BREAST CANCER HISTOLOGY PROFILE: A SIX-YEAR SURVEY OF BREAST CANCER HISTOLOGY SAMPLES IN FIJI (2009 TO 2014)

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ABSTRACT

Introduction: Breast cancer is a major health problem in Fiji. There are very few literature found on breast cancer in the Pacific. This study aims to provide a platform for future studies on breast cancer, by describing the demographics of breast cancer in Fiji, based on histological reports analysis.

Method: This was a retrospective study of histologically-diagnosed breast cancer specimens in Fiji between 2009 and 2014. Histological reports of the eligible samples were screened and information regarding the following variables were collected and analysed.

Results: Breast cancer cases are increasing over the years. There are 840 breast cancer cases noted, 20 of which were from male patients and 817 from females. The Ethnic group distribution shows 481 samples from the iTaukei Ethnic group, 327 samples were from the Fijian-of-Indian Descent (FID) group. Breast cancer is seen throughout all age groups, however majority of the cases are distributed between the age of 30 and 70 years. The majority of the Tumour sizes falls in between 2cm and 5cm. Grade 2 is the commonest grade that we see and there are usually more than 3 lymph nodes involved. The left and right breast have similar occurrence for cancer. There is an increase of Positive ER and PR cases. More ITaukei in the Central/Eastern division are diagnosed with Breast cancer, whilst there are more FID in the Western division diagnosed with breast cancer. Breast cancer incidence is 54.9/100000 population and this is lower than figures from Australia (118/100000) USA (125/100000) and UK (164/100000).

Conclusion: There is an increase in breast cancer cases in Fiji. The incidence of breast cancer is lower than figures from developed countries. People living in rural areas have lower incidence of developing breast cancer. Incomplete histology report is a problem in Fiji. Further studies need to be carried out, to profile each variable in detail.

Key Words: *Breast cancer, Histology*

INTRODUCTION

Fiji is a tropical and multicultural Island nation located in the South Pacific and it is 2000 km northeast of New Zealand [1]. The last national census, showed a population of 837,271 where 56.82% are iTaukei, 37.48% are FIDs and 5.70% makes up of other ethnic groups [2]. Males make up 51.09% of the population while females accounts for 48.91% [3]. There are 220 Health facilities in Fiji, but histology service is only offered in the 3 divisional hospitals – Colonial War Memorial Hospital (Suva), Lautoka Hospital and Labasa Hospital [4]. The Ministry of Health annual reports showed figures of breast cancer in Fiji from 2010 to 2014. The number of cases ranges from 164 to 217 new cases per year. In 2014 the rate of breast cancer in Fiji is 58 cases per 100,000 populations [4]. In comparison, Australia's breast cancer incidence is 118 cases per 100,000 [9], USA is 125 cases per 100,000 [10] and UK has got an incidence rate of 164 cases per 100,000 [11]. The incidence rate for breast cancer is actually low when compared to the international statistics.

Breast cancer is the commonest female cancer. Cancers are composed of uncontrollable cells that invade and indirectly destroy adjacent tissue [6]. The Nottingham Breast Cancer Index is used to predict the severity of breast cancers and the sum of score from variables determines the prognostic outlook of the cancer. [7] These variables include size of the tumour, and lymph node involvement. However, instead of tumour distant metastasis our study describes tumour grades.

Revolutionary studies have been conducted over the years and they are all promoting the superiority of molecular studies over normal histological studies. Lips et al confirmed that if clinical finding was used together with immunochemistry and histology grading (all available in Colonial War Memorial Hospital) the quality of information generated is just as good as the information received from molecular studies. It is also mentioned in Lips et al study that molecular investigation is expensive to be part of day to day, breast cancer investigation [26].

For cancer management, early detection is important in trying to cure the cancer [15]. Patient awareness of breast cancer will help in the making of decision to seek medical treatment early. They will need information on the nature of breast cancer, when to suspect it and the benefits of having regular check-up if one is at risk [16].

