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Breast Disease in Timor-Leste

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Breast Disease HNGV hospital Timor-Leste

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Abstract (<250 words)

Background

Surgically treatable conditions are well documented in high income countries. There is a gap in epidemiological understanding of breast pathology in many developing countries, Timor-Leste among them. This study was conducted to determine the burden of breast disease and to inform public health measures to address early detection, diagnosis and management.

Methods

A retrospective quantitative case control study was conducted at Hospital Nationale Guido Valadares (HNGV) in Dili. Patients were included if they attended surgical outpatients or had a pathology specimen recorded between 1st September 2016 and 1st September 2017.

Results

There were 444 female patients with a clinical diagnosis of breast disease over the 12 month period. The average age was 33.7 years. There were 188 (42.3% of total sample) cases of fibroadenoma and 122 (27.4% of total sample) diagnoses consistent with non-specific lumps. Of the 116 female patients presenting to HNGV who had a biopsy 62.6% were malignant or hyperplastic in nature, and 86% of those with a malignant biopsy had clinically locally advanced disease.

Conclusion
Breast conditions including cancer in Timor-Leste are relatively common and occur in young women in the prime of their lives (37 years of age). Developing a national cancer registry and funding directed towards improving early presentation and good clinical care of breast cancer patients will be critical for reducing early morbidity and mortality and improving other patient outcomes including income loss, gender health inequality the intergenerational effects of early parental death.

Keywords: breast cancer, breast disease, Timor-Leste, registry, women’s health

Introduction

Timor-Leste gained national sovereignty from Indonesian occupation in 1999 and became formally independent as a sovereign state in 2002.¹ The struggle saw destruction of national infrastructure alongside mass exodus of professional staff.² Economically, the country is placed 133 of 143 on the World Health Organisation’s (WHO) 2015 Human Development Index, reflected by the 64% poverty rate of its 1.2 million citizens.³ Poor economic status has resulted in an underfunded healthcare sector and a lack of medical resources for the population.⁴

Breast malignancy is ranked the second leading cause of premature death in Australian women and currently the most prevalent cancer among females worldwide.⁵,⁶ However, there is a gap in epidemiological understanding of breast pathology in many developing countries including Timor-Leste.⁷ Neighbouring Pacific low-and middle-income countries (LMICs) have reported a rising incidence of breast cancer with age standardised incidence reported to be 6.9 per 100 000.⁸ In these countries breast cancer is reported to be one of the most common cancers in women, alongside cervical and lung cancer. Established cancer registries and/or audits that have provided data for publications on the epidemiology and pattern of disease exist in economically comparable island nations, though not in Timor-Leste.⁹,¹⁰ Such lack of research leaves the health system vulnerable to a poor understanding of disease patterns, thus limiting the ability to develop affordable
and effective prevention and early detection measures, or improve management pathways. This also contributes to the current gender health disparity in many low and middle income countries (LMICs).\textsuperscript{6,11}

The risk factors for breast cancer are well documented and include genetic mutations, exogenous and endogenous hormonal factors and lifestyle issues such as diet, obesity and inactivity.\textsuperscript{12} Some of these risk factors are less common in developing countries, however as lifestyles change they are beginning to contribute to an increasing incidence of breast cancer. Population screening via mammography is not economically feasible or desirable in Timor-Leste, however other prevention and early detection strategies such as breast awareness, identification of risk factors and clinical examination are likely to improve earlier presentation and disease specific mortality.\textsuperscript{13} Understanding the pattern of disease for breast symptoms in Timor-Leste is a first step to instituting such measures, and this study seeks to address this knowledge gap by ascertaining the demographics, incidence and prevalence of breast pathology in Timor-Leste. It is hoped this will allow the healthcare system to align services, including surgery, accordingly, providing the community with thorough assessment, treatment and follow up for patients with symptomatic concerns.

This study aimed to investigate the incidence of surgically treatable breast conditions in Timor-Leste at its only tertiary referral hospital. This includes a description of patient demographics with an understanding of the clinical and pathological diagnoses related to breast presentations over a one year period from 1st September 2016 to 1st September 2017.

