

The Epidemiology of Breast Cancer in Oman

Shamsa AL Farsi

**A thesis submitted for the degree of Bachelor of
Medical Science with Honours at the University of
Otago, Dunedin New Zealand**

Abstract

Background

Breast cancer is the most common cancer in females around the world. Annually, more than one million women are diagnosed with breast cancer globally. In Oman, breast cancer is also the most common cancer in females and its incidence has been rising over the years. Published studies have shown that many Omani women have late stage breast cancer at presentation. Possible reasons for this have not been explored. Although Oman has in place a mortality registration database, no population-based mortality data from breast cancer are available. Likewise, the only data available about survival rate of people with breast cancer come from a hospital-based study.

Aims

The main aims of the research described in this thesis are:

- 1) To identify the extent of delay in breast cancer diagnosis in Oman.
- 2) To assess the relationship between delay and socio-demographic characteristics, medical and obstetric history, nature of presenting symptoms and women's knowledge about breast cancer.
- 3) To identify reasons for delay in seeking medical help for self-detected breast cancer symptoms in Omani women.
- 4) To calculate the population-based survival rate from breast cancer in Oman.

Methods

Aims 1, 2 and 3 were addressed by a study of 150 patients attending oncology clinics in both the Royal Hospital and Sultan Qaboos University Hospital, who were interviewed using structured questionnaires. Patient delay was defined as a period of three months or more between an individual's first awareness of a sign or a symptom of illness and the initial medical consultation.

In order to calculate survival rate, the National Cancer Registry records were to be linked to mortality databases in Oman (Directorate General of Civil Status and to the Parallel Mortality Database).

Results

The final analysis of delay included 144 patients with breast cancer. The median time taken by women in this sample between discovering the breast symptoms and seeing a doctor was 14 days. 56.9% of the patients had a medical consultation in less than a month after detecting symptoms, whereas 20.1 % had a consultation within 1 to 2 months. 22.9 % of the patients delayed consultation by ≥ 3 months. Of the socio-demographic characteristics examined in this study, it was observed that older age, low educational level and employment status were associated with patient delay. Practice of breast self-examination and having a history of chronic disease were also predictors of delay. 44% of patients had early stage disease (stage I/stage II) compared to 56% of patients with late stage disease (stage III/stage IV). However, patient delay was not associated with advanced stage cancer in this study.

The main reasons given for delay were: failure to recognise the symptoms to be breast cancer, not seeing oneself at risk for breast cancer, fear and embarrassment, use of alternative therapy and family and work commitments.

Due to ethical consideration, I was not able obtain data from Omani NCR and therefore the linking to mortality databases was not possible.

Conclusion

This study is the first in Oman to investigate the extent of patient delay for women with self-discovered breast symptoms and the factors that influence this delay. The findings of this study indicate the need for public education aimed at raising breast cancer awareness. Further, initiating a screening program in Oman should be considered to help women achieve diagnosis of the disease in its early stages.

Population-based cancer research should be encouraged in Oman, and efforts should be taken to improve the quality and completeness of cancer data, which are important in providing on-going monitoring of cancer.

Acknowledgments

I would firstly like to acknowledge the assistance of my supervisors Dr Patricia Priest and Dr Claire Cameron from the Department of Preventive and Social Medicine for their ongoing support and encouragement throughout the process of conducting the study and writing this thesis.

I am thankful to many people in Oman who made my project successful: Professor Mansour Al-Moundhri and Dr Ikram Burney from Sultan Qaboos University Hospital, Dr Bassim AL-Bahrani and Dr Suad Al- Kharusi from Royal Hospital for their efforts in helping me to interview the patients and complete data from the medical records, all the nurses and staff from both hospitals for making me feel welcome and helping me in meeting the patients, Dr Najla Al-Lawati from the Omani National Cancer Registry for helping me to obtain data from the registry.

This work would not have been possible without those many women with breast cancer and their families who participated in the interviews on which this thesis is based. My warm thanks go to them for taking the time to participate.

Most importantly, I am thankful and grateful for the ongoing support of my family in Oman, especially my brothers who were with me in every step during data collection. Lastly, I would like to acknowledge the support of many friends and their encouragement throughout the period of this thesis.

Table of Contents

Abstract.....	ii
Background.....	ii
Aims.....	ii
Methods	ii
Results	iii
Conclusion.....	iii
Acknowledgments	iv
List of Tables	viii
List of Figures.....	ix
List of Abbreviations	x
Chapter One - Introduction and Background	1
1.1 Introduction	1
1.2 Overview of the thesis	3
1.3 Search strategy for the background and literature review	3
1.4 Background.....	4
1.4.1 Pathology of the breast	4
1.4.2 Clinical aspects of breast cancer.....	6
1.4.3 Descriptive epidemiology of breast cancer	11
Chapter Two - Literature Review.....	18
2.1 Epidemiology of breast cancer in Gulf Cooperation Council Countries 18	
2.1.1 Cancer registration in Oman.....	22
2.1.2 Epidemiology of breast cancer in Oman	22
2.2 Breast cancer in the Arab population	24
2.2.1 Risk factors of breast cancer in the Arab population.....	27
2.3 Women’s perception of breast cancer risk	31

2.4	Delay in seeking medical care in patient with breast cancer	34
	Chapter Three: Delay in Seeking Medical Care for Self-Detected Breast Cancer Symptoms in Omani Women	45
3.1	Introduction	45
3.2	Aims.....	45
3.3	Methodology.....	45
3.3.1	Sample and sample recruitment.....	45
3.3.2	Data collection.....	47
3.4	Variable definition for analysis	48
3.5	Data analysis.....	49
3.6	Ethical considerations.....	50
3.7	Results	50
3.7.1	Study population.....	50
3.7.2	Knowledge and attitude toward breast cancer.....	55
3.7.3	Breast self-examination (BSE).....	55
3.7.4	Extent of delay.....	57
3.7.5	Influence of socio-demographic factors on delay.....	58
3.7.6	Influence of health characteristics, medical presentation and health behaviours on delay	59
3.7.7	BSE and patient delay.....	60
3.7.8	Reasons for patient delay.....	62
3.8	Discussion.....	65
3.8.1	Strengths and limitations	65
3.8.2	Patient delay in Omani women with breast cancer.....	66
3.8.3	Participants' characteristics and patient delay.....	67
3.8.4	Patient delay and breast self-examination	69
3.8.5	Stage at diagnosis and patient delay	71
3.8.6	Reasons for patient delay.....	73

3.8.7 Conclusion	79
Chapter Four - Mortality and Survival of Omani Breast Cancer Patients....	81
4.1 Introduction	81
4.2 Aim	82
4.3 Methodology.....	82
4.4 Data collection and ethical approval	83
4.5 Results	84
4.6 Discussion.....	84
Chapter Five - Conclusion.....	88
5.1 Main findings.....	88
5.2 Implications	89
References	91
Appendices	107
Appendix 1: Questionnaire.....	107
Appendix 2: The Omani National Cancer Registry Form.....	112
Appendix 3: Arab Women’s Breast Cancer Screening Practices.....	113

List of Tables

Table 1-1: Incidence of various types of breast malignant tumours.....	5
Table 1-2: TNM stage grouping of breast cancer.....	8
Table 3-1: Socio-demographic characteristics of participants	51
Table 3-2: Medical histories of the participants	52
Table 3-3: Reproductive histories of participants who had children.....	53
Table 3-4: Clinical presentations of the participants	54
Table 3-5: Patients' knowledge and attitude toward breast cancer	56
Table 3-6: Frequency distribution of patients presenting with breast cancer according to duration of patient delay	58
Table 3-7: Patient delay in breast cancer patient by socio-demographic factors	59
Table 3-8: Patient delay by health characteristics, presenting symptoms and health behaviour	61
Table 3-9: Reported main reasons for patient delay ≥ 3 months.....	63

List of Figures

Figure 1-1: Ten-year relative survival associated with AJCC/UICC (TNM) breast cancer stages.....	10
Figure 1-2: Age-specific breast cancer incidence in developed (white circles) and developing countries (black circles).....	13
Figure 1-3: Age standardized breast cancer incidence and mortality rates by world area	15
Figure 1-4: Age standardized incidence rate of breast cancer in selected developed countries	16
Figure 1-5: Age standardized incidence rate of breast cancer in selected developing countries	16
Figure 2-1: Age standardized incidence rate of female breast cancer in the GCC States, 1998- 2007.....	19
Figure 2-2: Average annual age specific incidence rates of breast cancer, 1998-2007 .	21
Figure 2-3: Age standardized incidence rate * of breast cancer in Omani women, 1999- 2011	22
Figure 2-4: Age standardized incidence rate of breast cancer in Oman and some selected countries	23
Figure 2-5 Age-specific incidence rates of common cancers in Omani females, 1998- 2006.....	23
Figure 2-6: Incidence of breast cancer by region (incidence rate are per 100,000 populations).....	24
Figure 4-1: Hospital-based breast cancer deaths.....	81