As discussed by Liao et al, it is crucial to incorporate multidisciplinary approaches to diagnosing breast cancer. Any of these discipline (histology, radiology or clinical) on its own can miss a significant amount of breast cancer or over diagnose cases [17]. Schmidt et al found that ultrasound (comes under the radiology department) alone can miss 16% of breast cancer cases [18].

At the moment tumour grade is not part of the Nottingham Breast Cancer index. It only includes PT (tumour size), PN (lymph node involvement) and PM (tumour metastases). A study conducted by Emad et al shows that lymph node involvement and tumour grade provides a more accurate prognostic index. The above group are recommending the inclusion of Tumour grade to the Nottingham Breast Cancer Index [23]. Tumour grade two is the most common tumour grade that is seen in Fiji. Limitations of the tumour grading system is that it is mainly subjective to the diagnosing Pathologist and it is difficult to reproduce the same results, amongst different pathologist to diagnose.

The hormonal receptor stain is a test that helps with decision on chemotherapy options. This study looks at some of those demographic variables together with variables that are measured by the Nottingham Breast cancer index.

AIM

To describe the demographics of histologically-diagnosed breast cancer reports in Fiji, between 2009 and 2014.

OBJECTIVES

1. To describe breast cancer in Fiji into gender, ethnicity, age groups, site of cancer, procedure, cancer grade, tumour size, lymph node involvement, hormonal status and medical zones.

2. To compare the local data with regional and global data

METHODOLOGY

This is retrospective study, where by the breast cancer cases from the three divisional hospitals in 2009 to 2014, were profiled. The reports were profiled according to each demographic and histological variable.

The studied variables for breast cancer cases include: Specimens, Age, Ethnicity, Gender, Site and Procedure, Tumour size, Cancer grade, Lymph node involved, Hormonal Receptor Stain status and Medical divisions.

The 'Documents and records data collection techniques' were used, whereby, the histology report for breast cancer cases were used as the source of data [19].

The inclusion criteria consist of histologically-identified breast cancer reports from the three tertiary hospitals between 2009 and 2014. Excluded are cases with multiple entries of the same patients and reports with absent or insufficient histological specimens

Ethical approval for conducting this study was obtained from College Health Research Ethics Committee (CHREC) and Fiji National Health Research Committee (FNHRC). Permission to collect the data from the three divisional hospitals was obtained from the respective medical superintendents. There were no confidentiality issues, since no personal identifiers were included (except the unique laboratory numbers to allow retracing of reports).

RESULTS

Out of all total specimens for histology collected in the study period (n= 32497), 6.9% (n=2244) were breast specimens, with breast cancer found in 2.6% (n=840) (Table 1). This accounts for 37.4% of the total breast specimens taken. Breast cancer is unanimously was a disease of the female, although there were 20 (2.4%) cases of breast cancer in males in the study period.

In terms of age distribution (Table 2), the percentage of cases that fall in between age of 30 and 69 is 85.1%. About 2.6% of the cases are below 30 years of age; 12.2% are older than 69. The youngest patient with breast cancer was less than 10 years.

Over the years, the number of breast cancer for the iTaukei ethnic group had increased dramatically compared to the other ethnic groups. Moreover, the total

number of breast cancer cases is high amongst the iTaukei ethnic group (48.6%) (Table 3). However, total population at risk for each ethnic group has to be taken into consideration. As an example, in 2014, there were estimated population of 513,022 iTaukei with 101 (19.7 per 100,000) having breast cancer; 338,703 FID with 70 (20.7 per 100,000) having breast cancer, and 40,644 Others with 5 (12.3 per 100,000) having breast cancer.

More iTaukei have breast cancer in the Central/Eastern division, while more FID have breast cancer in the Western division (Table 3). The northern division initially showed higher incidence of breast cancer amongst FID but then at the end of the study period the ITaukei figures passed the FID numbers. A significant number of received specimens were missing the size and ethnicity information. However, the FID women with breast cancer generally presented with small size tumours, while more iTaukei presented with big tumours that have already infiltrated the surrounding structure. There is consistent high numbers of tumour that size falls in between 2cm and 5cm (Table 4).

