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Global Burden of Breast Cancer and the Impact of Metabolic Factors from 1990 to 2019: Based on the Global Burden of Disease Study 2019

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Abstract: This study presents an assessment of the global breast cancer burden from 1990 to 2019, highlighting the current status and the impact of metabolic factors. Data on breast cancer incidence, deaths, disability-adjusted life years (DALYs), and the age-standardized rate in 204 countries and regions and its metabolic factors were obtained from the Global Burden of Disease Study 2019. The estimated annual percentage change (EAPC) was used to quantify the temporal trends. In 2019, the incidence cases of breast cancer globally reached 202,354, deaths reached 700,660. The age-standardized incidence rate (ASIR) of breast cancer globally increased by 0.33, while the age-standardized rates of deaths (ASMR) and DALYs decreased with EAPC of -0.56 and -0.5, respectively. In 2019, the EAPC in ASIR was negatively correlated with socio-demographic index (R = -0.21, $P < 0.01$). High fasting plasma glucose and high body mass index were the primary risk factors for breast cancer. Overall, the global burden of breast cancer is substantial, indicating the need for targeted prevention and control measures.

1. Introduction

Breast cancer is the most common malignant tumor among females and has the heaviest disease burden worldwide. Approximately 2,261,419 new cases of female breast cancer were diagnosed globally in 2020, accounting for 24.5% of all female cancers [1]. Breast cancer was the leading cause of cancer-related death among women in many countries, with approximately 684,996 deaths due to breast cancer worldwide, accounting for 15.5% of all female cancer deaths [1]. Modifiable factors such as obesity [2], have been identified as independent risk factors for breast cancer, influencing both the risk of developing the disease and the prognosis in those affected. Obesity is known to increase the risk of postmenopausal breast cancer [3], while a contrasting relationship has been observed in premenopausal women [4]. These varying associations underscore the complexity of metabolic influences on breast cancer risk.

With the global rise in obesity and associated metabolic disorders, there is an urgent need to

explore how these factors contribute to the changing landscape of breast cancer incidence and mortality. Therefore, using the latest data from the Global Burden of Disease Study 2019 (GBD2019), we analyzed the current state of breast cancer's global disease burden and the role of metabolic factors in its development, providing insights that could guide public health initiatives and clinical practices.

2. Methods

2.1 Data source

Breast cancer data were obtained through the Global Health Data Exchange online data collection tool (http://ghdx.healthdata.org/gbd-results-tool) [5-6]. The socio-demographic index (SDI) is a comprehensive parameter that integrates per capita income, the average educational attainment of the population aged 15 years and above, and the total fertility rate below 25 years, which is used to estimate the status of socio-demographic development [7]. The GBD database uses the SDI and geographical class to classify and describe 204 countries and areas (Table 1).

2.2 Risk factors

The GBD2019 study estimated the attributable risk factors through a comparative risk assessment framework and was recognized by the World Cancer Research Fund [6]. In this study, high fasting plasma glucose (greater than 4.8-5.4 mmol/L) and high body mass index (BMI greater than 20-25 kg/m^2) were selected to further explore the influence of metabolic factors on breast cancer.

2.3 Data analysis

This study used global incidence, age-standardized incidence rate (ASIR), deaths, age-standardized mortality rate (ASMR), disability-adjusted life years (DALYs), and the age-standardized DALYs (ASDR) of breast cancer from 1990 to 2019. The estimated annual percentage change (EAPC) was used to quantify the temporal trends of annual standardized rates (ASRs) of breast cancer.

The Spearman rank correlation was used to test correlations between the EAPC and the ASRs in 2019 and the SDI in 2019 by different countries and regions. The Local Weighted Scatterplot Smoothing Regression was used to characterize the nonlinear relationship between EAPC estimates and SDI.

All statistical analyses were performed using R software (version 4.2.3). Two-sided *P* values of less than 0.05 were defined as statistically significant.

