Income Disparity in Breast Cancer Incidence and Stage at Presentation: A National Population Study of South Korea

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ABSTRACT

Purpose: This study aims to explore income-based disparities in breast cancer (BC) incidence and stage at presentation in a national population in South Korea, where a National Cancer Screening Program (NCSP) has been implemented.

Methods: In 2007, new patients with BC were identified using the Korea Central Cancer Registry database. We calculated adjusted odds ratios (aORs) to evaluate the association between individual income level and the risk of distant stage BC at presentation, adjusting for women's age, body mass index, disability registration, employment, region of residence, and year of diagnosis.

Results: The cumulative age-standardized incidence of BC in the 11 years was highest among women in the richest quintile (2,040 per 100,000 women for 11 years), whereas the proportion of distant stage at presentation was the highest (10.2%) among the medical aid beneficiaries. The aOR of distant stage diagnosis at presentation was higher for lower-income quintiles, and the risk was the highest in the medical aid beneficiaries (aOR, 2.25; 95% confidence interval, 1.97–2.58) than in the richest quintile. The income-based gradient in aORs for distant stage did not differ between younger (< 40 years) and older patients.

Conclusion: A higher risk of distant stage BC at presentation among the lower-income and medical aid groups in the context of a NCSP was observed. A more focused approach toward women in lower-income groups is necessary to alleviate the disparity in the risk of advanced BC.

Keywords: Breast Neoplasms; Mass Screening; Republic of Korea; Socioeconomic Factors

INTRODUCTION

Breast cancer (BC) is the most commonly diagnosed form of cancer and the cause of cancer-related deaths in women worldwide in 2020 [1]. One-half of all BC cases and 58.3% of cancer deaths occur in Asian countries, where the overall incidence is lower compared to the global average [1,2]. Although BC mortality has modestly decreased, detection and treatment at an early stage are still of paramount importance for optimal survival among affected patients.
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The overall 5-year BC survival is reported to range from 27% to 98%, largely depending on the cancer stage at presentation [4,5].

The global burden of BC is characterized by inequality. Previous studies have provided evidence that higher socioeconomic status (SES) is associated with increased BC incidence, attributed to lower parity or hormonal contraceptive use, which leads to higher exposure to sex hormones [6]. However, many studies have reported that the survival of patients with BC with the higher income is more favorable than that of those with lower income [7-9]. As individuals with low SES are less likely to undergo regular screening, they are at a higher risk of advanced cancer at diagnosis [10].

South Korea has implemented the National Cancer Screening Program (NCSP) for BC in women aged 40 years and older in the medical aid program and the lower-income stratum (lower 50%) since 2004. Among the NCSP target population, 49.2%–63.8% of women were screened for BC in 2012–2017 [11]. Given that the screening rate for BC among Korean women in general in the same period was 82.9%–86.2% [12], the NCSP participation rate in the low-income population remains relatively low. In the context of a NCSP for a more deprived population, such as that in South Korea, the income gradient in the cancer stage at the time of diagnosis may vary. This study aimed to assess the socioeconomic gradient in the cancer stage in women who had been newly diagnosed with BC.

METHODS

Data source and identification of incident cases
A total of 177,835 BC cases diagnosed in 2007–2017 were extracted from the Korea Central Cancer Registry (KCCR) database. The KCCR is a population-based cancer registry that was established in 2000 by the National Cancer Center, covering approximately 90% of the new cancer cases in Korea. Since 2002, nationwide cancer incidence statistics have been produced by merging 11 population-based regional cancer registry programs, data from an ad hoc medical record review survey, and the cancer mortality database from Statistics Korea [13]. In the KCCR database, individuals with a primary cancer code beginning “C50” from the International Classification of Diseases 10th Revision were identified as incident BC cases. To construct a national cohort of newly diagnosed patients with BC, data on individuals with new BC diagnoses were linked to the database of the National Health Insurance Service (NHIS) in South Korea [14]. This database contains general demographics such as employment status, household income in percentiles, residential districts, and clinical information on diagnoses. Initially, we identified 179,881 new patients who were diagnosed with primary BC between 2004 and 2017. We excluded men with BC (n = 778), which is scarce. Restricting the study population to new cases linked to the NHIS database between 2007 and 2017, the final study population yielded 144,916 women (Supplementary Figure 1).

The KCCR database provides a summary of cancer staging information based on the staging system from the Surveillance, Epidemiology, and End Results (SEER) database of the United States National Cancer Institute. It classifies cancers according to their localized, regional, and distant stages. The “localized” and “regional” stages indicate the absence of cancer beyond the breast and its presence beyond the breast in nearby structures, respectively. In the distant stage, cancer spreads to distant parts of the body, such as the lungs, liver, or bones.
An unknown stage is separately recorded as “unknown.” We used 3 categories (locoregional, distant, and unknown) to assess the risk of distant or unknown stages at presentation.