Methods
This research is a retrospective quantitative case control study. Ethics approval in line with the Declaration of Helsinki was obtained from the Department of Health Ethics Division Timor-Leste ref: 1189/MS-INS/DE-DP/DEP-P/AL/X/2017. Data collection was performed using retrospective data capture and subsequent categorisation of diagnosis of breast disease by a surgical doctor.
We undertook a one year retrospective review of all outpatient presentations with a subjective clinical diagnosis of breast disease presenting to HNGV, between 1st September 2016 and 1st September 2017. Information collected included patient age, duration and type of symptoms and clinical cancer staging on presentation if available. These were the only data points entered into the HNGV records and did not include presentations to other health districts. Clinical diagnosis was defined as those made by the outpatient surgical doctor based on history and examination of the patient, whereas pathological diagnosis were those made on the basis of tissue examination (cytology) by a pathologist.

We also undertook a one year retrospective review of pathology department results at the national hospital between 1st September 2016 and 1st September 2017. The number of breast biopsies was recorded along with the age of the patient, and final pathological cell-based diagnosis. Biopsy at HNGV is done by ultrasound guided FNA performed by the duty pathologist of the day. The data was entered into an electronic database and descriptive statistical analysis was performed.

For a population of 1.2 million the health services nationally perform 315 procedures per 100,000. Timorese people experience delays in reaching urgent surgical care from onset of their disease until the surgical management of that disease in hospital. There is only one tertiary national hospital, GUIDO VALDARES NATIONAL HOSPITAL (HNGV), five secondary level health centres and over 302 primary Health Posts. The surgical service of HNGV has 14 surgeons, 3 anaesthetists and 3 obstetricians amongst the Timorese trained team and 18 expatriate surgeons and anaesthetists. Diagnostic services at HNGV are rudimentary, which is a similar experience for Timor’s LMIC neighbours. Two Timorese and one Cuban Medical Brigade pathologist/technician offer cytopathology services which can distinguish benign from malignant tissue as well as undertaking basic blood tests including limited tumour markers. There is no locally based anatomical pathology or immunohistochemistry available due to lack of functioning equipment and reagents. The Cuban
medical oncologist provides systemic therapy for selected breast cancer patients which is limited to Tamoxifen (poor supply and unknown compliance) as no cytotoxic therapy is available. No radiotherapy is available in Timor-Leste. To access radiotherapy patients have to travel to Indonesia, Singapore or Australia, with very limited funding available for this.

**Results**

A total of 444 female patients presented to HNGV where a clinical diagnosis of breast disease was recorded over the 12 month period. The average age was 33.7 (standard deviation = 14.2). Of the clinical diagnoses made, fibroadenoma and nonspecific breast lumps were the most common. There were 188 (42.3% of total sample) cases of fibroadenoma and 122 (27.4% of total sample) diagnoses consistent with non-specific lumps. The mean age for fibroadenoma was 31.5 (standard deviation = 13.2) years old and 35.5 (standard deviation = 15.1) years old for other presumed benign lumps. *(Table 1)* Breast cancer and abscesses were the next most prevalent with 57 (12.8% of total sample) and 30 cases respectively in the sample (6.8% of total sample).

Of the 116 female patients presenting to HNGV who had a biopsy within our capture dates and whom a pathological diagnosis was available, the average age was 37.7 (standard deviation = 15.8 years). Of this group, 45 patients were diagnosed with fibroadenoma (µ age = 25.7 ± 7.8) and 33 patients with invasive ductal carcinoma (µ age = 49.5 ±13). *(Table 2)* Of the pathological diagnosis 62.6% were malignant or hyperplastic in nature, and further to this 85.9% of the malignant diagnoses were at least locally advanced (lack of available imaging for staging means distant metastatic disease could not be confirmed).

Patients were on average required to travel 30km to reach breast clinic facilities. However, this was significantly skewed as the mode and median were 5km and 10km respectively and maximum distance 230km.

