Project title: Factors associated with delayed diagnosis of breast cancer and the impact of delays on the stage of cancer: A Bangladesh perspective

**Principal Investigators**

1. Mohammad SorowarHossain PhD, Biomedical Research Foundation, Bangladesh
2. Waheed Akhtar, Assistant Professor, Radiation Oncology Dept, National Institute of Cancer Research and Hospital

**Co-Principal Investigators**

1. Enayetur Raheem PhD, Biomedical Research Foundation, Bangladesh
2. Ferdous Shahriar Sayed MD, Oncologist, United Hospital Ltd, Bangladesh
3. Nova Ahmed PhD, Biomedical Research Foundation, Bangladesh
4. Professor Mahbubur Rahman, National Institute of Cancer Research and Hospital

**Theme :** Chronic Diseases Assessment

**Budget:** XX

**Duration:** 1 year

**Background**

Even though the incidence of breast cancer in developing countries is lower compared to their Western counterparts, it is on a rapid rise. According to GLOBOCAN estimates, more than half (52.9%) of 1.67 million new breast cancer cases was diagnosed in developing countries in 2012[1], while it was only 35% in 1980[2]. Although breast cancer is mainly a disease of postmenopausal women (≥ 50 years) in developed countries, almost half of all breast cancer cases (45%) in developing countries were diagnosed in women of reproductive age (15-49 years) in 2010 [2]. The mortality of breast cancer is significantly higher in developing countries than in high-income countries. Nearly 62% of breast cancer associated deaths occurred in developing countries in 2012[1].

In Bangladesh, approximately 45 million women are at reproductive age, while 13.5 million women are ≥ 50 years old [3]. Due to nonexistence of population-based cancer registry, the overall epidemiology of breast cancer is mostly unknown [4]. However, according to GLOBOCAN estimates based on the extrapolation of Indian data, 14,836 new breast cancer cases were diagnosed in 2012, with an age-standardized incidence rate (ASR) of 21.4 per 100,000[1].This figure is likely to be underestimated since many cases are missing due to lack of awareness, low level of education, misconceptions, poor socioeconomic status, insufficient access to health care as well as poor governance. Since there is no national cause of death registry in Bangladesh and patient’s follow-up system in hospitals, it is not possible to know about the mortality and survivorship of breast cancer respectively. However, a maternal health survey estimated that cancer was responsible for 21% of all women’s deaths at reproductive age range [5]. Another verbal autopsy study showed that 62% of all breast cancer associated deaths were in women less than 50 years old [6].

**Rationale**

Women are the key driver of Bangladesh economy and its social transformation through their enormous contribution in clothing industries, microcredit and microfinance-based development programs. Healthy women are vital for healthy families and communities. However, women’s problems generally get less priority in the society. None of the breast cancer cases is detected by organized screening in Bangladesh. Almost all breast cancer cases are detected clinically. Most of the patients (around 90%) seek medical attention at the advanced stages i.e. stage III and stage IV [4]. Delays in diagnosis and treatment of breast cancer are likely to result in advanced disease and low survival. Early diagnosis and treatment is associated with better prognosis when compared to worse outcomes related to significantly delayed diagnosis [7, 8]. Treatment of breast cancer diagnosed at a later stage is also associated with higher morbidity, due to more aggressive and disfiguring approaches, and is more expensive. Thus the reducing this delay is critical for better survival and outcome.

**Research objectives**

We hypothesize that some socioeconomic factors will be predictors of diagnosis delays. We also hypothesize that late- stage disease condition would be associated with delayed diagnosis. In both cases, analysis will be performed after adjusting for the sociodemographic and clinical factors.

1. Specifically, we would like to know--the factors associated with breast cancer diagnosis delay and how do socioeconomic determinants affect delay in diagnosis.
2. The impact of diagnosis delay on the stage of cancer as measured by size of the tumor.
3. Social implications regarding the delay (e.g., lack of awareness, support from family members etc.)
4. The study on the demography that is affected most through the delayed detection process (economically backward or not)

**Study design and methodology**

A multi-center retrospective cross-sectional study will be conducted in two primarily cancer care facilities located at Dhaka city-the capital of Bangladesh. Women aged 18 and older will be the target population. Participants will be recruited from the two providers following inclusion-exclusion criteria described in the following section.

Due to lack of patient registries, a convenience sampling methodology will be used. Patients visiting these facilities will be potential participants of the study. If they meet study inclusion-exclusion criteria, they will be requested to participate in the study. No compensation for participation will be given. Verbal informed consent will be taken prior to collecting data as per study protocol.

