



THE INCIDENCE AND MORTALITY OF ENDOMETRIAL CANCER AND ITS ASSOCIATION WITH BODY MASS INDEX AND HUMAN DEVELOPMENT INDEX IN ASIAN POPULATION

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Abstract – Objective: Endometrial cancer is the most common malignancy in women in many countries. Body mass index (BMI) is associated with an increased risk of endometrial cancer. The aim of this study was to investigate the incidence and mortality of endometrial cancer and its correlation with BMI and human development index (HDI) in Asia in 2012.

Materials and Methods: This study was conducted based on the world data of cancer and the World Bank including the HDI and its components. In this population-based study, we derived population attributable fractions (PAFs) using BMI estimates in adults by age, gender, and country. The incidence and mortality rate due to endometrial cancer in Asian countries were drawn. For data analysis, correlation test was used to investigate the relationship between incidence and death rate and two parameters BMI and HDI using the Stata software version 14. Significance level (p) was considered < 0.05.

Results: The highest incidence of endometrial cancer in Asia was reported for Armenia (26.7 per 100,000 population), followed by Israel (15.4 per 100,000 population) in the age group of 60-64 years, and the highest mortality rate due to this cancer for Armenia (1.6 per 100,000 population), followed by Afghanistan (1.4 at 100,00 population). The highest rate of endometrial cancer was reported for Kuwait (56.3%). The results showed a positive correlation between incidence of cancer and HDI ($r=0.44$, $p>0.001$). We observed no significant association between cancer-related death and HDI ($r=0.26$, $p>0.05$).

Conclusions: Overweight and obesity are associated with the risk of endometrial cancer. Therefore, to prevent this cancer and associated complications, the implementation of an intervention program for controlling obesity and also routine endometrial cancer screening programs in obese and overweight women is necessary.

KEYWORDS: Endometrial Cancer, Incidence, Mortality, Human Development Index, BMI, Asia.

LIST OF ABBREVIATION: Body mass index (BMI), Human Development Index (HDI), Relative risk (RR), Population attributable fraction (PAF).



INTRODUCTION

Endometrial cancer is the fifth leading cancer among women worldwide, with 320,000 new cases diagnosed in 2012, which accounts for 4.8% of all cancers in women^{1,2}. Endometrial cancer is the third leading cancer in the Western world, accounting for 6-9% of all cancers in women³⁻⁵. Endometrial cancer is often detectable in the early stages due to the nature of the disease and incidence of uterine and/or vaginal bleeding, with the 5-year survival rate of 85-91%⁶. About 73% of patients with endometrial cancer are diagnosed in stage I, and the diagnosis may be made in the stage II of the disease for about 10% of patients. It is, therefore, very important to identify risk factors followed by primary diagnostic interventions to modify the factors effective on cancer. Epidemiological studies^{3,7} have shown that body mass index (BMI) is a major risk factor for endometrial cancer. Every woman faces a 3% risk of developing cancers in her lifetime that increases for obese women. Studies have shown that about 57% of endometrial cancer cases in the United States occur due to overweight and obesity⁸. In a meta-analysis of 26 studies conducted by the American Cancer Research Institute, it was reported that per every five units of increase in body mass, the risk of developing endometrial cancer increases by 50%⁹. In addition, BMI increases the mortality rate of endometrial cancer. In a retrospective study in women with primary endometrial cancer, obese women had higher mortality rates than women with normal BMI⁸.

MATERIALS AND METHODS

AVAILABILITY OF DATA ON INCIDENCE AND MORTALITY

The method by which the death prevalence is measured is specific to each country and its quality is based on the comprehensiveness and quality of available data in the country. In each country, there are many methods to achieve this purpose and because these methods are complex and various, it is relatively impossible to definitely determine a qualitative value of death prevalence. However, there is an alphabetical, numerical scoring system that independently describes the death prevalence and its associated information on national level

INCIDENCE

The age and gender-based incidence of endometrial cancer in each country was assessed by using the following category:

1. Rates approximate to 2012 (38 countries);
2. The majority of recent rates were applicable to 2012 population (20 countries);

3. Estimates of national mortality by modeling, using incidence mortality rates obtained from data in national cancer registries (13 countries);
4. Estimates of national mortality by modeling, using incidence mortality ratios obtained from data in local cancer registries in border-sharing countries (9 European countries);
5. Estimates of national mortality by using modeled survival (32 countries);
6. Estimates of mortality according to the weighted average of the local rates (16 countries);
7. One cancer registry covering a part of the country considered to be representative of the country profile (11 countries);
8. Age/gender-specific rates due to all cancers partitioned using data on relative frequency of different cancers (according to age and gender) (12 countries);
9. The rates of neighboring countries or registries in the same region (33 countries).

