

Disparities in Cancer Incidence in Armenia, 2013-2016: Setting Priorities for Preventive Interventions

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Abstract: Many studies indicate increasing cancer burden in developing world with prominent sex and urban-rural disparities in the populations. However, internationally comparable research data about cancer incidence in Armenia is lacking. This study aimed to provide information about trends and inequalities in cancer incidence in Armenian population. A cross-sectional study was conducted to analyze data from all hospital-based cancer registries of Armavir province, western Armenia, from January 2013 to December 2016. For the 4-year study period, cancer crude and age-standardized incidence rates, as well as Incidence Rate Ratios were estimated by age-groups, sex, and urban-rural areas. A total of 1,894 cancer cases were recorded during the study period. Lung cancer was the most frequent in men and breast cancer was the most prevalent in women. ASIRs per 100,000 person-years of all cancers combined in men were significantly higher than in women (IRR=1.36, 95% CI: 1.24, 1.49; $p<0.001$) and were fluctuated over time, while in women they were fairly stable. Disparities in cancer incidence by urban and rural residence were also statistically significant considering overall outcome (IRR=1.57, 95% CI: 1.43, 1.72; $p<0.001$), as well as after adjustment by sex and age. Significantly higher rates for urban young women was particularly evident. The patterns observed here suggest priorities to reduce inequalities and prevent new cancer cases in revealed vulnerable groups. These findings about disparities in cancer incidence can be used by health planners for the development of targeted prevention programs for more efficient use of restricted resources in this developing country.

Keywords: Armavir province; Armenia; cancer incidence; developing country; epidemiology; urban-rural, geographical inequality.

I. INTRODUCTION

Cancer is one of the most important public health issues in the world with an ever-rising number of new cancer cases, and the situation is more alarming in developing countries where its incidence is expected to increase considerably in the future [1]. Another central concern for public health professionals in recent years has become health inequalities, with the epidemiological research as the first step to determine the extent of the disparity in the population and reveal vulnerable groups. Evaluations and analysis of cancer patterns are, therefore, indispensable particularly for low and middle-income countries for developing more effective health policy actions and improving the limited surveillance systems by resource allocation [2].

Armenia is located in West Asia and considered as developing country [3] with a lower-middle-income economy according to the World Bank [4]. As a post-Soviet state, a number of reforms in the public health care system are necessary due to emerged health challenges, in particular, significantly increased mortality rates from non-communicable diseases (NCDs) compared to communicable diseases [5]. According to national healthcare assessment report [6], cancer is one of the most prevalent diseases in Armenia with the second highest mortality rates which continuously rose during last decades, increasing the demand for the implementation of screening and prevention programs. For this reason, continued adapted application of the best international practices as well as utilization of quality population-based research

findings for public health care system improvements are essential. However, internationally comparable research data describing the patterns of the cancer burden in Armenian population is lacking. While recent worldwide estimates of cancer incidence and mortality published by the International Agency for Research on Cancer also include data for Armenia, the incidence of cancer for this country has been assessed from national mortality estimates and prevalence was based on the average of neighboring countries [7]. Therefore, the aim of this study is to provide more precise estimation and interpretation of incidence patterns and trends in Armenian population based on complete records of hospital-based cancer registries to facilitate the improvement of cancer control strategies and the development of targeted preventive interventions.

II. MATERIALS AND METHODS

Data:

A cross-sectional study with retrospective analysis of data from all hospital-based cancer registries of Armavir province of Armenia diagnosed from January 2013 to December 2016 was conducted. Armavir population estimates as of 01.01.2016 were obtained from the Demographic Handbook of Armenia 2016 [8]. Cancer cases were all taken from the normal resident population in Armavir, who lived in the province at least one year. Patients with a residence address outside of the province were excluded. Collected data were included demographic characteristics like age, sex, residency, date of diagnosis, and histopathology. All double entry cancer cases were excluded by cross checking name, age, sex, and address of each patient. Cancer cases presented by site according to the 10th edition of the International Classification of Diseases (ICD-10) with the following codes: C16 (stomach), C18-21 (colorectum, including anus), C33-34 (lung, including trachea), C50 (female breast), C53 (cervix uteri), C56 (ovary), C61 (prostate), C67 (bladder).