There were generally more mastectomies than biopsies of the breast, but since all of the excluded samples are biopsies, this lower biopsy numbers are false. There was similar numbers of left breast (42.3%) and right breast (43.4%) cancer occurrences (Table 5). Non-orientated breast sample accounts for 14.4%. Majority of breast cancer, with an identified grade shows intermediate (grade 2) tumour. Grade two cancers are the most common grade in Fiji and accounts for 46.5% followed by Grade 3 (30.1%) and then Grade 1 (23.4%) (Table 6). Majority of the tumours show metastasis to more than 3 lymph nodes. Most of the females in their 50s have more than three lymph node metastasis (Table 7).

A lot of mastectomy specimens did not have the hormonal status tested (51.4%). Out of the valid data, 26.8% of the tumours are positive for oestrogen receptors stain, while 21.7% test are negative. About 49.8% of the progesterone receptor test was not done; 26.8% of the tested breast cancers were positive and 23.4% were negative (Table 8).

Table 1: Specimens collected

Year	Total specimens	Breast specimens	Breast cancer
2009	5039	327	117
2010	5076	351	132
2011	5730	351	110
2012	5409	350	133
2013	5191	415	171
2014	6052	450	177
Total	32497	2244	840

Table 2: Age Distribution of Breast Cancer cases

Age	n	%
0 to 9y	1	0.1
10y to 19y	2	0.2
20y to 29y	19	2.3
30y to 39y	82	9.8
40y to 49y	204	24.3
50y to 59y	227	27.0
60y to 69y	188	22.4
70y to 79y	91	10.8
Over 80y	10	1.2
Missing data	16	1.9
Total	840	

Table 3: Ethnicity and Division Distribution of Breast Cancer cases

	Central / East	Northern	Western	Total (Ethnicity)
iTaukei	234	59	115	408 (48.57%)
FID	118	61	224	403 (47.98%)
Others	15	4	10	29 (3.45%)
Total (Division)	367 (43.69%)	124 (14.76%)	349 (41.55%)	840

Table 4: Tumour size in breast cancer cases

Size	n	%
0 to 2cm	46	5.5
2cm to 5cm	120	14.3
>5cm	107	12.7
Infiltrate adjacent structure	70	8.3
Missing data	497	59.2
Total	840	100

Table 5: Site and Procedure of Breast Cancer cases diagnosed

Site	n	%
Left breast biopsy	166	19.8
Right breast biopsy	167	19.9
Breast biopsy (side not recorded)	64	7.6
Left breast mastectomy	189	22.5
Right breast mastectomy	197	23.5
Mastectomy (side not recorded)	57	6.8
Total	840	100

Table 6: Tumour grade in breast cancer cases

Grade	n	%
Low (Grade 1)	88	10.5
Immediate (Grade 2)	175	20.8
High (Grade 3)	113	13.5
Missing data	464	55.2
Total	840	100

Table 7: Node involvement in breast cancer cases

Lymph node involvement	N	%
No lymph node involvement	79	9.4
1 to 3 node involvement	83	9.9
More than 3 node involvement	137	16.3
Missing data	541	64.4
Total	840	100

Table 8: Oestrogen and Progesterone receptor stain test			
Oestrogen receptor stain test	N	Progesterone receptor stain test	N
Positive	90	Positive	87
Negative	73	Negative	76
Not done	173	Not done	162
Missing data	504	Missing data	504
Total	840	Total	840

DISCUSSION

Specimens: Over the six years of study there are 32,497 histology specimens taken, of which 2,244 specimens were from the breast and 840 cases are cancer. Breast cancer makes up 37.4% of all breast samples taken. The other 62.6% are benign lesion. (Table 1)