MORTALITY

Based on the detail degree and precision of the countrywide mortality data, six methods below were applied in the following order of priority:

1. Rates approximate to 2012 (69 countries);
2. The majority of recent rates are applicable to 2012 population (26 countries);
3. Estimates of mortality according to the weighted average of the local rates (1 country);
4. Estimates of national incidence rates by modelling, using country-specific survival (2 countries);
5. Estimates of national incidence rates by using modelled survival (83 countries);
6. The rates of neighboring countries or registries in the same region (33 countries)⁹.

BODY MASS INDEX (BMI)

We used BMI average values and corresponding standard deviations based on age and gender for the adults over 20 years in each country during 1982-2002. The age groups included 20 – 34, 35 – 44, 45 – 54, 55 – 64, 65 – 74, and ≥ 75 years.

RELATIVE RISK (RR) ESTIMATES

Only the cancers for which sufficient evidence with respect to BMI was reported by World Cancer Research Foundation (WCRF) were reported, including adenocarcinoma and cancers of esophagus, rectum, large intestine, kidney, pancreas, bladder, and breast cancer following menopause, uterus, and ovary. The relative risk of a specific gender in various regions was derived from the analysis of the published standard measurements by the WCRF and its Constant Updating Project (CUP).

POPULATION ATTRIBUTABLE FRACTION (PAF)

The PAF was calculated using the method suggested by the Comparative Risk Assessment Collaborating Group, according to the formula below:

$$PAF = \frac{\int RR(x)P(x)dx - \int RR(x)P^*(x)dx}{\int RR(x)P(x)dx}$$

Where $P(x)$ represents the population distribution of BMI, $P^*(x)$ the distribution of the theoretical minimum BMI, and $RR(x)$ the relative risk of cancer related to a BMI of value x . The distribution of the theoretical minimum BMI was defined as a BMI distribution with a mean of 22 kg/m² and a standard deviation of 1, where the disease burden is assumed lowest at the population level. A log-logit function was applied to characterize the shape of the RR across BMI units. No risk^{10,11} was assumed for a BMI under 22 kg/m² and no risk increase for BMI over 40 kg/m².

CANCER INCIDENCE AND ATTRIBUTABLE CANCER BURDEN

Because of the slow effect of time on weight gain and cancer development (supposedly 10 years), the cancer load with respect to weight gain in adults aged ≥ 20 years appears only in cancers that have lasted 10 years or over. Accordingly, the number of cancer cases was calculated according to age (over 30 years), gender, and country based on GLOBOCAN in 2012. Countries were classified into 12 geographical regions: Sub-Saharan countries (East, Middle, South and West Africa), Middle East (Western Asia), and North Africa; Latin America (Central and South America), and the Caribbean; North America; East Asia (including China), Southeast Asia; South Central Asia (central and southern Asia including India); Northern Europe, Eastern Europe; Southern Europe; Western Europe, and Oceania (including New Zealand and Australia).

HDI

HDI is a combination index consisting of three dimensions: degree of studies, life expectancy, and dominance over required sources for a proper sensible life. All the regions and groups that have experienced a noticeable progress in all HDI components have developed more quickly in comparison with low or moderate HDI countries. According to this index, the world is unequal because national average value hides most of the various experiences in human life. Many inequalities exist in northern and southern countries. Income inequality has been intensified inside each country as well as between many countries^{12,13}.

STATISTICAL ANALYSIS

In this study, the correlation bivariate method was used to assess the correlation between the incidence and mortality rates of endometrial cancer and the HDI. Linear regression models were also used to assess the HDI effect on the incidence rate of endometrial cancer. Significance level was considered lower than 0.05. Data analysis was conducted by Stata software version 14.

