Clinicopathologic Features of Breast Disease in Jamaica: Findings of The Jamaican Breast Disease Study, 2000–2002

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ABSTRACT

Objective: *To describe the clinicopathologic profile of breast disease in Jamaica.*
Methods: *The Jamaican Breast Disease Study is an ongoing prospective, multidisciplinary investigation of breast disease at the University Hospital of the West Indies (UHWI). The initial phase was a prevalence survey comprising all consenting patients referred to the Surgical Outpatient Department (SOPD) UHWI, for breast disease. Demographic, clinical, radiologic and pathologic information were recorded for each patient and the data for the first three years (2000-2002) were analyzed.*
Results: *A total of 1189 patients was enrolled for the study period (28.8% of all new SOPD patients). The age range was10 to 93 years (mean/SD = 36.5 +/- 16.4 years) with a female : male ratio of 14:1. Most patients (67.8%) presented with a palpable lump and the clinical diagnosis was benign in the majority (70.4%) of patients. Fibroadenoma was the most common benign histologic result (39.4% of all biopsies) followed by non-proliferative (fibrocystic) disease (19.3% of all biopsies). Proliferative disease without atypia, complex fibroadenoma and atypical ductal hyperplasia accounted for 6.9%, 2.6% and 0.4% of biopsies respectively. Overall, 23.4% of biopsies showed malignant histology (10.8% patients); invasive ductal carcinoma accounted for the majority of these cases (69.5%).*
Conclusions: *The majority of patients with breast disease in Jamaica are young women with clinically benign disease. There was a low prevalence of clinically significant premalignant disease. This is the first study to prospectively describe the clinicopathologic features of breast disease in Jamaica and supports the need for advocating breast cancer screening to facilitate detection of significant premalignant disease and early stages of breast cancer.*

Características Clínico-patológicas de la Enfermedad de Mamas en Jamaica: Hallazgos del Estudio Jamaicano de la Enfermedad de Mamas, 2000–2002

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RESUMEN

Objetivo: *Describir el perfil clínico-patológico de la enfermedad de mamas en Jamaica.*
Métodos: *El "Estudio jamaicano de la enfermedad de mamas" – que continua realizándose en la actualidad en el Hospital Universitario de West Indies (HUWI) – consiste en una investigación prospectiva y multidisciplinaria de la enfermedad de mamas. La fase inicial fue un estudio de prevalencia que abarcó a todos los pacientes que dieron su consentimiento, y que fueron remitidos al Departamento de Cirugía Ambulatoria (DCA) de HUWI a causa de la enfermedad de mamas. Se registró información demográfica, clínica, radiológica y patológica de cada paciente, así como los datos referidos a los primeros tres años (2000–2002).*
Resultados*: Un total de 1189 pacientes fueron captados para el periodo de estudio (28.8% de todos los pacientes nuevos del DCA). El rango de edad fue de 10 a 93 años (media/SD = 36.5 + / - 16.4 años) con una proporción hembra:varón de 14:1. La mayoría de los pacientes (67.8%) presentó un nódulo palpable y el diagnóstico clínico fue benigno en la mayoría (70.4%) de los pacientes. El fibroadenoma fue el resultado histológico benigno más común (39.4% de todas las biopsias) seguido por la*

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enfermedad (fibrocística) no proliferativa (19.3% de todas las biopsias). La enfermedad proliferativa sin atipia, el fibroadenoma complejo y la hiperplasia ductal atípica representaron el 6.9%, 2.6% y 0.4% de las biopsias respectivamente. En general, el 23.4% de las biopsias mostraron histología maligna (10.8% de los pacientes); el carcinoma ductal invasivo representó la mayoría de estos casos (69.5%).

***Conclusiones**: La mayor parte de los pacientes con la enfermedad de mamas en Jamaica son mujeres jóvenes con enfermedades clínicamente benignas. Hubo una baja prevalencia de enfermedades premalignas clínicamente significativas. Este es el primer estudio dirigido a describir prospectivamente las características clínico-patológicas de la enfermedad de mamas en Jamaica, y respalda la necesidad de abogar por el pesquisaje del cáncer de mamas, a fin de facilitar la detección de enfermedades premalignas significativas y las fases tempranas del cáncer de mamas.*

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INTRODUCTION

Breast cancer is the most common invasive cancer in Jamaican women (1). There are a number of established factors that place women at increased risk for the disease such as a family history of breast cancer, various socio-economic factors, and reproductive factors such as early age at menarche and late age at menopause. It has also been shown that women with benign breast disease diagnosed on biopsy have an overall increased risk for development of breast cancer (2).

