RESEARCH ARTICLE

Global Trend of Breast Cancer Mortality Rate: A 25-Year Study

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Abstract

   Background: breast cancer is the most common cause of cancer death for women worldwide. In the past two decades, published epidemiological reports in different parts of the world show significant increase in breast cancer mortality rate. The aim of this study was to determine the 25-year trend of breast cancer mortality rate in 7 super regions defined by the Health Metrics and Evaluation (IHME), i.e. Sub-Saharan Africa, North Africa and Middle East, South Asia, Southeast Asia and East Asia and Oceania, Latin America and Caribbean, Central Europe and Eastern Europe and Central Asia, High-income. **Methods:** Our study population consisted of 195 world countries in the IHME pre-defined seven super regions. The age-standardized mortality rates from 1990 to 2015 were extracted from the IHME site. The reference life table for calculating mortality rates was constructed based on the lowest estimated age-specific mortality rates from all locations with populations over 5 million in the 2015 iteration of GBD. To determine the trend of breast cancer mortality rate, a generalized linear mixed model was fitted separately for each IHME region and super region. **Results:** Statistical analysis showed a significant increase for breast cancer mortality rate in all super regions, except for High-income super region. For total world countries, the mean breast cancer mortality rate was 13.77 per 100,000 in 1990 and the overall slope of mortality rate was 0.7 per 100,000 from 1990 to 2015. The results showed that Latin America and Caribbean the highest increasing trend of breast cancer mortality rate during the years 1990 to 2015 (1.48 per 100,000). **Conclusion:** In general, our finding showed a significant increase in breast cancer mortality rate in the world during the past 25 years, which could be due to increase in incidence and prevalence of this cancer. Low this increasing trend is an alarm for health policy makers in all countries, especially in developing countries and low-income regions which experienced sharp slopes of breast cancer mortality rate.

   Keywords: Breast cancer- mortality rate- Trend analysis

Introduction

   Cancer has one of the highest mortality rates worldwide. In 2015, there were estimated 17.5 million cancer cases followed by 8.7 million deaths (Global Burden of Disease Cancer Collaboration, 2017). Among different kinds of cancers, breast cancer is one the most important health problems around the world (Sharma, 2019).

   One of the most comprehensive assessment in 2004 showed that breast cancer was the most common cancer worldwide among women. It was the leading cause of death for women in the world, the second in Africa and Southeast Asia after Cervical cancer while it was in the fifth place in West Pacific (World Health Organization, 2008). The more recent studies confirm that these statistics are still remaining true. In 2012, breast cancer was the most common cancer type with 13.8% of all cancer cases (Ferlay et al., 2013). A study in China, India and Russia, showed that breast cancer was the second cause of death

among women after Lung cancer in 2014 (Goss et al., 2014).

   Because of several contributing factors, there has been a general increase in breast cancer cases in recent years. A study in 2017 showed an increase of cases by 33% from 2005 to 2015, while population growth was the reason for 12.6%, aging population for 16.4% and 4.1% was because of age-specific cases (Global Burden of Disease Cancer Collaboration 2017). In 2012 in the European Union, the number of death cases decreased by 91,000 (Ferlay et al., 2013), however from 2005 to 2015, there was an increase of 21.3% in breast cancer mortality from 439,800 to 533,600 (Wang et al., 2016).

   Regarding the increasing trend of breast cancer around the world, we decided to conduct the present study in order to assess the trend of this cancer in nearly all world countries. In this context, the present study aims to present a longitudinal analysis of breast cancer mortality rate in seven super regions of the world.

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Materials and Methods

Database used in the study

In this study, the data on age standardized breast cancer mortality rate from the GBD database according to a list of countries in world was used. The information includes age standardized mortality rate due to breast cancer in 195 countries, from 1990 to 2015 (in 5-year intervals; i.e. years 1990, 1995, 2000, 2005, 2010, 2015). The reference life table for calculating mortality rates was constructed based on the lowest estimated age-specific mortality rates from all locations with populations over 5 million in the 2015 iteration of GBD. We initially considered seven areas which were classified by the GBD: Sub-Saharan Africa, North Africa and Middle East, South Asia, Southeast Asia and East Asia and Oceania, Latin America and Caribbean, Central Europe and Eastern Europe and Central Asia, High-income. GBD has also classified countries under different regions and super regions. The mortality rate (per 100,000) due to breast cancer for each super regions, were considered as the main outcome of the study (Institute for Health Metrics and Evaluation, 2018).

