33.3)	2(66.7)
Non Hodgkin's	693(87.7)	97(12.3)	5 (100)		5 (100)	
Leukemia	1363(85.8)	226(14.2)	5(55.6)	4 (44.4)	4 (66.7)	2(33.3)

*Jordan Cancer Registry data 1996-2008

Table 5. Breast Cancer Cases by Histology

Histology		Arab Jordanian 5303	Circassians 42	Chechens 18
		N (%)	N (%)	N (%)
8000	Neoplasm, malignant	513(9.67%)	1(2.38%)	1(5.56%)
8140	Adenocarcinoma and Mixed*	287(5.41%)	2(4.76%)	3(16.7%)
8211	Tubular adenocarcinoma	10(0.19%)		
8500	Infiltrating duct carcinoma	3991(75.3%)	33(78.6%)	13(72.2%)
8510	Medullary carcinoma,	48(0.91%)		
8520	Lobular carcinoma	311(5.86%)	6(14.3%)	1(5.56%)
9020	Phyllodes tumour, malignant	23(0.43%)		
	Others	120(2.26%)		

*Adenocarcinoma and Mixed includes Papillary, Papillary adenocarcinoma, Intraductal Papillary adenocarcinoma, Infiltrating duct and lobular carcinoma, Infiltrating duct mixed with other types of carcinoma, Infiltrating lobular mixed with other types of carcinoma; **Jordan Cancer Registry data 1996-2008

(95% CI), in reference to Arab Jordanian rate, were 1.5 (0.76, 2.82) and 1.9 (0.88, 4.35) in Circassians and Chechens respectively Table 2. The percentage of leukemia within all types of cancer, in respective order, was 4.7%, 4.2% and 5.9% in Arab Jordanians, Circassians and Chechens Table 2. The adult to pediatric ratio was 6:1, 1.2:1 and 2:1 in the above three populations respectively Table 4.

Lymphomas

Non Hodgkin's lymphoma compromised 2.3% of Arab Jordanians' and Circassians' cancer and 4.9% of Chechens' cancer Table 1 and 4. In Hodgkin's lymphoma, the Arab Jordanians' and Chechans' crude rates of 3% were higher than Circassians' crude rate of 1.5% Table 1 and 4.

Brain tumor

The Arab Jordanian brain tumor crude rate was 2.7 per 100,000, which was almost twice the Circassians' rate of 1.6 with 95% CI of the rate ratio of (0.18, 1.74). On the other hand, Chechens' brain cancer crude rate was 5.0 per 100,000; 1.9 times Arab Jordanian rate with a 95% of the rate ratio of (0.78, 4. 5) Table 2. Brain tumor represented 4% and 5% of all cancer types in Arab Jordanians and Chechens while the corresponding percentage was 1.4% in Circassians Table 1.

Discussion

This is the first report on the rates of cancer in the Circassian and Chechan populations in Jordan and the Middle East. The objective of this study was to determine the incidence of various cancer types in genetically isolated populations in Jordan. The central hypothesis for the proposed research is that the relative genetic homogeneity of certain genetically isolated populations in Jordan including Circassians and Chechens results in incidences of complex diseases that differ from the general Jordanian population that consists mostly of Arabs. The rationale for the proposed research is that, such inbred and selected populations tend to be ideal for investigating the genetic factors involved various cancer types.

In the cancers; stomach, bones, kidney and Hodgkins Lymphoma there were no differences among populations studied. Lung cancer is usually related to smoking rates in different populations. A study reported no significant difference between the Circassian, the Chechan and the Arab Jordanian populations in rates of smoking (Dajani et al., 2012). Nevertheless our data, based on Jordan Cancer Registry data, showed higher probability for developing lung cancer in Circassians and Chechens compared to Jordanian Arabs though not significant. This correlates with the report that Circassians have a higher adenocarcinoma lung cancer risk than Jordanian Arabs general population based on the association shown of (MspI A2-BstUI A2) with lung adenocarcinoma (Mahasneh and Abdel-Hafiz, 2004). It is worth noting here that the most common cancer in male Circassians is not lung cancer.

Colorectal cancer was higher in Circassians compared to both Chechans and Jordanian Arabs. Surprisingly colorectal cancer among male Chechans was much lower than female Chechans and other populations in the study. Colorectal cancer is related to cultural behaviour, nutrition intake, BMI and physical activities. In a nutrition study there was significant differences in nutrient intake between the Circassian and Chechan population (Dajani, unpublished data). Chechans had lower BMI compared to Circassians who in turn have lower BMI compared to Jordanain Arabs (Dajani et al., 2013). This indicates that there is a genetic component to the higher incidence of colorectal cancer

among Circassians although they have a lower BMI compared to Arab Jordanians. Worldwide colorectal cancer is the third most common cancer in men (10%) and the second in women (9.4%) (Curado MP, 2007). This increase may be due to increase in type two diabetes (Ajlouni et al., 2008; Yang et al., 2005). It has been shown that colorectal cancer screening can be effective (Hawk and Levin, 2005) . In Jordan there is no screening for colorectal cancer.