Although pathologists had for many years recognized lesions occurring adjacent to invasive cancer in breast biopsies, it is only recently that the prognostic significance of these lesions has been documented. Page and Dupont proposed a classification scheme for benign breast disease in 1985 (3). Three major categories of disease were recognized: non-proliferative breast disease, proliferative disease without atypia and atypical hyperplasia. Non-proliferative disease (NPD) includes many of the entities previously designated as "fibrocystic disease" and women with NPD were found to be at no increased risk for breast cancer. Proliferative disease without atypia (PDWA) includes more severe forms of epithelial hyperplasia lacking any cytologic atypia as well as duct papillomas and a special form of adenosis known as sclerosing adenosis; women with this form of benign breast disease were found to be at slightly increased risk for cancer – 1.5 to 2 times that of women with NPD. Atypical hyperplasia (AH) can be ductal or lobular and shows features on biopsy that resemble but fall short of the corresponding *in-situ* or non-infiltrating forms of breast cancer; these patients were found to be at moderately increased risk of cancer – 4 to 5 times that of women with NPD. This risk for invasive cancer is approximately half that of women with *in-situ* carcinoma (CIS).

The increased risk for breast cancer following a diagnosis of some forms of benign breast disease diagnosed on biopsy has been confirmed by other studies (4–6). In addition, it has been shown that certain factors may modify the increased risk for cancer in women with PDWA and AH. For example, a family history of breast cancer essentially doubles the risk associated with these conditions (3, 7). Age at diagnosis has also been found to be a modifying factor – the risk for subsequent invasive cancer is greater in women younger than age 46 years compared to older women (8).

The concept of a spectrum of benign and pre-malignant disease has been generally accepted and has been endorsed by the College of American Pathologists (9, 10). Few studies however have been conducted in non-white populations (11–14). The prevalence of various forms of benign breast disease and the associated risks for invasive breast cancer have not been prospectively studied so far in the Jamaican population or in fact in the rest of the English-speaking Caribbean, where a variety of racial and ethnic groups are represented.

The Jamaican Breast Disease Study Group was therefore formed at the University of the West Indies (UWI) and comprised pathologists, surgeons, radiologists and epidemiologists with a particular interest in breast disease. The aim was to prospectively document in a multidisciplinary approach, the clinico-epidemiologic, pathologic and radiographic features of breast disease in a population predominantly of African descent and test current diagnostic classification schemes and prognostic indicators. The initial phase of the investigations was to describe the clinico-pathologic profile of breast disease in an outpatient population at a specialist hospital. This report documents the findings for the first three years of the study.

SUBJECTS AND METHODS

The study design was that of a prevalence survey in an outpatient clinic, to be followed by a cohort study of cases of premalignant disease. The study population comprised all consenting patients referred to the Surgical Outpatient Department facilities of the University Hospital of the West Indies (UHWI) for breast disease. The UHWI is the tertiary heathcare, multidisciplinary, 500-bed teaching hospital attached to the Faculty of Medical Sciences at the UWI in Jamaica. The protocol for the study was approved by the Ethical Committee of the UWI/UHWI.

Patients were required to give written informed consent prior to enrolment in the study. The relevant clinical and demographic data were entered on a pre-designed abstraction

form by research nurses assigned to the study. If fine needle aspiration (FNA) or biopsy was performed on a patient, the specimens were immediately placed into 95% ethyl alcohol and 10% neutral buffered formalin respectively, transported to the Pathology Department, UWI, and processed in the standard manner. Papanicolaou stained aspirates and haematoxylin and eosin stained slides from paraffin embedded biopsy material were examined by the pathologists on duty and were then independently reviewed by the designated study pathologist. Cases showing benign histology were classified using the scheme proposed by the College of American Pathologists (10). Significant disagreements affecting classification were resolved by review of the relevant slides. The study pathologist then abstracted the relevant pathologic data via a pre-designed abstraction form. If a mammogram and/or ultrasound was performed on a patient, the films were reviewed by the designated study radiologist and the relevant information documented. The frequency of AH, PDWA and NPD were calculated.

RESULTS

A total of 1189 patients were enrolled in the Jamaican Breast Disease Study between 2000 and 2002, representing 28.8% of all new patients seen in the SOPD for this period (Table 1).

Table 1: Number of patients enrolled in the Jamaica breast disease study between 2000 and 2002

Year	JBDS[a] Patients	All SOPD[b] Patients	%
2000	459	1355	33.9
2001	401	1413	28.4
2002	329	1355	24.3
2000–2	1189	4123	28.8

[a]JBDS = Jamaican Breast Disease Study
[b]SOPD = Surgical Outpatient Department

The patients ranged in age from 10 to 93 years (mean/SD = 36.5 +/- 16.4 years) with females representing 93.3% of the cohort [F:M ratio 14:1] (Fig. 1).

