

## Original Article

# HUMAN ERROR CAUSING INAPPROPRIATE MANAGEMENT OF PREGNANCY-ASSOCIATED BREAST CANCER, LITERATURE REVIEW AND EXPERIENCE IN NIGER DELTA UNIVERSITY TEACHING HOSPITAL, OKOLOBIRI, BAYELSA STATE, NIGERIA

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## Abstract

**Background:** Breast cancer is the commonest cancer in women in Nigeria. Pregnancy Associated Breast Cancer (PABC) is breast cancer occurring in pregnancy up to one year after delivery. Due to some misconceptions, mistakes occur in the management of these patients leading to poor outcomes. There may be difficulties in the diagnosis of PABC due to the clinical features being mistaken for the normal physiologic changes of pregnancy. The physiologic changes may interfere with radiological and pathological interpretations. Fine needle aspiration cytology (FNAC) or a trucut biopsy confirms the diagnosis. There have been debates on maternal versus foetal wellbeing in PABC. Chemotherapy is safe after 10 weeks of pregnancy when organogenesis is complete. Delaying chemotherapy till after pregnancy worsens the prognosis. Hormonal treatment is contraindicated in PABC.

**Method:** This is a retrospective observational study of cases of PABC at the Niger Delta University Teaching Hospital, Okolobiri, Bayelsa State, Nigeria, from January 2019 to January 2021.

**Results:** Seven cases were seen with ages ranging from 28 to 37. All patients presented with breast lumps. Diagnosis was by FNAC and trucut biopsy. None of the patients received care for the cancer during pregnancy as they were advised by their doctors not to and to present after delivery due to the perceived harmful effects of treatment on the foetus. All seven patients presented with advanced stage disease after delivery. They all received chemotherapy and hormonal therapy. Eventually all patients were lost to follow up.

**Conclusion:** Patients diagnosed with PABC in peripheral hospitals should be referred for specialist care. Treatment modalities like surgery and chemotherapy are feasible in PABC and should not be unduly delayed. Continuing education on the topic and feedback to colleagues at peripheral hospitals should be ensured.

**Keywords:** Breast Cancer, Pregnancy, Pregnancy-associated Breast Cancer, Human error, Inappropriate treatment

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## INTRODUCTION

Breast cancer is the most common cancer affecting women in Nigeria accounting for up to 50% of all cancer cases.<sup>1</sup> The role of human error in causing adverse events in the delivery of medical care was highlighted in the 1990s by Reason<sup>2</sup> who broadly classified human error into failures of execution, termed *slips* and *lapses*, and failures of intention, termed *mistakes*. There is the need for obstetrical care providers to be familiar with the

presenting signs and symptoms.<sup>3,4</sup> Pregnancy associated breast cancer (PABC) is defined as breast cancer diagnosed during pregnancy or up to 1 year of delivery.<sup>3,4</sup> It is a common malignancy in pregnant women and accounts for 3% of breast cancers in women worldwide.<sup>5,6</sup> It is responsible for about 21% of all premenopausal breast cancer diagnosis found in women in Nigeria.<sup>7</sup> Over 90% of patients with breast cancer in pregnancy or during lactation present with a palpable mass, and most often

(84%) these are self-reported by patients.<sup>1,3,7,6</sup> The management of PABC can be challenging because of the difficulties associated with its diagnosis and treatment.<sup>1-6</sup> The clinical manifestation may be obscured by the physiologic changes of pregnancy and lactation, and breast engorgement and density of the breast may make radiologic investigations misleading.<sup>8</sup> Presence of rapidly dividing cells of the pregnant or lactating breast that mimic malignant features may also alter pathologic decisions.<sup>9</sup> The treatment of PABC is also hindered by conflict between fetal and maternal wellbeing.<sup>4,6,7,8</sup> Symptoms of PABC are often recognized later than their non-pregnant counterparts, and this may be adduced to the fact that many pregnant women interpret pathologic bodily changes as being physiologic.<sup>4,6,7,8</sup> Although PABC is not a rare event, reports are scanty because of the challenges associated with the study population. Majority of the available reports are review articles and case reports.<sup>5,7,8,10</sup> In this retrospective study, we report our experience with the management of PABC in a tertiary health centre in Nigeria highlighting some errors leading to delay in referral and treatment which were caused the referring doctors.