Delayed diagnosis will be measured as the difference in months between first symptom onset to actual diagnosis of breast cancer. Stage of cancer will be measured by TNM system.

Univariate and multivariate analyses will be performed to measure association between sociodemographic and clinical measures on the presentation delay. Since the cutoff (>6 months) is somewhat arbitrary or based on experience, sensitivity analysis will be performed with different cutoffs to study stability of the estimates. Similar process will be carried out for finding association between clinical and sociodemographic factors on diagnosis delays. Results will be presented in terms of crude and adjusted odds ratio and confidence intervals for odds ratios.

***Participating centres:*** We will conduct our study in National Institute of Cancer Research & Hospital (NICRH) and United Hospital Ltd. NICRH is the only specialized public hospital dedicated for cancer treatment in Bangladesh, while United Hospital is one of few well-equipped private hospitals that serve cancer patients. However, due to high treatment cost, private hospitals are financially out of reach for most Bangladeshis. Most of the patients are referred to NICRH and United Hospital after a cancer diagnosis (presumptive or confirmed) at another facility. None of the breast cancer cases is detected by organized screening in Bangladesh. Almost all breast cancer cases are detected clinically.

### *Patients :* In this study, we will survey women aged ≥18 years with suspected breast cancer and patients diagnosed with breast cancer are being referred to our participating centres. These patients will only be included in the study if their initial stage is documented in the medical records or if their initial stage is unavailable but the initial diagnosis is made no more than 6 months prior to staging at our facilities. Face-to-face interview with a structured questionnairewill be conducted by previously trained interviewers who are not involved in the clinical management of the patients.

### *Key variables:*Total delay is defined as the time from identification of the problem (either through symptoms or screening) to the beginning of cancer treatment; patient delay is defined as the time from identification of the problem to the first medical consultation; and provider delay is defined as the time from the first presentation (first medical consultation) to the beginning of cancer treatment. Date of symptom discovery and date of presentation will be obtained from the patients through the questionnaire, whereas the dates of beginning of treatment will be obtained from the hospital charts. When patients will be unable to provide a date for when their symptoms began or the first provider visit, they will be asked to provide a month or month range and year. If they provide a month, the date will be estimated as the 15th of that month; if they provide a month range, the estimated date will be the midpoint between the 15th of those months. If patients are only able to provide a year, the estimated date will be coded as June 30th of that year.

The questionnaire covers demographic and clinical information and information regarding women’s experiences with their breast problem, including the dates of the initial symptoms and first healthcare facility presentation. We also asked patients which factors are the reasons for the delay.

***Data analysis:*** Data will be securely entered into an electronic data capture system (REDCap) with built in functionalities for maintaining data quality. The investigators and supervisors will review all data forms for accuracy, consistency and completeness. Data will be periodically checked by running frequency distribution and cross-tabulation. Data will be analyzed by data scientists/biostatisticians. SAS statistical software will be used for data management and analysis.

**Ethical consideration**

Our study protocol will be approved by the Ethical Review Committee of National Institute of Cancer Research and Hospital. No monetary incentives will be offered to the participants. Data will be securely stored on a computer which will be password protected. Privacy and confidentially of the collected information will be strictly maintained. No one other than the members of the study team will have access to the collected information. Before analysis, data will be deidentified by removing personally identifying information. Care will be taken during the presentation of the research findings so that the information presented is sufficiently aggregated to ensure that no individual can be identified. The study does not pose any major risk to the respondents or to the researchers. However, there is always some risk involved when working with human subjects.

**Limitations of the study**

This is a cross sectional study where participants were selected based on a non-random survey sampling method. Thus, the findings can only be relevant to the study participants and cannot be generalized to the entire population. However, the study results would serve as a baseline for future studies.

**Expected outcome**

1. Findings of our proposed study would promote the importance of breast cancer awareness and early detection.
2. Our study findings will be instrumental for developing smart device-based breast cancer early detection apps to make breast cancer awareness.
3. The outcome of our study will enrich the global knowledge on breast cancer from this part of the world.