RESULTS

According to the results recorded in GLOBOCAN in 2012, 6763030 cases (152.21 per 100,000 population) were registered in Asia, of whom 3694857 (174.1 per 100,000 population) were male and 3068173 (13.3 per 100 000 population) female. Besides that, the mortality rates for men and women were 2689472 (12.36 per 100,000 population) and 1810074 (77 per 100,000 population), respectively. The incidence and mortality rates for women due to endometrial cancer were 131819 (6 cases per 100000 population) and 34247 cases (1.5 cases per 100000 population), respectively. The highest incidence rate of endometrial cancer in Asia was reported for Armenia, followed by Israel and Georgia with the rates of 26.7, 15.4, and 14.2 cases per 100000 population, respectively. In addition, the highest mortality rate due to endometrial cancer was reported for Armenia, followed by Afghanistan and Tajikistan with the rates of 6.1, 4.1, and 4 cases per 100000 populations, respectively (Table 1, Figure 1, and Figure 2).

Regarding the incidence of the disease in different age groups in five countries with the highest incidence rates, namely, Armenia, Israel, Georgia, Singapore, Kyrgyzstan, the results showed that the highest incidence was observed in the age group of 60-64 years and the lowest incidence in the age group under 40 years, with the incidence gradually decreasing in the age group over 65 years old (Figure 3).

The results showed a positive correlation between incidence of cancer and HDI ($r = 0.44$, $p > 0.001$). We observed no significant association between cancer-related death and HDI ($r = 0.26$, $p > 0.05$).

Regarding the status of BMI and the incidence of cancer in Asia, the results showed that about 108900 cases in both genders were attributed to BMI. In women, about 80,000 cases of cancer were attributed to BMI. The highest percentages of all cancers associated with BMI were reported from the Western Asia, covering Kuwait (10.6%), Jordan (9.9%), Israel (9.5%), and Armenia (9.5%).



TABLE 1. Incidence and mortality rates for endometrial cancer in females in Asia in 2012.

Country	Incidence			Mortality			HDI
	Number	(%)	ASR (W)	Number	(%)	ASR (W)	
Asia	131720	4.3	6.0	34247	1.9	1.5	
Eastern Asia	89304	5.2	8.6	20823	2.1	1.9	
China	73109	5.9	8.6	17160	2.2	1.9	0.907
Japan	11449	1.6	10.6	2783	0.7	16	0.894
Korea, Democratic Republic of	766	2.6	5.0	333	1.7	2.0	—
Korea, Republic of	2016	1.9	5.8	291	0.9	0.7	—
Mongolia	20	1.1	1.9	15	1.1	1.4	0.720
South-Eastern Asia	15329	3.8	5.1	4432	1.9	1.5	
Brunei	26	9.0	12.6	4	3.7	2.2	0.860
Cambodia	161	1.9	2.5	56	1.0	1.0	0.546
Indonesia	6475	4.0	5.6	1947	2.1	1.7	0.677
Lao PDR	76	2.6	3.4	28	1.3	1.3	0.563
Malaysia	710	1.9	5.3	220	1.0	1.7	0.799
Myanmar	598	1.8	2.4	230	1.0	1.0	0.540
Philippines	2221	4.0	5.6	502	1.8	1.4	0.671
Singapore	539	7.0	13.9	77	2.4	1.8	0.920
Thailand	1852	3.0	3.9	512	1.4	1.1	0.733
Timor-Leste	32	6.3	9.3	12	3.5	3.8	0.620
Viet Nam	2639	2.1	5.4	844	0.9	1.8	0.668
South-Central Asia	19966	2.5	2.7	7227	1.5	1.0	
Afghanistan	727	6.9	7.9	308	4.2	4.1	0.470
Bangladesh	929	1.5	1.5	357	0.8	0.6	0.565
Bhutan	0	0.0	0.0	0	0.0	0.0	0.589
India	12323	2.3	2.3	4773	1.5	0.9	0.599
Iran, Islamic Republic of	795	0.2	2.5	196	0.8	0.6	0.769
Kazakhstan	1259	5.8	12.9	280	2.6	2.7	0.782
Kyrgyzstan	198	6.3	8.4	60	3.2	2.8	0.647
Maldives	3	2.8	3.1	0	0.0	0.0	0.683
Nepal	98	0.9	0.9	38	0.5	0.3	0.545
Pakistan	2171	2.6	3.6	797	1.5	1.4	0.538
Sri Lanka	207	0.9	1.5	53	0.4	0.4	0.757
Tajikistan	349	12.0	12.2	106	5.8	4.0	0.617
Turkmenistan	145	4.7	6.1	37	2.0	1.7	0.678
Uzbekistan	762	6.0	5.8	222	3.0	1.8	0.681
Western Asia	7121	2.2	7.6	1765	0.9	1.9	
Armenia	596	5.5	26.7	165	2.4	6.1	0.736
Azerbaijan	153	2.3	2.8	41	1.0	0.8	0.745
Bahrain	14	3.2	4.7	3	2.0	1.3	0.815
State of Palestine	88	2.5	7.8	27	1.2	2.7	0.684
Georgia	432	7.1	14.2	147	4.4	3.9	0.755
Iraq	144	1.0	1.5	47	0.5	0.5	0.659
Israel	830	2.8	15.4	131	1.2	2.0	0.891
Jordan	95	2.9	5.2	24	1.4	1.3	0.737
Kuwait	40	4.9	7.6	17	4.4	3.8	0.796
Lebanon	187	3.9	7.7	41	1.8	1.6	0.766
Oman	23	3.4	3.9	5	1.4	0.9	0.796
Qatar	13	1.3	5.7	1	0.2	1.0	0.843
Saudi Arabia	432	4.7	5.8	87	2.1	1.3	0.830
Syrian Arab Republic	239	1.1	3.3	69	0.5	1.0	0.635
Turkey	3787	6.1	10.1	951	2.9	2.5	0.754
United Arab Emirates	39	1.3	6.0	5	0.4	1.0	0.829
Yemen	9	0.1	0.1	4	0.1	0.1	0.498

