DOI: 10.1590/1413-81232018242.31672016

Social vulnerability and breast cancer: differentials in the interval between diagnosis and treatment of women with different sociodemographic profiles

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Abstract *This study aimed to identify the sociodemographic profiles of women diagnosed as breast cancer in the city of Belo Horizonte and to investigate its association with interval between diagnosis and treatment. A cross-sectional study from hospital records of 715 patients undergoing treatment between 2010 and 2013. Cluster analysis was used to delineate the profiles from the variables: age, color of the skin, education and cost of treatment. The association between profiles and intervals was investigated using multinomial logistic regression. Five profiles were identified: A (white skin color, years of schooling >15 and treatment through private healthcare systems); B (white skin color, years of schooling = 11 and treatment through the Unified National Health System (SUS); C and D (brown skin color, years of schooling = 11 and < 8 respectively, and SUS); E (black skin color, years of schooling < 8, and SUS). Profiles B, C, D and E were associated with increased diagnosis-to-treatment intervals regardless of cancer staging upon diagnosis; and profile E had 37- fold higher chances of interval > 91 days (OR: 37.26; 95% CI:11.91-116.56). Breast cancer patients with social vulnerability profiles wait longer for treatment even after overcoming barriers to access oncology units.*

Key words *Breast câncer, Interval to treatment, Social vulnerability, Health profile*

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Introduction

Malignant tumors stand out among chronic non-communicable diseases given their high incidence, mortality and treatment costs[1]. Breast cancer is the most frequent type of cancer in women, and ranks first as cause of cancer-related deaths in developing countries, and second in developed countries[2]. Worldwide, over one million women are diagnosed with cancer every year, and 40% of cases will progress to death[3]. While mortality has actually dropped in high income countries, increased breast cancer incidence and mortality rates have been documented in countries such as Brazil, Colombia and Venezuela[2]. Availability of and access to diagnostic and therapeutic technology partly explain these differences[4].

The estimated incidence of breast cancer among Brazilian women in 2016 was 56.2 per 100,000. Breast cancer incidence tends to be higher in Brazilian capital cities[5] and is similar to that reported in developed countries; however, age-adjusted mortality rates are higher[1]. Despite higher five-year survival rates in the country over the last two decades (78% to 87%), under-reporting of severe cases may underestimate incidence and overestimate survival[6].

Delays in making diagnosis and starting treatment have been associated with worse prognosis and decreased survival[5]. Delays between disease suspicion and first appointment with a cancer specialist are often associated with patient´s characteristics, such as old age, low level of education, lack of information about the disease, lack of health insurance coverage and lack of financial resources to afford medical services[7-9]. On the other hand, delays in the intervals between appointment, diagnosis and treatment are often related to the healthcare context[10].

The interval between diagnosis and treatment initiation is of particular concern in several countries. A study carried out by the Organization for Economic Co-operation and Development (OECD) on healthcare system administration, between 2001 and 2004, recommended reducing this interval to a minimum ranging from seven to 30 days[11]. A review study showed that intervals of up to 60 days between confirmation of diagnosis and initiation of treatment, particularly in the initial stages of cancer, have no impact on disease-free survival or overall survival[10]. In 2014, in an effort to reduce this interval, the Brazilian Ministry of Health determined that cancer treatment must be initiated within 60 days of diagnosis[12].

Belo Horizonte, like other Brazilian southeastern capital cities, has one of the highest incidence rates of breast cancer in the country. The estimated number of new cases in 2016 was 1020 (75.6 per 100,000)[5]. The healthcare system has a duty to provide early diagnosis and timely access to treatment for all women without distinction[12]. However, inequities in access to and utilization of healthcare services are observed in Brazil[13,14].

Socioeconomic and demographic characteristics are known be important determinants of individual behavior when seeking and using health services[8,15], and have been associated with delayed diagnosis of several types of cancer, including breast cancer[16-19]. However, Brazilian studies investigating the relation between individual characteristics and diagnosis-to-treatment interval delays in patients enrolled in cancer treatment unit programs are scarce[20].

Therefore, this study has two objectives: (1) to identify the sociodemographic profiles of women undergoing breast cancer treatment in oncology units in Belo Horizonte, Minas Gerais, and (2) to investigate potential associations between the patient profiles and intervals between diagnosis and initiation of treatment, regardless of cancer staging. The hypothesis being tested is that greater social vulnerability profiles are associated with increased time to initiate treatment.