List of Abbreviations

Age Standardized Incidence Rate	ASR
Breast Cancer Gene 1	BRCA1
Breast Self-Examination	BSE
Clinical Breast Examination	CBE
Directorate General of Civil Status	DGCS
Epstein-Barr Virus	EBV
Gulf Cooperation Council	GCC
International Agency for Research on Cancer	IARC
Mastectomy	MT
Metabolic Syndrome	MS
Ministry of Health	MOH
National Cancer Registry	NCR
Oestrogen Receptor	ER
Parallel Mortality Database	PMD
Royal Hospital	RH
Progesterone Receptor	PR
Single Nucleotide Polymorphism	SNP
Saudi Arabia	KSA
Sultan Qaboos University Hospital	SQUH
United Arab Emirates	UAE
United Kingdom	UK
United State	US
World Health Organization	WHO

Chapter One - Introduction and Background

1.1 Introduction

Breast cancer is the most common cancer among women. In 2008, there were around 1.38 million new female breast cancer cases diagnosed worldwide (Ferley et al., 2010). The incidence rate was almost two and a half times higher in more developed countries compared to less developed countries (Ferley et al., 2010). This is mainly as a result of a higher prevalence of the known risk factors for the disease in developed countries relative to less developed countries, and lack of awareness and organised screening programs in developing countries (Coughlin and Ekwueme, 2009, Ferlay et al., 2010). Breast cancer is the most common cause of cancer death in women worldwide, estimated to be responsible for around 458,500 female deaths in 2008 or nearly one in seven (around 14%) of all cancer deaths in women (Ferley et al., 2010).

In the Gulf Cooperation Council Countries (GCC), breast cancer is the most common malignancy among women with the incidence being higher in Bahrain, Kuwait and Qatar and lower in Oman, United Arab Emirates and Saudi Arabia (Al-Madouj et al., 2011). The incidence of breast cancer in the GCC countries starts to increase among women in their mid-20s and steeply increases for women in their late 40s then there is a slow increase in the rest of their lives. In 2011, the age standardized incidence rate (ASR) was 25.5 per 100,000 women accounting for 24.8% of all female cancer in Oman (Al Lawati et al., 2013).

Oman is a high-income developing country. It has a population of 2,137,807 Omani, and shows a gender ratio of 983 females per 1000 males. About 13.2% of the population is under 5 years, 34% is under 15 years and 3.8% of the total Omani population is above the age of 60 years (Al Lawati et al., 2013). Health care is free for all Omanis (Nooyi and Al-Lawati, 2011). The standards of health services in Oman have been brought up to those of industrialized nations and health services include treatments such as organ transplants and open-heart surgery. The establishment of the National Oncology Centre in the Royal Hospital in the capital, Muscat, has enabled the availability of comprehensive cancer care in Oman (Nooyi and Al-Lawati, 2011). However, findings indicate

that the majority of Omani women are being diagnosed at late stages of the disease (stage III and IV) (Al-Moundhri et al., 2004, Al-Moundhri et al., 2011, Al-Moundhri et al., 2003). It is well documented that prognosis of breast cancer depends on the stage at diagnosis and those diagnosed at an earlier stage show better survival rate (Kumar et al., 2007). Moreover, advanced stages of the disease are shown to be a result of longer delays in seeking diagnosis for breast symptoms and those who presented earlier usually have smaller tumours with more favourable outcomes (Unger-Saldaña and Infante-Castañeda, 2009). Early care seeking is a principle in oncology, and delay in diagnosis and treatment of cancer has been the subject of research for decades. As early as 1938, Pack and Gallo defined the term patient delay as ‘the time elapsing between first symptom and first visit with a physician’ (Pack and Gallo, 1938). The reasons for delayed care seeking among cancer patients have been thoroughly explored but not in Oman.

This study addresses the issue of patient delay among Omani women by assessing the magnitude of delay and also evaluates possible factors causing delay. Because early diagnosis of breast cancer is important for improving quality of life and survival rate, breast cancer screening is the best mode of obtaining this goal. Hopefully, this study may help to inform decision-making about whether a screening program should be implemented to downstage breast cancer cases in Oman.

Policies and programmes to address health problems in a population require an understanding of the nature and extent of the problems, their causes and changes over time (Mathers et al., 2005). Various statistics need to be provided: the incidence of the disease, prevalence in the population, mortality and survival rates. While incidence data on breast cancer in Oman is available (Al Lawati et al., 2013), information regarding mortality is still lacking. Likewise, survival data available on breast cancer come only from hospital based studies. In 2004, a vital registration system, the Directorate General of Civil Status (DGCS), was established where population-based deaths are recorded. Despite the establishment of the DGCS, no data on population-based mortality or survival from breast cancer were available. Therefore, as a result of this study, I am

hoping to close this gap and provide at least estimates of mortality and survival from breast cancer in Oman.

1.2 Overview of the thesis

The organization of the chapters is as follows:

- Chapter 1 provides an overview of the thesis and a background regarding descriptive epidemiology, the clinical features, and pathology of breast cancer.
- Chapter 2 will examine the available literature that addresses the epidemiology of breast cancer in GCC countries, risk factors in the Arab populations and the problem of delay in seeking medical help for self-discovered breast symptoms.
- Chapter 3 will describe the study conducted to examine patient delay among Omani women with breast cancer to measure the magnitude of delay and identify factors associated with delay.
- Chapter 4 will describe the attempt to calculate survival rate of breast cancer in Oman beside discussing the importance of actively collecting data on mortality and survival rates and their application to breast cancer in Oman.
- Chapter 5 provides the main findings and implications of this study.

1.3 Search strategy for the background and literature review

- *Database used:* The following databases were used to search for relevant articles and keywords on the topic: Ovid via the Medline database, PubMed, and Scopus. Reading started with the most recent review articles, and then sought out the important referenced sources. References from relevant studies were also used to trace other studies. Additionally, four websites were also valuable for the search, which were the World Health Organization Statistical Information System database (<http://www.who.int/whosis/en/>), the International Agency for Research on Cancer (IARC) (www.iarc.fr/), American Cancer Society (www.cancer.org/) and finally, Oman Ministry of Health (www.moh.gov.om/)

- *References and keywords:* The initial list of keywords used to identify relevant articles included: “epidemiology”, “breast”, “cancer”, “incidence”, “mortality”, “survival”, “survival analysis”, “ethnicity”, “aetiology”, “cause”, “risk factors”, “prognosis”, “pathology”, “histology”, “histopathology”, “treatment”, “therapy”, “clinical features”, “signs”, “symptoms”, “prevention”, “screening”, “Arab”, “Oman”, “delay”, “patient’s delay”, “late diagnosis”, “diagnosis delay”, “help seeking behaviour”, “late stage” “developing countries” and “Middle East”.

1.4 Background

This section will provide an overview of breast diseases followed by general information regarding the clinical aspects of breast cancer including signs and symptoms, diagnosis, treatment and prognosis. An overview of global breast cancer epidemiology is also provided.

1.4.1 Pathology of the breast

Breast diseases

Breast cancer is the most common malignancy among females (Ferley et al., 2010). Nevertheless, benign lesions of the breast are far more frequent than malignant tumours. Benign breast disease includes a heterogeneous group of lesions that may express a wide range of symptoms (Guray and Sahin, 2006). Benign breast lesions usually have a high incidence during the second decade of life and peak in the fourth and fifth decades (Guray and Sahin, 2006). The World Health Organisation stated that among 100 female patients aged 40-65 years presenting with breast complaints, the following is likely: 30% have no breast lesion, 40% have fibrocystic changes, 7% have a benign tumour diagnosis and 10% have carcinoma (Khatib and Modjtabai, 2006).

Acute and chronic inflammatory lesions of the breast like acute mastitis, duct ectasia, post-traumatic lesions and granulomatous mastitis together with non-proliferative cystic lesions are benign breast diseases that are not associated with increased risk for breast cancer (Fan and Thomas, 2011). On the other hand, fibrocystic proliferative changes such as lobular/ductal hyperplasia with

or without atypia and adenosis belong to the group of benign diseases, which are associated with increased risk of developing breast carcinoma (Thomas, 2011).

Tumours are the most important lesions of the breast. Fibroadenoma is by far the most common benign neoplasm of the female breast (Lioe and Cameron, 2013). Other tumours such as phyllodes tumours and intraductal papilloma are less frequent and though most of time they remain benign, progression to malignant lesions may occur.