**Relative level of household income**

Information on the relative level of household income was used as an SES indicator. The NHIS is a co-payment and contributory program covering approximately 96% of the Korean population. The main financial sources of the program are insurance premiums and government subsidies. The NHIS premium has been used as a proxy variable for the SES of Koreans because it is calculated based on employee wages. For self-employed Koreans, the premium is calculated based on household income, assets, vehicle ownership, and the age of household members. The Korean NHIS cohort database includes individually linked household income deciles. For those living under the national poverty line or with no identifiable income source, medical aid is provided as a non payable medical assistance program. Therefore, we divided the study population into 6 groups according to their relative income level (1, 90%–100%: highest income; 2, 70%−80%; 3, 50%−60%; 4, 30%−40%; and 5, 10%−20%: lowest income) and whether they were medical aid beneficiaries (level of income: 6) for analytical convenience. The 6 income categories are mutually exclusive because those who are medical aid beneficiaries do not have information on income levels.

**Statistical analysis**

First, using descriptive statistics, we tested for a linear trend of general incidence and the proportion of distant metastasis at the time of diagnosis, as well as the relative income gradient in the risk of the distant stage using Spearman’s rank-sum correlation. Second, to assess the incidence at the population level, we retrieved the total number of women based on age group and relative income level from the NHIS Statistical Yearbooks (https://www.hira.or.kr). The crude incidence rate was calculated by dividing the annual incidence of BC and distant stage BC by the total annual number of women. We computed the age-standardized cumulative incidence of BC using the number of women in each age/income group. Third, adjusted odds ratios (aORs) were calculated using multivariable analysis to evaluate the association between relative income level and risk of distant stage BC at presentation, excluding unknown stage cases. Because the NCSP for BC is for women aged 40 years, we tested for heterogeneity in the stratified risk estimates across women’s ages (< 40 and ≥ 40 years) to identify the impact of the NCSP. In addition, we computed the adjusted risk of unknown stage cases to assess the potential sources of selection bias. The covariates included age, body mass index (BMI), disability registration, employment, region of residence, and year of diagnosis. As more than 10% of the patients’ information did not include BMI (missing rate of 30.8%) or smoking (18.1%) details, we imputed the missing variables using the fully conditional method, which is reported to be a statistically valid method for imputation in large datasets [15]. In addition, we conducted a complete case analysis, as recommended by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [16]. All analyses were conducted using SAS software (version 9.4; SAS Institute, Cary, USA).

**RESULTS**

The crude annual incidence rate per 100,000 women increased from 54.0 in 2007 to 85.6 in 2017 ($p < 0.001$; Figure 1). The incidence rate of distant stage BC at presentation increased from 2.8 to 4.1 per 100,000 women-year, whereas the proportion of distant stage BC at
diagnosis among the new patients with BC for the year slightly decreased during the study period (from 5.1% in 2007 to 4.7% in 2017; $p = 0.041$). Both the annual incidence rate and the proportion of unknown stage BC have decreased.

The cumulative incidence of BC based on the average midyear female population was 4,324 per 100,000 women, and the incidence was most frequent among those aged 60 years and older and in the second income quintile (Supplementary Table 1). When stratified based on relative income level, the cumulative age-standardized incidence of BC in the 11 years (2007–2017) was the highest (2,040 per 100,000 women for 11 years) among women in the richest quintile (Figure 2). The age-standardized cumulative incidence was the lowest among the medical aid beneficiaries. By contrast, the proportion of new BC cases diagnosed at a distant stage was highest in the medical aid group (10.2%) and lowest in the richest quintile (4.2%). The risk of distant stage BC at presentation was also the highest in the medical aid group.

Among the 144,916 female patients with BC, most were under 60 years old (77.2%), unemployed (76.9%), and local subscribers to health insurance (62.0%) (Table 1). Ninety percent of the patients presented local or regionalized SEER stages, 5.2% (n = 7,562) showed distant metastasis, and 4.5% (n = 6,874) had unknown stage BC at presentation. The percentages of distant (7.5%) and unknown stages (8.8%) at presentation were the highest in the oldest group. Unemployed patients had a higher proportion of distant or unknown stages. The crude frequency of new BC was generally higher when the relative income level was higher, while the percentage of distant or unknown stage BC was higher when the income was lower or women were medical aid beneficiaries. When analyzing the 138,042 patients with BC, excluding those with unknown stage, the risk of distant stage diagnosis at presentation was consistently higher when the relative income level was lower, which was obtained more precisely with imputed data analysis (Supplementary Table 2). Medical aid beneficiaries were 2.25 times more likely to be diagnosed at the distant stage compared to those in the richest income quintile (95% confidence interval, 1.97–2.58). Although the income-based gradient in the distant stage at presentation was more evident among those
aged 40 years and older than among those aged less than 40 years, the difference was not statistically significant (Figure 3). Similarly, for the risk of unknown stage diagnosis, medical aid beneficiaries and those in lower-income quintiles showed a higher OR than women in the highest-income quintile among the 144,916 patients with BC (Supplementary Figure 2).