Method

A cross-sectional study involving a population of women with confirmed diagnosis of primary breast cancer and classified as C50 (International Classification of Diseases, version 10), regardless of age. All patients lived in Belo Horizonte and had received their first treatment (surgery, chemotherapy/hormone therapy or radiation therapy) in ten municipal oncology units, from 2010 to 2013. Of the 10 units included in the study, five were devoted exclusively for SUS patients, two exclusively for patients covered by private health insurance or private patients, and three were mixed (accessible to SUS and privately insured patients).

This study was based on sociodemographic, clinical and treatment data extracted from the hospital-based cancer registry Sis-RHC/INCA (*Sistema de Informação de Registros Hospitalares de Câncer*)[21]. Registration of all cancer cases in HCRs (hospital-based cancer registries) has been made compulsory by the Ministry of Health and must be complied with by all high complexity oncology assistance units and centers (UNACONs and CACONs)[22]. Despite issues regarding quality and completeness of records, the system is an important tool to plan actions regarding cancer surveillance, control and treatment in the country[23].

The inclusion of a postal code (ZIP code) in HCRs as of 2010 allowed the correct identification of patients' residence and served as a reference for determination of the study period.

A total of 1,405 records of women with a primary diagnosis of cancer and undergoing initial treatment were found. Indigenous and yellow women (n = 7) were present in small numbers and were therefore excluded; other exclusion criteria included cases with ZIP codes from different municipalities (n = 30) and patients with duplicate records (n = 31). Of the remaining 1,337 records, only those with complete data regarding the four variables selected for profile definition (n = 715) were retained; records with information gaps ("no information" - digit 9 or "missing data") were excluded. Selected variables did not differ significantly between women that remained in the study and those in the initial sample.

Breast cancer patient profiling was based on the following variables: "age" (continuous); self-reported "race/skin color" as w*hite, black or brown*; "schooling level" as *< 8 years, 8 years, 11 years* or ≥ *15 years*; "marital status" as *single, married/de facto relationship, widow* or *divorced*; "treatment financing" - *SUS* or *health insurance/ private coverage*.

Hypothesis verification was based on the dependent variable "diagnosis-to-treatment interval", defined as the number of days between diagnosis (histopathological confirmation) and initiation of cancer treatment (≤ *60 days, 61 to 90 days* or ≥ *91 days*).

"Cancer staging at diagnosis" was considered a potential intervening variable with respect to "diagnosis-to-treatment interval". Cancer staging was determined according to the TNM Classification of Malignant Tumors based on tumor size (T), presence and location of lymph nodes (N) and metastases (M)[24]. In this study, cancers were staged as "*in situ*" and I, II, III or IV, according to TNM category combinations.

Categorical variables were described by absolute and relative frequencies. Mean, median and standard deviation were calculated for the variable "age".

Profiles were delineated using cluster analysis (i.e., grouping of a set of cases/objects by similarity)[25]. The sociodemographic variables describing different and internally homogeneous groups of women were included in the model, as follows: "age", "race/skin color", "schooling level" and "treatment financing". The variable "marital status" had no (zero) significance for profile prediction and was therefore excluded. The two-step cluster method (SPSS® 19.0; *Statistical Package for Social Science for Windows, Inc., USA*), indicated for procedures involving large databases or databases comprising continuous and categorical variables, was used. The clustering models make the following assumptions: independent variables; normally distributed continuous variables; and ordinal or multinomial categorical variables. However, the procedure is quite robust to assumption violations[26,27]. The procedure is based on a series of agglomerative partitionings. First, pre-clusters corresponding to individual cases or small groups are formed; pre-clusters are then regrouped to yield final subprofiles according to an optimal number of clusters. The optimal number of clusters was determined using the Bayesian Information Criterium (BIC), as well as the log-likelihood distance measure (default program features).

Sociodemographic profiles were described and compared with respect to the variables "diagnosis-to-treatment interval" and "cancer staging at diagnosis", via analysis of differences in proportions (Pearson's chi square test or Fisher's exact test with Bonferroni correction). The level of significance was set at 5% ($p < 0.05$).

Multinomial logistic regression analysis was used to verify the power of associations between patient profiles and the variable "diagnosis-to-treatment interval", regardless of cancer staging upon diagnosis (level of significance, $p < 0.05$). The category time to treatment ≤ *60 days* was used as a reference for regression analysis, since it corresponds to the maximum waiting time to initiate treatment established by the Ministry of Health[12].

This study is part of the research project *Mulheres com câncer de mama em Belo Horizonte: perfil, trajetória e representações sobre o cuidado* [Women with breast cancer in Belo Horizonte: profile, trajectory and representations about care], approved by the Research Ethics Committee of the *Universidade Federal de Minas Gerais*.

