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RESEARCH ARTICLE

EVALUATION OF BREAST CANCER RISK ASSOCIATED WITH ATYPICAL HYPERPLASIA OF THE LOBULAR AND DUCTAL TYPES IN A JAMAICAN HOSPITAL 2007-2012: ACROSS-SECTIONAL STUDY

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ABSTRACT

Background: There is a paucity of significant data with regards to the high prevalence of breast cancer and its risk factors within the parish of Manchester. Atypical hyperplasia with a relative risk of 4-5% [5] has been demonstrated to have a positive association with the development of breast cancer. The objective the study is to clearly and concisely assess the association between atypical hyperplasia and breast cancer from convenient data obtain at a central Jamaica hospital over a five-year period.

Method: This study is essentially an analytical cross-sectional study in which the risk factor(s), atypical hyperplasia and associated outcome(s), and breast cancer are analysed within the same time frame. The data for all breast related surgical procedures during 2007 until 2012 were collated and the subset of patients who had atypical hyperplasia and breast cancer were selected for analysis. The descriptive statistics were conducted to included estimates of central tendencies and dispersion for quantity of procedures done, types of pathologies observed, age and gender of the patients. Additional evaluation included Pearson's correlation and linear regression. The cohort of patients with atypical hyperplasia and non-benign lesions were further selected for risk factor analysis and predictive risk assessment for breast cancer.

Results: The quantity of procedure done during the study period was 551 however, this did not reflect the quantity of complete histopathology reports due to that fact that there were missing data. The total sample size of persons was 147 which was predominantly females (142) and with a total of 210 breast pathologies of which 158 were benign breast disease (BBD), 4 were atypical hyperplasia (AH) and 48 were non-benign lesions. The linear regression analysis done demonstrated this equation; *non-benign lesion = (2.7)*(atypical hyperplasia) + 6.2* where 2.7 is the gradient and 6.2 the intercept. The Pearson's correlation analysis demonstrated a weak association with a p-value .213. The risk factors of; age at menarche (14 years), number of first degree relatives with breast cancer (1.3persons), age at current biopsy (57 years), age at first live birth (20 years), were the most salient among the cohort of atypical hyperplasia and non-benign lesion.

Conclusion: There was a positive weak association between atypical hyperplasia and non-benign lesions which were not statistically significant, which could be attributed to the missing data which made the study under powered.

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INTRODUCTION

The fact that breast cancer is one of the leading cause of mortality globally, with a sharp increase of 14% since 2008 (http://www.iarc.fr/en/media-centre/pr/2013/pdfs/pr223_E. pdf), affecting both men and women in a similar manner, with no regard for race, age or religion, perpetually motivates the scientific community to take a closer look at the disease process and its associated risk factors.

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The increased incidence of breast cancer worldwide, since 2008 has been estimated to be greater than 20% (http://www.iarc.fr/en/media-centre/pr/2013/pdfs/pr223_E. pdfm) which has been attributed to many factors and as such several attempts have been made to better understand these risk factors and eventually stem the prevalence. The reduction of associated risk factors has been attempted on many occasions with mixed results in several developed countries. A meta-analysis done on nine selective oestrogen receptor modulators (SERMs) prevention trials demonstrated that the incidence of oestrogen positive breast cancer was reduced (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3671272/). Within Latin America and the Caribbean breast cancer is