3. Results

3.1 Burden of breast cancer incidence and its changing trend

In 2019, there were 2,002,354 new cases of breast cancer diagnosed worldwide. (Table 1). The ASIR of breast cancer globally was 24.17 per 100,000 in 2019, and it increased from 1990 to 2019 (EAPC = 0.33) (Table 1).The highest ASIR for breast cancer (41.22) was found in the high SDI region in 2019. From 1990 to 2019, the ASIR of breast cancer decreased in the high SDI region and increased in the other four SDI regions (Table 1).

In the 21 GBD regions, the highest incidence cases of breast cancer were in East Asia (389,533)

in 2019. High-income North America (49.88) had the highest ASIR. Between 1990 and 2019, the ASIR increased in all GBD regions except high-income North America, Australia, and Western Europe (Table 1). From 1990 to 2019, the ASIR of breast cancer increased in 165 countries worldwide, including China, India, and South Korea. The ASIR for breast cancer decreased in 26 countries during this period, including the United States, United Kingdom, and Canada (Table S3).

Table 1: Incidence and age-standardized incidence rate for breast cancer in 2019- and its estimated annual percentage change from 1990 to 2019.

Characteristics	Incidence case (n, 95%UI)	ASIR per 100000 (n, 95%UI)	EAPC in ASIR (n, 95%CI)
Global	2,002,354 (1832150 to 2172540)	24.17 (22.11 to 26.24)	0.33% (0.28 to 0.37)
High SDI	678,945 (606,880 to 753,696)	41.22 (36.88 to 45.65)	-0.27% (-0.37 to -0.18)
High-middle SDI	516,515 (464,368 to 574,125)	26 (23.34 to 28.88)	0.68% (0.59 to 0.77)
Middle SDI	493,146 (437,195 to 552,894)	18.52 (16.43 to 20.76)	1.95% (1.92 to 1.98)
Low-middle SDI	230,769 (202,826 to 259,295)	15.38 (13.54 to 17.27)	1.54% (1.44 to 1.64)
Low SDI	81,721 (71,258 to 93,260)	13.51 (11.93 to 15.22)	1.28% (1.22 to 1.34)
Australasia	19,268 (15,570 to 23,873)	44.31 (35.73 to 54.87)	-0.29% (-0.45 to -0.12)
East Asia	389,533 (309,987 to 484,103)	18.37 (14.63 to 22.79)	2.81% (2.71 to 2.91)
High-income North America	283,122 (236,467 to 337,819)	49.88 (41.65 to 59.83)	-1.06% (-1.16 to -0.96)
Western Europe	341,500 (295,017 to 390,202)	45.15 (38.99 to 51.84)	-0.05% (-0.21 to 0.11)

3.2 Breast cancer mortality and DALYs and their spatial-temporal trends

In 2019, approximately 700,660 people globally died due to breast cancer (Table S1). Breast cancer was responsible for 20,625,313 DALYs globally (Table S2). From 1990 to 2019, the ASMR and ASDR of breast cancer showed a declining trend worldwide (Table S2).

Supplementary Table 1: Death case and age-standardized mortality rate for breast cancer in 2019, and its estimated annual percentage change.

Characteristics	Mortality case	ASMR per 100000	EAPC in ASMR
Global	700,660 (647,384 to 751,555)	8.62 (7.95 to 9.25)	-0.56 (-0.6 to -0.51)
High to middle SDI	165,934 (152,738 to 179,587)	8.31 (7.63 to 9)	-0.83 (-0.95 to -0.71)
High SDI	167,553 (151,809 to 176,807)	9.05 (8.36 to 9.47)	-1.52 (-1.56 to -1.47)
Low-middle SDI	127,410 (110,474 to 144,919)	8.94 (7.77 to 10.16)	0.63 (0.54 to 0.72)
Low SDI	54,467 (47,490 to 62,057)	9.83 (8.59 to 11.12)	0.75 (0.71 to 0.8)
Middle SDI	184,787 (166,334 to 205,342)	7.3 (6.6 to 8.12)	0.29 (0.26 to 0.32)
East Asia	101,023 (82,358 to 122,871)	4.91 (3.99 to 5.94)	0.09 (0.03 to 0.14)
Oceania	1,810 (13,85 to 2,297)	21.04 (16.32 to 26.53)	0.93 (0.89 to 0.97)
Southern Sub-Saharan Africa	7,259 (6,449 to 8,089)	13.33 (12.02 to 14.77)	1.03 (0.8 to 1.26)
Western Europe	98,409 (88,188 to 104,248)	10.9 (10.01 to 11.45)	-1.54 (-1.6 to -1.48)
Western Sub-Saharan Africa	24,643 (19,341 to 30,965)	12.27 (9.85 to 15.09)	1.2 (1.09 to 1.3)