Results

Study participants are described in Table 1. Mean age was 57 years; women with brown skin color, less than 8 years of education and married prevailed in the sample. In almost 75% of cases, cancer treatment was financed by SUS. Cancer stage upon diagnosis corresponded to 0, I or II in 53.7% of cases. Intervals of up to 60 days between diagnosis and treatment initiation were documented in 54.3% of cases, with mean and median intervals of 67.8 and 55 days, respectively.

Seven out of 715 records were classified as outliers and excluded from the analysis. The most significant variables for patient profile prediction (two-step clustering procedure) were "race/skin color" and "schooling level", followed by "treatment financing"; age was less important. Five different profiles were identified (Table 2).

Mean age varied little within clusters and was consistent with the age group with higher prevalence of this type of cancer (50 to 59 years)[5]. The following profiles were identified: (A) predominantly white women (68.8%) with higher levels of education (42.9%), treatment financed by health insurance/private (100%) and mean age of 56 years; (B) white women (100%) with up to 11 years of education (54.9%), treatment financed by SUS (100%) and mean age of 59 years; (C) predominantly brown women (100%), schooling level up to 11 years (53.3%), treatment predominantly financed by SUS (100%), mean age of 52 years; and (D) predominantly brown women (72.2%), < 8 years of education, treatment predominantly financed by SUS (95.3%) and mean age of 55 years. Finally, profile (E) black women, mostly with < 8 years of education

Table 1. Characteristics of women undergoing cancer treatment in Belo Horizonte, between 2010 and 2013.

Sociodemografic Characteristics	n = 715	%
Age (years)		
mean (± SD)	57.2 (±13.4)	-
median	56	
Skin color		
White	269	37.6
Black	78	10.9
Brown	368	51.5
Schooling level		
< 8 years	303	42.4
8 years	107	15
11 years	203	28.4
≥ 15 years	102	14.3
Marital status		
Single	195	27.3
Married/de facto relationship	316	44.2
Widow	130	18.2
Divorced	73	10.2
Missing data	1	0.1
Treatment financing		
SUS	528	73.8
Health insurance/private	187	26.2
Clinical and Care Characteristics		
Cancer staging at diagnosis		
In situ and I	178	28.0
II	206	32.4
III and IV	252	39.6
Total	636	
Missing data	79	11.0
Diagnosis-to-treatment interval (days)		
≤ 60	388	54.3
61 to 90	140	19.6
≥ 91	187	26.2

Source: RHC/SES-MG 2010 to 2013.

(65.3%), treatment financed by SUS (100%) and mean age of 59 years (Table 2).

Most women with profile A or B (86.5% and 53.7%, respectively) were treated within ≤ 60 days of diagnosis, compared to less than half of profile C, D or E women (43.6%, 43.4% and 36.1% respectively) initiated treatment within this time frame; and 41.7% of profile E women began treatment ≥ 91 days after diagnosis ($p < 0.05$). Significantly higher rates of stage III and IV cancer at diagnosis were documented in profile C, D and E women (48.1%, 45.3% and 50.0% respectively), while early cancer stages (*in situ* and I) were more common in profile A women (44.4%). Stage II cancer was diagnosed in 39.2% of profile B women (Table 3).

Profile B, C, D and E women had higher chances of initiating treatment within *61 to 90 days* or ≥ *91 days* after diagnosis compared to profile A women. Associations between profiles C, D and E and *61 to 90 days* intervals persisted following adjustment for cancer staging at diagnosis. All of these profiles were associated with ≥ *91 day* intervals; chances of initiating treatment within this time frame were up to 37 times higher in profile E compared to profile A (OR: 37.26; CI95%:11.91-116.56) (Table 4).

Discussion

Cluster analysis allowed identifying five different groups of women with an apparent continuum between race/skin color and schooling level, i.e., white women with higher levels of education and black women with low levels of education at opposite ends of the spectrum. Also, treatment financed by health insurance/private care set profile A apart from profiles B to E.

Multivariate analysis results sustain the initial hypothesis that the interval between breast cancer diagnosis and initiation of treatment is longer for women with more vulnerable social characteristics, regardless of disease staging.

There is a clear consensus in the literature that the shorter the interval between diagnosis and treatment, the better the prognosis and the longer the survival of the patient. Prompt intervention is paramount for treatment efficacy in more advanced stages of the disease, or for patient comfort in cases where treatment is palliative[28]. Cancer staging had little impact on diagnosis-to-treatment intervals in this study. However, social characteristics associated with different profiles were so robust that interval differences persisted following adjustment for cancer staging. Still, it should be noted that other potential confounding factors, such as health-related behaviors and obesity were not included in the analysis (missing data).