viewed as number one in incidence and mortality especially among females. This is mainly due to a lack of screening programmes and late stage diagnosing (http://www.paho.org/hq/index.php?option=com_docman&task), in conjunction with the lack of adequate funding for research. According to the report obtained from the initial phase of the Jamaican breast disease study carried out at the University of the West Indies during 2000-2002, (Arpino, 2005), the majority of breast diseases were benign in nature (70.4%), and within this was an even smaller subset the atypical hyperplasia (0.4%). The initial landmark study carried out by DuPont and Page in 1985 demonstrated that atypical hyperplasia has a relative risk of 4-5% for the develop breast cancer (Dupont, 2015). Benign breast disease is an important risk factor for breast cancer in patients 50 years and over, which can develop in either breast. Benign breast diseases constitute a heterogeneous group of lesions including developmental abnormalities, inflammatory lesions, epithelial and stromal proliferations, and neoplasms. These benign breast diseases have been classified using the Page and DuPont scheme[5]which states three major categories of disease: non-proliferative breast disease (nir), proliferative disease without atypia (sir 1.5-2%) and atypical hyperplasia (mir 4-5%). These increased risks for breast cancer were also demonstrated by a few other studies (Palli, 1991; London, 1992; Dupont, 1993). There are several other clearly accepted factors which contribute to breast cancer development such as advanced age (> 4%), family history first degree relative (>2%), family history of ovarian cancer (>5%), personal history (3-4%), personal history positive $BRCA_1/BRCA_2$ (>4%), history of breast biopsy with atypical hyperplasia (4-5%), history of breast biopsy withlobular carcinoma insitu (LCIS) or ductal carcinoma in situ (DCIS) (8-10%), reproductive history early age at menarche (2%), reproductive history late age of menopause (1.5-2%) (Stopeck, 2015). These risk factors when combined can also augment their individual relative risk as was observed by Dupont and Page in which 39 women with atypical hyperplasia and family history of breast cancer had a relative risk of 8.9%, (Dupont, 1985). These factors also modify the risk profile for developing breast cancer but mainly in the groups of the proliferative disease with atypia and atypical hyperplasia. Breast cancer is the most common invasive cancer in Jamaican women, Incidence rates of breast cancer in the Caribbean are considered intermediate between those of North America and Europe and those of the Far East (Brinton LA, Incidence, demographics and environmental factors), and within the Caribbean, Jamaica has been shown to have one of the highest rates (Brooks, 1992). The most recently reported age standardized rate for women in Jamaica is 43/100 000 (Gibson, 2008). The aim of this study is to document all breast pathology that have been treated at the Mandeville regional hospital by the surgical department and to correlate statistically the relationship between atypical hyperplasia of the breast and the risk for developing breast cancer. The parish of Manchester has the second highest breast cancer prevalence ~ 23% (Shirley, 2010), within the island. This alarmingly high prevalence of breast cancer encourages researcher aim at investigating the risk factors that have contributed to such startling findings. The latter has not come to fruition mainly due to the fact that there is no proper documentation with respect to the extent to which benign breast disease of atypical hyperplasia contribute to the alarmingly high prevalence of breast cancer observed in the parish of Manchester. The dilemma of breast cancer and the interaction with its risk factor of benign breast disease has been investigated on an international level by several key stakeholders. The associated relative risk of 4-5% in persons with atypical hyperplasia of the breast in subsequently developing breast cancer was initially demonstrated by Dupont and Page in 1985 and since then has been corroborated by several other studies (Shirley, 2002). There is aninadequacy of statistically significant data on breast cancer nationally although there is evidence which confirm the incidence rate of breast cancer in Jamaica to be one of the highest in the Caribbean (Brooks, 1992). The reason has not been researched in a scientific manner although there have been several assumptions made such as a greater accessibility to surgical care for the patients within the parish of Manchester (Shirley, 2010). The essence of this study attempts to shed some light as to the association between breast cancer and the benign breast disease of atypical hyperplasia (risk factor) within the parish of Manchester.

Literature review

The research on breast disease could clarify whether there is a continuum of breast alterations that culminates in breast cancer (Hartmann, 2005). However, the prevalence of various forms of breast disease and the associated risks (relative, cumulative and absolute risk) for invasive breast cancer have not been systematically studied thus far in the Jamaica (Shirley, 2002) hence it remains unclear which of the benign breast disease entities are the actual precursors to breast cancer and which reflect a background of increased risk involving all breast tissue. The Jamaica Cancer Registry, which was established in 1958 and has published a regular five-year report (Gibson, 2008), successfully demonstrating that breast cancer in women has an age standardised rate (ASR) of 43.0 per 100 000 per year. These results have been consistent when compared to previous reports and the major suggestion is that there is a lack of a national screening programme. This would help in elucidating on a national level what is the prevalence of breast cancer presentations and which benign breast pathology carries more risk. The screening mechanism which is widely accepted is one which entails self-breast examination and awareness for women in their 20's and 30's along with clinical breast examination every three years. For women in their 40's it is also recommended that the clinical breast examination be performed yearly along with a mammogram (American Cancer Society, 2014). Breast cancer is the leading cancer site for females in Jamaica (Gibson, 2008), and its development is related to several clearly documented risk factors such as age, family history, and previous cancer history, hormonal and environmental factor as well. There is however a specific group of risk factors, the benign breast diseases which were classified into non-proliferative breast disease, proliferative disease without atypia and proliferative breast disease with atypical hyperplasia (Dupont, 2015), which play a very important role. The benign breast diseases have been established as an important risk factor for breast cancer as was achieved through several landmark studies commencing with Page DL and Dupont WD, in 1985 (Dupont, 2015). These breast diseases arise through developmental abnormalities, inflammatory lesions, epithelial and stromal proliferations, and neoplasms. The relative risk associated acquiring breast cancers among in these lesions are as follows non-proliferative breast disease had no increased risk, proliferative breast disease without atypia had a 1.5 – 2% increased risk and proliferative breast disease with atypia had a 4-5% increased risk (Palli, 1991; London, 1992; Dupont, 1993). Atypia represents a high-risk premalignant lesion of the breast,