## LITERATURE REVIEW

Judgmental errors are usually discussed at conferences and are referred to as "errors" that are the result of inadequate knowledge or failure to employ knowledge<sup>2</sup>. These errors include failure to obtain appropriate consultation and failure to order the proper tests or to interpret them properly.<sup>2,3</sup> The obvious way to correct these deficiencies is education.<sup>4,6,8,10</sup> We as surgical educators spend inordinate amounts of time in such educational pursuits.<sup>8,9,11</sup> If there are unhappy consequences that are predictable, such as the death of terminally ill patients, we spend relatively little time in discussion.<sup>11</sup>

The incidence of PABC is said to be increasing and is related to the increasing age at first pregnancy due to postponed childbearing for academic reasons.<sup>1,5,7,8</sup> Delayed first birth is a risk factor for breast cancer.<sup>1,5,7,8,11</sup> Every year of increase in the age of first delivery above 25 years leads to a 3.5% to 5% increase in lifetime breast cancer risk.<sup>10,11</sup> It has been shown that the incidence rate of breast cancer jumps to a higher level during and just

after each pregnancy and the protective effect of pregnancy on breast cancer is not seen till 10 to 15 years after.<sup>10-12</sup> A delay in diagnosis increases the risk of lymph node involvement by up to 1.8% with every month delay.<sup>12</sup> The delay in presentation is usually due to the mass being attributed to normal breast physiologic changes.<sup>5,7,11,12</sup> Despite the difficulty in diagnosis of PABC, due to the effects of pregnancy on the breast, several investigative modalities with high specificity and sensitivity are available to aid the diagnosis.<sup>8,9,13</sup> Each should be interpreted with care and the presence of false positives and negatives should be entertained if investigative findings are incongruent with the clinical outlook.<sup>8,9,13</sup> Breast masses may be masked on mammography due to engorgement and increased density of the breast<sup>13</sup>; even though the amount of radiation exposure to mammography is small and inconsequential,<sup>13</sup> Many workers believe ultrasound is the preferred radiological modality of choice especially in the first trimester.<sup>13-15</sup>

Depending on the clinical scenario, PABC patients and their providers may be confronted with the choice to either proceed with local control or to initiate systemic treatment.<sup>4,16</sup> For patients diagnosed with early-stage PABC, both breast conservation and mastectomy are considered viable surgical options.<sup>17</sup> Termination of pregnancy was a routine protocol in the management of PABC for about 2 decades ago.<sup>17</sup> Reasons adduced are that the continuous hormonal milieu of the pregnant state encouraged rapid growth of the tumour and aborting the embryo/foetus may slow the progression of the disease.<sup>17</sup> Recent studies have debunked this.<sup>17-19</sup> There has been no difference in outcome in patients who have had termination of pregnancy on account of PABC and their counterparts who did not have termination of pregnancy and is therefore strongly discouraged for such purposes.<sup>11,16</sup> If maternal outcomes are not negatively impacted by the pregnancy itself, continuation of pregnancy seems not only reasonable but also recommended.<sup>11,15,17,19</sup> Nevertheless, in cases of advanced disease stage (stage III or IV) or for high-grade or aggressive primary tumours diagnosed in the early first trimester, termination of pregnancy may be considered (on account of teratogenic risk of chemotherapy during the first trimester.<sup>17</sup> Chemotherapy should be deferred

until after the first trimester (after 14 weeks) when organogenesis is considered complete (10 weeks).<sup>17</sup> The rate of malformations is up to 14% if chemotherapy is given in the first trimester<sup>17</sup> and even higher with combination chemotherapy.<sup>17</sup> However, if administered in the second or third trimester, the rate of malformation mirrors the baseline population's 3% risk of congenital malformations.<sup>18</sup> At least 3 weeks between a cycle of chemotherapy during pregnancy and delivery are recommended.<sup>19</sup> Reports of oncologic outcomes after chemotherapy during versus after pregnancy suggest that delaying systemic treatment in PABC patients may worsen prognosis.<sup>19</sup> Nettleton et al. found that by delaying chemotherapy by 3–6 months, the risk of metastases was increased by 5%–10%.<sup>12</sup>

Literature has suggested that the chemotherapeutic regimen of choice in PABC is adriamycin-based chemotherapy and this regimen has been adjudged to be safe in pregnancy.<sup>20</sup> Hormonal treatment of PABC is contraindicated.<sup>19-21</sup> Tamoxifen is associated with Goldenhar syndrome and ambiguous genitalia.<sup>21</sup>

## PATIENTS AND METHOD

This was a retrospective observational study of cases of PABC at the Niger Delta University Teaching Hospital, Okolobiri, Bayelsa State, Nigeria, from January 2019 to January 2021. In this context, a sample size analysis was not performed, as there were no data to indicate baseline rates of human error in our surgical caseload. Records of cases of PABC included age of patient, the duration of pregnancy when symptoms were first noticed, diagnosis made, previous care given and outcome.