Statistical methods

For descriptive purposes, the breast cancer mortality rate were presented using the mean (SD), separately for different region (Table 1) and super regions (Table 2).

To evaluate the trend of breast cancer mortality rate around the world, a general linear mixed effects model was fitted for each GBD super region. The model can be written as:

$$E(y_{it}) = \beta_0 + \beta_1 time + b_{0i}$$

Where y_{it} indicates the breast cancer mortality rate for ith country in tth year under study. In additional, b_{0i} shows the random intercept of the model which distributed as: $N(0; \sigma_b^2)$. The model parameters, β_0 and β_1, are common

fixed effect coefficients for model intercept and slope.

Results

Table 1 and table 2 show the descriptive statistics for mortality rate, respectively for the IHME regions and super regions during 1990 to 2015.

Comparing the average for regions reveals that Western Europe (year 1995) and Western Sub-Saharan Africa (year 1990) regions had, respectively, the highest and lowest average (38.04, 5.70).

Regarding table 2, the High-income super region had the highest and South Asia super region had the lowest breast cancer mortality rate during 25-year period, under study (32.56 vs 6.12)

In the next step, we fitted the described random effects model in methods section to the data, separately for each super region. Table 3 displays the obtained results.

The obtained results in Table 3 show that the world countries experienced a mean breast cancer mortality rate of 13.77 per 100,000 in year 1990. In addition, these countries had an annual mean increase of 0.7 per 100,000 from year 1990 to 2015.

Comparing the estimated intercepts reveals that the High-income and South Asia countries had, respectively, the highest and lowest breast cancer mortality rate in year 1990 (32.24 and 5.58 per 100,000). Moreover, the estimated slopes show that Latin America and Caribbean the highest increasing trend of breast cancer mortality rate during the years 1990 to 2015 (1.48 per 100,000). According the obtained p-value (last column table 3), one can conclude that all the super regions had significant positive trend of breast cancer mortality rate (p<0.01), except for the High- income super region which had a non-significant negative slope during the study period (p=0.489).

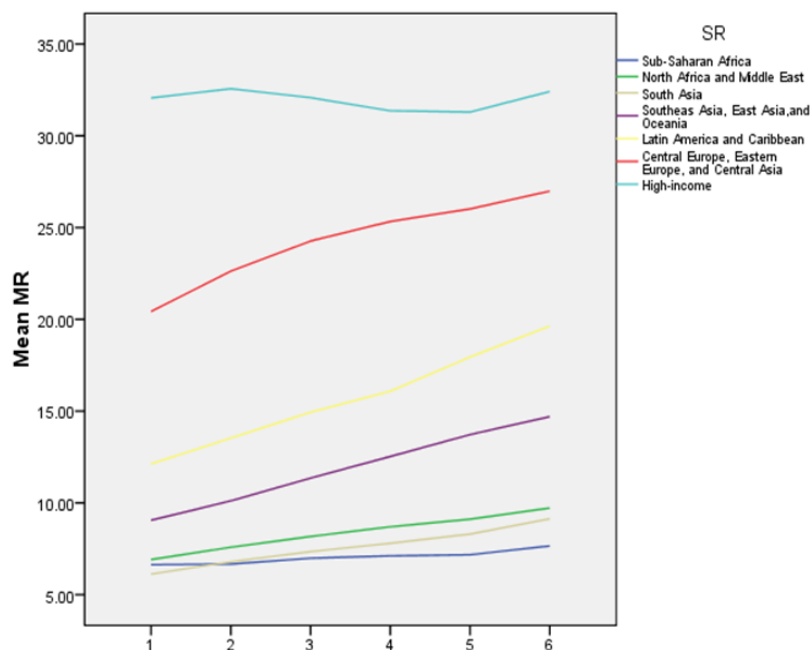Figure 1 displays the growth trajectories for seven super regions (each line shows mortality rate trend over

Figure 1. Breast Cancer Mortality Rate Trajectories of 195 World Countries

Global Trend of Breast Cancer Mortality

Table 1. Mean (SD) for Breast Cancer Mortality Rate for Each IHME Region from 1995 to 2015