The incidence of breast cancer was higher in both Circassian and Chechan populations. Breast cancer is related to genetic, environmental and cultural factors. The rate of breast cancer and how it relates to awareness and educational levels in each population is important. The more educated the population; the higher the awareness towards early screening. This leads to early diagnosis and therefore higher reported rates. In another study we had shown that the educational levels of Circassians and Chechans was higher than Jordanians (Dajani et al., 2013). In terms of genetics Circassians have a higher breast cancer risk than the Jordanian general population based on the shown association of (16bp A1-MspI A2) with breast cancer (Mahasneh and Abdel-Hafiz, 2004).

Circassians had a lower rate of brain cancer compared to Jordanian Arabs and Chechans. Since brain cancer is mostly genetic this would be interesting to study to shed light on the underlying genetic mechanisms of cancer. Circassians also showed a lower rate of Hodgkins lymphoma.

On the other hand Circassians had a higher rate of ovarian cancer and prostate cancer. Surprisingly, prostate cancer was the number one most common cancer in male Circassians compared to other populations in the study where lung cancer was more common. Prostate cancer has a genetic component.

There were no differences in the rates of Leukemia in all three populations. Leukemia has both environmental and geographical bases. There was a higher incidence of leukemia in Arab Jordanian pediatrics.

The differences in rates in cancer in general are attributed to differences in lifestyle including smoking, eating habits and physical activities and/or genetics. Although there are differences in lifestyles between Arab Jordanians and Circassians and/or Chechans we can attribute differences in cancer rates to genetics since the three populations share the same environment but are genetically very different.

Increasing incidence of cancer and its economic impact worldwide impose upon us to search for methods of early detection in order to lessen the crisis. In cancers where there is a clear genetic component this becomes very relevant. The presence of genetically isolated populations to study these particular types of cancer is rare and becoming even more rare with globalization and loss of cultural barriers among the young. Thus it is imperative to study these populations to try to identify genetic trends. In addition the majority of studies that have been conducted worldwide in studying the genetic components of cancer have been performed on European populations. There is a need to conduct studies on other world populations to discover novel risk factors from populations of different lineages that may shed new light on the genetic basis of diseases especially if we are to apply the discoveries on other populations.

This study sets the base for research into the genetic basis of cancer in these ethnic populations. Such inbred and selected populations tend to be ideal for investigating the genetic factors involved in various cancer types.

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References

Ajlouni K, Khader YS, Batieha A, et al (2008). An increase in prevalence of diabetes mellitus in Jordan over 10 years. *J Diabetes Complicat*, **22**, 317-24.

Al-Tarawneh M, Khatib S, Arqub K (2010). Cancer incidence in Jordan, 1996-2005. *Eastern Mediterranean health journal=La revue de sante de la Mediterranee orientale=al-Majallah al-sihhiyah li-sharq al-mutawassit*, **16**, 837-45.

Barbujani G, Nasidze IS, Whitehead GN (1994). Genetic diversity in the Caucasus. *Hum Biol*, **66**, 639-68.

Bulayeva KB (2006). Overview of genetic-epidemiological studies in ethnically and demographically diverse isolates of dagestan, Northern Caucasus, Russia. *Croat Med J*, **47**, 641-8.

Curado MP, Shin HR, Storm H, et al (2007). Cancer Incidence in five continents. IARC Scientific Publicatioins, 9.

Dajani R, Khader YS, Fatahallah R, et al (2012). Diabetes mellitus in genetically isolated populations in Jordan: prevalence, awareness, glycemic control, and associated factors. *J Diabetes Complicat*, **26**, 175-80.

Dajani R, Khader YS, Hakooz N, et al (2013). Metabolic syndrome between two ethnic minority groups (Circassians and Chechens) and the original inhabitants of Jordan. *Endocrine*, **43**, 112-9.

Ferlay J, Shin HR, Bray F, et al (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. International journal of cancer. *Int J Cancer*, **127**, 2893-917.

Freedman LS, Edwards BK, Ries LAG, et al (2006). Cancer incidence in four member countries (Cyprus, Egypt, Israel and Jordan) of the Middle East Conortium (MECC) compared with US SEER. (MECC Monograph) Bethesda, MAryland, NAtional Cancer Insitute (NIH Publication No. 06-5873).

Hawk ET, Levin B (2005). Colorectal cancer prevention. Journal of clinical oncology: official journal of the American Society of Clinical Oncology, **23**, 378-91.

Ismail SI, Soubani M, Nimri JM, et al (2013). Cancer incidence in jordan from 1996-2009: a comprehensive study. *Asian Pac J Cancer Prev*, **14**, 3527-34.

Kailani W (2002). Chechens in the Middle East: Between Original and Host Cultures. Caspian Studies Program.

Mahasneh AA, Abdel-Hafiz SS (2004). Polymorphism of p53 gene in Jordanian population and possible associations with breast cancer and lung adenocarcinoma. *Saudi Med J*, **25**, 1568-73.

Ministry of Health. 2008. Jordan National Cancer Registry, Jordan.

Nasidze I, Ling EY, Quinque D, et al (2004). Mitochondrial DNA and Y-chromosome variation in the caucasus. *Ann Hum Genet*, **68**, 205-21.

Rastogi T, Hildesheim A, Sinha R (2004). Opportunities for cancer epidemiology in developing countries. *Nat Rev Cancer*, **4**, 909-17.

Sener SF, Grey N (2005). The global burden of cancer. J Surg Oncol, **92**, 1-3.

Yang YX, Hennessy S, Lewis JD (2005). Type 2 diabetes mellitus and the risk of colorectal cancer. *J Am Gastroenterol Assoc*, **3**, 587-94.