The burden of cancers attributable to infection in Cluj County, Romania

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Introduction

Hepatitis B (HBV) and C (HCV) viruses, human papillomaviruses (HPV), Epstein-Barr virus (EBV), human herpesvirus 8 (HHV8), T-lymphotropic virus type-1 (HTLV-1) and *Helicobacter pylori* (Hp) have been identified as carcinogenic to humans according to the International Agency for Research on Cancer (IARC). In less developed countries, the proportion of cancers attributable to infections is much higher (22.9-26.3%) compared to more developed countries (3.5-7.7%) being related to higher prevalence of infectious agents.

Objective: To estimate the population attributable fraction (PAF) of infection-associated malignancies and the number of new cancer cases by infectious agent.

Methods:

The reported age and gender-specific incidence rates in the Cluj County, Romania, were provided from the North-Western Regional Cancer Registry (2006-2011) covering a population of 691,106 individuals according to 2011 census data. The estimated number of cancer cases attributed to each infection was calculated by multiplying the incident cases with PAF (Cole and Macmahon, 1971) .

The prevalence of infectious agents was obtained from local studies (HBV-5.6%, HCV-4.56%) and for Hp, HPV at anogenital sites, HHV8, and HTLV-1 global prevalence estimates were used since no evidence of regional variations was found in cases. Comparison with national and European data provided by IARC Globocan Project 2012 was done.

$$PAF = \frac{p(RR-1)}{1+p(RR-1)}$$

where RR is the relative risk for each infectious carcinogenic and 'p' the prevalence of exposure.

Results

Among 16,702 incident cancer cases (8781 in men, 7921 in women), 16.65% (2781) of cancer cases were attributable to infection with 1716 cases in women (21.66%) and 1065 cases in men (12.12%). HPV attributable cancers represented 6.99% (13.9% in women, 0.77% in men), followed by Hp (4.89%), HBV and HCV (4.08%) attributable cancers. Among all cancers the main localizations were: cervix uteri cancer (6.2%), non-cardia gastric cancer (4.7%) and liver cancer (HBV-2.07%, HVC-1.83%) accounting for 95.9% (2666) of all infection-attributable cancers.

Human papillomavirus (HPV, high-risk types)	RR	PAF%	Attributable cases			% of all cancers		
			M	F	Total	M	F	Total M+F
Cervix uteri (C53)	>100	100	-	1035	1035	-	13.1	6.2
Vulvar carcinoma (C51)	NR	43	-	27	27	-	0.34	0.16
Vaginal carcinoma (C52)	NR	70	-	14	14	-	0.18	0.07
Anal carcinoma (C21)	NR	90	14	17	31	0.16	0.21	0.19
Penile carcinoma (C60)	NR	50	14	-	14	0.16	-	0.08
Mouth (C01.9-C06.9)	NR	3	6	1	7	0.07	0.01	0.04
Oropharynx (CC09.9-10.9)	NR	25.6	34	6	40	0.39	0.08	0.24
Total			68	1100	1168	0.78	13.89	6.99

Table 1. Estimated numbers of HPV-related cancers, Cluj County,, 2006-2011

	Prevalence %	RR	PAF %	Attributable cases			% of all cancers		
				M	F	Total	M	F	Total
Hepatitis viruses									
HBV Liver cancer (C22)	5.6	20	52	201	145	346	2.29	1.83	2.07
HCV Liver cancer (C22)	4.56	20	46	178	128	306	2.03	1.62	1.83
HCV NHL (C82-85,C96)	4.56	2.5	8.2	17	13	30	0.19	0.16	0.18
Total				396	286	682	4.51	3.61	4.08
Helicobacter pylori									
Non-cardia gastric cancer (C16.1-C16.9)	74	5.9	78	499	286	785	5.68	4.63	4.70
NHL of gastric location MALT (C82-85,C96)	74	6	79	20	11	31	0.23	0.18	0.19
Total				519	297	816	5.91	3.75	4.89

Table 2. Estimated numbers of hepatitis viruses and Hp-related cancers, Cluj County,, 2006-2011