**Discussion**
Fibroadenoma was the most common presentation of breast pathology to the tertiary referral hospital in
Timor-Leste. Invasive ductal carcinoma (IDC) was the most common breast carcinoma and presented most
frequently among women aged in their late forties. The 2012 WHO Globocan report includes Timor-Leste
within the South East Asian data, but without confirmed prevalence or incidence data. Our results provide a
clearer understanding of the previously unreported breast pathology prevalence in Timor-Leste. From our
cohort, the mean age of invasive carcinoma at diagnosis was 49.5 years old. This is difficult to compare with
other developing countries that typically have minimal or no data, however the mean age at diagnosis is
approximately a decade less compared to developed countries such as Australia. Without mortality data
prognosis relative to other countries also cannot be determined from this study, although of malignant
diagnoses 85.9% were at least locally advanced conferring worse prognosis generally.

The results of our study suggest the average distance to travel for treatment was relatively modest for the
population demographics of Timor-Leste, suggesting many patients from distant areas simply do not reach the
tertiary treatment centre. However, the data was highly skewed and suggests there are residents who may
face transportation challenges, with even relatively short journeys sometimes being very difficult to
undertake. There are two important caveats to this; firstly the time travelled is more important than
distance, as time and difficulty would be seen as the barrier rather than the nominal distance. This reinforces
the importance for more accessible breast services in the primary and secondary health clinics in order to
promote breast health and diagnosis.

There are numerous obstacles contributing to this inadequate care, and these impact on patient outcomes.
These include low numbers and inadequate training of many health professionals, poor infrastructure and
equipment, and access barriers for patients including geographic, financial and cultural. We acknowledge
shortcomings in our data - we were unable to infer or explore the reasons why all patients with clinically
concerning breast symptoms did not proceed to biopsy. Surgical management (inclusive of support services

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such as pathology, radiology, wound care in the community and rehabilitation) has been under-resourced, partly as a result of inaccurate assumptions and competing priorities; like much of the developing world, there is a presumption that surgery is too costly for the benefits accrued, with many agencies and health professionals focusing on more “cost effective interventions”. Furthermore, where surgical procedures are performed in substandard conditions, the risk of adverse outcomes and complications rises. As a consequence, despite less access to surgical management, LMICs such as Timor-Leste account for a greater proportion of global burden of disease attributable to complications.

Limitations of our study also include sampling bias as data from people unable to access clinics could not be retrieved. As many of the clinics around Timor-Leste are inaccessible by road from remote communities, there is a high possibility that people with undiagnosed conditions are not included in the data. Moreover, not all patients given a clinical diagnosis were given a pathological diagnosis through further investigation. This is due to poor access to pathology, poor follow up and/or lack of resources. Furthermore, human error and lack of rigorous breast-related pathology specialist training compounds the lack of clinical accuracy. In view of this we were unable to link data sets between the clinical and pathological diagnosis groups as patient records were missing and incomplete for both clinical and demographic data.

This study has encouraged the development of a rudimentary breast cancer registry in Timor-Leste thereby prompting the potential for further audit and research. In addition a regular clinic at HNGV to assess patients with breast symptoms has been formed and patient information resources developed. Information regarding long term outcomes, as well as population data rather than that limited to the tertiary centre, is now required. The data presented within this study provides a retrospective statistical insight for only a 12-month period. Further work would involve development of a long-term cohort study examining patient risk factors, presentation, treatment, disease progression and mortality.
Conclusion

Breast conditions including cancer in Timor-Leste are relatively common and occur in young women in the prime of their lives (37 years of age). Developing a national cancer registry is critical for understanding local demographics, improving access to care, advancing health outcomes, measuring outcome changes over time and directing funding. Funding directed towards improving early presentation and good clinical care of this population will be critical for reducing early morbidity and mortality and improving other patient outcomes including income loss, gender health inequality and the intergenerational effects of early parental death. To improve breast cancer services in Timor-Leste a comprehensive plan aimed at screening, diagnostic services (radiological and pathological), service equity, surgical management and postsurgical care for all citizens needs to be optimized. Appendix 1 outlines such a plan.
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Appendix 1

INITIATIVE 1: Governmental department

Develop an Office of Cancer Control within NCD section of Ministry of Health.

