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Breast cancer incidence in Mongolia

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Abstract

Purpose—Data on international variation in breast cancer incidence may help to identify additional risk factors. Substantially lower breast cancer rates in Asia than in North America and Western Europe are established, but differences within Asia have been largely ignored despite heterogeneity in lifestyles and environments. Mongolia's breast cancer experience is of interest because of its shared genetics but vastly different diet compared with other parts of Asia.

Methods—Age-standardized breast cancer incidence and mortality rates obtained from the International Association of Cancer Registries are presented for several Asian countries. Mongolian incidence rates obtained from its cancer registry describe incidence within the country.

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Results—Breast cancer incidence in Mongolia (age standardized 8.0/100,000) is almost a third of rates in China (21.6/100,000), and over five times that of Japan (42.7/100,000) and Russia (43.2/100,000). Rates within Mongolia appear to have increased slightly over the last decade and are higher in urban than rural areas (annual percentage increase of age-standardized rates from 1998 to 2005 was 3.60 and 2.57%, respectively). The increase in breast cancer incidence with age plateaus at menopause, as in other Asian populations.

Conclusions—Mongolia's low breast cancer incidence is of particular interest because of their unusual diet (primarily red meat and dairy) compared with other Asian countries. More intensive study of potential dietary, reproductive and lifestyle factors in Mongolia with comparison to other Asian populations may provide more clarity in what drives the international breast cancer rate differences.

Keywords

Mongolia; Breast cancer; Urban-rural; Asia; International

Introduction

Breast cancer incidence rates in Northern and Western Europe, and North America are greater by approximately four to five times those of East and Southeast Asian countries [1]. Furthermore, rates increase rapidly among Asian migrants to Western countries, reaching those of the host country by the second generation [2]. Although the major causal hypothesis to explain these observations has been differences in established breast cancer risk factors, including endogenous hormone concentrations, evidence in support of this is lacking.

There has been the assumption that Asian-Western differences in breast cancer incidence are uniform and reflect the benefits of the Asian lifestyle. Asian populations have generally been treated as homogeneous, and variation in breast cancer incidence among the countries that make up this large, culturally and environmentally diverse geographic area has been overlooked. Just as Western countries vary in breast cancer incidence, so do Asian countries. As we show in this paper, Mongolia's breast cancer rate is at least as low as, and possibly lower than rates in other parts of Asia, whereas their diet is unique among Asian countries and more closely resembles the diets in Western countries. Considerable variation in rates among Asian countries may provide further opportunity for generating novel hypotheses to determine what factors contribute to the international differences (i.e., Asian vs. Western) that have been observed in breast cancer. In particular, countries such as Mongolia still allow the evaluation of the possible influence of lifestyle change associated with economic development and with migration from rural to urban areas. Additionally, certain aspects of the Mongolian lifestyle, such as their diet, could have a direct impact on hypotheses for explaining incidence differences.

In this report, we describe breast cancer incidence rates in Mongolia, overall and for urban and rural populations by age, calendar year, and stage at diagnosis.

Materials and methods

Breast cancer rates for Mongolia were obtained from two sources: the International Association of Cancer Registries (IARC) and the Mongolian National Oncology Center.

Breast cancer incidence rates for women based on the 2008 estimates from the IARC are presented for Mongolia and other countries. The calculated incidence and mortality rates are expressed per 100,000. The world standard population used in Globocan is as proposed by

Segi [3] and modified by Doll et al. [4]. The age-standardized rate is calculated using 10 age groups.

The Mongolian Ministry of Health, National Center for Health Development publishes an annual health report providing data on demographics, and incidence, prevalence, and mortality for selected diseases and health conditions [5]. Annual breast cancer incidence rates from 1998 to 2005 were available from the Mongolian National Oncology Center. In Mongolia, cancer cases are reported to provincial authorities (there are 23 provinces or “aimags”) who then provide them to the National Oncology Center. Although incidence rates for calendar years through 2007 were available, the analysis was truncated at 2005 to address completeness of the registry data. Age-specific breast cancer incidence rates for women in Mongolia from 1998 to 2005 were calculated for each 5-year age group using annual data by province. Each age-specific rate (i.e., number of cases divided by the number of women in that age group) was multiplied by the number of women in that age group in the World Standard Million (one of several standard populations that can be obtained from the SEER) [6] divided by the total female population for ages 20+ years in the World Standard Million, the products were summed across age groups (for each calendar year and province), and then all multiplied by 100,000. In other words, a weighted average of the age-specific rates was calculated, weighing each rate by the corresponding fraction of the World Standard Million. These age-standardized rates were presented overall, by calendar year, urban/rural residence, and breast cancer stage.