Supplementary Table 2: DALYs case and age-standardized DALYs rate for breast cancer in 2019, and its estimated annual percentage change.

Characteristics	DALYs case	ASDR per 100000	EAPC in ASDR
Global	20,625,313 (19,043,049 to 22,174,397)	247.63 (228.68 to 266.08)	-0.5 (-0.56 to -0.45)
High-middle SDI	4,570,253 (4,209,331 to 4,954,003)	230.43 (212.17 to 249.87)	-0.99 (-1.1 to -0.87)
High SDI	4,083,850 (3,816,265 to 4,354,647)	252.68 (237.71 to 269.32)	-1.53 (-1.58 to -1.48)
Low-middle SDI	4,194,850 (3,622,482 to 4,785,991)	271.67 (235.41 to 309.31)	0.6 (0.49 to 0.7)
Low SDI	1,837,382 (1,599,786 to 2,101,742)	283.77 (248.24 to 323.37)	0.67 (0.61 to 0.72)
Middle SDI	5,923,359 (5,318,524 to 6,558,618)	219.85 (197.35 to 243.15)	0.25 (0.22 to 0.28)
East Asia	3,106,704 (2,558,341 to 3,748,533)	146.32 (120.33 to 176.17)	-0.1 (-0.16 to -0.03)
Oceania	68,335 (51,802 to 88,227)	690.8 (530.35 to 880.44)	0.96 (0.91 to 1.01)
South Asia	4,218,058 (3,461,522 to 5,024,210)	264.62 (218.07 to 314.62)	0.81 (0.69 to 0.93)
Southern Sub-Saharan Africa	210,438 (185,318 to 239,360)	335.75 (297.05 to 378.56)	0.84 (0.62 to 1.07)
Western Europe	2,184,732 (2,032,712 to 2,339,874)	290.47 (272.68 to 311.07)	-1.67 (-1.73 to -1.61)

Supplementary Table 3: Incidence case and age-standardized incidence rate for breast cancer in 204 countries in 2019, and its estimated annual percentage change.

Location	Incidence case	ASIR per 100000	EAPC in ASIR
Australia	15,656 (12,089 to 20,129)	42.61 (32.85 to 55.11)	-0.3 (-0.52 to -0.09)
China	375,484 (296,626 to 469,983)	18.32 (14.5 to 22.93)	2.84 (2.74 to 2.95)
India	146,090 (112,452 to 183,482)	11.81 (9.15 to 14.82)	1.73 (1.55 to 1.91)
Republic of Korea	20,328 (16,423 to 24,533)	23.79 (19.29 to 28.65)	3.48 (3.13 to 3.84)
United Kingdom	53,010 (42,241 to 65,883)	49.21 (38.91 to 61.75)	-0.38 (-0.47 to -0.3)
America	254,486 (210,821 to 308,184)	50.22 (41.23 to 61.11)	-1.09 (-1.19 to -0.99)

In 2019, the highest number of breast cancer deaths occurred in South Asia, followed by East Asia and Western Europe. Similarly, South Asia had the highest DALYs of breast cancer. From 1990 to 2019, regions such as Oceania experienced an increase in both ASMR and ASDR. In contrast, high-income regions like North America, Australia, and Western Europe showed a favorable trend.

Supplementary Table 4: Deaths case and age-standardized mortality rate for breast cancer in 204 countries in 2019, and its estimated annual percentage change.