INITIATIVE 2: Advocacy.

Using the power of the patient voice along with those delivering care is one of the most effective means to achieve health system change – it can influence government policy and stimulate policy change and
development, call for better care and resources for cancer patients including accessing international resources (UICC, 2017) and provide support for patients and families.

**INITIATIVE 3: Awareness in the community.**

Fund a number of initiatives around community awareness and strengthening the Haliku programme, with assistance from the Breast Cancer Network Australia and UICC.

**INITIATIVE 4a: Health worker education – early detection.**

Existing education materials (bettercare programme and Breast Course 4 Nurses) will be explored to use as templates for teaching both metropolitan and rural nurses and health workers as well as the newly trained Timorese doctors in regional centre and health posts.

**INITIATIVE 4b: Health worker education – breast cancer care.**

Develop appropriate educational material for health professionals managing women diagnosed with breast cancer.

**INITIATIVE 5: Data collection and cancer registry.**

A hospital based cancer registry could be developed from the MD clinic with all patient tumour and treatment details discussed at MD meetings entered into a data base. A national cancer registry will require legislation around notification of cancer cases by both pathology labs and treating clinicians, and establishment of this could be done with assistance from organisations such as the International Association of Cancer Registries, part of the International Agency for Research on Cancer.

**INITIATIVE 6: Develop a multidisciplinary team.**

The proposed establishment of a Breast Clinic at HNGV needs urgent action. Along with the physical location and governance of the clinic, establishment of regular MD meetings in which ALL breast cases referred
to HNGV are discussed and treatment plans devised and recorded. Attendance at these MD meetings is a requirement of all surgeons who manage breast cases, but should also include the oncologist, pathologist, radiologist, nurses, physiotherapy and Haliku staff.

Development of local treatment protocols needs urgent attention to guide MD care. International surgical colleagues will assist with this process.

INITIATIVE 7: Diagnostic services at HNGV.

- Imaging – mammography and CT scan equipment needs to be sourced along with servicing, staff training and quality control arrangements. All patients with breast symptoms need access to mammography and breast ultrasound. Patients with advanced cancer require staging with whole body CT and/or chest X-ray and liver ultrasound.

- Pathology – anatomical pathology services require urgent update. Histopathology including adequate formalin supplies, H&E staining and immunohistochemistry (IHC) for hormone receptors and HER2 are mandatory.

- Blood bank services need to be made secure via a national Blood Bank Service.

- Biochemical tumour markers should ideally be made available in the pathology services at HNGV or via the private clinic.

INITIATIVE 8: Treatment services.

The long term goal is a Comprehensive Cancer Centre at HNGV which meets international standards of care. For breast cancer this will include surgery, hormone therapy, chemotherapy, avenues for referral for radiotherapy, and supportive care.

In the short term, key aspects of treatment services which require urgent development include MD care and protocols (see Initiative 6), developing advanced skills in breast surgery, sustained access to
endocrine drugs including a stable procurement process for Tamoxifen as well as adding goserelin to the
formulary, and development of a small 4 chair, 2 bed chemotherapy unit with 2 trained chemotherapy nurses,
a pharmacy and equipment for drug dispensing, and access to a basic suite of chemotherapy agents notably
CMF, anthracycline and platinum agents, and protocols for administration and management of side effects,
including access to anti-emetics and steroids.

Development of basic allied health support is considered important including staff development (see
Initiative 4.b) and physiotherapy.

Treatment of metastatic disease including access to bisphosphonates.

The Ministry may wish to develop better pathways for those requiring radiotherapy.

INITIATIVE 9: A national Palliative Care Plan (home-based and community palliative care to all patients with
life limiting cancer - protocols for symptom management, education and training and access to appropriate
drugs).

Importantly access to opioid analgesia may need legislative action.

INITIATIVE 10:

The Health Minister ratify the World Cancer Declaration 2008 and in doing so join the UICC.

INITIATIVE 11:

A detailed resourcing plan to be formulated to accompany the cancer plan.