Carcinoma is by far the most common malignant neoplasm of the breast. It affects the left breast slightly more often than the right. About 4% of women with breast cancer have bilateral primary tumours or sequential lesions in the same breast. 50% of tumours occur within the upper outer quadrant of the breast. The remaining quadrants are each involved into about 10%, and the subareolar area is the initial site of presentation in 20% of tumours. Breast cancer can be divided into two main groups: non-invasive or carcinoma in situ, and invasive carcinoma. Table 1-1 presents the incidence of various breast carcinomas globally.

Table 1-1: Incidence of various types of breast malignant tumours

Type	Incidence
In situ carcinoma	15-30%
Ductal carcinoma in situ	80%
Lobular carcinoma in situ	20%
Invasive carcinoma	70-85%
Ductal carcinoma (no special type)	79%
Lobular carcinoma	10%
Tubular/ cribriform carcinoma	6%
Mucinous carcinoma	2%
Medullary carcinoma	2%
Papillary carcinoma	1%

Note: data adapted from (Khatib and Modjtabai, 2006)

1.4.2 Clinical aspects of breast cancer

Breast cancer signs and symptoms

The American Cancer Society highlighted signs and symptoms of breast cancer in its publication *Breast Cancer Facts and Figures: 2009-2010* (2010). It states that breast cancer usually produces no symptoms when the tumour is small and most treatable. A lump is by far the most common presentation. Most of the time it is painless, shows irregular borders, is firm and appears fixed to the underlying tissues or to the overlying skin. Pain is not usually present in breast cancer; only 5 % of patients with malignant mass present with breast pain. Another uncommon and alarming symptom is nipple discharge particularly when the discharge is blood stained. Other nipple abnormalities may indicate breast cancer such as erosion, inversion and tenderness. Less common signs and symptoms include heaviness and persistent changes to the breast such as swelling, thickening or redness of the skin of the breast. In some cases breast cancer may spread to the axillary lymph nodes and cause a lump or swelling, even before the original breast tumour is felt.

Diagnosis of breast cancer

It is recommended that any abnormal lesion, which is detected by the woman herself or through breast screening, to be evaluated using the 'triple assessment' approach (Lioe and Cameron, 2013). Triple assessment has an overall accuracy of 99.3% in evaluating patients with breast lumps and detecting patients with breast cancers (Jan et al., 2010). Lioe and Cameron (2013) described the process of this assessment, which usually starts with a clinical examination where symptomatic patients are referred to designated breast clinics, and assessed by multidisciplinary teams. Then radiological imaging is performed where a diagnostic mammography is used to determine size and location of the abnormalities in older women. Otherwise, ultrasonography is indicated for younger women. Sometimes the ipsilateral axilla is scanned using ultrasound to assess any enlarged or abnormal lymph nodes. Finally, any detected abnormality or suspicious areas of microcalcifications are further investigated using aspiration and/or biopsy. Clinicians may perform fine needle biopsy to characterize the cellular components of cystic lesions or use core needle biopsy

to investigate non-nodular or non-palpable lesions detected as mammographic microcalcifications.

Histological assessment of the tissue is then carried out to characterize the tumour based on microscopic organisation and growth pattern of cancer cells (Bateman, 2006). Tumour marker assay is now widely used to determine subtypes of breast cancer along with immuno-histochemistry of oestrogen and progesterone receptor status. Histopathological parameters are also used to determine tumour stage to achieve a prognosis.

Stage

The staging of breast tumours provides a description of the extent and spread of a tumour (Phipps and Li, 2010). The most common system used to describe the stages of breast cancer is the American Joint Committee on Cancer (AJCC) TNM system (Compton et al., 2012). Specifically, tumour stage is determined by the size of the tumour, number of involved lymph nodes, and whether the cancer has spread to other parts of the body.

The TNM staging system classifies cancers based on their T, N, and M stages:

- The letter T followed by a number from 0 to 4 describes the tumour's size and spread to the skin or to the chest wall under the breast. Higher T numbers mean a larger tumour and/or wider spread to tissues near the breast.
- The letter N followed by a number from 0 to 3 indicates whether the cancer has spread to lymph nodes near the breast and, if so, how many lymph nodes are affected.
- The letter M followed by a 0 or 1 indicates whether the cancer has spread to distant organs for example, the lungs or bones.

Once the T, N, and M categories have been determined, this information is combined in a process called stage grouping (Table 1-2). Cancers with similar stages tend to have a similar outlook and are often treated in a similar way. The stage is expressed in Roman numerals from stage 0 to stage IV. Stage 0 breast cancer (i.e., in situ breast cancer) is characterized by an accumulation of malignant cells that have not invaded into surrounding tissue. Breast tumours

designated as stage I, II, III, or IV involve some invasion of tumour cells beyond the basement membrane, and are thus referred to as invasive tumours. Stage I breast cancer is confined to the breast tissue and has a maximum diameter of less than 2 cm while stage IV breast cancer involves distant metastases.

Table 1-2: TNM stage grouping of breast cancer

<i>Stage</i>	<i>T</i>	<i>N</i>	<i>M</i>
Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T0	N1mi	M0
Stage IIA	T1	N1mi	M0
	T0	N1	M0
Stage IIB	T1	N1	M0
	T2	N0	M0
Stage IIIA	T2	N1	M0
	T3	N0	M0
	T0	N2	M0
	T1	N2	M0
	T2	N2	M0
Stage IIIB	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
Stage IIIC	T4	N1	M0
	T4	N2	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1

Note: data adapted from (Compton et al., 2012)

Grade

Tumour grade provides a description of how closely breast tumour cells resemble normal breast tissue when viewed microscopically (Phipps and Li, 2010). In situ ductal carcinoma and all invasive tumours are routinely graded. The grade is defined according to three morphologic features of breast tumour cells: (1) the degree of tumour tubule formation, (2) mitotic activity, and (3) nuclear pleomorphism (Fabbri et al., 2008). The three values are added together to produces scores of 3 to 9, to which the grade is assigned:

- Point total 5: grade 1, well differentiated;

- Point total 6–7: grade 2, moderately differentiated;
- Point total 8–9: grade 3, poorly differentiated

Thus, across grading scales, a lower grade is indicative of slower growing cancer that is less likely to spread and a higher grade is indicative of more aggressive, rapidly progressive disease. The grade is an important predictor of both disease free and overall survival (Phipps and Li, 2010).

Treatment

Surgery is considered the primary treatment for primary breast cancer. Many patients are cured with surgery; otherwise, adjuvant treatment involving radiation and systemic therapy (including chemotherapeutic, hormonal, and biologic agents) might be undertaken to treat micrometastatic disease.

Jatoi (2010) outlines in Management of Breast Diseases the surgical options for patients with breast cancer. Breast conserving surgery is an option for patients with lateral breast cancer showing small and localised tumours. Usually the surgery is followed by radiotherapy to eliminate occult tumour foci remaining in the ipsilateral breast (Sainsbury et al., 2000). Larger tumours require a modified radical mastectomy (MT) in which the entire breast tissue and the ipsilateral lymph nodes are removed leaving the muscle of the chest intact. It is recommended that patients choosing this treatment must undergo postmastectomy radiation if the primary tumour is $> 5\text{cm}$, and involves ≥ 4 lymph nodes (Recht et al., 2001). Additionally, some women with unilateral breast cancer might be treated with a modified radical MT and a contralateral prophylactic MT (i.e., bilateral MT), particularly if they carry the BRCA 1 or BRCA 2 gene mutations or have anxiety over the possibility of developing a new cancer in the opposite breast.

Chemotherapy is the initial therapy for ER-negative/Progesterone Receptor-negative metastatic breast cancer, or metastatic breast cancer with widespread, symptomatic visceral disease (Kurian and Carlson, 2010). The type and duration of chemotherapeutic agents should be adjusted according to patient tolerance to avoid cumulative toxicity.

Finally, postoperative mammography should be performed as a follow-up for all patients who have had surgery (Mariani and Gianni, 2008) (Sainsbury et al., 2000). The first mammogram is best-performed six months postoperatively to provide a baseline for the new postoperative and post-irradiation changes. Thereafter, mammography may be performed every 6-12 months for screening and follow-up. Monitoring of any metastatic disease is also recommended for high-risk patients, which should include monthly evaluations consisting of a history, and physical examination to evaluate any progression of disease.

Prognosis

As the range of options for treatment of breast cancer widens, so it becomes increasingly important that the clinician is provided with accurate prognostic information on which to base therapeutic decisions. Prognostic factors are tumour characteristics that are associated with the risk of breast cancer recurrence and death. Many prognostic factors have been identified over the years.