Analysis:

Crude incidence (CIR) and age-standardized incidence (ASIR) rates were estimated for each year and for the 4-year study period 2013-2016 inclusive [9]. CIRs and ASIRs were further categorized by gender, urban-rural residence, and age groups. Age at diagnosis of cancer was classified into 15 categories of 5 years each (<19, 20-24, 25-29, 30-34, ..., 80-84, 85+) and expressed per 100,000. To compute 4-year incidence rates, the number of annual cases were summed and the population in each age-group multiplied by four. Age standardization was conducted using the direct method based on the 2000 projected U.S. population [10].

Sex disparities were estimated calculating age-standardized incidence rate ratios (IRRs) stratified by age. Geographical (urban/rural) disparities were estimated calculating crude IRRs stratified by sex and age. The 95% CIs for IRRs were calculated assuming of Poisson distribution [11]. Comparisons among CIRs and ASIRs were performed by z-test using the appropriate Standard Errors and *p* values obtained according to Altman and Bland [12].

III. RESULTS

Cancer incidence by sex:

During study period 2013-2016 inclusive, there were a total of 1,894 newly diagnosed cases of cancer in Armavir province. These cases were all in the normal resident population in Armavir. The mean age of the patients at the time of diagnosis was 60.6 years (SD=14.3), the majority of new cancer cases being diagnosed in “Ejmiatsin” Medical Center (Table 1). Over the 4 years of the study period, slightly more cancer events were observed in women than men, 50.1% and 49.9% respectively (Table 1); however, both CIRs and ASIRs were higher in men.

Table 1: Distribution of new cancer cases by sex from hospitals in Armavir province, 2013-2016.

SN	Hospital name	Location	Males		Females		Total	
			Cases	%	Cases	%	Cases	%
1	“Armavir Medical Centre after Zarishat (Aram) Martin Mkrtchyan”	Armavir	354	51.5	334	48.5	688	36.3
2	“Ejmiatsin” Medical Centre	Vagharshapat	494	49.4	505	50.6	999	52.7
3	“Metsamor” Medical Centre	Metsamor	29	34.1	56	65.9	85	4.5
4	“Children of Jesus” Medical Centre	Myasnikyan village	68	55.7	54	44.3	122	6.4
Total			945	49.9	949	50.1	1894	100

The most common cancer in men was lung cancer, while in women was breast cancer. Colorectal and stomach cancers were among five most frequent cancers in both sexes. The number and percentages of cases by site (ICD-10), as well as ASIRs of the most prevalent cancers for males and females are given in Table 2.

Table 2: Collected data for the most prevalent cancers in men and women in Armavir province, 2013-2016

SN	Cancer site	ICD-10	Cases	%	ASIR ^a
Men					
1.	Lung	C33-34	314	33.2	84.5
2.	Bladder	C67	104	11.0	27.1
3.	Stomach	C16	89	9.4	21.8
4.	Colorectum	C18-21	82	8.7	20.7
5.	Prostate	C61	46	4.9	15.1
6.	All cancers	-	945	100	237.1
Women					
1.	Breast	C50	355	37.4	64.8
2.	Cervix uteri	C53	89	9.4	16.1
3.	Colorectum	C18-21	71	7.5	13.3
4.	Ovary	C56	51	5.4	8.9
5.	Stomach	C16	42	4.4	8.0
6.	All cancers	-	949	100	174.8

^aAge-standardized incidence rate per 100,000 person-year

Gender differences in CIRs for all cancers combined were not statistically significant ($z=-0.95$, $p=0.34$): CIR was 181.6 (95% CI: 170.0, 193.1) and 173.8 (95% CI: 162.8, 184.9) for males and females correspondingly, with IRR=1.04 (95% CI: 0.95, 1.14). Meanwhile, ASIR for males was 237.1 (95% CI: 225.6, 248.7) and 174.8 (95% CI: 163.8, 185.9) for females, revealing significantly higher risk for men by almost 36% (IRR=1.36, 95% CI: 1.24, 1.49, $p<0.001$) (Table 3). ASIRs for each year of the study period in men were fluctuated over time with an increasing tendency, while in women they were fairly stable with an overall decreasing trend (Fig. 1).