Region	Year					
	1990	1995	2000	2005	2010	2015
Eastern Sub-Saharan Africa	5.94 (1.75)	6.13 (1.78)	6.19 (1.62)	5.80 (1.49)	6.00 (1.62)	6.65 (1.81)
Western Sub-Saharan Africa	5.70 (1.24)	5.75 (1.24)	5.85 (1.32)	5.85 (1.50)	5.98 (1.66)	6.34 (1.81)
Southern Sub-Saharan Africa	7.63 (3.62)	7.58 (3.66)	9.64 (4.34)	11.56 (4.64)	10.95 (4.44)	11.35 (5.45)
Central Sub-Saharan Africa	10.30 (2.79)	10.01 (2.86)	9.92 (3.21)	9.93 (3.13)	10.14 (2.60)	10.67 (2.63)
North Africa and Middle East	6.91 (3.15)	7.58 (3.43)	8.17 (3.67)	8.70 (3.99)	9.12 (4.06)	9.72 (4.00)
South Asia	6.12 (3.49)	6.79 (4.29)	7.35 (4.81)	7.80 (5.17)	8.30 (5.20)	9.14 (5.25)
Southeast Asia	7.73 (1.21)	8.75 (1.63)	10.05 (1.82)	11.33 (2.11)	12.19 (2.56)	12.70 (2.91)
East Asia	8.06 (4.09)	9.22 (4.70)	10.71 (5.57)	11.99 (6.15)	13.22 (6.66)	14.30 (7.35)
Oceania	10.46 (5.02)	11.42 (5.57)	12.38 (5.98)	13.40 (5.85)	14.65 (5.94)	15.64 (6.33)
Central Latin America	6.17 (2.13)	6.92 (2.31)	7.56 (2.47)	8.41 (2.74)	9.52 (3.19)	10.73 (3.58)
Andean Latin America	5.97 (0.96)	6.59 (0.87)	7.03 (0.42)	7.45 (0.34)	8.20 (0.63)	8.89 (0.88)
Caribbean	16.52 (6.62)	18.44 (7.43)	20.41 (8.28)	21.76 (8.72)	24.23 (9.69)	26.36 (10.59)
Tropical Latin America	8.58 (1.41)	9.55 (1.73)	10.81 (1.45)	12.43 (0.79)	13.89 (0.65)	15.33 (1.03)
Eastern Europe	24.69 (3.46)	28.46 (4.21)	29.50 (5.03)	30.29 (4.70)	30.48 (4.01)	31.92 (4.18)
Central Europe	24.74 (9.11)	27.04 (9.55)	29.25 (9.94)	30.70 (9.32)	31.69 (8.41)	32.53 (8.78)
Central Asia	10.88 (7.08)	11.71 (7.69)	13.01 (9.20)	13.71 (9.74)	14.36 (10.10)	15.15 (10.69)
Southern Latin America	25.54 (13.08)	26.61 (13.61)	27.85 (13.84)	28.54 (13.43)	30.00 (13.22)	32.33 (13.77)
Western Europe	37.57 (10.00)	38.04 (9.08)	37.06 (8.15)	35.77 (6.96)	35.20 (7.14)	36.00 (7.59)
High-income Asia Pacific	9.48 (3.23)	10.57 (3.93)	11.93 (4.48)	13.51 (4.56)	15.28 (4.96)	17.04 (5.06)
Australasia	31.67 (4.56)	31.32 (3.48)	30.27 (3.64)	28.97 (2.97)	29.04 (3.11)	30.11 (3.49)
High-income North America	28.52 (8.85)	28.50 (8.17)	27.83 (6.16)	27.27 (5.92)	26.80 (6.14)	28.24 (6.86)

time for each super region). Except High-income (which had a non-significant negative slope during the study period), these trajectories show similar increasing trends for these super regions. "Sub-Saharan Africa" shows a mild decrease from 1990 to 1995, while during 1995 to 2010 here is an insignificant yet steady increase, with a considerable increase for 2015. "North Africa and Middle East" region and "South Asia" region have steady increasing rate from 1990 to 2015. This steady increasing rate is much sharper for "Southeast Asia, East Asia, and Oceania" region, "Latin America and Caribbean" region and "Central Europe, Eastern Europe, and Central Asia" region. For "High-income" region is mildly unsteady, after an increase in 1995, there is decrease to 2010, while there is a relatively sharp increase for 2015.