A brief outline of common prognostic factors as stated in Robbins Basic Pathology (Kumar et al., 2007). The TNM staging of the tumour is important. Ten-year survival estimates in the US according to breast cancer stage are presented in Figure 1-1. Patients with small invasive carcinomas and no distant metastases have a better prognosis. Similarly, nodal involvement is a significant prognostic factor where absence of axillary node involvement shows a 5-year survival rate close to 90%. The survival rate decreases with each involved node and is less than 50% with 16 or more involved nodes.

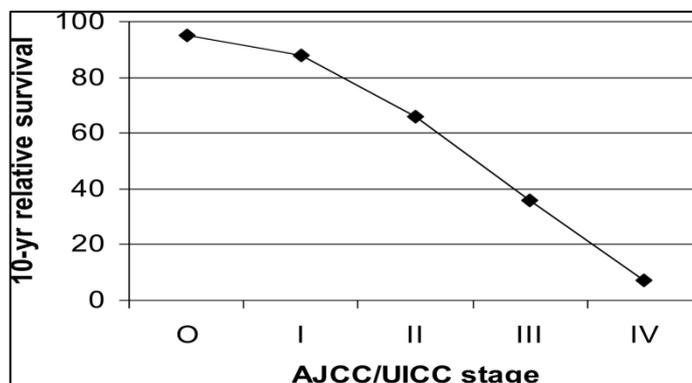


Figure 1-1: Ten-year relative survival associated with AJCC/UICC (TNM) breast cancer stages
Note: Figure adapted from (Singletary and Connolly, 2006)

A number of other tumour pathologic factors are used to further refine estimates of breast cancer prognosis, including tumour grade, tumour histology, level of steroid hormone receptor expression, and amplification or overexpression of the HER-2/NEU oncogene. Well-differentiated tumours have a significantly better prognosis compared to poorly differentiated tumours. Moderately differentiated carcinomas have a better prognosis initially, but survival at 20 years approaches that of poorly differentiated carcinomas.

Approximately 80% of breast cancers in developed countries are of ductal histology with approximately 10–15% of tumours being of lobular histology (Li, 2010). The less common tubular and mucinous histological types usually grow slowly and therefore have a more favourable prognosis (Li, 2010). The presence of hormone receptors offer a better prognosis where higher levels of expression of receptors for oestrogen and progesterone associate with improved survival. The reason is that tumours with oestrogen and progesterone receptors show high rates of response (80%) to anti-oestrogen therapy. In contrast, tumours with only one receptor present show lower rates of response (25%-45%) and only 10% response if both receptors are absent (Kumar et al., 2007). Amplification or over-expression of the HER-2/NEU oncogene correlates with early recurrence and worse outcomes. Age is a prognostic factor, in part, because breast cancers diagnosed before menopause often have unfavourable pathologic features, and young patients, therefore, have shorter survival (Kumar et al., 2007).

1.4.3 Descriptive epidemiology of breast cancer

By person

Breast cancer exhibits gender differences. Though most cancer types occur more among males compared to females, male breast cancer is rare, accounting for an incidence of less than 1 per 100,000 man-years (Ly et al., 2013). Male breast cancer makes up less than 1% of all cancers in men (Miao et al., 2011). In the other hand, breast cancer is by far the most frequent cancer among females. In 2008 breast cancer represented 23% of all invasive cancer diagnosed amongst females (Ferley et al., 2010). The female-to-male incidence ratio for breast cancer for the period 1988-2002 is calculated to be 122 (Ly et al., 2013). Due to

lack of awareness of its occurrence among men and lack of an early detection programme for men, male breast cancer is usually diagnosed at a more advanced stage and with a more severe clinical presentation than in women (Ly et al., 2013) (Miao et al., 2011). Because breast cancer in males is less common and because the main interest of this research is female breast cancer, the rest of the background concentrates only on breast cancer in women.

Age is considered to be the greatest risk for developing breast cancer (Kamangar et al., 2006). While the incidence of most epithelial cancers increases steadily with aging, breast cancer has a unique age-specific curve (Figure 1-2) (Kamangar et al., 2006, Bray et al., 2004). Before menopause (age 40-50 years), there is a rapid increase in incidence rate of breast cancer; then after that, and due to low levels of circulating oestrogens, the rise in incidence is slow (Bray et al., 2004, Ferlay et al., 2010). The midlife inflection in the age-specific curve is termed 'Clemmesen's hook' and has been attributed to menopause (Kamangar et al., 2006). It is noted that the slope of the curve after menopause varies worldwide. While it continues to rise more slowly in more developed (high risk) countries, it flattens or falls in less developed (low risk) countries (Bray et al., 2004). Some investigators attribute this to increased risk of occurrence in consecutive generations of women rather than a real decline in risk with age (Kamangar et al., 2006, Ferlay et al., 2010). Others link it with the existence of two types of breast cancer according to oestrogen receptors (ER) expression (Anderson et al., 2002, Kamangar et al., 2006). ER-positive tumours are more common in carcinomas occurring in more developed countries such as lobular and tubular carcinomas. The rate of ER-positive tumours rises rapidly until the age of 50 years and then slowly decreases after that, consistent with the age-specific curve observed in more developed countries. In contrast, ER-negative tumours are most common in medullary breast carcinomas, which are rare tumours occurring in women in less developed regions. The ER-negative tumour incidence rate follows that of less developed countries in which it rises rapidly till menopause and then reaches a plateau (Kamangar et al., 2006).

The mean age of diagnosis of breast cancer in less developed countries is younger than in more developed countries due to the young age structure of population coupled with a flatter postmenopausal age-incidence curve in less

developed countries (Ferlay et al., 2010, Bray et al., 2004). Worldwide, 89% of breast cancers are diagnosed from the age of 40 onwards (Ferley et al., 2010) but there is a difference between more developed countries (95%) and less developed countries (85%) (Youliden et al., 2012).

Breast cancer is characterized by marked differences in the incidence rate by ethnicity. For example, breast cancer incidence in the United States (US) was highest among white women followed by African Americans, Asian American/Pacific Islanders, Hispanics/Latinas, and American Indians/ Alaska Natives (Smigal et al., 2006). Research shows that while the incidence is highest among white women, they are more likely to be diagnosed with localized tumours compared to groups with lower incidence where they are diagnosed at regional/distant stages. This difference is also noted in South Africa where Stages III and IV of breast cancer were more common in black women compared with the nonblack women (Vorobiof et al., 2001).

Another finding for ethnic differences comes from New Zealand, with Māori women having the highest rates followed by Pakeha, and Pacific and Asian women, who experience the lowest rates (Ellison-Loschmann et al., 2013).

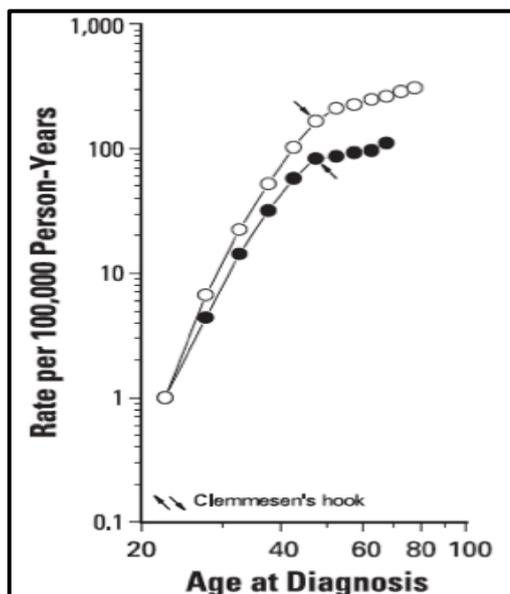


Figure 1-2: Age-specific breast cancer incidence in developed (white circles) and developing countries (black circles).

Note: Figure adapted from (Kamangar et al., 2006)

By place

In 2008, there were around 1.38 million new female breast cancer cases diagnosed worldwide (Ferley et al., 2010). Incidence rate was almost two and a half times higher in more developed countries compared to less developed countries (66.4/ 100,000 and 27.3/100,000, respectively) (Ferley et al., 2010). Female breast cancer incidence rates varied internationally by more than 13-fold in 2008, ranging from 8.0 cases per 100,000 in Mongolia and Bhutan to 109.4 per 100,000 in Belgium (Figure 1-3). In general, the highest rates are observed in Western and Northern Europe, Australia/New Zealand and North America; intermediate rates in South America, Caribbean, and Northern Africa; and low rates in sub-Saharan Africa and Asia (Bray et al., 2004, Ferlay et al., 2010).