Age: Increasing age is one of the well-established risk factor for breast cancer [6]. According to the Cancer Research UK [11], about 45% of Breast cancer in the United Kingdom are aged 65 and above, however, in Fiji 23.3% of breast cancer are from the same age group range. This signifies that Fiji's peak breast cancer age group includes younger age groups compared to international breast cancer peak age groups. Familial/genetic related breast cancer often develops in younger (less than 40 years) females, which is linked to BRAC 1 and BRAC 2 gene mutation. Females younger than 40 years accounts for about 5% of breast cancer cases in the United States of America [21]. Younger age group (Birth to 39 years) accounts for 12% in Fiji. If Fiji were to set up a BRAC gene mutation screening programme, a potential of 12% of breast cancer patients may benefit from knowing their risk of developing breast cancer. A shortcoming was that 14.4% of all the breast cancer specimens did not have the age entered on the form.

Ethnicity: The Centre for Disease and Control (CDC) confirmed that Asian and Pacific Islanders ethnic group have the second lowest incidence for breast cancer, while the Hispanic have the lowest in the United States of America [22]. Over the years, the number of breast cancer for the iTaukei ethnic group has increased dramatically compared to the other ethnic groups. The total number of breast cancer is high amongst the iTaukei ethnic group. However the incidence rate for FID ethnic group is higher than the iTaukei ethnic group. The FID shows 21 cases per 100,000 populations while the iTaukei showed 20 cases per 100,000 populations. The Others ethnic groups accounted for only 12 cases per 100,000 populations. Overall the Fiji incidence rate is much lower than the Pacific Islanders and Asian in the United States which is 88.3 per 100,000 [10]. The ethnic group distribution per medical zones shows obvious differences. The Central/Eastern division show

predominance of iTaukei with breast cancer. Western division shows a predominance of FID cases of breast cancer and the Northern division initially shows high FID numbers (later in the study it changed to the iTaukei ethnic group). This may be reflective of the different population density of each ethnic group per medical division. The correlation of age group and ethnicity showed that more iTaukei have breast cancer very early and later in life.

Gender: Being a woman is the greatest risk factor for breast cancer. In 2014 the incidence for breast cancer amongst females in Fiji is 38.8 per 100000 population, while Male are 0.7 per 100000 population. The incidence for male breast cancer in this study is the same as male breast cancer incidence in Fiji described by Singh et al (2010), which is 0.7 per 100000 populations [12].

Site and Procedure: There is generally more mastectomy than biopsies of the breast. There should be equal or more biopsy compared to mastectomy. Due to the exclusion criteria a lot of biopsies were eliminated. There are similar numbers of left to right breast cancer occurrences; right breast in 43.4% and left breast in 42.3%.

Tumour size: The size of the tumour is mainly reported on mastectomy samples. Biopsy samples do not have the tumour size reported in the description of the tumour. There are 397 biopsies, but there are 497 samples that do not have the tumour size reported. It is 100 specimens more and this extra 100 specimens are mastectomy cases that do not have the size entered. Most of the reported tumours are between 2cm to 5cm, followed by tumours more than 5cm in size (31.2%) and then tumours less than 2cm in size (13.4%). The smaller breast tumour groups are slowly increasing at the end of the study period.

Breast Cancer Grade: Breast cancer samples from mastectomies should consist of the entire tumour, in order to measure the size of the tumour. The worst looking area is used to predict the grade of the tumour, and tumour grade is important in the prediction of the behaviour of the cancer. Majority of breast cancer, with an identified grade shows intermediate (grade 2) tumour. Grade two cancers as the most common grade in Fiji and accounts for 46.5% followed by Grade 3 (30.1%) and then Grade 1 (23.4%). In the USA the commonest grade is grade 3 (45.6%) followed by grade 2 (35.6%) and then grade 1 (18.6%) [10]. There are smaller size tumours in low grade cancer compared to higher grade tumour; generally high grade tumours show bigger tumour size.

Node Involvement: With the high frequency of multiple node involvement, it is hypothesised that most of the breast cancer patient present late to hospital, as it takes

a long time from development of cancer to the removal of the cancer.