conveying a relative risk of approximately 4 for a later breast cancer [11, 12] with a cumulative incidence of 29% at 25 years [13, 14]. Atypical ductal hyperplasia (ADH) is generally considered a direct precursor of low-grade ductal carcinoma in situ (DCIS) and thus, low-grade invasive ductal cancer, whereas the precursor(s) of higher-grade DCIS and invasive ductal cancer remain unknown (Wellings, 1973; Allred, 2008). Atypical lobular hyperplasia (ALH) is thought to occupy a position in the evolution of lobular carcinoma but is also considered a risk indicator for a later breast cancer in either breast (Bombonati, 2015; Lewis, 2012 and Anderson, 2006). Atypical hyperplasia of the breast confers a relative risk of 4-5% [5] however it was observed that when this was combined with other situation such as family history, age at first live birth and number of biopsy can attenuate or augment its effect. It was observed that a combination of family history of breast cancer and atypical hyperplasia of the breast augmented the relative risk from 3.5% to 8.9% (Dupont, 1985). It was also observed in a study conducted by the mayo clinic in 2005 and 2014 that when atypical hyperplasia of the breast is diagnosed in younger women it was more likely for breast cancer to develop (Hartmann, 2015). The other risk modifiers that affect atypical hyperplasia are the quantitation of foci and involution of background lobular units; with greater numbers of foci increases the risk and with greater involution decreases the risk (Hartmann, 2015). The Jamaican scenario suggest that the vast majority of lesions that occur in the breast are benign (70.4%) with only 0.4% being atypical hyperplasia and with the premalignant prevalence being low (Shirley, 2008), as was demonstrated in the initial phase of The Jamaican breast disease study. The parish with the most exceptionally reported prevalence of breast cancer is Manchester with 23% (Shirley, 2010). The reasons for this finding has never been studied and could be related to environmental, socio-economic, genetic/ hereditary, and medical factors.

MATERIALS AND METHODS

Data collection

The study will be done through the collection of data from the histopathology reports of breast biopsies done and subsequently through revision of the dockets of the patients who had breast cancer and/or atypical hyperplasia. The information was collated over a five-year period so as to give an appropriate sample size and power.

Exclusion and inclusion criteria

Only patients who have had a surgical intervention/procedure (biopsy) done to their breast at the main operating theatre (regardless of their age and sex) during the stipulated time period were included into this study. The subset of patient that have had trauma to the breast were also excluded and only considered if this initial trauma led to the more serious breast pathology. The patients who had breast cancer prior to the start of this research had their subsequent biopsies of the ipsilateral side excluded.

Study Design

This study is essentially an analytical cross-sectional study in which data is retrieved from the list of biopsies done at the operating theatre at Mandeville regional hospital. Thus the outcome as well as the independent variables is looked at within the same time frame. There was documentation of the quantity of biopsies done and the varying types of breast pathologies obtained. There was documentation of the presenting complaints of the patients (solitary lump, nodularity, nipple discharge, pain, etc.), the presenting side (left, right or bilateral), clinical and radiological diagnosis, the time period from diagnosis to biopsy to report was also documented and the demographics of the selected patients (gender, age, and geographic location,). A thorough review of the dockets for the selected patients (patients with atypical hyperplasia and also those with breast cancer) with a view of documenting other known risk factors for breast cancer within this subset of patients. These risk factors are: age (>25), family history (first line relative with breast cancer, etc.), history of previous cancer (ovarian, breast, etc.), hormonal factors (menarche, menopause, nulli-parity, age of 1st live birth, obesity), environmental (radiation, etc.).

Sampling

The selection of subjects was done in the form of recognizing the study population as those patients who present to Mandeville regional hospital with varying breast pathology and then subsequently only those patients that had procedures (biopsy) done at the operating theatre were eventually considered; hence this would be a form of non-probability purposive sampling.

Statistical analysis

The objective to document all breast pathologies and to retrieve from same measures of central tendencies: mean, mode, median and extrapolated to measures of dispersion: standard deviation, variance and the range will aid in the creation of a data base for subsequent statistical inferences. The period prevalence values obtained from was used to calculate the odds ratio and subsequent deduction with regards to relative risk. The appropriate correlation analysis was done between breast cancer patients and those with atypical hyperplasia as well as regression modelling. This aided in the establishing a predictive risk assessment model, which will be corroborated with other breast cancer risk assessment such as: the BCRAT (breast cancer risk assessment tool), also called the GAIL model and the IBIS (international breast cancer intervention study).