Results

The population in Mongolia was close to 3 million (2 2,996,081) in 2008 (<https://www.cia.gov/library/publications/the-world-factbook/>). Mongolia is experiencing a demographic transition, with mortality and birth rates declining, and the population aging. Nevertheless, the current population is young: 32.6% of its population is <15 years of age and only 3.5% is over age 65 years. Also, there has been a substantial move from rural to urban residence. In 2008, approximately 60% of the population lived in Ulaanbaatar (the capital; UB), whereas in 1986, only 500,200 people lived in UB, or only 25% of the nation's population at the time. From 1998 to 2005, the proportion of the female population living in Ulaanbaatar (the capital; UB) increased from 31 to 42%.

Median life expectancy for women in Mongolia is estimated to be 69.8 years of age [7]. Mortality in Mongolia among persons older than 45 years is largely due to circulatory diseases and neoplasms, respectively [5]. Liver cancer is by far the most prevalent cause of cancer mortality (44.0%), followed by tumors of the stomach (14.8%), lung (11.7%), and cervix (7.2%) [5]. The overwhelming majority, about 90%, of incident cancer cases are diagnosed at late stage with distant metastasis, and mortality is 75% in the first year after diagnosis [5].

Table 1 shows IARC breast cancer incidence and mortality rates as of 2008 for Mongolia, adjacent and other Asian countries, and for comparison, Europe and Northern America. The age-standardized breast cancer incidence rate in Mongolia was 8.0/100,000 ranking it among the lowest in the world with only countries in Southern and Western Africa also having rates in the single digits. Breast cancer incidence rates in Mongolia's neighboring countries of China (21.6/100,000), Kazakhstan (35.5/100,000), and the Russian Federation (43.2/100,000) were two and a half to over five times higher than in Mongolia. Rates were highest in North America (76.7/100,000) and Europe (66.6/100,000). The cumulative risk of developing breast cancer was ten times higher in Northern America (~8.0) compared with Mongolia (0.80). Mortality rates for breast cancer also were lowest in Mongolia, and the

incidence to mortality ratio was lower than for Europe, North America, Japan, China, and Eastern Asia, but comparable to or higher than other parts of Asia and adjacent countries.

Breast cancer incidence rates in Mongolia are presented in Figs. 1, 2, and 3. The “world population” used by Globocan includes a larger proportion of young ages where rates are low, whereas the second standardization method used for the Mongolian rates omits all age groups less than 20 years of age. Therefore, incidence rates presented for Mongolia are higher than in Table 1. (See supplemental Tables 1 and 2 for case counts.) The Mongolian breast cancer rates increase with age but plateau around the menopause (Fig. 1). Incidence rates appear to have slowly increased from 1998 to 2005 (Fig. 2); the annual percentage increase of age-standardized rates from 1998 to 2005 was 3.60 and 2.57%, respectively, for urban and rural areas. When data through 2007 were included in Fig. 2, the rates showed some decline (data not shown). Rates were higher in the capital city of Ulaanbaatar, with a population of about 300,000 women 20 years of age or older, compared with rural provinces all of which include less than 40,000 women 20 years of age or older (Fig. 3). Extent of disease at diagnosis appeared similar between cases living in Ulaanbaatar and those living outside of Ulaanbaatar with 78.2 and 78.5% diagnosed at stages III or IV, respectively. Furthermore, the distributions of stage for women diagnosed in and outside of Ulaanbaatar have changed only slightly over the last decade. For example, 75.7 and 80.2% of breast cancers in women in and outside of Ulaanbaatar, respectively, were diagnosed at stages III or IV in 1998–2002, whereas the proportions were 80.0 and 77.2% in 2003–2007.