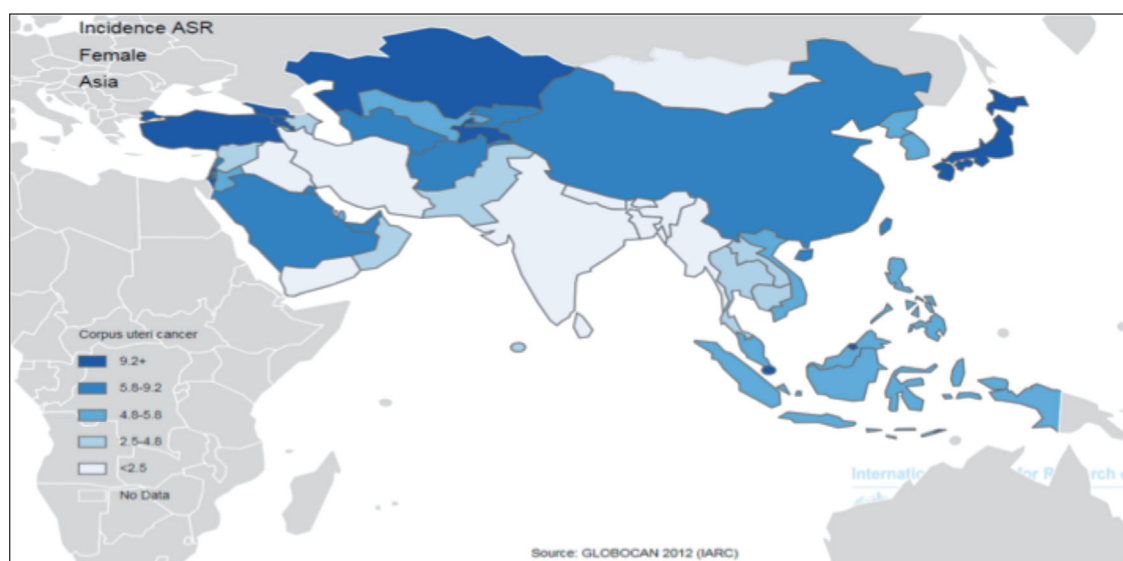


Fig. 1. Incidence of endometrial cancer in women in Asia [extracted from GLOBOCAN 2012].