Data Analysis

The data was analyzed using the Statistical Package for the Social Sciences Software (SPSS version 20). Utilizing this software, both descriptive and inferential analyses was conducted. There was measures of central tendency and measures of dispersion for the data collected (demographics, presenting complaints, presenting side of lesion/unilateral or bilateral, time period from diagnosis to histopathology reporting), which was demonstrated by the patterns and trend of all breast pathology being treated at Mandeville regional hospital during 2007 until 2012. The subset of patients that have atypical hyperplasia of the breast (including the risk modifiers) and/or breast cancer was used to conduct correlation coefficient. There was also a regression analysis done with the subset of patients that have atypical hyperplasia of the breast (including the risk modifiers) and/or breast cancer and finally odds ratio of atypical hyperplasia of the breast (exposure) to the breast cancer (outcome) was conducted.

RESULTS

The above Table (information taken from the operating theatre registry) demonstrates that during a six-year period over 551 procedures were done as there were several missing data with the most noticeable being that of 2008 where no data was available after the month of June.

Table 1. Table showing the types of procedures performed on a yearly basis obtained from operating theatre registry

Year	Right biopsy	Left biopsy	Bilateral biopsy	Right mastectomy	Left mastectomy	Bilateral mastectomy	Total no. of procedures/year
2007	80	57	8	9	16	0	170
2008	31	35	4	12	5	1	88
2009	47	44	6	12	10	0	119
2010	28	48	3	9	13	0	101
2011	19	23	1	6	5	0	54
2012	9	4	1	5	0	0	19
Total	214	211	23	53	49	1	551

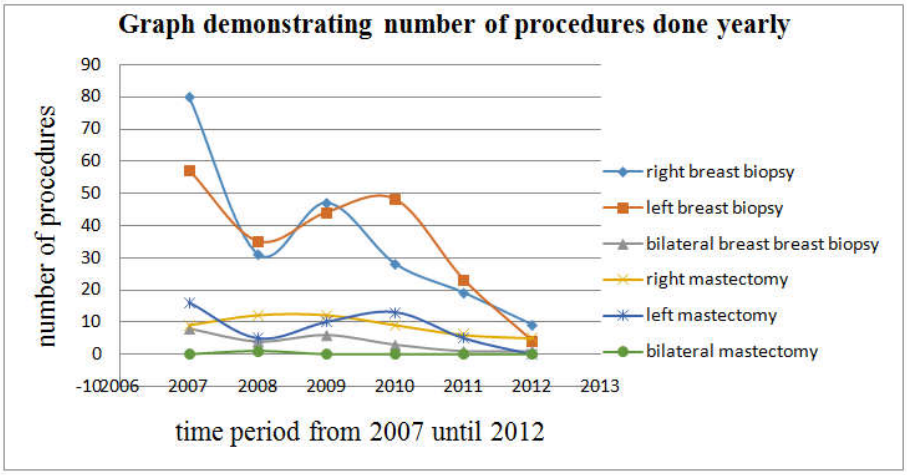

Figure 1. Line graph showing the number of procedures done within the study period

Table 2. Table demonstrating the breast pathologies from available histopathology reports

Categories of BBD	Number diagnosis	% benign Biopsies (n=162)	% total biopsies (n=210)
Moderately Increased Risk (Mid/4-5%)			
Atypical Hyperplasia	4	2.5	1.9
Slightly Increased Risk (Sir/1.5-2%)			
PDWA	23	14.2	10.95
Complex Fibroadenoma	1	0.62	0.48
Fibroadenoma	43	26.5	20.5
Non-proliferative disease (NPD)	54	33.3	25.7
Mammary duct ectasia	7	4.3	3.33
Gynaecomastia	5	3.1	2.4
Galactocele/lactational changes	1	0.62	0.48
Mastitis	1	0.62	0.48
Hamartoma	2	1.23	0.95
Fat necrosis	2	1.23	0.95
Fibrocystic lesion	3	1.9	1.43
Epidermal cyst	5	3.1	2.4
Papilloma	6	3.7	2.9
Phylloides tumour benign	1	0.62	0.48
Lipoma	4	2.5	1.9
Non-benign lesion	48		22.86
Total	210	100	100