Table 2. Profiles ofwomen receiving firstbreast cancer treatment, according to sociodemographic and economic characteristics. Belo Horizonte, 2010 to 2013.

Characteristics	Profile A n=170 (23.8%)	Profile B n= 82 (11.5%)	Profile C n= 149 (20.8%)	Profile D n= 235 (32.9 %)	Profile E n= 72 (10.1 %)
Age (years)					
mean (± SD)	56 (±13)	60 (±13)	52 (±12)	55 (±14)	59 (±14)
median	56	59	52	56	57
Skin color (%)					
White	68.8	100.0	0.0	29.8	0.0
Black	0.0	0.0	0.0	0.0	100.0
Brown	31.2	0.0	100.0	70.2	0.0
Schoolinglevel (%)					
< 8 years	11.2	0.0	0.0	100.0	65.3
8 years	7.6	30.5	37.6	0.0	16.7
11 years	38.2	54.9	53.0	0.0	18.1
≥ 15 years	42.9	14.6	9.4	0.0	0.0
Treatmentfinancing (%)					
SUS	0.0	100.0	100.0	95.3	100.0
Health insurance/private	100.0	0.0	0.0	4.7	0.0

Source: RHC/SES-MG/INCA 2010 to 2013.

Table 3. Profile distribution of women with breast cancer according to clinical and care characteristics. Belo Horizonte, 2010 to 2013.

Characteristics	Profile A	Profile B	Profile C	Profile D	Profile E	p value
Diagnosis-to-treatment interval (days)						0.000
≤ 60 days	**86.5** $_{\mathbf{a}}$	**53.7** $_{\mathbf{b}}$	**43.6** $_{\mathbf{c}}$	**43.4** $_{\mathbf{c}}$	**36.1** $_{\mathbf{c}}$	
61 to 90 days	11.2 $_{a}$	18.3 $_{a\ b}$	20.8 $_{b}$	24.3 $_{b}$	22.2 $_{b}$	
≥ 91 days	2.4 $_{a}$	28.0 $_{b}$	35.6 $_{b}$	32.3 $_{b}$	**41.7** $_{\mathbf{b}}$	
Cancer staging at diagnosis						0.000
In Situ or I	**44.4** $_{\mathbf{a}}$	25.7 $_{b}$	19.5 $_{b}$	25.5 $_{b}$	19.1 $_{b}$	
II	34.7 $_{a}$	**39.2** $_{\mathbf{a}}$	32.3 $_{a}$	29.2 $_{a}$	30.9 $_{a}$	
III or IV	20.8 $_{a}$	35.1 $_{b}$	**48.1** $_{\mathbf{b}}$	**45.3** $_{\mathbf{b}}$	**50.0** $_{\mathbf{b}}$	

Source: RHC/SES-MG/INCA 2010 to 2013.

Pearson's chi-square test or Fisher's exact test with Bonferroni correction. Different superscript letters (a, b, c, d) denote different category subsets with similar proportions ($p < 0.05$).

Table 4. Associations between breast cancer patient profile and intervals between diagnosis and initiation of treatment. Belo Horizonte, 2010 to 2013.

PROFILE	Interval 61 to 90 days	Interval ≥ 91 days	Interval 61 to 90 days	Interval ≥ 91 days
	OR (IC 95%)		OR (IC 95%) ajustada	
Profile A	1,00	**1,00**	**1,00**	**1,00**
Profile B	2,64 (1,24 - 5,62)	19,21 (6,31 -58,52)	2,17 (0,97 - 4,85)	**15,31 (4,93 - 47,6)**
Profile C	3,69 (1,94 - 7,01)	29,97 (10,41 -86,27)	**3,17 (1,59-6,33)**	**25,85 (8,815 - 75,78)**
Profile D	4,32 (2,43 - 7,70)	27,38 (9,71 - 77,21)	**3,7 (1,97 -6,93)**	**25,28 (8,86 - 72,1)**
Profile E	4,76 (2,17 - 10,44)	42,40 (13,78 - 130,42)	**3,69 (1,60 - 8,53)**	**37,26 (11,91 - 116,56)**

Souce: RHC/SES-MG 2010 to 2013.

OR (CI95%): Odds ratio (95% confidence interval). Adjusted OR (CI 95%) = Odds ratio adjusted for "cancer staging at diagnosis" using multinomial logistic regression; the interval corresponding to "up to 60 days" was used as a reference in the analysis.

The findings of this study could be compared to those of a retrospective cohort including 137,593 women seen at SUS facilities from 2000 to 2011, and listed in Sis-RHC. In that study, diagnosis-to-treatment intervals of up to 60 days were documented in more than 50% of cases, and delays were more common among nonwhite women with less than eight years of education and (different from this study) early stage cancer[20].