Discussion

The majority of deaths due to cancer now occur in the developing world because of the sheer size of its populations, the gradual increase in overall life expectancy over the last several decades due to better control of communicable diseases, and the changing risk profile of the populations with increasing rates of tobacco use, obesity, and inactivity [8]. Breast cancer incidence rates remain several times greater in the developed than the developing world. The assumption has been that this higher incidence is due to differences in established breast cancer risk factors. There is some evidence, however, suggesting that higher rates in the West are not actually due to differences in recognized reproductive breast cancer risk factors that change with acculturation. In one study of Asian migrants to the United States in which breast cancer rates were six times greater in the most acculturated compared with the least acculturated women [2], adjustment for breast cancer risk factors (i.e., nulliparity, nulligravidity, age at first live birth, number of live births, breastfeeding, age at menarche, and menstrual cycle length) barely impacted on the breast cancer risk estimates for migration status [9]; the risk estimates for breast cancer with and without adjustment for these factors were 0.20 and 0.25, 0.67 and 0.69, 0.48 and 0.48, and 0.75 and 0.78 for the least to most acculturated women compared with Asian–American women who had always lived in the United States. Likewise, differences in weight and weight change [10], oral contraceptive use [11], and tofu consumption [12] seemed to explain little of the increase in breast cancer risk associated with migration from Asia to the United States.

Speculation also has focused on lower pre- and post-menopausal hormone concentrations in Asian than Caucasian women as a possible explanation for lower breast cancer rates among Asians living in Asia. Indeed, several studies have assessed endogenous hormone concentrations in pre- and postmenopausal Asian women living in the East, and Caucasian women living in the West, with most, but not all, showing approximately 25–50% lower levels in the former [13]. In addition, estrogens have been shown to increase in premenopausal migrant women to the United States with greater acculturation [14]. However, even a 100% increase in estradiol has been estimated to correspond only to a 30% breast cancer risk increase [15]. The much smaller differences in circulating hormone

concentrations observed between Asians and Caucasians are unlikely to explain the roughly 400–500% lower breast cancer risk in Asians. Yet, there are likely clues in the large international differences in breast cancer that might point to novel risk factors.

Mongolia is situated north and west of China and south of Siberian Russia, covering an area of approximately 1.5 million square kilometers. It is one of the least densely populated countries in the world. By the end of 2004, the population of Mongolia reached 2.5 million with about half residing in urban areas and the rest widely spread in rural areas, many living as nomadic or semi-nomadic herdsman. The Ministry of Health is responsible for health care delivery, which is generally free of charge. Mongolia has a three-tiered medical service system. The rural population is served by small district (Soum) hospitals that provide treatment and preventive checkups. Secondary level medical services are provided by larger, provincial (Aimag) general hospitals that provide more specialized services, including surgical care. Tertiary care is based in the capital, Ulaanbaatar with full medical and surgical services. Health care availability is generally high; for example, 98% of deliveries in urban areas and 92% in rural areas occur in a health care facility, in the latter despite many of the patients not living in close proximity to the hospital. In Mongolia, cancer is a reportable condition and cancer cases are referred to the National Oncology Center (NOC) in Ulaanbaatar. Provincial hospitals report new cancer cases to the NOC, and these reports are combined with those from patients in Ulaanbaatar who are directly admitted to the NOC to form the basis for a developing cancer registry. From interviews with the individuals involved in the registry, we believe that reporting is generally high. Accuracy or completeness of making the diagnosis in the first place, however, is unknown. Although localized disease may need to advance before being diagnosed, the non-localized stage of many of the cancers suggests that advanced disease is being diagnosed and reported to the NOC. While completeness of diagnosis is a concern, it is unlikely to explain the three-fold difference between breast cancer rates in Mongolia and China and the even greater difference in rates between Mongolia and developed countries.