The above graph shows the quantity of procedures being done on a yearly basis where in 2007 had the most procedures being recorded (missing data especially from 2008), could be the reason the other years did not record as much. The above Table demonstrates the quantity of pathology generated from procedures done on 148 persons. There are 162 benign breast diseases and within this non-proliferative diseases, fibroadenoma, and proliferative disease without atypia had 33.3%, 26.5% and 14.2% respectively, there were 48 non-benign diseases (cancer) also. The above Table depicts the spread of pathology as they occur on a yearly basis with a very peculiar occurrence where the highest quantity of non- benign lesions was documented for 2008. The above graphical representation demonstrates the quantity of the pathologies on a yearly basis that were generated from the histopathology report of the 147 patients. There is alarmingly high amount of benign breast disease for 2011 while 2008 recorded the highest amount of non-benign lesions. There were a total of 48 cases of non-benign lesion over the six-year period and 4 cases of atypical hyperplasia within the same time period, with a mean of 8 and 0.7 respectively. The above Table illustrates that they were 147 person involved in this study with 142 females and 5 males. The average age for the persons involved was 43 years.

The above ANOVA Table demonstrates the relation between and within the groups of atypical hyperplasia (independent variable) and non-benign lesions (dependent variable) where F-ratio is (F (1, 4) = .786, P = .425).

benign lesions. Equation for regression (y = mx + c); *non-benign lesion = (2.7)*(atypical hyperplasia) + 6.2*. The above graph depicts the association between atypical hyperplasia and non-benign lesions, with the outcome variable the non-benign

Table 3. Table demonstrating the benign breast disease, atypical hyperplasia and non-benign lesions from available histopathology reports

Year	Benign breast disease	Atypical hyperplasia	Non-benign lesion
2007	28	0	7
2008	29	2	15
2009	28	0	14
2010	10	0	1
2011	50	1	5
2012	13	1	6
Total	158	4	48

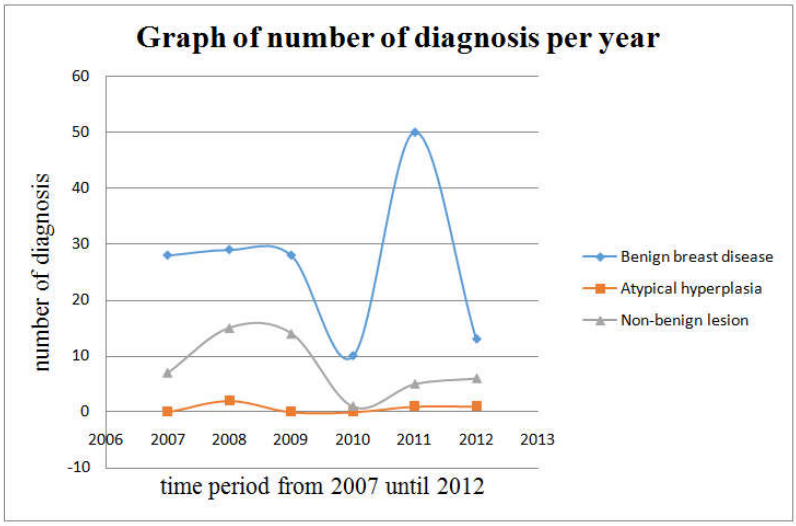

Figure 2. Line graph showing the number of diagnosis within the study period

Table 3a. Table demonstrating the mean and standard deviation of the non-benign lesions and atypical hyperplasia

Variables	Mean	Std. Deviation	N	Total
Non-benign lesion	8.0000	5.44059	6	48
Atypical hyperplasia	0.6667	0.81650	6	4

Table 4.Table demonstrating the demographic of the gender, and mean age of patients from available histopathology reports

Year	Gender		Mean age of persons	Descriptive for age			
	Male/%	Female/%		N	Min.	Max.	St. dev.
2007	3	26	38	28	14	67	13.31
2008	1	32	45	31	16	78	17.86
2009	0	37	46	35	17	81	20.28
2010	0	8	43	6	18	59	15.82
2011	0	28	36	27	13	76	18.10
2012	1	11	52	11	18	84	19.58
Total	5	142					

The above Table illustrates the linear regression analysis done between atypical hyperplasia and non-benign lesions which generated the following equation;

non-benign lesion = (2.7)(atypical hyperplasia) + 6.2*

The above Table illustrates the R squared value which determines the proportion of the variance explained by the linear regression model. In this case only 16.4% is explained by this model which is a very low value. The above Table demonstrates the Pearson's correlation between atypical hyperplasia and non-benign lesions. There is a weak not statistically significant association between AH and non-lesions being that of the y-axis and the independent variable atypical hyperplasia is on the x-axis. The above Table demonstrates the MANOVA test done with AH, non-benign lesions, and age as variables. There is no statistical significance F value which suggest that there are significant difference of AH among the two groups of dependent variables of age and non-benign lesions (supporting the alternative hypothesis) with the Wilk's = .55, F(4, 4) = .345, p < .836. The above Table illustrating the Levene's test of equality of error variance in which there is no statistical significance for non-benign lesion and the opposite for age which together suggest that there was partial violation of the assumption and that the data in its entire can be deemed as correct.

