ORIGINAL ARTICLE

Socioeconomic inequalities in metastasis, recurrence, stage and grade of breast cancer: a hospital-based retrospective cohort study

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Keywords

Socio-Economic Status • Inequality • Concentration Index • Breast Cancer

Summary

Introduction. *This study aims to estimate the Socio-Economic Status (SES) inequality on the metastasis, recurrence, stage and grade in Breast Cancer (BC).*

Methods. *This retrospective cohort study conducted on 411 BC patients in Arak, Iran. Asset-based questionnaire used to estimate the household SES. For calculate of SES inequality was used from Concentration Index (C). Moreover for investigate the association between recurrence and metastasis with other variables were used from multilevel logistic regression and analysis of variance were used to investigate the relationship between SES and other variables. The data were analyzed with Stata (v.13) software.*

Results. *Results of analysis of variance showed statistical significant relationship between SES with, insurance, surgery, grade, stage, recurrence and metastasis (p-value < 0.05). Moreover the Odds Ratio (OR) were significant of recurrence with age, academic level of education, supplementary insurance history of BC in first-degree relatives, stage and grade, also, metastasis with age of > 80 years, insurance, supplementary insurance, history of BC in first-degree relatives, chemotherapy, radiotherapy, stage and grade four. The total C index obtained 0.015 (0.002, 0.026), 0.011 (0.003, 0.031), – 0.014 (– 0.034, – 0.001) and – 0.042 (– 0.061, – 0.002) for metastasis, recurrence, stage and grade of BC respectively.*

Conclusions. *Our results showed evidence of inequality in the metastasis, recurrence, stage and grade in BC patients.*

Introduction

Breast cancer (BC) accounts for about one-third of all cancers in women. This cancer is the second most common cancer after lung cancer and the most common cause of cancer deaths among women [1].

BC with nearly 1.7 million cases was considered as the most prevalent cancer among women in 2016 [2]. Breast cancer has led to 535,000 deaths and 15.1 million DALYs [2]. The incidence and mortality rate of BC has increased in recent years in Asian countries as well as Iran [2-4].

Some factors such as age, estrogen receptor status and lymph node involvement as factors influencing recurrence [5]. One of the most important problems in this cancer was the metastasis of cancer cells to other organs, which was, in fact, one of the main causes of failure in the treatment [6]. The metastasis was seen among the 5-10% of patients [7]. Also, the factors affecting the metastasis was identified, such as the initial size of the tumor, lymph node involvement, disease grade, estrogen receptor status, and the interval between surgery, and local recurrence [8]. Moreover, the tumor stage, access to health-care services, comorbidity, cigarette smoking, Body Mass Index (BMI), stress, and social support were associated with the prognosis and the risk of death of BC. The SES was related to hormone therapy, smoking, and access to health-care and affects metastasis, recurrence, stage, and grade of diagnosis [9]. The SES and the level of education lead to a difference in the stage and subsequently survival of BC [10, 11]. Early diagnosis with treatment was an appropriate strategy for improving prognosis. Population-based screening programs reduce the incidence and death of cancer, due to extensive population coverage and improved follow-up and control. The SES was referred to socio-economic factors such as education level, income and occupation, which can affect a person's or group's situation in the community [12]. However, the role of SES inequality in outcomes of BC cancer remains uncertain.

Despite the many efforts in different periods to reduce the difference between the poor and the rich, through the redistribution of wealth to create an equal society, social inequalities have not disappeared and even seems increased globally. Health inequality is one of the most important indexes of inequality. It has been shown in various studies, that the overall incidence and mortality