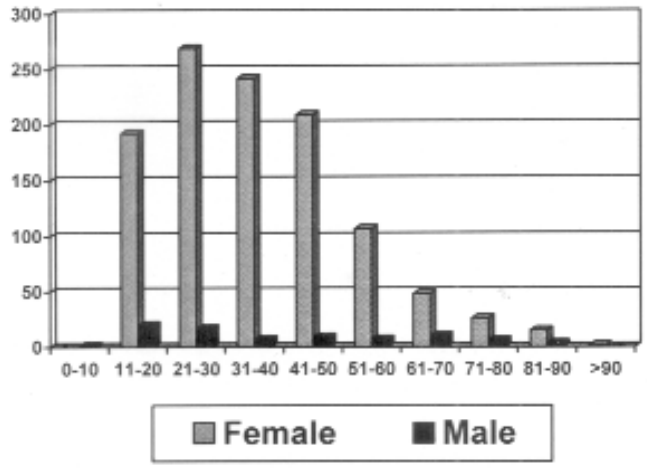

Fig. 1: Age and sex distribution for study patients

The most common presenting symptom was that of a lump (67.8% patients); diffuse nodularity and nipple discharge were the next most common complaints and were reported in 14.5% and 7.3% of patients respectively. Lesions were left-sided in 39.2% of patients, right-sided in 38.4% and bilateral in 22.4%. The clinical diagnosis was classified as benign in the majority of cases (70.4%) as were subsequent radiologic and pathologic investigations (Figs. 2 and 3).

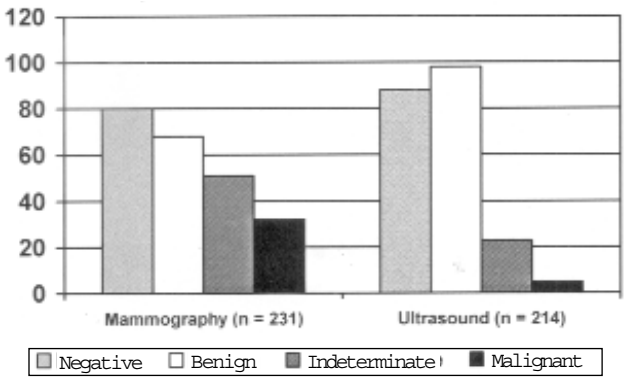

Fig. 2: Distribution of imaging results.

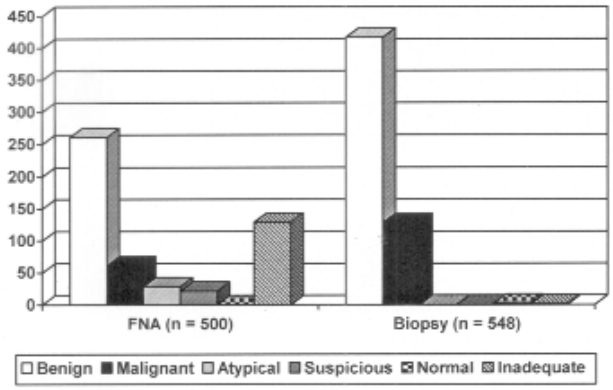

Fig.3: Distribution of pathology results.

Hookwire localization biopsies were performed in 42 cases (7.7% of biopsies).

The distribution of benign biopsy results is detailed in Table 2. The most common benign lesion sampled was fibroadenoma, seen in 39.4% of biopsies overall, with the complex variant accounting for 6.5% of these lesions. In some cases, a definitive distinction could not be made between fibroadenoma and benign phyllodes tumour, and these lesions were designated fibroepithelial lesions (3% biopsies). Non-proliferative disease was the second most common histologic diagnosis, seen in 19.3% of biopsies. Overall, 23.4% of biopsies showed malignant histology (10.8% patients) with invasive ductal carcinoma being the most common histologic type of malignancy (69.5% cases).