Table 5. Table demonstrating the ANOVA that is done using AH and non-benign lesion

Model		Sum of Squares	DF	Mean Square	F	Sig.
1	Regression	24.300	1	24.300	0.786	0.425[b]
	Residual	123.700	4	30.925		
	Total	148.000	5			

a. Dependent Variable: non-benign lesion
b. Predictors: (Constant), atypical hyperplasia

Table 6. Table demonstrating the linear regression between AH and non-benign lesion

Model	Unstd. Coefficients		Std. coefficients	T	Sig.	95% C.I. for B	
	B	Std.error	Beta			Lower bound	Upper bound
Constant	6.200	3.046		2.036	0.112	-2.257	14.657
AH	2.700	3.046	0.405	0.886	0.425	-5.757	11.157

a.Dependent variable: non-benign lesion.

Table 7. Table demonstrating the R squared values (0.164) and the significance

R	R squared	Adjusted R squared	F change	Sig.
0.405	0.164	- 0.045	0.786	0.425

Predictors (constant): atypical hyperplasia.

Table 7a. Table demonstrating the correlations between AH and non-benign lesion and the significance

		Non-benign lesion	Atypical hyperplasia
Pearson Correlation	Non-benign lesion	1.000	0.405
	Atypical hyperplasia	0.405	1.000
Sig. (1-tailed)	Non-benign lesion	-	0.213
	Atypical hyperplasia	0.213	-

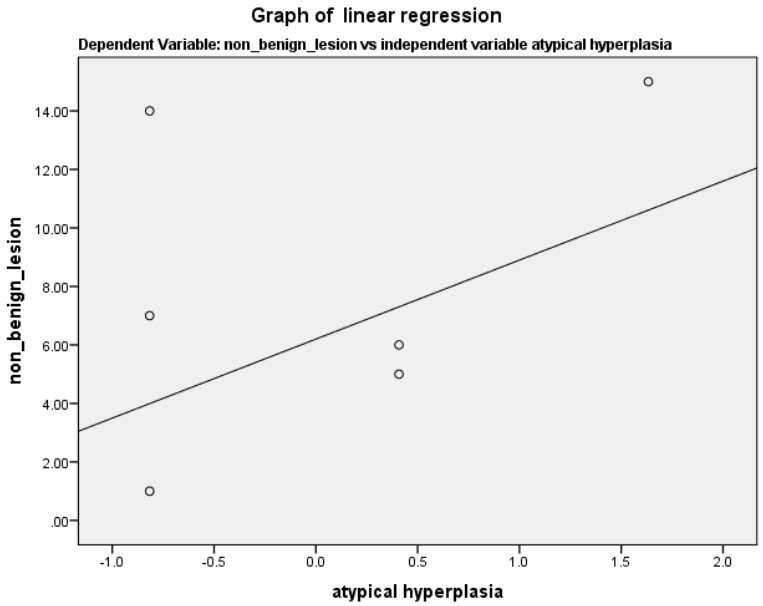

Figure 3. line graph showing the linear regression between atypical hyperplasia and non-benign

Table 8. Table demonstrating the multivariate test done for AH, mean age and non-benign lesions

Effect		Value	F	Hypothesis df	Error df	Sig.
Intercept	Pillai's Trace	.983	58.645[b]	2.000	2.000	.017
	Wilks' Lambda	.017	58.645[b]	2.000	2.000	.017
	Hotelling's Trace	58.645	58.645[b]	2.000	2.000	.017
	Roy's Largest Root	58.645	58.645[b]	2.000	2.000	.017
Atypical hyperplasia	Pillai's Trace	.461	.449	4.000	6.000	.771
	Wilks' Lambda	.553	.345[b]	4.000	4.000	.836
	Hotelling's Trace	.785	.196	4.000	2.000	.921
	Roy's Largest Root	.753	1.129[c]	2.000	3.000	.431

a. Design: Intercept + atypical_hyperplasia
b. Exact statistic
c. The statistic is an upper bound on F that yields a lower bound on the significance level.

