Breast cancer in pre-menopausal women in West Africa: Analysis of temporal trends and evaluation of risk factors associated with reproductive life ☆

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ABSTRACT

Background: In West Africa, trends and risk factors for breast cancer (BC) have been rarely studied.
Methods: Here we have analyzed trends of BC over two periods in two population-based cancer registries, in Mali-Bamako (1987–1997; 1998–2009) and in The Gambia (1988–1997; 1998–2006). We have conducted a case–control study (n = 253 cases, 249 controls) on risk factors associated with reproductive life stratified by menopausal status in Bamako.
Results: Between the two periods, BC incidence rates increased by 20% (incidence rate ratio (IRR) 1.20 (95% CI [1.07−1.35])) in Bamako, with an annual percentage change of 2% (95% CI [0.4−3.6]). The increase was of 30% in women under 55 years (IRR 1.30 (95% CI [1.14−1.60])). A similar pattern was observed in The Gambia for women under 50 years (IRR 1.47 (95% CI [1.07−2.01])). Overall, pre-menopausal breast cancer was predominant in both countries. In contrary to what is well established, case−control study showed that late age at menarche (>14 years) increased the risk of BC among pre-menopausal women (OR: 2.02 (95% CI [1.08−3.78])) while it tended to be protective in post-menopausal women (OR: 0.61 (95% CI [0.29−1.29])). Later age at a first pregnancy (>20 years) was associated with a reduction of risk in pre-menopausal women (OR: 0.41 (95% CI [0.18−0.89])).
Conclusion: These results indicate that the burden of pre-menopausal BC is increasing in West African countries. These cancers appear to be associated with distinct reproductive risk factors, highlighting the need for better understanding the biological bases of early BC in African populations.

Introduction

Worldwide, breast cancer (BC) is the most common cancer among women.[1] This cancer shows important differences in age-related incidences in relation with geography and socio-economic status, perhaps reflecting differences in population structures with a lower average life expectancy among African women, as well as the possible influence of risk factors associated with reproductive life and hormonal status. Other factors such as genetic susceptibility may also play a role. Although breast cancer incidence rate is more than 2.4-fold higher in developed regions (66.4 compared to 27.3 in less developed regions) mortality rate is only 1.4 higher compared to less developed regions (15.3 in more developed regions compared to 10.8 in less developed regions),[2] suggesting that forms of BC with poor outcome are more equally distributed among populations. In recent years, ductal carcinoma of the breast (which is the most common form of invasive breast cancer[3,4]) has been shown to consist into distinct molecular subtypes with different prognosis and responses to therapy, and may

correspond to different forms of disease, which differ by their risk factors, their age of occurrence and their prognosis.

In Sub-Saharan Africa, 70% of breast cancer patients present at age of 50 years or less, and most of them occur before or around menopause. The highest incidence is observed in multiparous women aged 40–44 years (average number of children: 5).[5,6] Most of these early cancers seem to be more frequently negative for estrogen and progesterone receptors (ER/PR).[7,8] Nevertheless, a study by Adebamowo et al. showed that the majority of women with BC presenting at the oncology clinic of the University College Hospital of Ibadan in Nigeria were positive for ER and PR.[9] In Caucasian/ Western women, most of BC occurs after the menopause and are ER/PR+, whereas parity is a well-defined protective factor. Noteworthy, in the US, early onset of BC is more common among African American as compared to Caucasian American women and these cancers tend to be negative for ER/PR. This type of BC has a worse prognosis than BC arising in older women, independent of the ethnic background.[10]

Reliable data on cancer incidence are scarce in West Africa. In this study, we have analyzed data from two population-based cancer registries, the National Cancer Registry (NCR) of The Gambia and the cancer registry of Mali (Bamako) to assess BC incidence rates and their temporal variations. Using a hospital-based data collection in Bamako, we have designed a case–control study in order to assess the effects of several reproductive life factors on the risk to develop breast cancer.