DISCUSSION

In the 11 years of increasing BC incidence, we observed a consistently higher incidence of BC among women with higher incomes than among those with lower incomes. Unlike the reverse income gradient in BC incidence, the risk of distant metastasis at presentation is associated with a lower level of income or medical aid beneficiaries. Although the national BC screening program is only for women aged 40 years and older, the income-based gradient in the risk of distant stage BC did not differ between younger and older patients. This pattern of income-based disparity was also observed in the risk of unknown-stage diagnosis in the registry. This finding supports our hypothesis of a higher risk of advanced-stage BC at presentation when SES is low. Using the national cancer registry data, we observed a consistent association between a higher risk of advanced-stage BC at presentation and lower income in contemporary Korean women.

Historically, a higher SES has been established as a risk factor for a higher BC incidence, which is attributed to earlier menarche, mammography screening, hormone therapy, and lifestyle factors [17]. BC was once considered an illness subject to reverse socioeconomic disparities, showing a lower incidence and mortality for those in lower socioeconomic positions [7]. In many Asian countries, the incidence of BC increases with economic development and urbanization, affecting women of higher socioeconomic positions [18-20]. A Swiss study showed that women with lower SES are less likely to undergo screening tests.
Table 1. Demographic characteristics and Surveillance, Epidemiology, and End Results stage at the time of diagnosis of women who were newly diagnosed with breast cancer in 2007–2017 (n = 144,916)

| Variables                                      | Locoregional (n = 130,480) | Distant (n = 7,562) | Unknown (n = 6,874) | Total (n = 144,916) |
|------------------------------------------------|-----------------------------|--------------------|---------------------|---------------------|
| Age (yr)                                       |                             |                    |                     |                     |
| < 30                                           | 1,208 (89.0)                | 82 (6.0)           | 67 (5.0)            | 1,357               |
| 30–39                                          | 13,915 (89.4)               | 920 (5.9)          | 725 (4.7)           | 15,560              |
| 40–49                                          | 46,924 (91.2)               | 2,259 (4.4)        | 2,268 (4.4)         | 51,451              |
| 50–59                                          | 39,339 (90.4)               | 2,302 (5.3)        | 1,859 (4.3)         | 43,500              |
| 60–69                                          | 19,260 (90.4)               | 1,124 (5.3)        | 918 (4.3)           | 21,302              |
| ≥ 70                                           | 9,834 (83.7)                | 875 (7.5)          | 1,037 (8.8)         | 11,746              |
| Body mass index (kg/m²)                        |                             |                    |                     |                     |
| < 18.5                                         | 1,766 (92.5)                | 63 (3.3)           | 80 (4.2)            | 1,909               |
| 18.5–25                                        | 62,649 (93.0)               | 2,273 (3.4)        | 2,412 (3.6)         | 67,334              |
| 25–30                                          | 26,606 (92.2)               | 1,121 (3.8)        | 1,141 (4.0)         | 28,868              |
| ≥ 30                                           | 2,010 (91.0)                | 114 (5.2)          | 86 (3.8)            | 2,210               |
| Smoking                                        |                             |                    |                     |                     |
| Past or current smoker                         | 5,051 (91.7)                | 240 (4.4)          | 219 (4.0)           | 5,510               |
| Never smoked                                   | 104,578 (92.4)              | 3,727 (3.3)        | 4,853 (4.3)         | 113,158             |
| Employment status                              |                             |                    |                     |                     |
| Employed                                       | 23,078 (92.9)               | 854 (3.4)          | 905 (3.6)           | 24,837              |
| Not employed                                   | 107,402 (92.4)              | 6,709 (5.6)        | 5,969 (5.0)         | 120,079             |
| Relative income (quintiles and medical aid)    |                             |                    |                     |                     |
| 1st (highest)                                  | 37,813 (91.6)               | 1,639 (4.0)        | 1,809 (4.4)         | 41,261              |
| 2nd                                            | 34,301 (90.6)               | 1,817 (4.8)        | 1,736 (4.6)         | 37,854              |
| 3rd                                            | 20,908 (88.9)               | 1,449 (6.2)        | 1,153 (4.9)         | 23,510              |
| 4th                                            | 16,053 (89.1)               | 1,084 (6.0)        | 883 (4.9)           | 18,020              |
| 5th (lowest)                                   | 11,862 (88.0)               | 913 (6.8)          | 697 (5.2)           | 13,472              |
| Medical aid*                                   | 4,005 (85.0)                | 388 (8.2)          | 319 (6.8)           | 4,712               |
| Disability registration                        |                             |                    |                     |                     |
| Disability                                     | 6,257 (85.1)                | 524 (7.13)         | 569 (7.74)          | 7,350               |
| No disability                                  | 123,959 (90.3)              | 7,017 (5.1)        | 6,272 (4.6)         | 137,248             |
| Region                                         |                             |                    |                     |                     |
| SMA                                            | 72,736 (90.4)               | 4,061 (5.1)        | 3,650 (4.5)         | 80,447              |
| Non-SMA                                        | 57,744 (89.57)              | 3,501 (5.43)       | 3,224 (5.0)         | 64,469              |