https://doi.org/10.15167/2421-4248/jpmh2019.60.3.1162

rates in poorer economic groups are higher, due to an increase in inequality index in particular areas [13]. The relation between inequality and health is an important issue. Inequality is an issue at the social level that imposes a lot of costs on society. Health is one of the most important indicators of human capital. Therefore, inequality has the greatest effect on health [14]. Income inequality affects people's health in many ways. The high level of inequality undermines social capital, also, caused stress among individuals in the community, which set these behaviors affects general health [15]. At the individual level, the person's income increases the health, but community-based studies do not endorse this theory. Because there are countries that, although lower income than high-income countries have high health status, because they have less inequality [16]. The BC is curable and also can be prevented with early detection and if does not metastasize to other tissues. Achieving health care and screening services can lead to early diagnosis and prevention of disease severity. SES inequality can also play an important role in people's health. To date, no study has been performed yet, that can identify the role of SES inequality in recurrence, metastasis, grade and stage of BC. This gap was addressed in this study.

Methods

Study design and sampling

This retrospective cohort study conducted on 411 BC patients referred to hospitals of Arak University of Medical Sciences. The sampling method is accessible (non-randomized). In this study, we analyzed all cases during the study period.

Instrument

Two questionnaires were used to data collection in this study: 1) the demographic and disease information questionnaire includes age, marital status, education, job, insurance, supplementary insurance, history of BC in first-degree relatives, chemotherapy, radiotherapy, surgery, stage and grade of BC patients; 2) a questionnaire designed by Gorramoodi et al. was used to measure the SES. This questionnaire includes questions about the level of women's education, the education of her husband, the area of the infrastructure, the cost of home, the number of rooms and the facilities and amenities (personal car, personal computer, more than one TV, refrigerator, washing machine, dishwasher, mobile phone and traveling abroad. The correlation of these factors with a score reliability was obtained 0.87 and validity was obtained 0.88 respectively [17].

Statistical analysis

To investigate the relationship between recurrence and metastasis with other variables, binary logistic regression was used because these two variables were dichotomous. Using this method, the OR for each variable is calculated with constant considering effect of other variables. Moreover to evaluate the relationship between SES with other variables, analysis of variance was used. All statistical analyzes were performed using Stata (v.13) software.

Measurement of SES and Inequality

In this study, a new variable was created as an SES, using the Principal Component Analysis (PCA) method. The PCA method identifies the variables that have the greatest effect on the variance of the total variables, and then constructs the new variable. The first component derived from the analysis, explains the most variance in the variables and gives each family a score that is considered as an indicator of its SES [18, 19].

The Concentration index (C) was used to determine the inequality in this study. The value of this index varies between + 1 to – 1. When the line of equality and the C curve fit together, the C index will be zero, which means that there is no inequality. The C index is defined by the area under the C curve multiplication in two. With the greater interval between the C curve of the inequality line the amount of inequality also increases. When the C curve is above the equality line, the C index will be negative, which means that, the concentration of the investigated factor (in this study: metastasis, recurrence, stage and grade of BC is more in lower SES. Also when the C curve is under the equality line, the C index will be positive, which means that the concentration of the investigated factor is more in highest SES [20, 21].

The C index is a common inequity measure in health outcomes and has been used continually in recent studies [20, 22]. The C was calculated by the Kakwani et al. formula [20] (formula 1).

$$C = \frac{2}{\mu}\sum_{t=1}^{T} f_t \mu_t R_t - 1$$

In this formula, μ is the mean in studied patients with cancer and μ_t is that for the tth group. In addition, f_t, is the group share of patients. Also, R_t, is the relative rank of the tth educational level of the participating patients, which was obtained through formula 2:

$$R_t = \sum_{t=1}^{T} f_r - \frac{1}{2} f_t$$

Therefore, R_t indicates the cumulative proportion up to the midpoint of each SES group interval. The correspondence confidence interval for C is calculated based on Wagstaff and Van Doorslaer method [20, 23].