Breast cancer incidence rates in Mongolia were about one-third those of China and other neighboring countries, consistent with the relative, but unexplained, decrease in rates noted from the south to the north of Asia [8]. Incidence rates in Mongolia appear to be slowly increasing over time, like those for Eastern and Southeastern Asia [8, 16, 17]. When data for incidence in more recent years were added, however, the rates appeared to decline slightly, which is consistent with incomplete data for later years. Rates were higher in urban compared with rural areas. Both the increase over time and the higher incidence rates in more urban areas could reflect better detection and reporting of breast cancer, or greater registration of cases. A proportion of cancer cases may be missed due to the lack of diagnostic equipment (the NOC is the only hospital with mammography facilities) and because the primary tumor site may be undetermined in the large proportion of cases that are of advanced stage at presentation. We did not have access to the number of cancer cases with unknown primary site, which might have demonstrated whether increases in breast cancer rates over time and higher rates in rural compared with urban areas were due to difficulty in identifying breast cancer as a primary tumor site. The proportion of late-stage breast tumors was much higher in Mongolia (~80%) than that reported for China (about 8% in Shanghai [19]), although in India 60% of women presented with stage III and higher tumors [20]. Stage of disease at diagnosis was roughly similar over time in Mongolia and between cases diagnosed in urban and rural areas suggesting that varying proportions of unknown primary cancers do not explain the rural–urban or timetrend observations within Mongolia. We also addressed the possibility of underascertainment of primary breast tumors by reviewing incidence rates for other tumor sites diagnosed at late stage and found that the rates of stomach cancer were as high or higher in Mongolia than in neighboring countries, whereas liver cancer rates were much higher in Mongolia, likely due to highly elevated

prevalence of hepatitis C and cirrhosis in Mongolia [21, 22]. In addition, the incidence of lung cancer, a major metastatic site for breast cancer, was not elevated in Mongolia compared with other countries. The incidence to mortality ratio for breast cancer in Mongolia (2.4) is low compared to the west; however, it was similar to ratios for Southeastern Asia (2.3) and South Central Asia (2.0), although lower than for Eastern Asia (4.0). This provides some evidence that the extent of disease at diagnosis did not differ dramatically among most countries adjacent to Mongolia and suggests that the lower breast cancer incidence rate in Mongolia is not due to the underascertainment of cases and/or a larger proportion of unknown primaries. The possibility of greater registration of cases in urban areas and over time cannot be excluded.

Routine screening mammography is not performed in Mongolia due to the lack of equipment and low health care priority given the paucity of breast cancer. Although the opportunity to be screened may be increasing in urban areas in China and other parts of Asia, it would represent only a small minority of the population. Thus, the differences in breast cancer rates between Mongolia and other Asian countries are unlikely to be due to screening. In addition, as has been previously discussed [18], the long-term low incidence of breast cancer in Asia relative to the west existed long before screening mammography.

Alternatively, the urban–rural incidence rates may hint at a real difference emerging between women living in traditional settings and those moving to urban areas. In the early 1990s, a major economic transition resulted in a sharp decline in average income in Mongolia. Mongolians responded by moving to urban areas in search of economic opportunity. Between 1990 and 2000, Ulaanbaatar’s population grew by 27%. Currently, one-third of Ulaanbaatar’s population is composed of migrants from rural areas. Concurrently, a decrease in the marriage rate, greater use of contraceptives and abortion, and longer intervals between births contributed to a drop in birth rates by 52% between 1989 and 1999, which was especially pronounced in urban areas. Increases in the prevalence of smoking and greater exposure to air pollution generated from the city’s reliance on fossil fuel [23] also have accompanied migration from rural to urban areas. Whether these factors play a role in the urban–rural difference in incidence rates is currently unknown.

As in China, breast cancer incidence rates rose exponentially with age but leveled-off around the time of menopause. This age-incidence pattern is in contrast to that observed in the United States where rates continue to rise after the menopause, albeit more slowly [24]. The difference in incidence rates by age between Chinese and US populations appears independent of birth cohort and age-period effects and may reflect age-related environmental exposures [25].

Diet, namely fat consumption, is one of the most commonly hypothesized risk factors to explain breast cancer rate differences between Asian and Western countries. There are major differences in dietary intake among Asian countries. Mongolia, for instance, relies almost entirely on meat and dairy products for calories [26] and less on cereals than China and other countries in South and Southeast Asia [26]. Lower breast cancer incidence rates in Mongolia compared with other Asian countries would seem to argue against the importance of dietary fat but other dietary factors may play a role.