Values are presented as number (%). The sum of column frequencies may not be equal to the total population because of missing values.

SMA = Seoul metropolitan area.

*Under national poverty line.

Figure 3. Adjusted odds ratios of distant stage diagnosis at presentation across relative income levels, for younger (< 40 years) and older (40 years and older) among 138,042 patients with stage information, National Cancer Registry of Korea linked with the National Health Information Database of the National Health Insurance database in 2007–2017. The estimates are adjusted for age, body mass index, employment, disability, year of diagnosis, and Seoul metropolitan area residence.
for BC, even with increased BC screening coverage, which results in less optimal survival compared to their counterparts [21]. In Japan, the age-standardized incidence of BC was higher in higher-income areas, where effective screening programs are readily available and accessible, than in lower-income areas [22]. A lower incidence and higher mortality in lower socioeconomic positions were also observed in an Israeli cohort study, which supports the socio-behavioral mechanism underlying disparity [23]. Given the association between low SES and aggressive cancer [24-26], BC in the more deprived group may have more aggressive features, resulting in a faster progression than that in the less deprived group. Our observations confirmed the high risk of BC in higher socioeconomic strata and the income disparity that persists in advanced-stage BC screening programs for the population. The consistent income-based gradient in the distant stage at presentation, regardless of women's age, suggests that implementation of the NCSP may not be sufficient to resolve income-based disparities in the timely diagnosis of BC.

Although the results were similar, the estimates from the imputed data analysis were more precise and greater than those from complete data. The estimates from imputed data can be biased depending on the missing patterns in the dataset [15]. Many studies on social disparities in health outcomes have performed complete dataset analysis. However, given that information on BMI or smoking is more likely to be missing for lower-income groups, this approach may ameliorate the magnitude of disparity across different social groups. We present both results to increase the transparency and understanding of the research findings.

Therefore, the findings of this study should be interpreted with caution. Given that the lead time from exposure to carcinogenesis is several years, the relative income level assessed at the time of BC diagnosis and SES at the time of BC development may have been different. The income status at the time of BC diagnosis was used in the analysis. As data on changes in income status before 2007 were not available, we could not capture the impact of income on the incidence and stage at presentation. Second, there may have been residual confounding effects from unmeasured variables, such as diet and occupational exposure. However, as a population-based study using the National Cancer Registry, our findings provide valid evidence of a positive association between the relative income level and BC stage at presentation. Finally, there is a potential competing risk of other cancers, which could have affected our risk estimates. To confirm our findings, the impact of competing risks needs to be assessed using the complete data of all primary cancers.

In conclusion, we observed a higher risk of distant stage BC at presentation in Korean women with lower income who received medical aid in the context of a NCSP for low-income populations. A more focused approach is necessary for women in lower-income groups to alleviate disparities in the risk of advanced BC.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1
Cumulative frequency, total number of population, cumulative incidence (per 100,000 women) per age and income levels, total female new BC patients in 2007–2017, South Korea (n = 144,916)

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Supplementary Table 2
Distant stage at presentation and stage unknown among 144,916 patients of the National Cancer Registry of Korea linked with the National Health Information Database of National Health Insurance database in 2007–2017

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Supplementary Figure 1
Selection flow of study population, total female new breast cancer patients in 2007–2017, South Korea (n = 144,916).

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Supplementary Figure 2
Adjusted odds ratios for stage unknown at presentation across relative level of income, (A) complete case analysis and (B) imputed data analysis, 144,916 patients of the National Cancer Registry of Korea linked with the National Health Information Database of National Health Insurance database in 2007–2017. Estimates are adjusted for age, body mass index, employment, disability, year of diagnosis and Seoul metropolitan area residence.

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