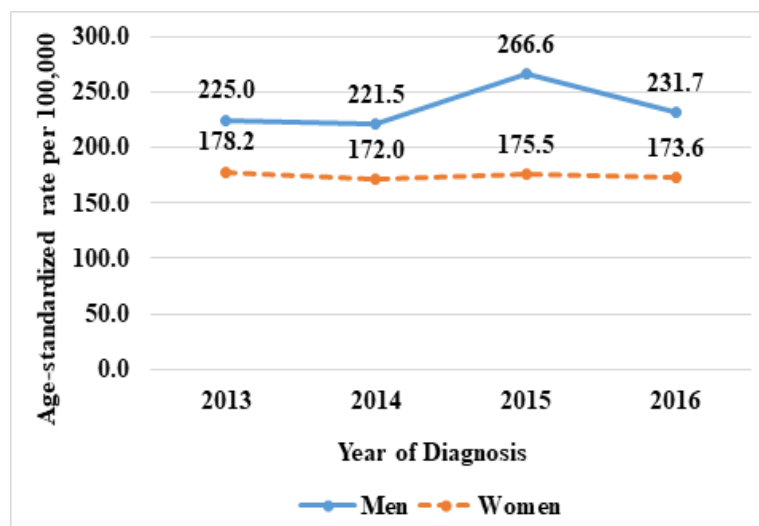


Fig 1: Age-standardized incidence rates for all cancers combined in men (solid line) and women (dashed line) per 100,000 in Armavir province, 2013-2016.

Age-specific ASIRs in men increased gradually at elder ages with the highest rate for 70-74 age-group, which after a decline, slightly increased in the 85+ years old men (Fig. 2). Different patterns were recorded in females showing a sharp increase in 35-39 age-group continued with a gradually rising trend with slight fluctuations up to the 70-74 age-group and then decreased (Fig. 2). Overall, for younger age-groups, age-specific ASIRs were higher in women, and the differences were statistically significant for 35-39 and 45-49 age-groups, while from the 55-59 age-group, the situation changes with significantly higher ASIRs in men for all remaining age-groups (Supplementary Table 1).

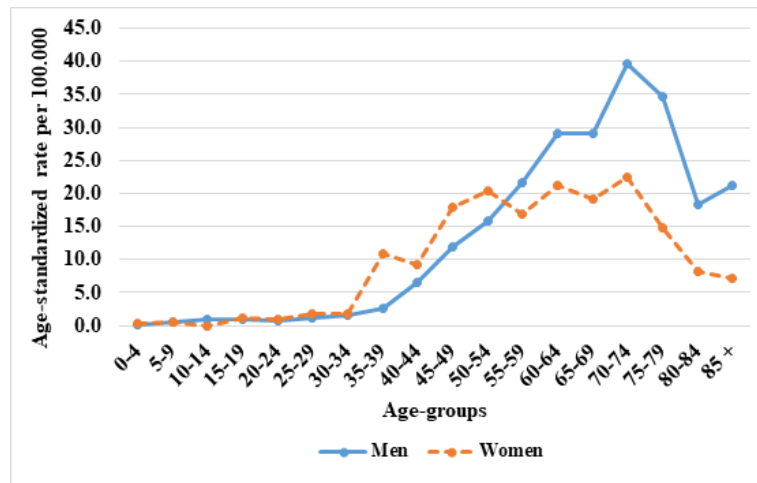


Fig 2: Age-specific age-standardised incidence rates for all cancers combined in men (solid line) and women (dashed line) per 100,000 person-year in Armavir province, 2013-2016.