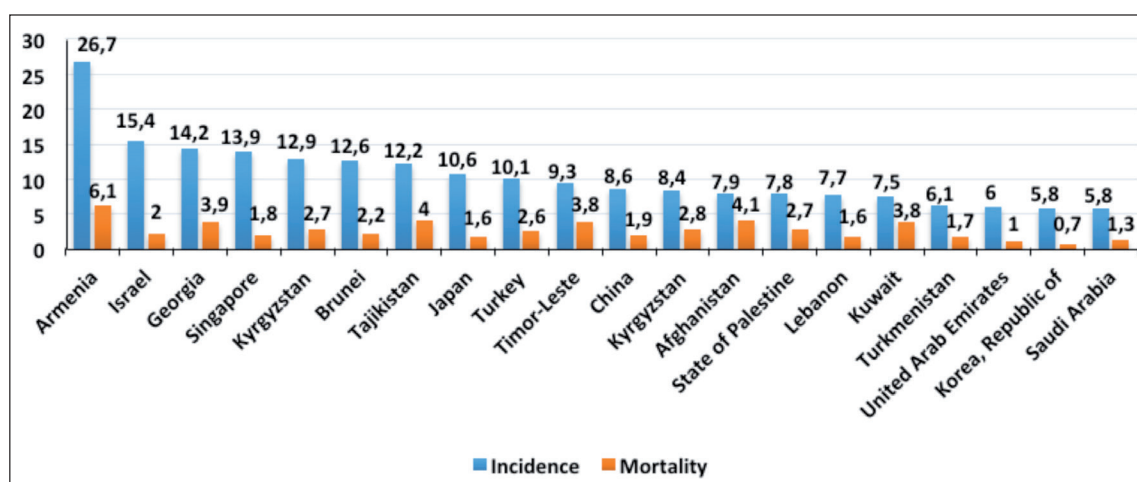


Fig. 2. The highest incidence rates for endometrial cancer in women in Asia [extracted from GLOBOCAN 2012].

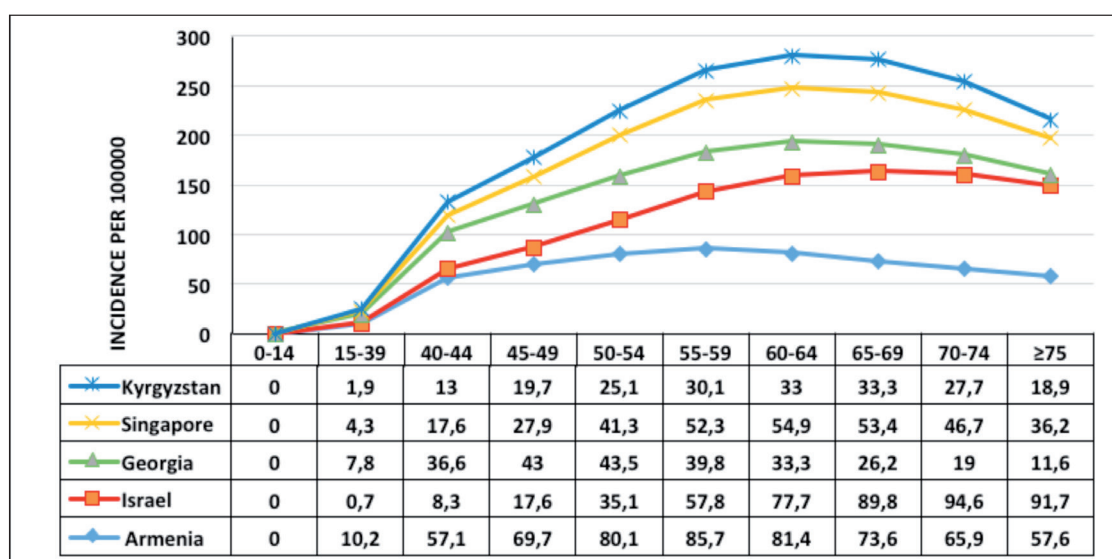


Fig. 3. Incidence of endometrial cancer in Asian women in different age groups in 2012.



The lowest percentage of all cancers associated with BMI was reported from Bangladesh (0.35%), Nepal (0.61%) and Vietnam (0.65%). The results also showed that 26,000 (21%) of endometrial cancer cases in Asia were attributed to BMI. The highest percentage of endometrial cancer associated with BMI was observed in Kuwait (56.3%), followed by Jordan (54.5%) and Saudi Arabia (52.8%). The most preventable levels of endometrial cancer associated with BMI were reported from Maldives (29.1%), Lebanon (21.4%), Bahrain (21.1%), and Iran (21.1%) (Table 2, Figure 2).

The results showed a positive correlation between the percentage of cancers associated with BMI and HDI ($r = 0.569$, $p < 0.05$). The results showed that the correlation between endometrial cancer and BMI and HDI was 0.51 ($p < 0.05$) (Figure 4).