The large variation in breast cancer incidence rates between less developed and more developed countries reflects differences in risk factors. In general, the high incidence rates of breast cancer in more developed countries are the result of a higher prevalence of the known risk factors for the disease relative to less developed countries (Ferlay et al., 2010, Jemal et al., 2011). Women in developed countries, for example, tend to have fewer children, give birth at an older age and are less likely to breastfeed. In addition, obesity, alcohol consumption and exposure to exogenous hormones (example, oral contraceptive and hormonal replacement therapy) may also contribute to the higher rates. Over diagnosis of some cancer cases in developed countries as a consequence of organised screening programmes might also add to the rise in cases compared to less developed countries where some cases remain undetected due to lack of diagnostic and health care facilities (Youlten et al., 2012).

Incidence by stage also exhibits a geographical variation. In less developed countries breast cancer tends to be diagnosed at a late stage compared with more developed countries where cases are diagnosed much earlier. For example, in the US and Australia, 60% of cases diagnosed were localised in contrast to 25% of cases diagnosed in less developed countries (Youlten et al., 2012). Lack of public awareness and organised screening programs in less developed countries may explain the variation in stage observed between countries (Coughlin and Ekwueme, 2009, Agarwal et al., 2009). It is also important to acknowledge that

the availability and quality of primary health care might also contribute to the difference noticed. In less developed countries even if the women present early, they may still be faced with delay or inadequate treatment (Agarwal et al., 2009, Coughlin and Ekwueme, 2009).

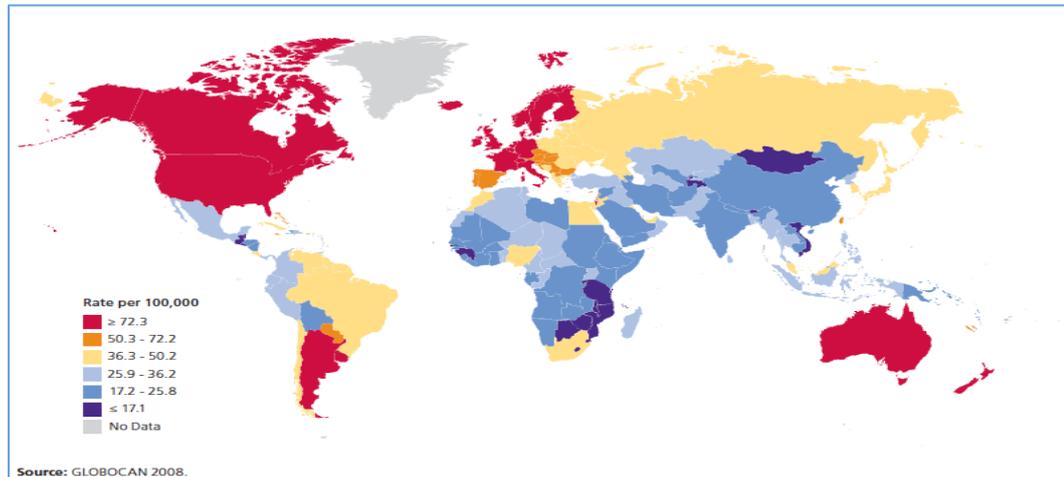


Figure 1-3: Age standardized breast cancer incidence and mortality rates by world area

*Estimated age-standardized rates (World) per 100,000. Note: Figure from GLOBOCAN 2008 (Ferley et al., 2010)

By time

Breast cancer incidence rate has increased worldwide over the past several decades. The largest increase in incidence occurs in populations with historically low-incidence rate, often in developing countries whereas relatively recent decrease in incidence rates have been observed in several, mainly western countries (Ferlay et al., 2010). The incidence rate of breast cancer increased by 30% in westernised countries between 1980 and the 1990s (Althuis et al., 2005).

Figure 1-4 demonstrates trends in breast cancer incidence observed in some developed countries from 1965 to 2005. In countries of Northern America including US and Canada, there was a rise in incidence between 1980s and 1987, which was related to increase in mammography-detected incident cases (Bray et al., 2004). In the US, the incidence rate of breast cancer decreased between 1999 and 2003 and research suggests it might be due to saturation in screening programs and/or due to decreased use of postmenopausal combined hormonal therapy (Ferlay et al., 2010). The incidence rates increased substantially across various European countries through the mid-1990s (Ferlay

et al., 2010, Bray et al., 2004). A mean global increase of 56.5% was observed between 1990 and 2002 across all age groups, and the greatest increase was observed across central and eastern European countries (Héry et al., 2008).

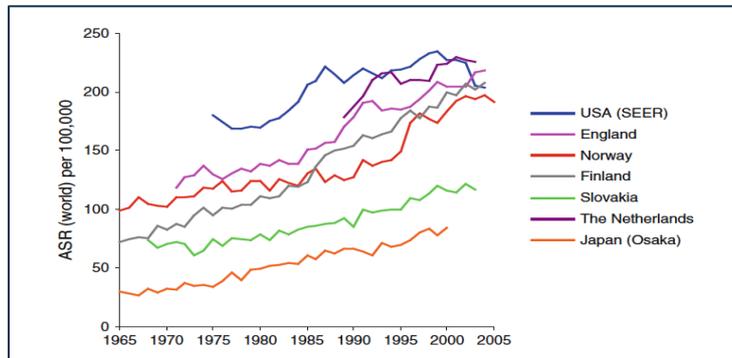


Figure 1-4: Age standardized incidence rate of breast cancer in selected developed countries
 Note: Figure adopted from (Ferlay et al., 2010)

Figure 1-5 shows breast cancer incidence in some developing countries between 1968 and 1998. Developing countries have low to moderate rates of breast cancer incidence compared with that in developed countries (Ferlay et al., 2010). Breast cancer incidence rates have been rising in these countries. Between 1983-1987 there was a 40% increase in the rate of breast cancer in India (Bray et al., 2004). In Singapore there was a threefold increase in the rate between 1968 and 2002 (Ferlay et al., 2010). Countries of Africa including Uganda, Nigeria experienced a twofold increase between 1960s and the late 1990s (Parkin et al., 2003). Similar trends were observed in the countries of Latin America (Bray et al., 2004).

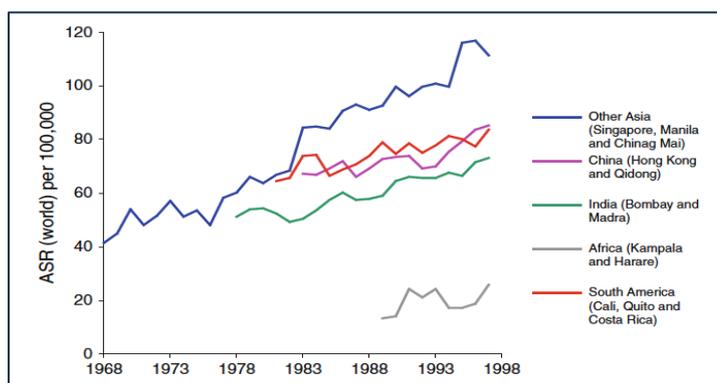


Figure 1-5: Age standardized incidence rate of breast cancer in selected developing countries
 Note: Figure adopted from (Ferlay et al., 2010)

The rising rates of breast cancer observed in developing countries might be attributed to the “westernization” of lifestyles, in particular to delayed childbearing, lower parity, lower breastfeeding duration, consumption of calorie-dense food, physical inactivity and obesity (Bray et al., 2004, Jemal et al., 2011)

Chapter Two - Literature Review

This chapter examines the available literature on breast cancer related to this thesis. There will be an outline of the epidemiology of breast cancer in Gulf countries and then in Oman followed by an overview of risk factors for breast cancer among Arab women. Then, a summary of women's perception of breast cancer and perceived personal risk will be provided as they are important concepts that influence women's decisions regarding health behaviour and involvement in prevention programs. Finally, literature on patient delay and breast cancer will be summarised to identify the most common factors which influence women to delay seeking medical help.