## RESULT

Seven cases were seen during the period of study. Ages range from 28 – 37 years with average of 35.4. All cases presented with history of lumps noticed during pregnancy, 4 cases within first trimester, 2 cases second and 1 in the third. Five were on the right breast, 2 cases left and 1 bilateral. All had histological diagnosis made at onset of the noticing of the lumps at peripheral Health Centres. All had no care given as they were advised not to have treatments for fear of adverse effects on the babies by the obstetrical care providers at peripheral Health Centres. All cases presented to us at very advanced stages

2 – 3 months after delivery as shown by the clinical picture (Figure 1) of one of the cases in this study. All were placed on hormonal and chemotherapy cyclically to down stage the disease process for possible surgical interventions. Four cases declined treatment due to financial reasons, 1 had a dose of chemotherapy and two had 2 doses. They were all lost to follow up.



**Figure 1: Advanced Pregnancy-Associated Breast Cancer in a 36-year-old.**

## DISCUSSION

Thomas<sup>22</sup> stated that all recognize and accept that adverse events occur with some frequency in surgery and that all departments meet regularly to review them. Since adverse events and "mistakes" have the potential for delaying recovery and injuring surgical patients, an ethical mandate exists to do all that can be done to prevent harm.<sup>22-24</sup> The incidence of breast cancer in pregnancy is rising as increasing number of women are postponing childbearing until middle age, and delays in diagnosis are more common.<sup>23</sup> It is necessary for women to undergo periodic breast examinations during antenatal visits.<sup>22-24</sup> Pregnancy-induced changes in the breast and some level of radiation-associated risk to the developing fetus later in pregnancy makes mammography of limited value among the investigations.<sup>8,9,13</sup> Fine-needle aspiration or core needle biopsy has emerged as the diagnostic tool of choice in pregnant women with breast cancer.<sup>23</sup> All our patients were diagnosed with FNAC or trucut biopsy.

The goals of breast cancer treatment are not different for pregnant and non-pregnant women, that is, to control the cancer locally and prevent systemic spread.<sup>19-21</sup> Systemic treatment includes adjuvant or neoadjuvant chemotherapy, patient's age or stage at diagnosis notwithstanding.<sup>24</sup> A diagnostic delay of 2 to 15 months was noted by Olatoke et al<sup>25</sup> in their patients with PABC, with a mean delay of about 6 months. The risk of lymph node involvement is increased by up to 1.8% with every month of delay in diagnosis.<sup>25</sup> Matted axillary lymph nodes was found in 45% of their patients at presentation, typical of the aggressive nature of PABC which have early lymph node involvement and spread.<sup>25</sup> Attribution of the mass to normal breast physiologic changes is the usual cause of delay in presentation.<sup>5,7,11,12</sup> All our patients presented at an advanced stage not due to a delay in diagnosis but rather a delay in seeking specialist care due to wrong decisions taken by the obstetrical care providers at peripheral Health Centres causing inappropriate management of Pregnancy-associated breast cancer.

Studies of PABC are yet to be documented in our locality. Fente and Alagoa<sup>26</sup> reported that out of 42 patients with Breast Cancers, twelve patients (28.6%) were of the 31-40 years age group, followed by 21-30 years age group with 10 patients (23.8%). Thirty-one patients (73.8%) between the ages of 21-50 years were premenopausal. Late presentation at least Stage 3 was seen in 38 (90.5%) patients mainly due to illiteracy, poverty, poor health seeking behaviour, access to health care and traditional and religious believes. These factors may have been in play in their late presentation, advanced stage at presentation and eventual loss to follow up of all 7 patients. These 7 cases of PABC are the first we are seeing from not acceptable sources and reasons. Despite the reduced complications achieved during the past several decades through implementation of systems-based and team-based care approaches to ensuring patient safety, preventable patient harm still persists.<sup>27-29</sup>

## CONCLUSION

PABC is not uncommon in our environment, though specific studies of PABC seem scarce as compared to the epidemiology mirrors of breast cancers patients. All suspicious lumps should be investigated by FNAC or trucut biopsy. Women diagnosed with PABC should

receive prompt specialist care like their non pregnant counterparts as delay worsens the overall outcome. The mother's life takes precedence over that of the fetus. All patients with suspicious or confirmed PABC should be promptly referred to the General Surgeon. There is the need for continuing education and constructive feedback on PABC to practitioners involved in obstetric care. Women undergoing antenatal care should be educated as well.

## CONFLICT OF INTEREST

Authors declared that there are no conflicts of interest

## AUTHOR CONTRIBUTIONS

All authors made substantial contribution to the study and manuscript.

## ETHICAL CONSIDERATIONS

**Informed Consent:** An informed consent was obtained from the patient to take pictures for academic purpose.

**Confidentiality:** The patient's face was removed from the image to maintain confidentiality.

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