INITIATIVE 12:

An evaluation framework for the cancer policy to measure outcomes and system change, in relation
to the specific goals for breast cancer control.
Table 1: Frequency of breast related suspected diagnoses made clinically and age of patient made for patients presenting to the outpatient department of HNGV hospital between 1/9/16 - 1/9/17

<table>
<thead>
<tr>
<th>Complaints</th>
<th>Number of Presentations</th>
<th>AVERAGE of Age 'Years'</th>
<th>STDEV of Age 'Years'</th>
<th>MEDIAN of Age 'Years'</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroadenoma</td>
<td>188</td>
<td>31.5</td>
<td>13.2</td>
<td>28</td>
</tr>
<tr>
<td>Lump</td>
<td>122</td>
<td>35.5</td>
<td>15.1</td>
<td>31</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>57</td>
<td>34.8</td>
<td>13.6</td>
<td>32</td>
</tr>
<tr>
<td>Abscess</td>
<td>30</td>
<td>38.5</td>
<td>16.1</td>
<td>34.5</td>
</tr>
<tr>
<td>Mastalgia</td>
<td>13</td>
<td>30.9</td>
<td>15.7</td>
<td>25</td>
</tr>
<tr>
<td>Mastitis</td>
<td>10</td>
<td>35.0</td>
<td>14.6</td>
<td>29</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>24.7</td>
<td>9.1</td>
<td>21</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>444</strong></td>
<td><strong>33.7</strong></td>
<td><strong>14.2</strong></td>
<td><strong>30</strong></td>
</tr>
</tbody>
</table>
Table 2

Table 2: Number of breast related cell-based pathological diagnoses and age of patients recorded in the results of pathology department of HNGV hospital between 1/9/16 - 1/9/17.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Results</th>
<th>AVERAGE Age 'Years'</th>
<th>STDEV Age 'Years'</th>
<th>MEDIAN Age 'Years'</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abscess</td>
<td>3</td>
<td>31.00</td>
<td>13.86</td>
<td>23.0</td>
</tr>
<tr>
<td>Ductal hyperplasia with atypia</td>
<td>2</td>
<td>28.50</td>
<td>4.95</td>
<td>28.5</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>45</td>
<td>25.69</td>
<td>7.81</td>
<td>24.0</td>
</tr>
<tr>
<td>Fibroadenoma with atypia</td>
<td>2</td>
<td>34.50</td>
<td>6.36</td>
<td>34.5</td>
</tr>
<tr>
<td>Fibrocystic disease of the breast</td>
<td>7</td>
<td>35.14</td>
<td>6.67</td>
<td>37.0</td>
</tr>
<tr>
<td>Fibrolipoma</td>
<td>1</td>
<td>64.00</td>
<td>0</td>
<td>64.0</td>
</tr>
<tr>
<td>Granulomatous infection</td>
<td>2</td>
<td>35.50</td>
<td>0.71</td>
<td>35.5</td>
</tr>
<tr>
<td>Gynaecomastia</td>
<td>1</td>
<td>37.00</td>
<td>0</td>
<td>37.0</td>
</tr>
<tr>
<td>Inflammatory breast cancer</td>
<td>2</td>
<td>23.00</td>
<td>9.90</td>
<td>23.0</td>
</tr>
<tr>
<td>Invasive carcinoma</td>
<td>43</td>
<td>49.76</td>
<td>14.09</td>
<td>49.0</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Count</td>
<td>Proportion</td>
<td>Mean</td>
<td>Median</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-------</td>
<td>------------</td>
<td>-------</td>
<td>--------</td>
</tr>
<tr>
<td>Lipoma</td>
<td>1</td>
<td>33.00</td>
<td>0</td>
<td>33.0</td>
</tr>
<tr>
<td>Liposarcoma of the breast</td>
<td>1</td>
<td>55.00</td>
<td>0</td>
<td>55.0</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td>6</td>
<td>50.67</td>
<td>15.00</td>
<td>54.5</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td><strong>116</strong></td>
<td><strong>37.68</strong></td>
<td><strong>15.76</strong></td>
<td><strong>36.5</strong></td>
</tr>
</tbody>
</table>
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