Location	Deaths case	ASMR per 100000	EAPC in ASMR
China	96,306 (77,323 to 118,090)	4.85 (3.91 to 5.92)	0.06 (0 to 0.12)
India	83,510 (64,550 to 105,994)	7.12 (5.53 to 9.01)	0.75 (0.59 to 0.91)
Micronesia	16 (10 to 26)	22.82 (14.73 to 35.65)	1.56 (1.43 to 1.68)
Pakistan	32,118 (24,388 to 43,374)	26.34 (20.2 to 34.86)	1.53 (1.34 to 1.73)
Solomon Islands	153 (117 to 196)	37.1 (29.18 to 46.81)	5.97 (5.36 to 6.59)
America	55,021 (51,008 to 57,900)	10.07 (9.45 to 10.55)	-1.7 (-1.79 to -1.61)

In 2019, China, India and America had the highest breast cancer deaths. Solomon Islands, Pakistan, and Federated States of Micronesia had the highest ASMR (Table S4). The highest ASDR of breast cancer was observed in China. The highest ASDR was found in the Solomon Islands, Pakistan, and Papua New Guinea (Table S5).

Supplementary Table 5: DALYs case and age-standardized DALYs rate for breast cancer in 204 countries in 2019, and its estimated annual percentage change.

Location	DALYs case	ASDR per 100000	EAPC in ASDR
China	2,957,454 (2,408,511 to 3,590,166)	144.15 (117.26 to 174.99)	-0.13 (-0.19 to -0.06)
Pakistan	1,119,378 (847,412 to 1,520,925)	783.3 (597.3 to 1054.53)	1.4 (1.19 to 1.62)
Papua New Guinea	49,888 (36,209 to 67,731)	704.24 (515.69 to 938.66)	0.55 (0.51 to 0.58)
Solomon Islands	6,079 (4,597 to 7,916)	1,306.47 (1004.77 to 1,673.33)	6.27 (5.61 to 6.93)

3.3 Association of the disease burden of breast cancer with socio-demographic index

We found that the EAPC in ASIR had a moderate-intensity negative correlation with the initial ASIR (R = -0.61). The EAPC in ASMR was negatively correlated with the baseline ASMR (R = -0.58) (Figure 1A). This finding indicates that countries with higher baseline ASIR and ASMR had a significant reduction in breast cancer incidence and mortality (Figure 1B). In addition, our study found that the EAPC of ASIR had a weak negative correlation with the SDI in 2019 (R = -0.21), indicating that the ASIR of breast cancer in middle SDI countries was on the rise (Figure 1C). The EAPC of breast cancer ASMR had a significant negative correlation with SDI (R = -0.48), indicating that the ASMR of breast cancer in countries with a high SDI decreased gradually during the study period (Figure 1D).