This method has been used in other studies [24-29] and is as given below.

$$Var(C) = \frac{1}{n}\left[\sum_{t=1}^{T} f_t\, a_t^2 - (1+C)\right] + \frac{1}{n\mu^2}\sum_{t=1}^{T} f_t\, \sigma_t^2 (2R_t - 1 - C)^2$$

In this formula σ_t^2 is the variance of μ_t,

$a_t = \frac{\mu_t}{\mu}(2R_t - 1 - C) + 2\text{-}q_{r-1} - q_t$ and $q_t = \frac{1}{\mu}\sum_r^t \mu_r f_r$,which is the ordinate of *L (P)*, $q_0 = 0$ and $p_t = \sum_{r=1}^{t} f_r R_r$

Results

In total, 411 women with mean age of 20-87 participated in this study. Mean score of SES was 0.29 ± 0.94 (– 2.71, 2.2). Of all patients, 19.7% had a good SES, 71.04% had a middle and 9.26% had a poor SES.

The crude and adjusted OR of relationship between the recurrence and other variables showed in Table I. According to these results, the OR was significant for relationship between recurrence and supplementary insurance, history of radiotherapy, stage 4 and grade 3 of BC patients.

The crude and adjusted OR of relationship between the metastasis and other variables showed in Table II. According to these results, the OR was significant for relationship between the metastasis and history of surgery, stage 4, grade 2, and grade 3 of BC patients.

Differences in mean of subgroups of variables in this study by SES showed in Table III. These results shown significant relationship between SES with supplementary insurance and grade of BC (p-value < 0.05).

C index obtained – 0.0025 (– 0.0153, 0.0103) and – 0.00001 (– 0.01623, 0.01620) for recurrence and metastasis respectively. Also for stage and grade of BC, C index obtained 0.0013 (-0.009, 0.011) and – 0.004 (– 0.0145, 0.0059) respectively, that showed there was not concentration of metastasis, recurrence, stage and grade by SES levels (Tab. IV). In addition, the concentration curve for recurrence and metastasis showed that there was no concentration of these outcomes by SES level (Figs. 1, 2).

Tab. I. The crude and adjusted OR of recurrence with other variables.

Variables	Subgroups	Crude	Adjusted*
		OR (95% CI)	OR (95% CI)
Age	< 40	Reference	Reference
	40-60	2.91 (0.36, 23.27)	4.28 (0.48, 37.84)
	> 60	3.54 (0.43, 28.94)	2.91 (0.26, 32.25)
Marital status	Single	Reference	Reference
	Married	1.65 (0.20, 13.65)	2.29 (0.26, 19.71)
	Widow/divorced	0.94 (0.09, 9.53)	1.39 (0.12, 15.60)
Education	Illiterate	Reference	Reference
	Primary	0.33 (0.12, 0.87)	0.27 (0.08, 0.89)
	Diploma	0.85 (0.31, 2.32)	1.06 (0.3, 3.71)
	Academic	0.27 (0.05, 1.27)	0.43 (0.05, 3.69)
Job	Housewife	Reference	Reference
	Retired	0.31 (0.04, 2.45)	0.28 (0.02, 2.81)
	Unemployment	2.26 (0.41, 12.28)	2.73 (0.44, 16.81)
	Permanent/temporary	0.75 (0.16, 3.49)	1.14 (0.18, 7.29)
Insurance	No	Reference	Reference
	Yes	0.48 (0.04, 4.80)	0.43 (0.02, 6.69)
Supplementary insurance	No	Reference	Reference
	Yes	2.19 (1.00, 4.77)	2.94 (1.21, 7.14)
History of BC in first-degree relatives	No	Reference	Reference
	Yes	1.43 (0.66, 3.13)	1.12 (0.47, 2.68)
Chemotherapy	No	Reference	Reference
	Yes	2.91 (0.98, 8.71)	2.67 (0.82, 8.61)
Radiotherapy	No	Reference	Reference
	Yes	2.42 (1.12, 5.24)	2.73 (1.17, 6.34)
Surgery	No	Reference	Reference
	Yes	0.32 (0.13, 0.78)	0.38 (0.14, 1.05)
Stage	One	Reference	Reference
	Two	0.17 (0.01, 3.00)	0.15 (0.001, 2.99)
	Three	1.04 (0.12, 9.02)	1.09 (0.10, 10.86)
	Four	27.5 (3.03, 249.48)	49.24 (4.06, 596.2)
Grade	One	Reference	Reference
	Two	3.42 (0.91, 12.77)	2.93 (0.75, 11.44)
	Three	9.47 (2.52, 35.59)	9.43 (2.34, 38.06)

*: adjusted for age, marital status, education level, and job.