2.1 Epidemiology of breast cancer in Gulf Cooperation Council Countries

Countries of the Gulf Cooperation Council (GCC) share similarities in culture, lifestyle, and environment, and hence it is believed they share similar health risks (Chouchane et al., 2013). Nonetheless, cancer incidence and prevalence are reported at differing levels among populations of the GCC countries (Al-Hamdan et al., 2009). Incidence data in GCC countries reported in this section of the thesis are obtained from the report 10-Year Cancer Incidence Among Nationals of the GCC States, 1998-2007 published by the Gulf Centre for Cancer Registration (GCCR) (Al-Madouj et al., 2011). The GCCR was established in 1998 to create a population-based incidence database for the GCC countries which includes United Arab Emirates (UAE), Kingdom of Bahrain, Kingdom of Saudi Arabia (KSA), Sultanate of Oman, State of Qatar, and State of Kuwait (Al-Madouj et al., 2011). The NCR in each country is responsible for data collection at the national level from health facilities. Most of the national cancer registries in the Gulf countries were established in the 1990s (Al-Mahrouqi et al., 2011) except for Kuwait which was started in 1971 (Curado et al., 2008). To ensure comprehensive data collection, a ministerial decree in each of the GCC countries has rendered cancer a reportable disease by all Ministry of Health hospitals, and government and private hospitals, clinics and laboratories (Al-Hamdan et al., 2009). Mandatory reporting started in 1998 or earlier in

Kuwait, Bahrain, Saudi Arabia and Qatar and was only around the beginning of 2001 that it started in Oman and UAE (Al-Mahrouqi et al., 2011). Data on cancer site, histology, stage, behaviour and extent of the disease, basis of diagnosis and methods of treatment are collected from patients' medical records, histopathology and radiology reports, clinical notes, and death certificates at National Cancer Registries (NCRs) in each member state. Data are sent to the GCCR in different formats (e.g. Excel, Epi-Info) and at the GCCR all files are converted to CanReg format, validated software for processing cancer data developed by the International Agency for Research on Cancer (IARC), and subsequently analysed (Al-Hamdan et al., 2009).

Between 1998 and 2007, there were 95,183 cancer cases (47,250 males, 47,933 females) diagnosed among nationals of the GCC states. Breast cancer was the most common cancer in almost all the GCC countries. It represented 11.8% of all diagnosed cancers in both genders and 23.5% of the total female cancer cases.

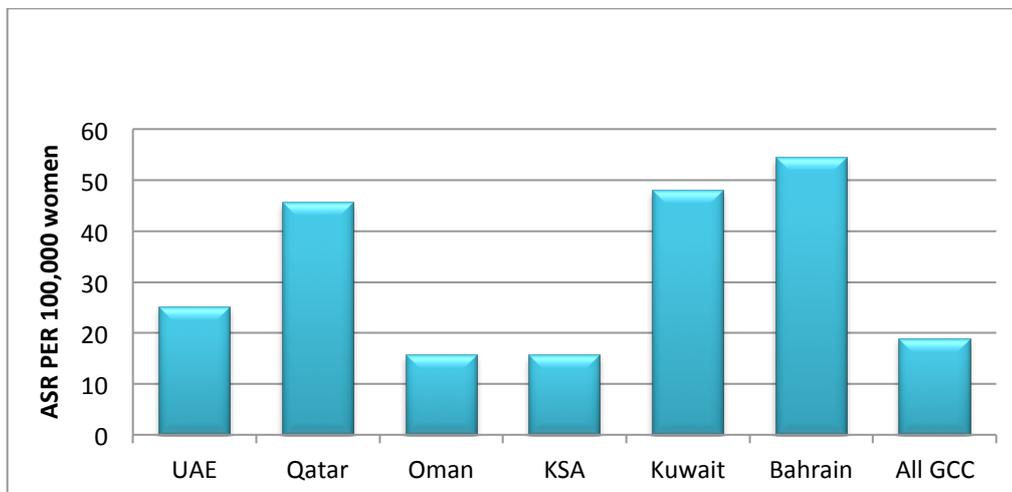


Figure 2-1: Age standardized incidence rate of female breast cancer in the GCC States, 1998- 2007.
 Note: Figure created using data from (Al-Madouj et al., 2011)

Figure 2-1 illustrates the age standardized incidence rate (ASR) of female breast cancer in GCC countries between 1998 and 2007. The overall ASR for all GCC states was 18.8 per 100,000 women. The highest incidence was reported in Bahrain with ASR of 54.4 per 100,000 women, followed by ASR of 48.0 and 45.6 per 100,000 women reported in Kuwait and Qatar respectively. In UAE,

the ASR was 25.2/100,000 women. The lowest incidence of breast cancer was reported in Oman (15.7) and KSA (15.6).

Differences in reproductive factors could partially explain the gap in observed rates between high incidence countries (Bahrain, Kuwait and Qatar) and low incidence countries (UAE, Oman, and KSA). Fertility rates were higher in the low incidence countries and breastfeeding duration was reported to be shorter among females residing in Qatar and Kuwait compared to other GCC countries. There has been a reduction in breastfeeding time in all the GCC countries along with a steady rise in the age at first childbirth (Ravichandran and Al-Zahrani, 2009). Along with the decrease in fertility rate, there was a rapid increase in usage of contraceptives among GCC women. Moreover, UAE is the only GCC country that has established a screening program and this factor might account for the higher incidence rate to some extent (Al Khaja and Creedon, 2010).

There is no current comprehensive review of the completeness and quality of cancer registration in all of the GCC countries which might explain some of the differences seen in breast cancer incidence among Gulf countries. However, there is a suggestion that cancer incidence in Saudi Arabia and UAE might be under-reported (Al-Mahrouqi et al., 2011). Al-Mahrouqi et al. (2011) provided some evidence for this suggestion after analysing data from three different resources, the Cancer Incidence in Five Continents reports (published by the International Agency for Research on Cancer, IARC), the IARC Globocan database (which contains country-specific estimates of cancer incidence throughout the world in 2002) and the GCCR report. The Cancer Incidence in Five Continents report publishes cancer incidence data from cancer registries from all over the world, but only data of sufficiently high quality and completeness are included. Only three of the GCC countries: Bahrain, Kuwait and Oman were included in the latest report (Curado et al., 2008). Data submitted by Saudi Arabia were excluded because of concerns about completeness, while UAE and Qatar did not submit data. The Globocan estimates of cancer incidence rates for Oman, Qatar, Bahrain and Kuwait were based on the original data from these four GCC countries and thus were similar to those published in the GCC cancer incidence report 1998–2002 (Ferley et al., 2010). However, because under-reporting was suspected on data from Saudi

Arabia and UAE, their incidence rates were estimated using data from Oman, Kuwait, Israel, and Jordan (Ferley et al., 2010). Therefore, the resulting incidence rates were higher than those published in the GCCR report. The 1998 - 2002 GCCR report also revealed a very high percentage of microscopic verification as a basis for diagnosis in Saudi Arabia, a quality indicator which suggests that some cases could have been missed.

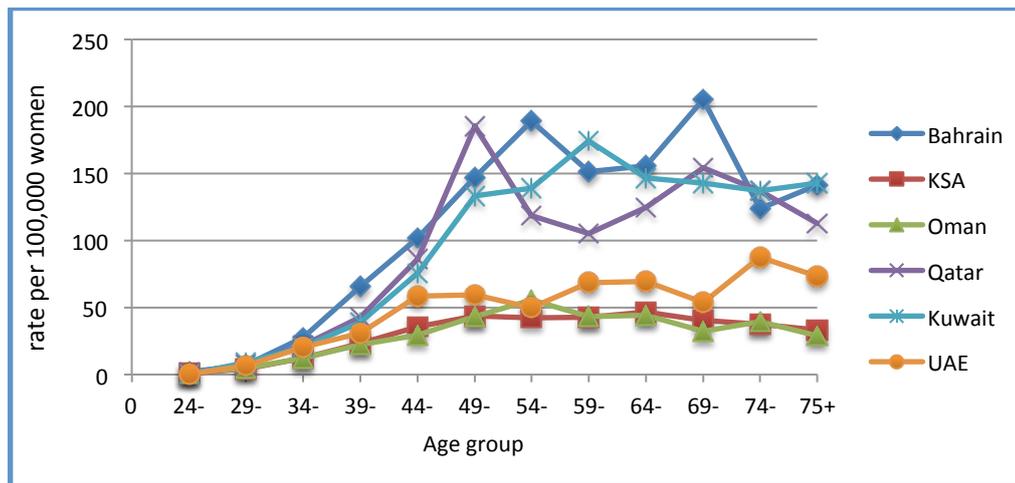


Figure 2-2: Average annual age specific incidence rates of breast cancer, 1998-2007
 Note: Figure created using data from (Al-Madouj et al., 2011)

With regards to the histopathology types, infiltrating duct carcinoma was the most commonly occurring type. 57.8% of all diagnosed types of breast cancer showed metastasis and only 22.2% of tumours were localised.

For all GCC countries, breast cancer incidence gradually increased with age (Figure 2-2). In Bahrain, Kuwait and Qatar, the highest incidence was reported among women aged 65-70 years. In Qatar, the incidence peaked at age between 45-50 years. In Oman the highest incidence was observed among women aged 50-60 years and the highest incidence was observed in Saudi women aged >40 years. As with most developing countries and due to change in lifestyle, breast cancer seems to be increasing over time in all GCC countries. Between 1998 and 2007, there was a 20% increase in number of new breast cancer cases diagnosed among nationals of the GCC.