Discussion

Breast cancer is an important health concern with an increasing trend of prevalence and mortality rate globally. In the present study, the data obtained from GLMM showed a positive slope of 0.7 for the total of countries of the world which means that the breast cancer mortality rate increases (on average) about seven in million every 5 years in the world.

Regarding Table 1, one can conclude that during 1990 to 2015 the highest increasing rate belongs to the Caribbean region, with 16.52 in 1990 to 26.36 in 2015. The decreasing rate most belongs to the Western Europe with 37.57 in 1990 to 36.00 in 2015.

This study, (Table 2), indicates that the highest increasing rate belongs to the Latin American and Caribbean super region (from 12.12 to 19.64) while the lowest increasing rate belongs to High-income super

Table 2. Mean (SD) for Breast Cancer Mortality Rate for Each IHME Super Region from 1995 to 2015

Super region	Year					
	1990	1995	2000	2005	2010	2015
Sub-Saharan Africa	6.63 (2.52)	6.67 (2.46)	6.99 (2.76)	7.11 (3.16)	7.18 (3.00)	7.66 (3.24)
North Africa and Middle East	6.91 (3.15)	7.58 (3.43)	8.17 (3.67)	8.70 (3.99)	9.12 (4.06)	9.72 (4.00)
South Asia	6.12 (3.49)	6.79 (4.29)	7.35 (4.81)	7.80 (5.17)	8.30 (5.20)	9.14 (5.25)
Southeast Asia, East Asia, and Oceania	9.06 (4.40)	10.11 (4.90)	11.35 (5.43)	12.53 (5.63)	13.72 (5.95)	14.70 (6.47)
Latin America and Caribbean	12.12 (7.16)	13.53 (8.01)	14.94 (8.92)	16.08 (9.36)	17.95 (10.39)	19.64 (11.25)
Central Europe, Eastern Europe, and Central Asia	20.43 (9.74)	22.63 (10.76)	24.27 (11.45)	25.33 (11.49)	26.02 (11.25)	26.99 (11.61)
High-income	32.06 (12.94)	32.56 (12.37)	32.08 (11.30)	31.36 (10.01)	31.29 (9.56)	32.42 (9.64)

Table 3. Breast Cancer Mortality Rate (Per 100,000) and Estimates from the GLMMs by Global Burden of Disease Study Super Regions

Super regions	Parameter	Estimate	SE	P
Sub-Saharan Africa	Intercept	6.36	0.42	< 0.001
	Slope	0.19	0.03	< 0.001
North Africa and Middle East	Intercept	6.45	0.79	< 0.001
	Slope	0.55	0.04	< 0.001
South Asia	Intercept	5.58	1.95	0.004
	Slope	0.57	0.15	< 0.001
Southeast Asia, East Asia, and Oceania	Intercept	7.89	1.01	< 0.001
	Slope	1.15	0.07	< 0.001
Latin America and Caribbean	Intercept	10.52	1.61	< 0.001
	Slope	1.48	0.09	< 0.001
Central Europe, Eastern Europe, and Central Asia	Intercept	19.87	2.02	< 0.001
	Slope	1.26	0.09	< 0.001
High-income	Intercept	32.24	1.86	< 0.001
	Slope	-0.078	0.11	0.489
Total	Intercept	13.77	0.86	< 0.001
	Slope	0.7	0.04	< 0.001

region (from 32.06 to 32.42). A less than 3 in 100,000 increase could be observed in the North Africa and Middle East region.

Based on the American Cancer Society reports, breast cancer has the second highest cancer death after lung cancer for women. One out of eight American women may experience this cancer which is an average risk of 12%. In 2017, it was estimated that 252,710 invasive and 63,410 non-invasive (CIS) cases would be diagnosed, while it was predicted about 40,610 deaths due to this cancer. From 1989 to 2015, there was a 39% drop in mortality rate. Since 2007 the mortality rate amongst women over 50 declined while it has stayed steadily for those under 50 (American Cancer Society, 2017).

Cancer Research UK shows that in 2014 there were 357,000 new cancer cases, with 181,000 males and 176,000 females. Breast cancer was the most common cancer for women in the UK. In compare to early 1990s there was an increase rate of 12% for all cancers, with the increase rate of 16% for females and 4% for males (Cancer Research UK, 2014b). The trend for breast cancer was 55,200 new cases which was 15% of all new cases, of which 390 cases were males and 54,800 females. The increase rate of breast cancer since 1990 was 19%. While breast cancer for males has a stable rate, its increase rate for females is 24%. In the UK, breast cancer death was 11,400 cases in 2014, with 75 cases males and the rest were females. breast cancer was the second most common cause of cancer death for women with over 11,300 deaths in 2014. It is also estimated that between 2014 and 2035 the number of breast cancer cases will increase by 2% in this country (Cancer Research UK, 2014a).