Cancer incidence by urban-rural residence:

First of all, geographical differences in cancer incidence based on urban and rural residence were estimated by comparing CIRs per 100,000 stratified by age-groups. Rate ratios by urban-rural residency revealed significantly higher cancer incidence in urban population compared to rural one (IRR=1.57, 95% CI: 1.43, 1.72, $p<0.001$) (Table 3), and this geographical disparity was more pronounced in the 40-59 aged population (Supplementary Table 2).

Table 3: Sex and geographical disparities in cancer incidence estimated as rate ratios in Armavir province, 2013-2016

Disparity	IRR ^a	95% CI	Z score	p value
Men/Women	1.36	1.24 1.49	6.562719	<000.1
Urban/Rural	1.57	1.43 1.72	9.576051	<000.1
Urban men/Rural men	1.37	1.20 1.57	4.591775	<000.1
Urban women/Rural women	1.77	1.55 2.01	8.612597	<000.1
Urban men/Urban women	0.86	0.75 0.99	-2.12953	0.033
Rural men/Rural women	1.11	0.98 1.25	1.681108	0.092

^aIRR-incidence rate ratio. Statistical significance is indicated in bold.

When urban-rural cancer CIRs were further stratified by sex, significantly higher rates were observed for urban women compared to rural women (IRR=1.77, 95% CI: 1.55, 2.01, $p<0.001$) and to urban men (IRR=0.86, 95% CI: 0.75, 0.99, $p=0.033$) (Table 3). Rates in urban men were also significantly higher than in rural men (IRR=1.37, 95% CI: 1.20, 1.57, $p<0.001$), but no significant disparity was observed between rural men and women (IRR=1.11, 95% CI: 0.98, 1.25, $p=0.092$) (Table 3). Importantly, age-specific geographical disparities were more pronounced in younger age-groups (Supplementary Table 2), revealing considerably higher rates in particular for urban young women.

IV. DISCUSSION

This is the first report on cancer incidence from Armenia based on complete records from all the hospital-based cancer registries of the western province of Armavir for the period 2013-2016 inclusive which comprises the most recent cancer data for the estimation of CIRs as well as globally comparable ASIRs. Armavir is also the smallest province of the country with an area of 1,242 km² and a population of 266,613 as of January 2016 (130131 men and 136482 women), and health and environmental issues are of great concern in this area especially following construction of the Armenian Nuclear Power Plant in the end of 20th century located in the Armavir province area. It is the only nuclear power plant in the South Caucasus which has been the subject of debates for closure due to the lack of internationally accepted nuclear safety standards [13]. Concerns about elevated cancer risks for people living nearby due to accidents or plant emissions arose several decades ago [14, 15], and it is already well established that occupational or environmental exposure to such radiation can cause the most of cancer types [16]. Obviously, high doses of radiation, mainly after nuclear power plant accidents, lead to a number of short- and long-term health issues [17] but continuous radiation exposure, even at low levels, can also lead to cancer, especially in younger subgroups of the population [18].

Increased cancer incidence with population aging is also well documented, presenting advanced age as one of the greatest risk factors for developing the disease [19, 20]. Due to demographic changes which mainly occurred during the post-Soviet period, the number and proportion of older persons in Armenia have rapidly increased [5]. All demographic drivers of population aging, including mortality, fertility, and migration have contributed to current accelerated aging trends in Armenia. Additionally, as a result of higher mortality among Armenian men than women, the gender disparity became more pronounced in the elder population aged 50 and over.

Rapid industrialization and urbanization of the country during the post-Soviet period further contributed to increased rates of NCDs, including cancer. The cancer incidence in men is particularly alarming. Indeed, according to GLOBOCAN 2012, Armenia has the second highest lung cancer incidence in the world and is among five countries with the highest incidence of stomach, bladder, colorectal, and prostate cancers in Western Asia in men [7]. Similarly, our findings showed higher rates in Armavir province compared to provincial incidence rates of neighboring and other countries [21-23]. This phenomenon, at least partly, may be explained by greater exposure of men to risk factors, mainly smoking. Although recent data about the trends of smoking and cigarette consumption in Armenia is not available, a previous Tobacco Consumption Survey showed that the prevalence of smoking in Armenian men was one of the highest in the world (63.7 %) [24].