Tab. II. The crude and adjusted OR of metastasis with other variables.

Variables	Subgroups	Crude	Adjusted*
		OR (95% CI)	OR (95% CI)
Age	< 40	Reference	Reference
	40-60	1.29 (0.45, 3.67)	1.91 (0.59, 6.15)
	> 60	1.32 (0.44, 3.91)	2.07 (0.53, 8.06)
Marital status	Single	Reference	Reference
	Married	0.68 (0.20, 2.30)	0.73 (0.20, 2.61)
	Widow/divorced	0.57 (0.14, 2.26)	0.58 (0.13, 2.46)
Education	Illiterate	Reference	Reference
	Primary	0.77 (0.39, 1.52)	0.83 (0.37, 1.86)
	Diploma	0.80 (0.34, 1.90)	1.06 (0.39, 2.84)
	Academic	1.03 (0.44, 2.40)	2.31 (0.68, 7.86)
Job	Housewife	Reference	Reference
	Retired	0.68 (0.22, 2.11)	0.42 (0.11, 1.62)
	Unemployment	1.85 (0.42, 8.02)	1.82 (0.39, 8.39)
	Permanent/temporary	0.65 (0.21, 1.99)	0.44 (0.12, 1.58)
Insurance	No	Reference	Reference
	Yes	0.39 (0.08, 1.80)	0.29 (0.05, 1.63)
Supplementary insurance	No	Reference	Reference
	Yes	1.38 (0.79, 2.43)	1.52 (0.81, 2.86)
History of BC in first-degree relatives	No	Reference	Reference
	Yes	0.99 (0.57, 1.74)	0.90 (0.50, 1.64)
Chemotherapy	No	Reference	Reference
	Yes	1.07 (0.57, 2.01)	0.95 (0.48, 1.88)
Radiotherapy	No	Reference	Reference
	Yes	1.06 (0.60, 1.88)	1.14 (0.62, 2.07)
Surgery	No	Reference	Reference
	Yes	0.38 (0.19, 0.78)	0.35 (0.16, 0.76)
Stage	One	Reference	Reference
	Two	1.10 (0.76, 3.23)	0.91 (0.05, 8.41)
	Three	1.87 (0.65, 4.56)	1.92 (0.23, 8.42)
	Four	9.72 (2.11, 73.21)	11.28 (3.56, 45.12)
Grade	One	Reference	Reference
	Two	4.02 (1.67, 9.65)	3.91 (1.58, 9.62)
	Three	8.27 (3.18, 21.50)	9.24 (3.35, 25.44)

*: adjusted for age, marital status, education level, and job.

Tab. III. Relationship between SES and other variables.

Characteristics	Subgroups	Mean	SD	P-value
Insurance	No	– 0.46	1.08	0.055
	Yes	0.04	0.93	
Supplementary insurance	No	– 0.08	0.91	0.006*
	Yes	0.16	0.95	
Chemotherapy	No	– 0.058	0.89	0.160
	Yes	0.079	0.96	
Radiotherapy	No	0.05	0.96	0.421
	Yes	– 0.02	0.90	
Surgery	No	-0.032	0.87	0.578
	Yes	0.042	0.95	
Grade	One	– 0.1	0.84	0.011*
	Two	0.063	0.93	
	Three	0.094	0.89	
	Four	0.022	0.49	
Stage	One	0.16	0.65	0.865
	Two	– 0.12	0.99	
	Three	0.30	0.85	
	Four	– 0.50	0.95	
Recurrence	No	0.02	0.90	0.926
	Yes	0.04	0.72	
Metastasis	No	0.07	0.88	0.785
	Yes	0.04	0.93	

*: significant.