DISCUSSION

Obesity is one of the most common medical disorders and also one of the most important public health issues³. In 2016, the prevalence of obesity (BMI: 25-29.9 kg/m²) and obesity (BMI > 29.9 kg/m²) was 38% in men and 39.2% in women¹⁴. A study (2015) showed that about 3.6% of patients with cancer in 2012 were overweight or obese. Previous studies have shown that obesity is associated with an increased risk of various types of cancers including cancers of stomach^{15,16}, liver¹⁷, ovary¹⁸, pancreas^{19,20} and colon²¹. It has been estimated that 38.4% of endometrial cancer cases in 2012 were associated with diabetes and BMI^{22,23}. The analysis of cohort and case studies also confirms the positive correlation between overweight and obesity and the risk of developing endometrial cancer among both Asians and non-Asians^{3,24}. Overweight is responsible for about 30% of endometrial cancer in 30 European countries²⁵. With increasing prevalence of obesity in the following years, endometrial cancer incidence seems to increase. Evidence has shown that relatively lean women with the BMI of 20 kg/m² have the lowest risk of developing endometrial cancer. Different epidemiological studies have investigated obesity and the risk of developing endometrial cancer²⁶⁻²⁸. In a large cohort study in American women,

obesity was strongly associated with the incidence of endometrial cancer. Adipose tissue produces a lot of estrogen, and high estrogen levels increase the risk of endometrial cancer. Obese people often have high levels of insulin and insulin-like growth factor (IGF) in the blood (IGF-1)²⁹. This complication, called hyperinsulinemia or insulin resistance, is a preliminary stage of type 2 diabetes. High levels of insulin and IGF-1 play an important role in the development of colon, kidney, prostate cancers and endometrial cancer³⁰⁻³². In the United States in 2013, approximately 49560 endometrial cancer cases were detected, making this cancer recognized as the fourth leading cancer in women³³. The study of Esposito et al³² showed that the risk of endometrial cancer is higher in people with high BMI. An important role of obesity was also reported by Friedreich et al^{34,35}. In a large study by Bjorge et al³⁰ on a total of 287320 cases, high BMI was reported in 917 cases of endometrial cancer. Various studies have shown the association between BMI and increased risk of mortality in patients with endometrial cancer^{35,36}. In a meta-analysis of 221 databases, a significant association was found between BMI and endometrial cancer³⁷. Studies have shown that the risk of endometrial cancer can be reduced by weight loss through diet and physical activity strategies³⁸.

CONCLUSIONS

Overweight and obesity are major contributors to endometrial cancer and increase the risk of developing endometrial cancer. Therefore, to prevent this cancer and associated complications, the implementation of an intervention program for controlling obesity and also routine endometrial cancer screening programs in obese and overweight women is necessary.

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CONFLICT OF INTEREST:

The authors declare no conflict of interest

TABLE 2. Fraction (%) of all cancer cases (at all anatomical sites), endometrial cancer and preventable fraction attributable to BMI in Asia in 2012 by country.

Sites	Fraction (%) of all cancer cases (at all anatomical sites) attributable to BMI)						Fraction (%) of all endometrial cancer attributable to BMI		Preventable fraction (%)
	Female		Male		Both Sexes				
	(%)	Number	(%)	Number	(%)	Number	(%)	Number	
Asia	108900		29600		80000		26000	21	
Eastern Asia									
China	49000	1.7	14000	0.76	36000	3.0	14000	20	3.0
Japan	15000	2.2	5800	1.4	9400	3.2	1900	16.7	4.4
Korea, Republic of	4600	2.2	1800	0.8	2800	2.8	458	23.1	9.6
Mongolia	49	1.3	13	0.65	36	1.9	7	34.8	8.8
South-Eastern Asia							2800		
Brunei	15	2.9	4	2.0	10	3.7	5	18.8	1.0
Cambodia	66	0.48	6	0.09	61	0.8	16	10.3	0.0
Indonesia	3600	1.3	481	0.37	3200	2.1	1200	18.4	0.0
Lao PDR	38	0.68	4	0.13	35	1.3	10	12.9	0.0
Malaysia	1100	3.2	308	1.8	810	4.5	237	33.9	19.7
Myanmar	439	0.72	43	0.15	395	1.3	80	13.6	0.0
Philippines	1600	1.8	300	0.76	1300	2.6	455	21.8	0.0
Singapore	521	3.4	154	2.0	376	4.9	131	24.6	0.0
Thailand	2400	2	416	0.69	2000	3.4	539	29.3	13.4
Timor-Leste	8	0.84	1	0.22	7	1.5	4	11.1	0.0
Viet Nam	368	0.31	37	0.06	330	0.65	181	7.1	0.0
South-Central Asia							3200		
Afghanistan	109	0.64	12	0.16	96	1.1	50	7.4	0.0
Bangladesh	249		45	0.08	204	0.35	29	3.3	0.0
Bhutan	3	0.76	1	0.48	2	1.1		0.0	0.0
India	7000	0.73	956	0.22	6000	1.2	1400	11.7	0.0
Iran	2400	3.1	681	1.6	1700	4.7	310	40	21.1
Kazakhstan	1700	4.5	353	2.0	1400	6.6	479	39.2	4.5