No less worrying is the high cancer ASIRs found in very young age-groups of women (Figure 2). Factors responsible for the observed patterns are yet to be discovered; meanwhile, breast cancer and cancers of female genital organs have been identified as the main contributions to oncological morbidity in Armenia [25]. Importantly, greater emphasis should be given particularly to younger urban women who had significantly higher cancer incidence compared to urban men in Armavir (Table 3), in contrast with the overall substantially greater risk of oncological diseases in Armenian men revealed by this and previous research [26]. Additionally, for men and women combined, urban residents had 57% higher risk of developing cancer than the rural population (Table 3). Various factors could contribute to this difference in cancer incidence between urban-rural areas, including lifestyle and environmental alterations that are very rapidly invading the developing countries [27]. In fact, many cancer-related risk factors such as tobacco use, overweight and obesity, physical inactivity, alcohol abuse [28] as well as environmental issues [29] are rather prevalent in Armenia; although, no significant steps are being taken to adequately address or reduce them. Further differences among urban and rural residents of Armenia have been revealed regarding their awareness of the risk factors, in particular, significantly less knowledge of the link between smoking and lung cancer in urban populations [30]. Several sociodemographic factors and cancer screening or other health care system variables may also explain urban-rural disparities in cancer incidence [31-33]. Improving these aspects in more susceptible groups of people could significantly ameliorate not only the differences in cancer incidence between urban and rural areas but also reduce the overall incidence of the disease in the whole population. Particular emphasis should be placed on prevention and education programs since even considering the improvements in primary healthcare in Armavir province after implementation of community health partnership project, several issues such as high prevalence of risk factors or poor practice and lack of knowledge about preventive medical care as well as early detection and screening programs in the region remained unchanged [34].

V. CONCLUSION

The results of this study are based on hospital cancer registries, and cancer cases from the residents of Armavir who have been diagnosed outside of the province hospitals were not included in this study. Thus, the actual numbers of cancer cases may be higher in the province than presented in this study as its eastern extremity borders with the capital Yerevan and many residents might have been diagnosed and treated at cancer centers there.

During the study period, increasing cancer incidence trend and significantly higher ASIRs were observed in men than women, in particular for 55+ aged men. However, in younger age-groups, ASIRs were higher in women. Geographical disparity was also more pronounced in younger population with alarming higher cancer incidence in urban young women. From this point of view, the initial epidemiological studies such as this are of crucial importance for identifying the more vulnerable groups to elicit priorities for cancer surveillance and to facilitate the development of targeted cancer control and prevention programs for more efficient use of restricted resources, particularly in developing countries. Future studies providing more information on cancer incidence in the population as well as the correlated risk factors can additionally contribute to better public health planning and quality improvement strategies to eventually reduce the burden of cancer in this population.

APPENDIX - A

Supplementary Table 1.

Age-specific ASIRs per 100,000 person-year by sex for all cancers combined in Armavir province, 2013-2016.

Age group	Males			Females			IRR	95% CI
	Cases	ASIR	95% CI	Cases	ASIR	95% CI		
< 19	14	2.6	1.25, 4.01	10	2.2	0.84, 3.56	1.2	0.52, 2.74
20-24	5	0.7	0.09, 1.35	6	0.9	0.17, 1.54	0.84	0.25, 2.83
25-29	10	1.2	0.47, 2.02	14	1.7	0.82, 2.61	0.73	0.32, 1.66
30-34	10	1.6	0.60, 2.57	12	1.8	0.78, 2.81	0.88	0.38, 2.08
35-39	11	2.5	1.04, 4.03	51	10.9	7.93, 13.93	0.23	0.12, 0.45
40-44	23	6.6	3.92, 9.33	36	9.2	6.16, 12.14	0.72	0.42, 1.23
45-49	48	12.0	8.57, 15.34	82	18.0	14.08, 21.86	0.67	0.46, 0.96
50-54	93	15.9	12.69, 19.16	136	20.5	17.04, 23.92	0.78	0.59, 1.02
55-59	166	21.7	18.39, 24.98	140	16.8	14.04, 19.61	1.29	1.02, 1.62
60-64	172	29.1	24.72, 33.40	149	21.3	17.86, 24.69	1.37	1.09, 1.71
65-69	111	29.1	23.68, 34.51	91	19.1	15.16, 23.00	1.53	1.15, 2.02
70-74	77	39.6	30.79, 48.49	66	22.4	17.00, 27.81	1.77	1.27, 2.47
75-79	123	34.7	28.56, 40.83	91	14.7	11.70, 17.75	2.36	1.79, 3.11
80-84	50	18.4	13.31, 23.52	40	8.2	5.68, 10.78	2.24	1.46, 3.42
85 +	32	21.2	13.88, 28.60	25	7.2	4.39, 10.06	2.94	1.72, 5.01
Total	945	237.1	225.57, 248.72	949	174.8	163.75, 185.87	1.36	1.24, 1.49