Tab. IV. Calculation of C indexes and their 95% CI, for metastasis, recurrence, stage and grade of BC patients.

Outcomes	Concentration index	95% Confidence intervals
Recurrence	– 0.0025	– 0.0153, 0.0103
Metastasis	– 0.00001	– 0.01623, 0.01620
Stage	0.0013	– 0.009, 0.011
Grade	– 0.004	– 0.0145, 0.0059

Discussion

The results of our study showed that most patients were housewives, also were in middle level of SES. Moreover the most of patients had a primary level of education. In a study, most of the patients, had a under diploma level of education. In evaluating the status of employment, the results showed that most of the patients were housewives and other were employed, also had a middle level of income, which is consistent with our study result [30].

The results of this study showed that there was no the significant relationship between the metastasis and

Fig. 1. Concentration Curve of SES inequality in recurrence.

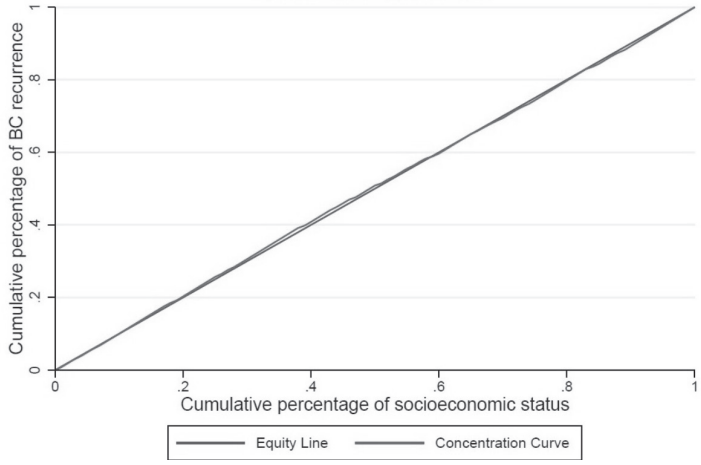
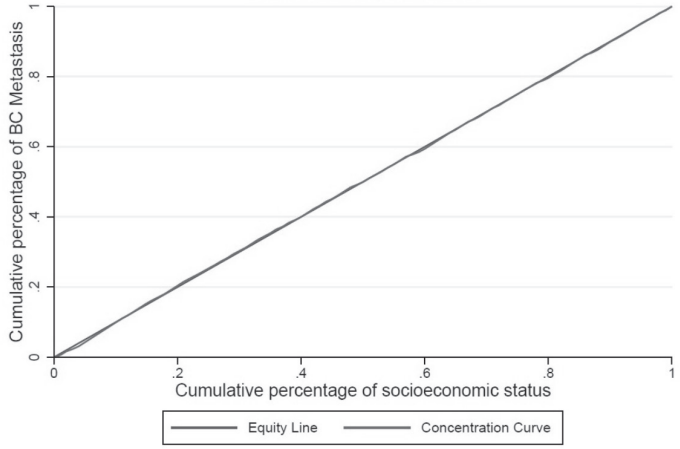


Fig. 2. Concentration Curve of SES inequality in metastasis.



recurrence of BC with age of patients. In some studies, it has been concluded that metastasis occurs at an earlier age, which is not consistent with our findings [31]. In some studies the role of age has proven to be an important factor in causing a bad prognosis in patients with a variety of cancers [32]. Results of Bennier's study in French showed the probability of recurrence and metastasis of BC was higher in patients older than 35 years. Also shown that patients with age of 35 years, before menopause had a better prognosis than the first group and patients over 60 years of age had a worse prognosis than the second group [33].