The above Table for the univariate ANOVA indicate that both age and non-benign lesions were not significantly different for AH: age $F(2, 3) = .062$, $p < .941$ and non-benign lesions $F(2, 3) = 1.107$, $p < .437$ and hence the linear representation that could be generated would have similar characteristics as that generated before for AH and non-benign lesions. This entailed a detailed revision (identifying other risk factors) of the patient's dockets that were found to have atypical hyperplasia (4 cases) and non-benign lesions (48 cases), however due to the difficulties encountered at the clerical department at the Mandeville Regional Hospital only 28 of the total of 52 were found. The above Table illustrates the types of complaint that the patients (28) presents with. The most salient presentation being that of a solitary breast lesion which was seen in combination with the other presenting complaints at times.

The side of presentation within this cohort seemed to be relatively equal with only a few persons depicting a bilateral presentation. The definitive procedures that were performed were that of a modified radical mastectomy with the left side being operated on more frequently and only one case that had atypical hyperplasia being given the option of continued surveillance.

A thorough review of the dockets of these 28 patients with a view of highlighting the most salient risk factors (risk factors identified through Gail predictive risk assessment and Rangan A.) has yielded that age above 50 years at the time of biopsy, age at first live birth, age at menarche and geographic location of Manchester as being the most outstanding.

Table 8a. Table demonstrating levene's test of equality of error variances

	F	df1	df2	Sig.
mean_age_of_pt	10.150	2	3	.046
non_benign_lesion	1.507	2	3	.352

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.
a. Design: Intercept + atypical_hyperplasia

Table 8b. Table demonstrating the reiterated ANOVA of AH measured against mean age and non-benign lesion

Tests of Between-Subjects Effects

Source	Dependent Variable	Type III Sum of Squares	Df	Mean Square	F	Sig.
Corrected Model	mean_age_of_pt	6.667[a]	2	3.333	.062	.941
	non_benign_lesion	62.833[b]	2	31.417	1.107	.437
Intercept	mean_age_of_pt	9408.242	1	9408.242	175.673	.001
	non_benign_lesion	422.561	1	422.561	14.885	.031
atypical_hyperplasia	mean_age_of_pt	6.667	2	3.333	.062	.941
	non_benign_lesion	62.833	2	31.417	1.107	.437
Error	mean_age_of_pt	160.667	3	53.556		
	non_benign_lesion	85.167	3	28.389		
Total	mean_age_of_pt	11434.000	6			
	non_benign_lesion	532.000	6			
Corrected Total	mean_age_of_pt	167.333	5			
	non_benign_lesion	148.000	5			

a. R Squared = .040 (Adjusted R Squared = -.600)
b. R Squared = .425 (Adjusted R Squared = .041)

Table 9.Table demonstrating the presenting complaints of the patients for surgical intervention

		Number of cases
Presenting complaints	Pain	6
	nipple discharge	3
	solitary lump	29

Table 9a. Table demonstrating the presenting side (breast) that prompted surgical intervention

		Number of cases
Presenting side	Right	15
	Left	12
	Bilateral	3
	Total	30

Table 9b. Table demonstrating the definitive procedure performed and the corresponding side

		Number of cases
Definitive procedure	Right MRM	9
	Left MRM	11
	Bilateral MRM	2
	Surveillance	1
	Unknown	3
	Total	28

Table 10. Table demonstrating the risk factors that have been found within the cohort of 28 patients

Risk factors		Number of cases (mean)	Relative risk
Age at menarche		13.7 (mean for 10 persons)	1.099
Age at menopause		Unknown	?
Number of previous breast biopsy		2 (mean for 4 persons)	2.882
Age at first live birth		20 (mean for 6 persons)	1.224
Parish	Clarendon	3	?
	Manchester	13	??
	St. Elizabeth	10	??
	Trelawny	1	?
	Unknown	1	?
Age at current biopsy		57 (mean for 27 persons)	1.273(1)/1.620(2)
Number of first degree relatives with breast cancer		1.3 (mean for 10 persons)	2.834
Gender	Male	0	
	female	30	
Atypical hyperplasia		1	4-5
Ionising radiation		1	2.1
Mammographic increased breast density		2	2.1
Previous history of breast cancer or other cancer		4 (3 persons previous breast cancer contralateral).	2.1
$BRCA_1/BRCA_2$		Unknown	?

*this table is the combined risk factors as obtained from the Gail predictive risk assessment and the Rangan A., BCI westmead breast cancer institution.