2.1.1 Cancer registration in Oman

The Oman National Cancer Registry (NCR) was established in 1985 as a hospital-based registry. Only cases treated in tertiary hospitals were registered. In 1996, the cancer registry started functioning as a population based registry. By 2000, a cancer notification form was created and distributed to all hospitals to record patient's details. In 2001, cancer notification by hospitals was made mandatory. In December 2004, radiotherapy services became available in Oman in addition to the other modalities of treatment, which already existed. This minimised the number of patients sent abroad for treatment and provided the registry with an extra source of cancer notification. Details of the patients sent abroad for treatment (mainly for radiotherapy) were obtained from the Department of Treatment Abroad and from Tuwam Hospital (the main referral hospital for radiotherapy in the neighbouring United Arab Emirates) (Curado et al., 2008). Cancer data from Oman were included in the publication of the IARC, Cancer Incidence in Five Continents, both 8th and 9th editions (Parkin et al., 2002) (Curado et al., 2008).

2.1.2 Epidemiology of breast cancer in Oman

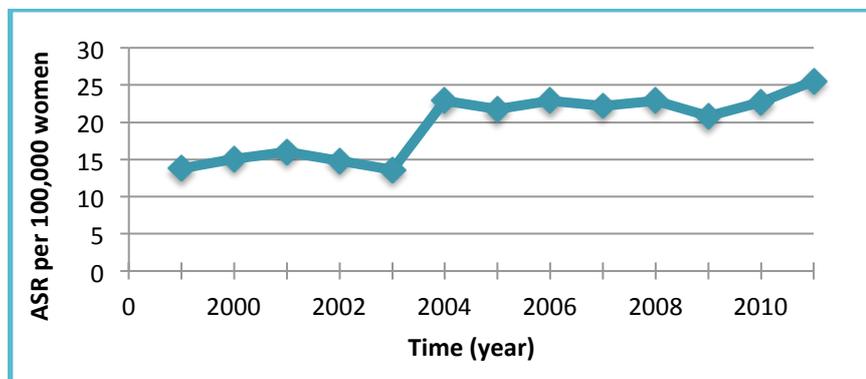


Figure 2-3: Age standardized incidence rate * of breast cancer in Omani women, 1999-2011

* Age standardized using the World Standard Population of Segi.

Note: Figure created using data reported in the Omani cancer incidence reports (Al Lawati et al., 2013)

Breast cancer is the most common cancer among females in Oman. Figure 2-3 demonstrates the ASR of breast cancer per 100,000 women in Oman from 1999 to 2011. The incidence of breast cancer has been rising over the years. It was 13.8 per 100,000 women in 1999 and rose to reach 25.5 per 100,000 women in 2011. In 2011, in total there were 162 cases of breast cancer diagnosed in

Oman: 6 males and 156 females of which 9 cases were carcinomas in situ. This accounted for 24.8% of all cancer in Omani women.

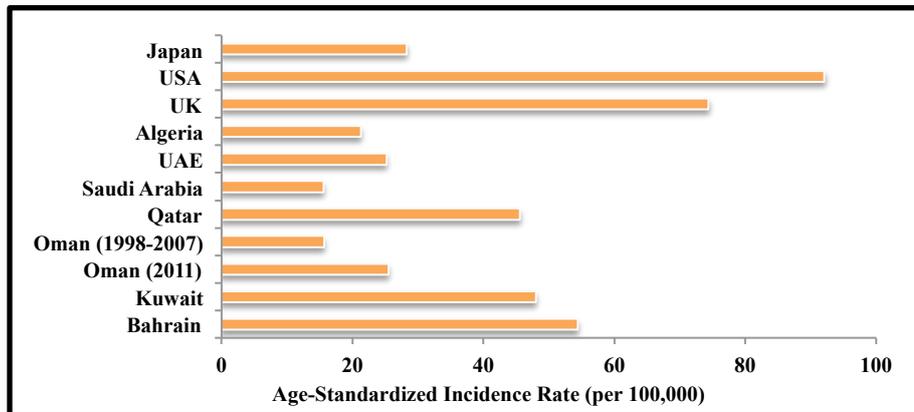


Figure 2-4: Age standardized incidence rate of breast cancer in Oman and some selected countries
 Note: Figure from (Al Lawati et al., 2013)

The incidence of breast cancer in Oman is in line with that in other developing countries but it is much lower than those reported in industrialised countries such as the United Kingdom (UK) and US (Figure 2-4). It has been suggested that the relatively lower incidence in Oman (15.7/100,000) is due to the still prevalent traditional cultural practices like the early age of the mother at childbirth, and multi-parity practiced in most regions in the country (Nooyi and Al-Lawati, 2011).

Breast cancer rates in Oman increase after 29 years of age and peaked between 50-59 years, unlike cancers in other sites like stomach and cervix, which increase gradually with age (Figure 2-5).

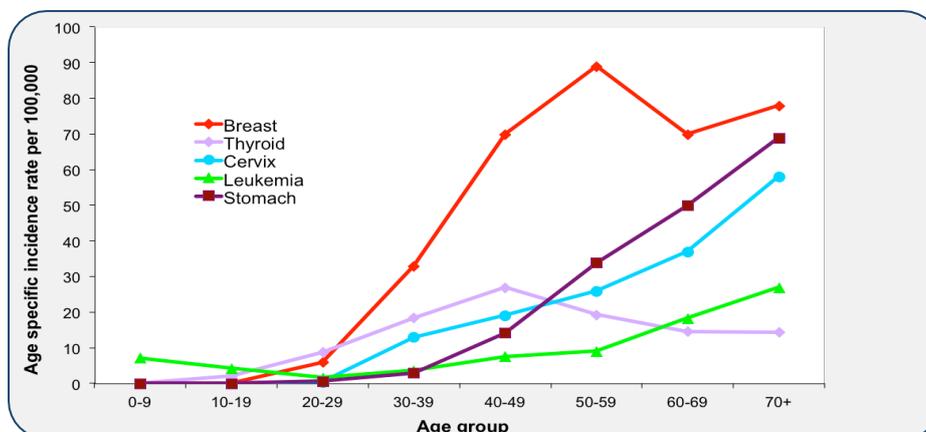


Figure 2-5 Age-specific incidence rates of common cancers in Omani females, 1998-2006
 Note: Figure from (Nooyi and Al-Lawati, 2011)

Incidence according to regions of Oman in 2011 is shown in Figure 2-6. High incidence is reported in Muscat (28.2 per 100,000 women) followed by 19.3 in Dhofar, 17.4 in Musandam, 12.2 in Adakhliyah and 11.4 in Adhahirah. Incidence rates below 10 per 100,000 women were reported in rest of the country. The high frequency of cancer reported from Muscat could be biased since the majority of the cancer cases are referred to the Royal Hospital in Muscat, and people sometimes give a local address in Muscat, rather than giving their original place of residence.

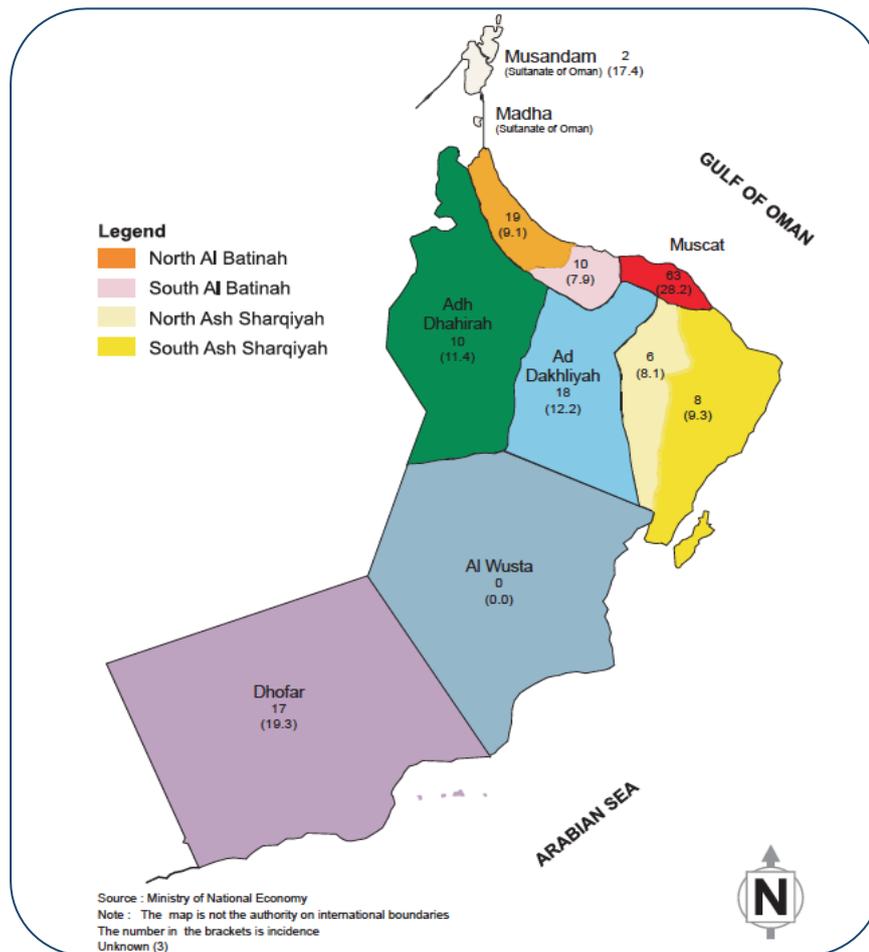


Figure 2-6: Incidence of breast cancer by region (incidence rate are per 100,000 populations)
 Note: Figure from (Al Lawati et al., 2013)