**References**

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**Questionnaire : Breast Cancer Diagnosis Delay Study**

**Sociodemographic variables**

1. Form Number / Identification Number
2. Date of Interview (today’s date)
3. Patient’s Name
4. Contact: XX, XX
5. Current place of residence (City)
6. Current place of residence (District)
7. Education (highest level completed) (primary, secondary, higher secondary, university)
8. Husband’s education (Primary, secondary, higher secondary, university)
9. Age in years (whole year)
10. Home district (permanent residence)
11. Marital status (single/widowed/never married/ married)
12. Access to communication and media (Select ALL that apply)
    1. have access to social media,
    2. own a smartphone,
    3. own a computer
13. Family history of breast cancer: yes/no

**Estimation of delays and associated factors for delays**

**1. Discovery of health problem**

1.1 When did you first realize that you haveproblem with your breast?

(Enter date in dd-mm-yyyy format)

1.2 What was the first symptom you noticed? (select ALL that apply)

Lump /Skin changes/Breast pain/Nipple discharge/Bone pain/ Others :………………

1.3 Did you feel shame to discuss about problem? Yes/No

**2. Perception of discomfort**

2.1 When you noticed for the first time, did you think this might be serious? (Select ONE)

Nothing serious

Somewhat serious

Serious

Very serious

2.2 How much did you worry at that time? (Select ONE)

Not at all

Some what worried

Normal worried

Very much worried

2.3 When you noticed symptom for the first time did you think that it could be cancer? (Yes/No)

2.4 Have you experienced following discomfort?

1. Lump in the armpit, neck or trunk? Yes/No
2. Pain in breast (Yes/No)
3. Pain in arm on the same side as the affected? (Yes/No)
4. Color changes in the breast skin (like red, brown or purple)? (Yes/No)
5. Ulcer or sore on the skin of the breast? (Yes/No)
6. Itching in the breast?(Yes/No)
7. Changes in breast shape?(Yes/No)
8. Liquid or blood came out from the nipple?(Yes/No)

2.5 What was it that made you decide to go to a doctor?

1. Felt discomfort
2. It got worse
3. Suggested by a friend or relative
4. Suggested by spouse

2.6 Why did not seek attention sooner? Please respond for each of the queries (Yes/No)

*Emotional barriers*

1. Because you thought that the problem would disappear by itself? Yes/No
2. Fear/ too scared?(Yes/No)
3. Too embarrassed(Yes/No)
4. Negligence or carelessness?(Yes/No)
5. Embarrassed to talk about symptom?(Yes/No)

*Practical barriers*

1. Lack of money to use health services? (Yes/No)
2. Too busy?(Yes/No)
3. Because I had to take care of the family (children, elderly or sick)?(Yes/No)

*Health-Service barriers*

1. Because I did not know where should I go?
2. Difficult to make appointment?(Yes/No)
3. Difficult to arrange transport?(Yes/No)
4. For some other reason? \_\_\_\_\_\_\_\_\_\_\_\_\_

**3. Use of health services**

3.1 What medical centerdid you visit before coming to the cancer treatment centre? (Select ONE)

1. Physician (Private clinic/hospital)
2. General hospital
3. Upzila health complex
4. NGO clinic
5. Pharmacy
6. Others (please specify)

3.2 Do you remember the date when you first visited a medical center?

(Enter date in dd-mm-yyyy format)

3.2 Have you tried to treat at home or taken alternative remedy for this problem? Yes/No

**4. Family a support**

4.1 Who is the person you talked first about your health problem? (Select ONE)

Husband/Mother/Sibling/Friend/Other/None

4.2 Who recommended you to consult with a doctor? (Select ONE)

1. Husband/Mother/Sibling/Friend/Others\_\_\_\_\_\_\_\_/No one

4.3 Did you fear or uncomfortable to tell about the problem to your spouse? Yes/No

4.4 Did you receive support from spouse after diagnosis? yes/no

4.5 If no, did you receive negative behavior from spouse? (Yes/No)

4.6 Did you receive support from social circle? yes/no

4.7 If no, any suggestions on what could be different?

[open ended]

**5. Knowledge and practices of early detection of cancer**

5.1 Did you usually check your own breasts? (Yes/No)

5.2 Before this health problem, did a doctor or nurse check your breasts Yes/No

5.3 Before your breast problem have you heard of mammography or mammogram? Yes/No

5.5 Did you know about breast cancer before? 5.4 Do you know someone close to you who had or has cancer? Yes/No (THIS IS ABOUT CANCER, NOT BREAST CANCER)

5.6 Any particular information you wish you knew before and want others to know?

**6. Pathological status after diagnosis of breast cancer**

: T……… N ……… M………. Tumor size :……………………..cm

Stage I/Stage II/Stage III/Stage IV

Interviewed by :