DISCUSSION

This study presents findings of the breast pathology cross-sectional research carried out during a five-year period at the Mandeville Regional Hospital. It was observed that a total of 551(Table 1) breast procedures (there were segments of the operating theatre registry that were missing with the most noTable being that of 2008) were done at the main operating theatre where 448 of those were biopsies. There were142 females and only 5 males (Table 4) which generated a total of 210 pathologies (Table 2). There was a predominantly high quantity of benign breast disease (162) (Table 2) and the rest being non-benign lesions (48). The non- proliferative disease had a total of 54 (25.7%) occurrences meanwhile fibroadenoma and proliferative disease without atypia had 43 (20.5%) and 23 (10.95%) respectively, meanwhile non-benign lesion represented 22.86% of the total. The ANOVA (Table 5) between atypical hyperplasia (independent variable) and non-benign lesions (dependent variable) yielded a no statistically significant difference between the groups, ($F(1, 4) = .786$, $P = .425$) and although the F-ratio is close to unity which would support the null hypothesis (that there is no association between the groups with atypical hyperplasia and the non-benign lesions) the alternative has to be accepted (there is an association between atypical hyperplasia and non-benign lesions).

The regression analysis that was obtained yielded (Table 6) *non-benign lesion = (2.7)*(atypical hyperplasia) + 6.2*which would suggest there is a weak positive association which is confirmed with Pearson's correlation (Table 7a) of 0.405 with a p-value of 0.213. The results of the MANOVA test (Tables 8, 8a, 8b) also demonstrated that the alternative hypothesis should be accepted by analysis of the WILKS- lambda, levene's test of equality of error variance and the individual univariate performed. Further analysis was conducted by selecting all non-benign lesions and atypical hyperplasia patients which were essentially 52 and doing a thorough docket review in order to create a database of established risk factors for breast cancer that might be present. The difficulty encountered here is that there were a lot of missing data which and only 28 of this was found. The explanation as to this could be due to death; and the dockets would be filed away in some other location, dockets being genuinely misplaced, or the dockets being used for other purposes or involved in other research. The cohort consisted of 27 patients with non-benign breast lesions and one person with atypical hyperplasia. The initial data obtained from this docket review demonstrated that the presenting complaints for most of the patients was solitary lump in 25 (Table 9) situations (this value is at times combined with the other presentation as there might be more than one location to be biopsied). The side of most frequent presentation was relatively even in the sense that the right had 13 and the left had 12 (Table 9a). The definitive procedures that was done throughout most of these case was modified radical mastectomy where a total of 24 (Table 9b) were performed with a slightly higher left sided predominance of about 11. The risk assessment tabulation from the established risk factors obtained from GAIL model of predictive risk assessment for breast cancer of Table 10 yielded the most frequent risk factors as being age above 50 years at the time of biopsy, age at first live birth, age at menarche and geographic location of Manchester.

The combination of several risk factors has an accumulative effect and tends to augment or attenuate the overall relative risk of the patients. Hence the fact that someone is diagnosed at a young age with atypical hyperplasia and a family history of breast cancer may increase or decrease the risk of developing breast cancer [22], however what is found in this study is that the one case of atypical hyperplasia which had docket review had one first degree relative with breast cancer, age at menarche 15 years, age at biopsy was 47 with two previous biopsies, is a female from St. Elizabeth and whose age at first live birth was 17. The accumulative risk would be calculated over a time period not less than 25 years.Limitation to the study; patients who fall out of the study due to death, migration and no follow up within the public system and also missing data due to missing histopathology reports and dockets and operating theatre registry were the main limitation.

Conclusion

There is a weak association between the atypical hyperplasia and non-benign lesions which support the alternative hypothesis although not statistically significant which could be attributed to the missing data and a small sample size. The fact that there were only four atypical hyperplasia presentations

from a cohort of 210 pathologies during this six-year period would suggest that this should not be eliminated as a formidable risk factor in the development of breast cancer. The analysis of the data obtained through this study would suggest that with improved data management of breast cancer cases there could be a better understanding of the association of the various established risk factors along with probable causation within this geographic setting.

Recommendations

The Current situation within the parish of Manchester, for best practice, healthcare workers should understand that atypical hyperplasia does confer a risk of developing breast cancer. To completely understand the association between atypical hyperplasia and non-benign lesion additional research is needed. This study highlighted that fact that there was poor data management in the form of its collection and storage. The average age at current biopsy being above 50 years suggest the need for a properly constructed and well adhered to set of guidelines for early detection and management of breast cancer (a screening programme). The current situation is that the local guidelines for breast-cancer screening of women should include guidelines from the national comprehensive cancer network (NCCN), the American Cancer Society (ACS), and the American College of Radiology. This would be a valiant effort by the healthcare system to implements these guidelines as this would improve awareness of this devastating disease.

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