ASIR-age-standardised incidence rate, CI-confidence interval, IRR-incidence rate ratio. Statistical significance is indicated in bold.

Supplementary Table 2.

Age-specific cancer incidence rate ratios by urban-rural residency and sex in Armavir, 2013-2016.

Age-group	UW/RW		UM/UW			UM/RM			RM/RW			Urban/Rural		
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
< 19	4.93	1.24 19.59	0.57	0.16 2.00	0.84	0.26 2.76	3.33	0.89 12.44	1.79	0.79 4.06				
20-24	5.28	0.93 29.86	0.25	0.03 2.34	0.66	0.07 6.18	2.00	0.35 11.30	2.20	0.66 7.39				
25-29	1.40	0.46 4.27	0.80	0.21 3.06	1.68	0.46 6.11	0.67	0.23 1.91	1.51	0.65 3.51				
30-34	1.08	0.32 3.69	0.50	0.09 2.83	0.54	0.11 2.63	1.00	0.37 2.72	0.81	0.31 2.12				
35-39	1.37	0.77 2.41	0.14	0.04 0.49	0.73	0.19 2.84	0.27	0.12 0.59	1.23	0.73 2.08				
40-44	2.60	1.33 5.08	0.35	0.15 0.84	0.91	0.37 2.25	1.00	0.49 2.03	1.75	1.04 2.96				
45-49	1.98	1.27 3.09	0.44	0.24 0.81	1.27	0.69 2.34	0.70	0.44 1.10	1.69	1.18 2.42				
50-54	1.63	1.15 2.32	0.57	0.36 0.89	1.22	0.78 1.90	0.76	0.54 1.06	1.45	1.10 1.91				
55-59	1.87	1.33 2.62	0.85	0.59 1.22	1.06	0.77 1.47	1.49	1.10 2.02	1.39	1.10 1.75				
60-64	1.30	0.94 1.81	1.10	0.79 1.54	1.20	0.88 1.63	1.20	0.89 1.62	1.25	1.00 1.56				
65-69	1.22	0.80 1.86	1.12	0.73 1.70	1.04	0.71 1.52	1.31	0.89 1.93	1.12	0.84 1.48				
70-74	1.22	0.74 2.00	1.17	0.71 1.94	1.23	0.78 1.95	1.16	0.74 1.82	1.22	0.87 1.71				
75-79	1.91	1.25 2.90	1.18	0.79 1.77	1.47	1.02 2.12	1.52	1.04 2.22	1.65	1.25 2.16				
80-84	1.80	0.96 3.40	1.05	0.55 2.00	1.33	0.75 2.37	1.43	0.81 2.52	1.52	1.00 2.33				
> 85	1.22	0.52 2.87	1.88	0.78 4.50	2.29	1.13 4.64	1.00	0.50 1.99	1.75	1.02 3.01				
Total	1.77	1.55 2.01	0.86	0.75 0.99	1.37	1.20 1.57	1.11	0.98 1.25	1.57	1.43 1.72				

IRR-incidence rate ratio, CI-confidence interval, UW-urban women, RW-rural women, UM-urban men, RM-rural men.

Statistical significance is indicated in bold.

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Conflict of interest statement:

The authors declare that they have no conflict of interest.

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