In our study, there was no the significant relationship between education levels with metastasis and recurrence. In various studies, appropriate prevention and treatment of BC have relationship with education. Also, there is a significant relationship between knowledge of risk factors for BC and the level of education, which this knowledge can prevent the metastasis and recurrence [34]. Our results showed that there was a significant relationship between the existences of supplementary insurance in patients with recurrence. In other words, the recurrence in patients with supplementary insurance was occurred more than other patients. Having supplementary insurance helps to encourage individuals for treatment and screening and causes more diagnosis and sooner discovering the disease. Therefore, it can be concluded that SES directly affect the stage, grade, recurrence and metastasis of BC [35]. Also, in a study, the insurance status had an important role in the outcomes of BC, even with adjusting for SES [36].

Some studies had identified a number of genes that causes metastasis in various tissues in BC [37]. However, there was not association between history of BC in first degree relatives with recurrence and metastasis. Cancer patients receive different therapies after surgery that can affect the survival, recurrence and metastasis [38]. In our study, the effect of surgery on metastasis was evident. In some studies, the role of radiotherapy has been shown to reduce metastasis [39]. Also results of our study showed grade and stage of BC had a relationship with recurrence and metastasis. Other studies showed a significant correlation between tumor size with recurrence and metastasis also with staging of BC [40].

The C index for health expenditure has always been positive, stating that health costs in higher deciles is

higher than lower deciles. This can be due to the low pay ability of low income deciles or lack of access to health services. The C index is closer to zero, indicating a more equality concentration on health costs among different deciles. The C index was 0.498 at 2009 in Iran, which indicates significant inequalities in health costs. An increase in inequality could be affected by rising prices due to economic policies or discriminatory health policies. An increase in inequality, can have a more negative effect on the health expenditure of lower SES groups [41]. According to the results of this study, there was not SES inequality in recurrence, metastasis, stage and grade of BC. This was the first study in this field. Although the role of SES inequality in health has been evaluated in some studies [42-45]. In some studies, the effect of SES on the incidence of cancer is reversed. For example in a study by Tweed et al., BC had a low incidence in areas with lower SES [46]. In a study in European countries the role of SES inequality evaluated in health. The C index varied from 0.0034 in the Netherlands to 0.0218 in Portugal. Also in this study patients with high SES are more likely to use diagnostic and therapeutic test, which leads to early detection of the disease [47].

Conclusions

BC is the most common cancer among women. Many complications of this cancer can be prevented with early detection. To date no study has been performed that evaluate the role of SES inequity in recurrence, metastasis, grade, and stage of BC. Therefore, our study results can be good evident of the importance of this topic. Due to the important role of SES and the existence of insurance and supplementary insurance, in early detection and treatment of BC, it is suggested that measures be taken to allow BC diagnostic and screening services to be available at a lower cost to the public. Also, with the reduction of SES inequality and increase in screening test, BC can be detected earlier and metastasis and recurrence decrease eventually.

Ethical statement

The Research Ethics Committee of Shahid Beheshti University of Medical Sciences approved this study and participants provided written informed consent for voluntary participation in the study (Ethical Code: IR.SBMU.RETECH.REC.1396.839).

Acknowledgements

Funding/Support sources: this research has been supported by Shahid Beheshti University of Medical Sciences grant number: 11361.
This study is part of PhD thesis of Dr. Majid Taheri in the field of Medical Sociology that funded by Shahid Beheshti University of Medical Sciences. The authors also gratefully acknowledge the cooperation of oncologists, without whom this investigation would not have been possible. We would also like to thank all patients who participated in this research.

Conflict of interest statement

None declared.

Authors' contributions

MT, MT, MEA, AAH, RA, AAA and MT contributed to project design and its development. MT, MT, AAH, RA and MA wrote the manuscript. MT, AAH, MT and MA analyzed data.

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Received on December 28, 2018. Accepted on June 17, 2019.

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How to cite this article: Taheri M, Tavakol M, Akbari ME, Anoshirvani AA, Aghabozorgi R, Almasi-Hashiani A, Abbasi M. Socioeconomic inequalities in metastasis, recurrence, stage and grade of breast cancer: a hospital-based retrospective cohort study. J Prev Med Hyg 2019;60:E262-E269. https://doi.org/10.15167/2421-4248/jpmh2019.60.3.1162