Continued

TABLE 2 (Continued). Fraction (%) of all cancer cases (at all anatomical sites), endometrial cancer and preventable fraction attributable to BMI in Asia in 2012 by country.

Sites	Fraction (%) of all cancer cases (at all anatomical sites) attributable to BMI)						Fraction (%) of all endometrial cancer attributable to BMI		Preventable fraction (%)
	Female		Male		Both Sexes				
	(%)	Number	(%)	Number	(%)	Number	(%)	Number	
Kyrgyzstan	189	3.5	29	1.1	160	5.5	69	35.4	1.2
Maldives	6	2.7	1	0.43	5	5.1	1	45.4	29.1
Nepal	69	0.4	10	0.14	59	0.61	5	5.3	0.0
Pakistan	2300	1.7	193	0.35	2100	2.7	494	23.5	9.4
Sri Lanka	283	1.2	26	0.27	257	2.0	44	21.2	0.0
Tajikistan	128	2.6	22	0.96	106	4.1	71	21.9	0.0
Turkmenistan	120	2.2	35	1.3	85	3.0	38	26.2	1.2
Uzbekistan	622	2.2	111	1.3	510	4.4	226	30	10.5
Western Asia							17000		
Armenia	580	5.5	71	1.4	510	9.5	246	41.3	8.0
Azerbaijan	336	2.6	81	1.2	255	4.0	70	45.8	2.9
Bahrain	43	5.2	14	3.3	29	7.1	7	48.1	21.1
Georgia	403	3.3	63	1.0	340	5.6	159	36.9	0.61
Iraq	834	3.7	176	1.8	659	5.3	67	47.5	12.1
Israel	1900	6.6	571	3.9	1300	9.5	393	47.5	19.7
Jordan	417	7.2	127	4.5	290	9.9	51	54.5	9.4
Kuwait	107	7.2	30	3.9	77	10.6	23	56.3	15.1
Lebanon	464	5.4	91	2.2	372	8.3	91	48.8	21.4
Oman	50	3.8	17	2.4	33	5.5	9	40.4	12.2
Qatar	45	4.9	20	3.5	25	7.3	6	48.8	8.8
Saudi Arabia	1000	6.8	290	4.0	742	9.2	225	52.8	15.6
Syrian Arab Republic	1100	5.5	287	3.0	802	7.7	120	50.8	16.3
Turkey	6600	4.8	1700	2.1	4900	8.5	1900	50.7	13.4
United Arab Emirates	126	4.8	45	3.4	81	6.3	21	52.7	11.0
Yemen	220	2.5	59	1.5	161	3.3	3	36.2	15.8

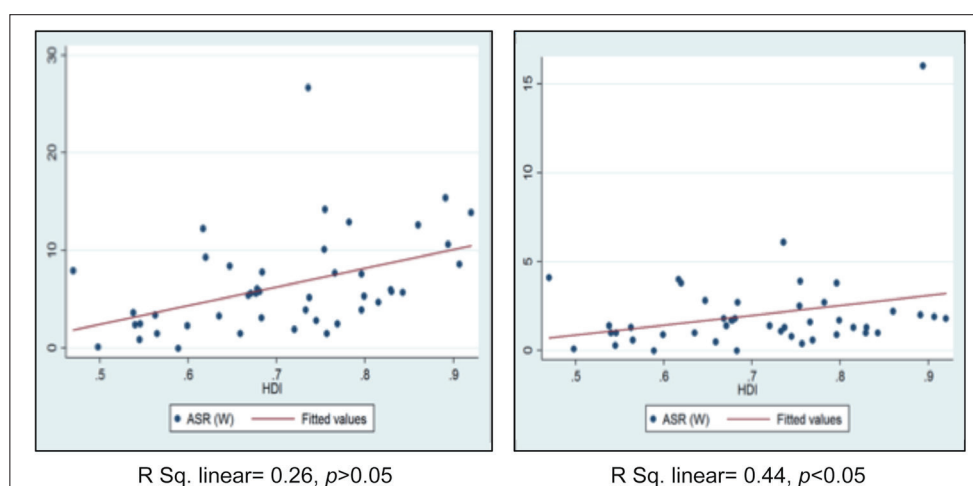


Fig. 4. Correlation between the HDI and incidence and mortality rates of endometrial cancer in Asia in 2012.