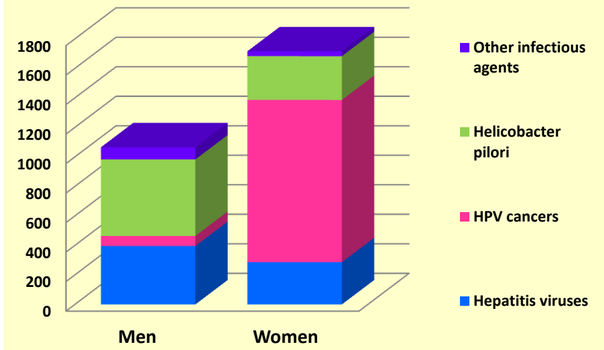
	Attributable cases			% of all cancers		
	M	F	Total	M	F	Total
Bacteria						
Helicobacter pylori	519	297	816	5.91	3.75	4.89
Viruses						
Human papillomavirus (HPV; high-risk types)	68	1100	1168	0.77	13.89	6.99
Hepatitis viruses	396	286	682	4.51	3.61	4.08
Epstein-Barr virus	71	27	98	0.80	0.34	0.59
Human herpes virus type 8 (HHV-8)	11	5	16	0.13	0.06	0.10
Human T-cell lymphotropic virus type 1 (HTLV1)	-	1	1	-	0.01	0.006
Total	1065	1716	2781	12.13	21.66	16.65

Table 3. Estimated numbers of cancers attributable to different infectious agents, Cluj County

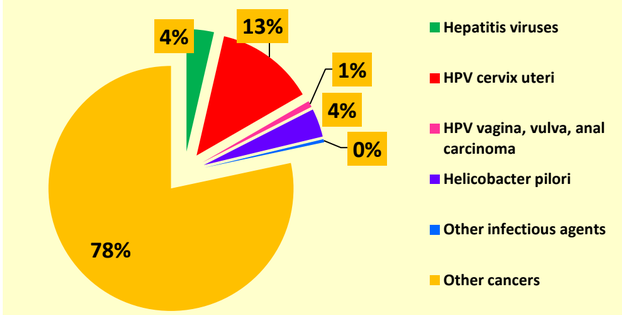
	Cluj No/%	Romania Globocan No/%	Europe Globocan No/%	Cluj/Romania 95%CI, P value	Cluj/ Europe 95%CI, P value	Romania/Europe 95%CI, P value
Women - Total infection related cancers*	1651/20.84	6682/18.76	169649/9.72	1.10-3.07 < 0.0001	10.23-12.03 < 0.0001	8.63- 9.46 < 0.0001
Men - Total infection related cancers*	984/11.2	4673/10.82	161595/8.2	NS	2.35-3.68 < 0.0001	2.32-2.91 < 0.0001

Table 4. Comparison - incident cases and proportion of cancers attributable to infection Cluj County/Romania/Europe
*Only the types of cancers reported to Globocan 2012 were included

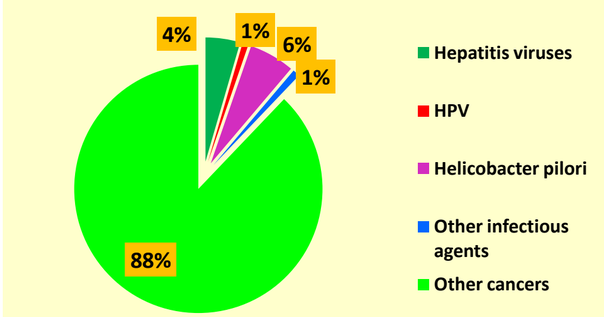
Number and proportion of cancer cases attributable to infection 2006-2011, Cluj County, Romania



Proportion of cancers attributable to infection in women Cluj County, Romania



Proportion of cancers attributable to infection in men Cluj County, Romania



Conclusion

Our assessment of infection-associated cancers highlights the burden of disease in women. From the public health perspective, the primary, secondary and tertiary preventive measures should be outlined, primarily for the infections caused by HPV, Hp and hepatitis viruses.