In Europe, studies showed after a peak of cancer death rate in the late 1980, despite differences in different countries, there had been a 10% decline in mortality rate until 2000 (Karim-Kos et al., 2008; La Vecchia et al., 2009; Bosetti et al.; 2013). However, in 2002, statistics showed that 26% of global cancer cases belonged to Europe (Parki et al., 2005). In 2006, there were 3,191,600 new cancer cases among them 429,900 were breast cancer cases (about 13.5%). Among 1,703,000 cancer death, breast cancer was the third cause of death after lung and colorectal cancer with 131,900 (about 7.5%) of cancer death cases (Ferlay et al., 2007).

In 2012, data from 54 African countries including three quarters of 47 Sub-Saharan African countries, showed 846,961 (about 6%) of global new cancer cases, of which 362,037 male and 484,924 female. There were also 591,169 (about 7.2%) of global cancer deaths, of which 277,849 were male and 313,320 female. The results of this study showed the breast cancer was the leading cancer type for women with a large difference with 133,900 (about 27.6%) of all cancers. The study suggested that by 2030 there would be 70% increase in new cancer cases as well as the cancer death rate in Africa due to population growth and aging (Parkin et al., 2014).

The reports from study in china revealed that cancer was the second most common cause of death, (1 out of 5 deaths with annual 2.82 million new cancer cases and 1.96 million death(Goss et al., 2014). National Cancer Registry Programmed in India monitored six populated regions (Bangalore, Barshi, Bhopal, Chennai, Delhi, and Mumbai) between 1990 and 1996. Their data showed 160,017 new cases of which 79,954 were male and 80,063 female. Their findings indicated that cervical and breast cancers were accountable for 40% of all cancer cases in women (Nanda, 2001). A more recent study in 2012 by GOLOBOCAN showed annual 1 million new cases of cancer followed by about 700,000 cancer death in India. Since 2009 breast cancer became the most common type of cancer for women and the first cause of cancer death. Breast cancer was the cause of fifth of all female cancer death with 144,937 new cases and 70,218 deaths in 2012 pushing cervical cancer to the second place (Mallath et

al., 2014).

Another study in 2009 gathered data for 10 Arab countries in the Middle East and North Africa (Salim et al., 2009). Age-standardized breast cancer cases was 38.0 in Jordan, 38.5 in Palestine Authority (Freedman et al., 2006), 11.8 in Saudi Arabia (Bazarbashi et al., 2004), 42.5 in Egypt, 18.8 in Algeria, 29.8 in Tunisia, 14.6 in Oman, 46.8 in Bahrain, 43.1 in Kuwait (Curado et al., 2007), 30.1 in Qatar (Bener et al., 2008). In addition, age-standardized cancer cases 112 in Jordan, 134 in Palestine Authority (Freedman et al., 2006), 58 in Saudi Arabia (Bazarbashi et al., 2004), 122 in Egypt, 85 in Algeria, 106 in Tunisia, 91 in Oman, 143 in Bahrain, 129 in Kuwait (Curado et al., 2007), 87 in Qatar (Bener et al., 2008).

During 1965 to 2000, breast cancer had become the most common type of cancer among women (Mousavi et al., 2007). The cancer registry reports of Iran Ministry of Health for years 2000 to 2006 showed that breast cancer was the most common type of cancer among women with an increase rate of 21.4% to 24.4% of all new cancer cases. This report also revealed that breast cancer was the fifth cause of cancer death among Iranian females (Lamyian et al., 2007; Mousavi et al., 2008; Jafari-Koshki et al., 2014). In 2004 another study showed that the mean age of Iranian breast cancer patients about 10 years less than developed countries (Harirchi et al.; 2004).

Overall our findings showed a substantial increase in breast cancer mortality rate in the world during the past 25 years. This could be because of increase in number of new incidents of this type of cancer. This increasing trend is an alarming sign for health policy makers in all countries, in particular in developing and low-income regions which have experienced sharp slopes of increasing breast cancer mortality rate.

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