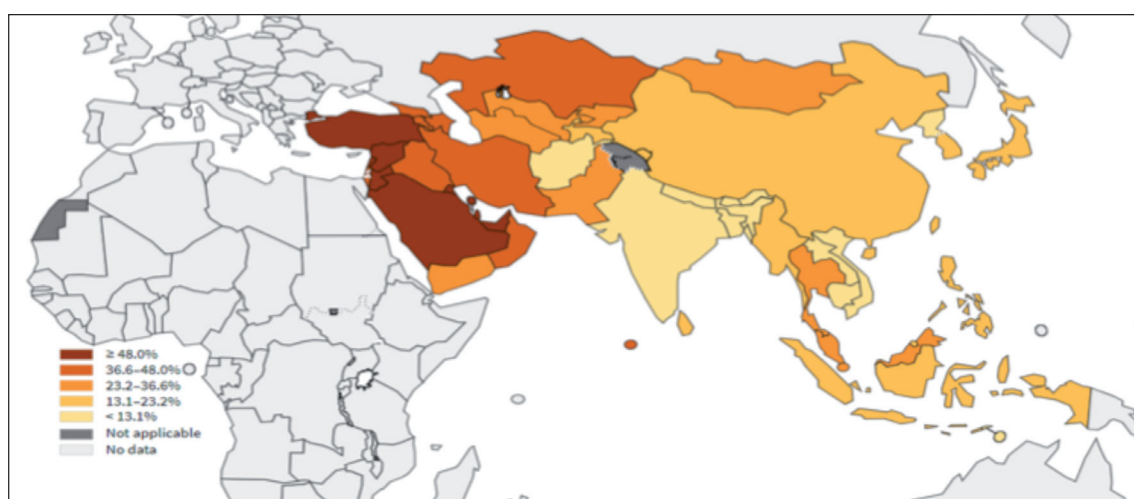


Fig. 5. Fraction (%) of all endometrial cancer cases among women in Asia in 2012 attributable to excess body mass index by country [Extracted from GLOBOCAN 2012].

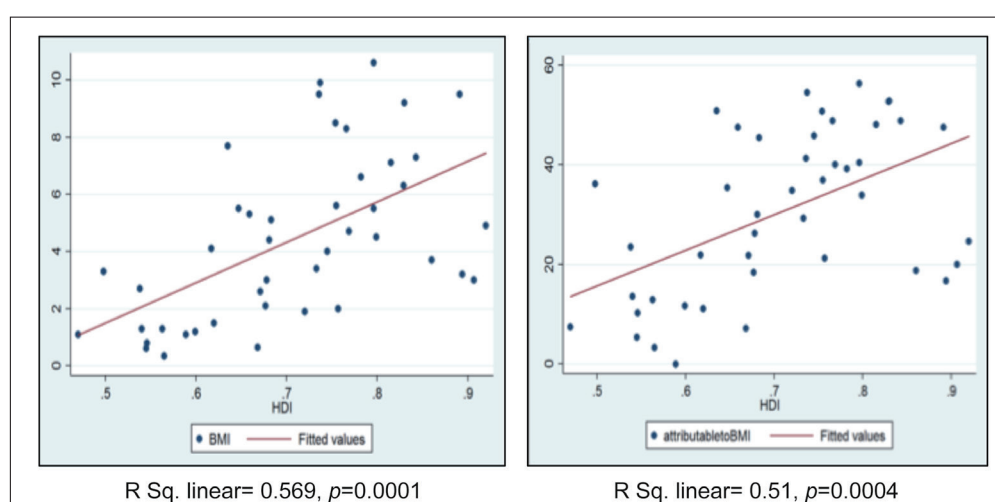


Fig. 6. Correlation between the Human Development Index and Fraction (%) of all cancer cases (at all anatomical sites) and endometrial cancer in Asia in 2012.



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