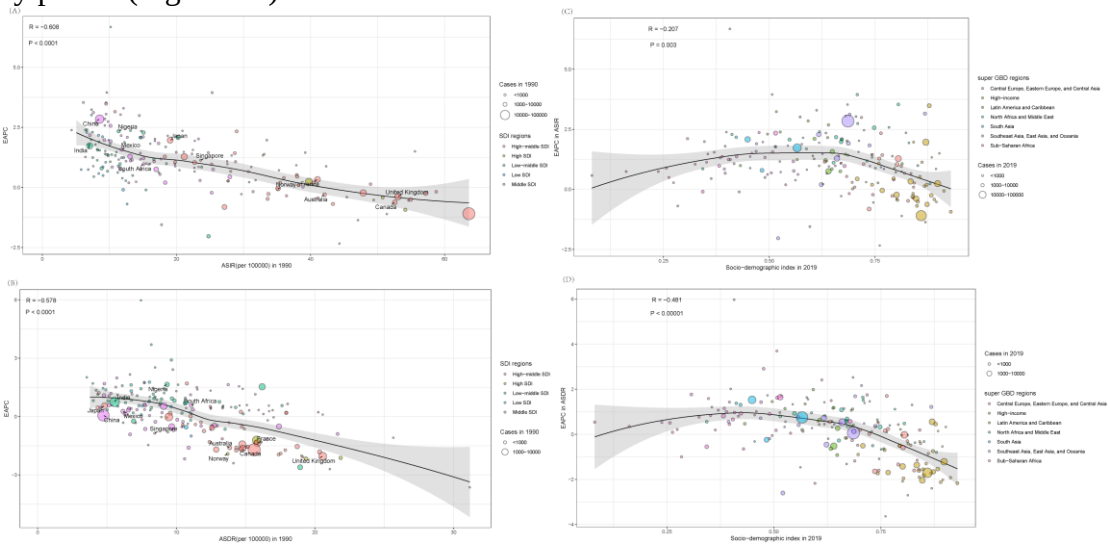

Figure 1: The Influential factors for the EAPCs in age-standardized rate of breast cancer from 1990 to 2019 at the national level. (A) EAPC in ASIR and ASIR in 1990; (B) EAPC in ASMR and ASMR in 1990; (C) EAPC in ASIR and SDI in 2019; (D) EAPC in ASMR and SDI in 2019. The blue line was an adaptive association fitted with adaptive Loess regression based on all data points.

3.4 Risk factors of the disease burden of breast cancer

High fasting plasma glucose (deaths: 7.4%, DALYs: 6.1%) and high BMI (deaths: 6.6%, DALYs:

4.7%) were the dominant risk factors of the disease burden for female breast cancer in 2019 (Figure 2).High fasting plasma glucose was the main attributable risk factor for females aged over 70 years (deaths: 10.3%, DALYs: 10.3%)). The results revealed that high BMI was a risk factor for breast cancer among females aged 50 years or older and a protective factor for breast cancer in females aged 15 to 49 years (Figure S1).These findings underscore the complex role of metabolic factors in breast cancer risk across different age groups.

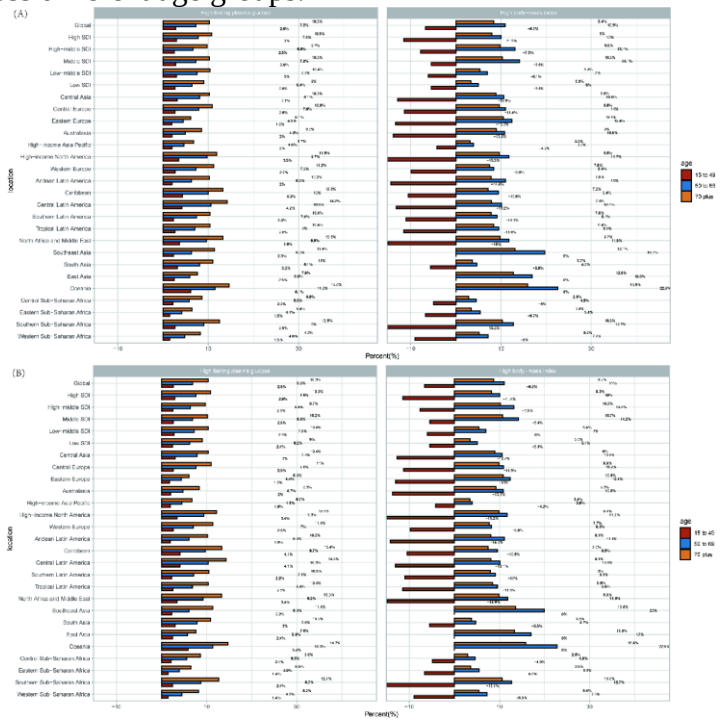

Figure S1: The percentage contribution of metabolic factors to the burden of female breast cancer by age group and regions in 2019. (A) The mortality percentage of female breast cancer; (B) The DALYs percentage of female breast cancer.