Social inequalities – or the inequalities that, when associated with individual characteristics such as schooling level, income and race, among others, place some groups at disadvantage compared to others[29] – may translate not only into worse health conditions, but also into inequalities in access to and utilization of services. The use of healthcare services is a complex resulting from interactions between several factors, including socioeconomic, demographic, cultural and psychic characteristics, health-related needs, characteristics of services and of healthcare professionals and geographic and social access availability, among others[30]. These factors may have different impacts on access to health depending on the type of care (prevention, cure or rehabilitation), service (inpatient or outpatient) and level of complexity (primary, specialized or high complexity) involved[31]. That said, differences in diagnosis-to-treatment intervals between the five profiles described in this study may reflect inequalities in utilization of highly complex oncologic services, resulting from interactions between the following conditions: lower levels of education, brown or black race/skin color and lack of access to health insurance/private appointment.

Differences in breast cancer diagnosis and treatment within the public and private healthcare systems were reported, and demonstrated advantages of the private system[32-34]. In a multicenter study, Liedke et al. (2013) observed higher rates ($p < 0.001$) of advanced disease upon diagnosis and shorter survival in stage III and IV cancers ($p < 0.002$ and $p < 0.008$, respectively) in SUS patients compared to privately insured patients[32]. Aside from expected differences between women seen by health insurance/private networks and SUS facilities, this study suggests a synergistic effect between brown or black race/skin color and low levels of education leading to poorer outcomes among women receiving care at SUS. Despite the not precise classification of the variable "race/skin color" in this study, the complex relation between race as a social construct and socioeconomic conditions has been demonstrated and is thought to be associated with poor health outcomes[35,36].

Marmot (2005) suggested that ethnic inequalities in health are largely a reflex of socioeconomic factors, such income and level of education[37]. Moreover, there is evidence to show that racial harassment and discrimination experiences, alongside the perception of living in a discriminative society, contribute to inequalities in health[38]. The issue was addressed by Travassos and Bahia (2011) in an article suggesting that affirmative policies in Brazil reinforce subgroup identities (racial, gender and others), promoting stigma and shifting the focus away from the true causes of discrimination to the institutional domain; discrimination would be "fundamentally derived from relationships between healthcare professionals and patients"[39].

Different from the situation in the United States, skin color related iniquities are not commonly investigated in health literature, in spite of expressive social inequality between black and white citizens[35,40]. The relevance of the topic has been widely demonstrated. Discrimination in access to prenatal care and delivery based on education level and skin color, in both private and public health care services has been reported[41]. Black women are also more likely to present with advanced stages of breast cancer at diagnosis[8]; moreover, studies investigating diagnosis-to-treatment intervals pointed to associations between non-white skin color and treatment delay in Brazil[20].

Several authors have investigated the mechanisms through which social inequalities may affect health[34,37,42]. However, little is known about the impact of such inequalities on healthcare services utilization once access has been gained. Therefore, further investigation of the impact of social inequalities on the healthcare trajectory of breast cancer patients, particularly of those seen at the public health system, is warranted for deeper understanding of the results of this study.

This study has some limitations that should be mentioned. The use of an administrative database with a high percentage of incomplete records limits the applicability of our results to the study population, which does not reflect the total number of women undergoing breast cancer treatment in Belo Horizonte during the study period. It is worth mentioning the characteristics of patients included in the final analysis and those in the initial sample were not statistically different. However, the quality of data entry in medical registries of Sis-RHC must be improved, given the potential contribution of such databases for cancer surveillance and organization and planning of oncology services.

This is a cross-sectional study; nevertheless, the possibility of reverse causality (i.e., the disease having impacted sociodemographic profiles) is highly unlikely, since only women in the in the early stages of cancer treatment were included in the sample. Data concerning patient income were missing; therefore, "treatment financing" was used as a proxy for individual socioeconomic status, in light of the association between private healthcare services utilization, higher levels of education, formal employment and personal assets in Brazil[43].

For the most part, diagnosis-to-treatment intervals in this sample fell within the timeframe set by the Brazilian Ministry of Health (up to 60 days). Still, this study revealed interval differences placing women with more vulnerable social profiles at disadvantage even after the barriers to accessing oncology treatment units are overcome.

Collaborations

ALLV Cabral, L Giatti and ML Cherchiglia worked on the methodology, data analysis, design and final writing of the article; ALLV Cabral and C Casale worked on data collection and processing; all authors worked on critical review of the article, read and approved the final version.

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Article submitted 09/08/2016
Approved 16/03/2017
Final version submitted 18/03/2017