Hormonal Receptor Status: Performing hormone receptor study on breast infiltrating ductal carcinoma is important to the clinical course and treatment of patient. If the tumour is positive for oestrogen receptor stain, the patient will do well with target therapy (example tamoxifen) [25]. Initially there were a lot of Oestrogen receptor stain and Progesterone receptor stain negative tumour in 2009. The number of both hormonal status negative tumours gradually declined over the years while both hormonal status positive tumours increases over the similar period. Apart from the actual change in the tumour hormonal status over that particular period, another explanation for the trend could be gravitated towards technical skills of the immunohistochemistry technician, performing the test. All of the immunohistochemistry tests are done manually, and the outcome of the test is dependent on the skills of the technical officer. In the beginning of the study in 2009 the technical officer was relatively new to the art of performing immunostains. Over the years, as the technical officer's skills improved, there was an increase in the number of oestrogen and progesterone receptor stain positive tumours.

Medical Division: The incidence of getting a histology sample taken from a certain geographical division is highest in the Western division, followed by Central/Eastern Division and lowest in the Northern Division. Central and Western Division are generally urban areas while the Northern division is a mix of semi urban and rural region of Fiji.

Statistics: Australia, United States of America and the United Kingdom cancer statistics estimated in 2012 that in every 8 females 1 will develop breast cancer in their life time [24]. However figures from Fiji shows that in every 44 females 1 will develop breast cancer. This figure is not directly comparable since the calculation depends on the life expectancy of the particular geographical community. The life expectancy in those developed country ranges from 84 to 87 years for females and for Fiji it is 79 [13, 14, 15] Mortality rate for breast cancer is estimated to be as high as 60% and less than 50% of this breast cancer patient received standard medical treatment [5].

Conclusion

Each year there is an increase in the number of histology samples and the number of breast cancer samples. The incidence of breast cancer is the same for left and right breast, thus breast cancer do not have any predilection for which hand the person uses/do not uses. The incidence for breast cancer in Fiji is lesser compared to Australia, USA and the UK incidence. The incidence of breast cancer between the iTaukei and FID are similar. This is attributed the high iTaukei population in the Central/Eastern division and the higher in the western division. Others ethnic group shows lesser incidence rate. Male rate for breast cancer is similar to international values, while female rate is lower than international values. Breast cancer is common from thirties to the sixties. Majority of breast cancer shows grade 2 cancer. Common breast cancer size ranges from 2cm to 5cm. Majority of the mastectomies with axillary clearance shows more than 3 lymph node having tumour metastasis. The information from the tumour grade, tumour size and lymph node involvement showed that people present late to hospitals for examination and investigation. There are more awareness programme for breast cancer being disseminated, thus people are coming to hospital early and the diagnosed breast cancer sizes are a lot more compared to previous years. Incomplete breast cancer reports are a serious issue detected. Missing data ranges from Age, ethnicity, site of breast cancer, Tumour size, tumour grade, lymph node involve and hormonal status

Strengths of study: This is the first study to look at the demographics of breast cancer in Fiji. The study looks at data from the whole of Fiji and all the histology breast cancer reports are being included in the study. The study can be used as a base line for future studies, the results can be used as supporting evidence to get advance medical equipment's and tests.

Limitations of study: When searching for breast cancer in CWM with the programme Microsoft access, the search parameter used under the specimen column was the word "breast" and "mastectomy". Breast specimens that were labelled with any other name apart from the above mentioned have been missed out. An example would be the breast cancer cases labelled with anterior chest wall mass will be missed out. Significant numbers of report were missing some information vital information like age, ethnicity, grades, sizes, and hormonal status. To have better coverage for breast cancer histology, samples from Suva private hospital and Autopsy sample of breast cancer are supposed to be included. Figures and comments made to the biopsy versus mastectomies are not accurate and cannot be used to make meaningful interpretations since most of the samples were excluded by the exclusion criteria. But if we were to purely look at the numbers of the biopsies and mastectomy than all those excluded samples due to repetition needs to be included.

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