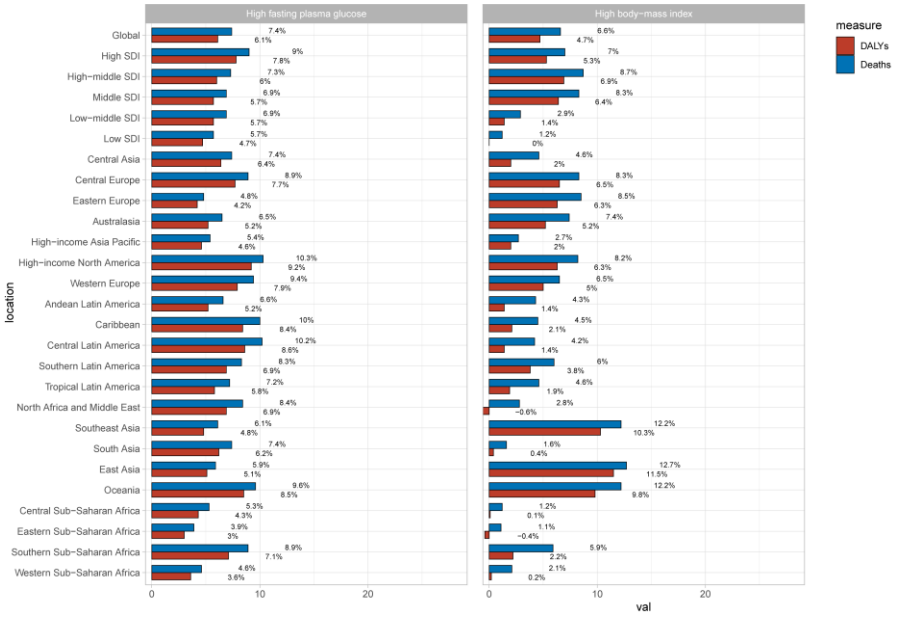

Figure 2: The percentage contribution of risk factors to the burden of breast cancer by regions in 2019. DALYs, disability-adjusted life-years.

4. Discussion

This study offers a comprehensive overview of the global disease burden of breast cancer from 1990 to 2019, and assesses the metabolic factors. First, the results show that the global ASIR of breast cancer increased. The ASMR and ASDR of breast cancer showed a downward trend. Meanwhile, we found that breast cancer burden decreasing in high SDI regions and increasing in low SDI regions. In addition, high BMI was a major risk factor for breast cancer death and DALYs in females, with differences observed across age groups.

The changing trends of global breast cancer incidence and disease burden were significantly different between high and low SDI countries, which is consistent with many previous studies. Previous studies [8-9] have suggested that regional differences in breast cancer disease burden are due to ethnic factors, lifestyle habits, and socioeconomic development levels. First, relevant studies [10] suggested that the geographical differences in breast cancer are caused by racial differences in innate immune procedures. There may be racial differences in the occurrence, development, and prognosis of breast cancer. Secondly, the gradual westernization of lifestyle in developing countries and reproductive factors [11] are important risk factors for increasing breast cancer burden. In addition, the levels of economic development and social welfare affect breast cancer screening, treatment and prognosis [12-13]. Therefore, developing countries should improve screening efficiency and develop targeted breast cancer public health policies and treatment programs to alleviate the breast cancer burden.

Our results showed that high fasting plasma glucose and high BMI are consistently important risk factors for breast cancer. The study also found that obesity had an opposite effect on breast cancer burden in premenopausal and postmenopausal women. A previous study [14] showed a strong linear relationship between high BMI and invasive breast cancer in postmenopausal women, especially estrogen receptor-positive breast cancer. Another study [15] found that obesity was negatively associated with breast cancer risk in premenopausal women and positively associated with breast cancer risk in postmenopausal women. This is consistent with our results that obesity has some protective effect in premenopausal women. However, a case-control study [16] indicated no obvious correlation between obesity in premenopausal women and breast cancer. At present, the impact of obesity on breast cancer is controversial, and extensive experimental studies are needed to test the mechanisms behind this phenomenon.

Our study has some unavoidable limitations. First, our data were collected and sorted by GBD, and no statistical analysis was performed on individual original data; therefore, the results may be biased. In addition, our study did not include the effects of breastfeeding, early age of menarche, environmental trace elements, and other factors on the incidence, death and DALYs of breast cancer.

5. Conclusion

In summary, from 1990 to 2019, the incidence of breast cancer has been increasing globally, but its mortality and DALYs have declined. However, by 2019, breast cancer burden gradually increased in low SDI regions. Obesity is a major risk factor for female breast cancer. Targeted breast cancer prevention measures should be taken to reduce breast cancer burden and narrow the gap between developed and developing countries.

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