There are few population data available for other breast cancer risk factors in Mongolia overall and by urban versus rural status. In general, age at menarche is lower in China than in the West [29, 30]; we are not aware of population data on age at menarche in Mongolia but a recent study (unpublished, Daavasaambuu G, et al.) of premenopausal women living in Ulaanbaatar suggests that the age is similar. Mongolia experienced a drop in its fertility rate from 6 to 3 children per woman of reproductive age by 1998 [31]. Current estimates of the

fertility rate in China are about half of those in Mongolia with 1.5–1.7 children per woman [30, 32]. Higher parity is associated with modest long-term reductions in breast cancer risk (10% for each birth) and each 5-year increase in age at birth increases risk by only 5–14% depending on the birth order [33]. Moreover, in comparisons with breast cancer risk in Asian migrants to the United States mentioned above [2], menstrual and reproductive factors did not explain the observed differences by migration status. Therefore, differences in parity and other established reproductive breast cancer risk factors seem unlikely to explain the 300% difference in incidence rates between Mongolia and other Asian countries. While pregnancy termination rates are high in both Mongolia [34] and China [35], abortion is not a risk factor for breast cancer.

Vitamin D status is generally low in many parts of Asia, including Mongolia and follows a north-to-south gradient [27]. There is no reliable information on vitamin D in rural and urban areas. The association between vitamin D and breast cancer is inconsistent, although some data indicate a protective effect. Given the likelihood that Mongolia's vitamin D levels are lower than in more southern parts of Asia, it is unlikely that vitamin D differences explain their lower breast cancer incidence rates. Environmental factors such as BPAs could be speculated to explain some of the difference in breast cancer incidence in Asia, but data on the levels of BPA and other factors are not available, and their association with breast cancer in humans is still unclear. More intensive study of factors that differ among Asian countries, including dietary intake, may uncover new environmental agents related to risk.

The transition from a rural lifestyle to a more urban lifestyle characterized by changes in reproductive factors, smoking, and other exposures mostly likely including diet and physical activity, creates an opportunity to study the effects of these factors on the incidence of breast and other cancers. Identifying factors that explain the substantial variation in breast cancer rates within Asian countries may provide further opportunity for identifying breast cancer risk factors active in all populations. Studies of a range of established breast cancer risk factors and biological parameters, and lifestyle factors already known to differ among different racial/ethnic populations, would be informative.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.
Age-specific breast cancer incidence rates in Mongolia (cases/100,000)

Fig. 2.
Age-standardized (World Standard Million) breast cancer incidence rates in Mongolia
(cases/100,000)

Fig. 3.
Age-standardized (World Standard Million) breast cancer incidence rates in Mongolia by population density (cases/100,000)

Table 1

Region and country-specific breast cancer incidence and mortality rates: crude and age-standardized (world) [ASR(W)] per 100,000 women (Globocan IARC 2008)

Country/region	Incidence		Mortality		Incidence: mortality	
	Cases	Crude rate	ASR (W)	Cases	Crude rate	ASR (W)
Eastern Asia	240,318	31.5	25.3	61,742	8.1	6.3
Southeastern Asia	86,945	30.1	31.0	36,764	12.7	13.4
South Central Asia	172,887	20.6	24.0	82,563	9.8	12.0
Western Asia	28,537	26.3	32.5	12,259	11.3	14.3
Europe	424,755	111.8	66.6	128,770	33.9	16.9
Northern America	205,515	117.6	76.7	45,563	26.1	14.8
China	169,452	26.2	21.6	44,908	6.9	5.7
Japan	45,853	70.3	42.7	11,796	18.1	9.2
Kazakhstan	3,376	41.6	35.5	1,839	22.6	18.9
Kyrgyzstan	691	25.2	27.2	358	13.1	14.1
Mongolia	92	6.9	8.0	36	2.7	3.4
Tajikistan	386	11.2	16.6	189	5.5	8.7
Turkmenistan	702	27.4	30.9	341	13.3	15.6
Uzbekistan	2,174	15.9	19.4	1,111	8.1	10.2
Russian Federation	52,469	69.0	43.2	22,946	30.2	17.2