Table 2: Distribution of benign histology results

Categories of Benign Breast Disease	No.	% Benign Biopsies (n = 417)	% Total Biopsies (n = 548)
Moderately Increased Risk	2	0.5	0.4
Atypical ductal hyperplasia	2	0.5	0.4
Slightly Increased Risk	52	12.5	9.5
PDWA[a]	38	9.1	6.9
Complex fibroadenoma	14	3.4	2.6
No Increased Risk	363	87.0	66.2
Fibroadenoma	180	43.2	32.8
Non-proliferative disease (NPD[b])	84	20.1	15.3
Fibroadenoma and NPD	22	5.3	4.0
Fibroepithelial lesion, NOS[c]	16	3.8	3.0
Mammary duct ectasia	8	1.9	1.5
Gynaecomastia	7	1.7	1.3
Galactocele/lactational changes	5	1.2	0.9
Mastitis	5	1.2	0.9
Hamartoma	4	1.0	0.7
Fat necrosis	3	0.7	0.5
Other[d]	29	6.9	5.3
Total	**417**	**100**	**76.1**

[a]PDWA = Proliferative disease without atypia; [b]NPD includes adenosis, simple cysts, apocrine metaplasia and fibrosis; [c]NOS = Not otherwise specified [d]"Other" includes skin/stromal/lymph node lesions, 2 cases of accessory breast tissue and 1 case each of medial calcific sclerosis and haematoma

DISCUSSION

Breast disease is a common health problem in Jamaica, accounting for just under thirty per cent of new patients registering at the Surgical Outpatient Department facilities of the UHWI during the study period. The majority of patients with breast disease in Jamaica are female, relatively young, presenting with a palpable lump and having benign disease, a similar clinicopathologic profile to that described for other populations (11–13, 15).

Biopsy confirmed disease in the present study revealed that fibroadenoma was the most commonly sampled lesion, similar to a Nigerian study (11) whereas a previous retrospective review from another hospital in Jamaica showed fibrocystic disease (NPD) to be the most common histologic result (14). The preponderance of fibroadenoma in the index study may reflect a local bias towards biopsy of these lesions and does not necessarily imply that this is in fact the most common lesion in the population; it is generally accepted that NPD is the most prevalent form of benign breast disease (15). Only 6.5% of the fibroadenomas in the present study exhibited complex features, a much lower percentage than has been reported by other groups (16) and implies that the majority of these lesions in our population are not biologically significant. The problem in distinguishing fibroadenomas in some cases histologically from other fibroepithelial lesions, as documented in 3% of our biopsies is also recognized (17), and definitive diagnosis may be facilitated in the future by molecular genetic testing.

Other challenges in histologic diagnosis are reflected in the variations in diagnostic criteria for proliferative lesions, particularly for AH. Various quantitative and qualitative criteria have been proposed by different groups of workers to aid in the distinction of AH from CIS (18, 19) but this area can be a diagnostic dilemma. Major differences in diagnosis have been documented even amongst experienced pathologists who have reviewed these pre-malignant lesions with the same lesion being interpreted as PDWA, AH or CIS by different pathologists (20, 21). High-grade forms of DCIS including the classic "comedo" pattern are usually easily diagnosed. The problem that arises is the distinction of AH from low-grade forms of DCIS which can display minimal cytologic atypia. The distinction is critical however because important clinico-epidemiologic differences have been reported between AH and CIS, such as the observation that AH confers a bilateral risk for subsequent invasive cancer, in striking contrast to DCIS that confers a distinctly ipsilateral risk (4, 7, 22, 23). These observations support the concept that AH is a general marker for invasive cancer for both breasts while DCIS is a more direct precursor and these lesions should remain different diagnostic entities, regardless of the terminology to be adopted. Genetic analyses have tended to support this viewpoint (24). In this study, we attempted to deal with any problems regarding classification by slide review and consultation, although given the paucity of truly borderline lesions, the vast majority of biopsies did not prove to be diagnostically challenging.

The low prevalence of clinically significant forms of benign breast disease such as AH in the present study is most likely explained by the fact that the study population largely represents referrals for palpable or clinically detected lesions, as opposed to abnormalities detected by screening mammography. The relatively small percentage of biopsies performed by imaging guidance in this study (7.7%) supports this. In a country where breast cancer is the most common type of malignancy in women, the findings underscore the importance of advocating nation-wide screening to facilitate the detection of significant premalignant disease as well as early stages of cancer. This would also reduce the prevalence of invasive cancers at the time of diagnosis (69.5% of cancer cases) as has been demonstrated in other studies (25). In addition, mammographic screening has been shown to reduce mortality associated with breast cancer (26).

In conclusion, this study has described the clinicopathologic profile of breast disease in a Jamaican population. The majority of patients were young women with clinically benign lesions. Radiologic and pathologic tests also revealed benign disease in the majority of cases investigated by these modalities, with a low prevalence of clinically significant premalignant disease. This report represents the preliminary findings from an ongoing, prospective, multidisciplinary sur-

vey of breast disease at the UWI/UHWI, and supports the need for advocating breast cancer screening in a population where this is the most common form of cancer in women.

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