Methods

Cancer registration data

Mali is one of the largest countries of Africa (1,241,238 km^2), with an estimated population of 14,517,176 in 2009. According to the National Institute of Statistic of Mali, in 2006, the average number of children per women was 6.6 and the life expectancy was 65.4 years (http://www.instat.gov.ml/voir_domaine.aspx?dom=5) but, according to the CIA world factbook, the life expectancy in Mali was 53.06 years in 2011 (https://www.cia.gov/library/publications/ the-world-factbook/geos/ml.html). Mali has a pyramidal health care system. The base of the pyramid consists of the community health centers specialized in primary health care, followed by the reference centers (6 in Bamako, one for each township) specialized in surgery, gynecology, pediatric, etc. followed by the regional hospitals (8 in the country, one for each region) and, at the top level, three university (general) hospitals, two of which are located in Bamako (the university hospitals of Point G and Gabriel Touré) and the third one in Kati (the university hospital of Kati). Currently, there is no cancer center in Mali, but, a radiotherapy center is under construction in Bamako. A population-based cancer registry covering the district of Bamako has been established in 1986. This registry covers the capital city (2009 population estimated at 1,809,106 http://www.instat.gov.ml/documentation/bamako.pdf) and its immediate surroundings (including the city of Kati, within 15 km of Bamako). The procedure of data collection of the cancer registry of Mali has been described in a previous study.[11] Cases are notified by in-charge nurses at in- and out-patient services, and details of cancer cases diagnosed by the medical staff are recorded. Completeness of records is verified against other documentary sources by the registry clerks (pathology interns) who actively collect on a monthly basis all cases of cancer diagnosed in all medical service units (public or private clinics and hospitals) and in the death registry. Items of information collected for each cancer case are: source of information (e.g. hospital/service), hospital or laboratory number, names, age, sex, usual residence, ethnic group, date of diagnosis, site of the tumor, most valid method of diagnosis

(e.g. histology/cytology, clinic, death certificate etc.), topography, morphology, date of diagnosis and causes of death (if available). Data are computerized using the software CanReg 4. Tumors are coded according to ICD-O third edition. The cancer registry is maintained by pathologist interns under the supervision of trained pathologists and is located since 2010 in the department of pathology of the university hospital of Point G (Bamako).

On average 449 cases are collected every year with a minimum of 294 cases collected in 1987 and a maximum of 743 in 2006. Overall, 45% of cases are collected in Point G hospital, 40% in Gabriel Touré hospital and 10% in private structures.

The Gambia is the smallest country of continental Africa, with a population of 1,360,681 in 2003, and an average number of 5.13 children per women (http://www.accessgambia.com/information/ demographic-statistics.html; http://www.accessgambia.com/infor mation/population.html). According to the World Health Organization, in 2009, the life expectancy was 58 years for men and 61 years for women (http://www.who.int/countries/gmb/en/). A National Cancer Registry (NCR) covering the entire population was created in 1986. As in Mali, the registry performs active monitoring of all medical service units on a regular basis. The NCR is located in the office of the Gambia Hepatitis Intervention Study (GHIS), a Hepatitis B vaccination intervention trial jointly managed by the International Agency for Research on Cancer, the Medical Research Council of UK and the Government of the Republic of The Gambia. The methods and characteristics of the NCR of The Gambia have been extensively described elsewhere.[12]

For the purpose of this study, cancer incidence data from 1987 to 2009 were used. The first years of registration were excluded due to collection bias (1986 for Bamako and 1986–1987 for The Gambia). The rest of available years of cancer registration activity (1987– 2009 for Bamako and 1988–2006 for the Gambia) were arbitrary divided into two periods (1987–1997 and 1998–2009 for Bamako; 1988–1997 and 1998–2006 for The Gambia).

Population data

The cancer registry records cancer patients who are residents of Bamako district, diagnosed in medical services based in Bamako and/or its immediate surroundings and only a fraction of patients from other cities and villages referred to Bamako for diagnosis. Therefore, breast cancer patients who were residents of locations outside of the district of Bamako were excluded from incidence data analysis. Bamako residents are defined as being in residence for at least 3 months in the district prior to diagnosis.[11]

Demographic data for Bamako district in person-years from 1987 to 1997 were obtained by the interpolation of data extracted from the national censuses of 1976 and 1998. For years 1999–2009, we have used person-years estimated from the National Institute of Statistics of Mali (http://www.instat.gov.ml "Prospects of the resident population in Mali (1999–2024), Central Census Office, February 2003"). For The Gambia, annual population data were interpolated and extrapolated from demographic censuses of 1993 and 2003 as described previously.[13]

Case–control study

Since 2005 an independent case series of women affected by breast diseases has been developed by the staff of the cancer registry, with parallel collection of information on matched women free of any breast diseases. Cases were identified after the reception of biopsy in the pathology laboratory for histological confirmation. They were then traced back to their hospital of referral and/or place of residence where a standard structured questionnaire was administered to volunteer patients by the staff of the cancer registry and to