2.2 Breast cancer in the Arab population

By 2004, the Arab world had a population exceeding 300 million, living in 22 countries spread across Northern Africa and Western Asia (El Saghir et al., 2007). There are many shared demographic features among Arab countries

including large family size, high rates of consanguinity, and rapid population growth (Najjar and Easson, 2010).

As with most countries in the world, breast cancer is the most frequent cancer among females in Arab population (Salim et al., 2009). It accounts for 14-42% of all tumours diagnosed (Chouchane et al., 2013). Though the incidence of breast cancer in Arab countries is low compared to countries in Europe and America, it is steadily increasing (El Saghir et al., 2007).

Despite the fact that breast cancer is poorly researched in Arab nations, it was noted across published studies that breast cancer in Arabs manifests different characteristics when compared to nations in Europe and America. In particular, Arabs are diagnosed on average at a younger age. They have more advanced stages of cancer at diagnosis with larger and more poorly differentiated tumours. Additionally, they show more lymph node involvement and a large proportion of negative hormonal receptors (Shaheen et al., 2011, Chouchane et al., 2013, Zidan et al., 2012, Salim et al., 2009).

Breast cancer in younger women has been shown to have poorer clinicopathological features, which indicate aggressive behaviour (Chouchane et al., 2013). Tumours tend to be larger in size, lymph nodes positive, poorly differentiated and show higher oestrogen and progesterone receptors negativity and higher Human Epidermal Growth Factor Receptor-2 (HER-2). Indeed, supporting results have been documented in different Arabic studies, for example, a study carried out in Tunisia reported that 81% of patients with breast cancer had a tumour size of >2 cm in diameter, 34% had a tumour size of >5 cm (Missaoui et al., 2011). Further, 48% of cancers were at stage II, 41% were at a more advanced stage (stage III and IV), and only 11% had early stages (0 and I). In another study comparing Arabs and Jews with breast cancer, Zidan et al. (2012) reported that smaller tumour size < 2cm was more common among Jews compared to Arabs (53% and 25%, respectively). Additionally, nodal involvement was present in 64% of Arab compared to 37.2% of Jews, and stage I disease was present in 42% and 11.3% respectively. Similarly, when comparing French with Arab Mediterranean populations, tumours were smaller in French patients, and grade III predominated in Arab patients (Chalabi et al.,

2008). Similar patterns of tumour size, grade and staging have been reported in studies from Arab countries (Alshatwi et al., 2012, Al-Ajmi et al., 2012, Al-Tamimi et al., 2009).

It has been reported in many studies from the US and Europe that younger age at diagnosis is a predictor of low survival rates (Najjar and Easson, 2010, Albain et al., 1994, Fowble et al., 1994, El Saghir et al., 2006). In Lebanon, a review of 1320 patients with breast cancer concluded that younger age at presentation is also an independent adverse prognostic factor (El Saghir et al., 2006). Interestingly, this negative impact is retained in younger patients studied despite the fact that they had an increased rate of positive hormonal receptors and received more aggressive chemotherapy than older patients. In contrast, reports from other developing countries like Saudi Arabia and Singapore found that younger age had no impact on survival of breast cancer patients (Chia et al., 2004, al-Idrissi et al., 1992).

Women in the Arab world are diagnosed on average a decade earlier than western individuals. In a review carried out in 18 articles from the Arabic countries, it was calculated that the average age at diagnosis was 48 years (Najjar and Easson, 2010). 11 out of the 18 articles reviewed reported that 65.5% of breast cancer patients were younger than 50 years old. In Saudi Arabia, 78% of the diagnosed patients were below 50 years (Ezzat et al., 1999). Published statistics from western countries show that the median age at diagnosis is around 63 years and only 25-30% of breast cancer patients are younger than 50 years (Chouchane et al., 2013). Similar results come from a study comparing North Mediterranean (France) with South Mediterranean (Tunisia, Morocco, and Lebanon) (Chalabi et al., 2008). Northern patients were on average 60.1 years old when diagnosed whereas southern patients were 49.1 years old. Tunisian patients were on average more than 13 years younger.

Interpretation of differences in age at diagnosis of breast cancer observed in Arab population and other low risk countries is controversial (Hemminki et al., 2011). While some have attributed the difference to a cohort effect of rapidly increasing rates in the young population, others attribute it to incomplete registration of cancer in older patients. Others have suggested that it is caused

by differences in tumour biology, which are assumed to vary between low-risk and high-risk ethnic groups or regions because of genetic and environmental risks factors (Hemminki et al., 2011).

Evidence seems to show that Middle Eastern Arab women have a tendency to manifest a high-grade pathway in breast cancer development. Striking evidence appears in an analysis of two consecutive breast cancer series from Switzerland and Saudi Arabia (Al-Kuraya et al., 2005). 65% of Saudi patients had grade III tumours and only 32% were diagnosed with grade III in Switzerland. Consequently, Saudi women appear to have an almost 14-fold lower risk for developing lower grade breast cancer than Swiss women. However, further study is required to assess this finding in other Arab populations.

2.2.1 Risk factors of breast cancer in the Arab population

Hereditary risk factors

Recently there have been some studies describing different variations in genetic presentation of breast cancer in Arab population and their contribution to breast cancer risk. Because the genetic aspect of breast cancer is beyond the scope of this research, only a brief account of common genetic variations will be described here.

It is estimated that 5-10% of breast cancer cases are hereditary (Mahfoudh et al., 2012, Shan et al., 2012, Bener et al., 2010), in which 4-5% are caused by high penetrance genes inherited in an autosomal dominant pattern (Chouchane et al., 2013). Breast cancer gene1 (BRCA1) and BRCA2 genes are two such genes that play a substantial role in developing breast cancer (El-Harith et al., 2002). BRCA1 carriers have 47-66% risk of developing breast cancer and the risk is 40%-57% in BRCA2 carriers (Litton et al., 2012). BRCA genes mutations explain some of breast cancer risk in Arab world. In recent years, few published studies have emerged to describe frequency and spectrum of BRCA mutations in Arab countries. It was suggested that BRCA aberrations could be higher in Arab women compared to other populations (Rouba et al., 2000). In Tunisia, a study screened 16 high-risk breast cancer families for BRCA1 mutations and

calculated the frequency to be 37.5%(Mahfoudh et al., 2012). The study also revealed a founder mutation in Tunisian patients.

A Lebanese study found nine carriers of BRCA deleterious mutations among a cohort of 72 related patients with breast cancer (Jalkh et al., 2012). 21.8% of identified variants on BRCA genes were novel to this study population. Atoum and Al-Kayed (2004) studied a total of 135 Jordanian women with breast cancer for BRCA1 mutations. Only 50 patients had a family history of breast cancer and five germline mutations were identified in these patients given that only parts of the gene were screened. Another result comes from a pilot study of 43 Omani women with breast cancer, which reported duplication and deletion in BRCA1 at a rate of 9.7% (Al-Ansari et al., 2013). These results are similar to other published studies in the US (8%) and France (9.6%) (Al-Ansari et al., 2013).

Most studies in different populations reveal that patients with BRCA mutations have a risk of an early onset breast cancer and they are usually younger compared to non-mutation carriers at the age of cancer diagnosis (Tommasi et al., 2005, Mahfoudh et al., 2012). Litton et al. (2012) assessed the age at diagnosis of breast cancer in two generations of families with known BRCA mutations. The study reported a median age at diagnosis of 48 years in the older generation and 42 years old in the younger generation concluding that BRCA mutations carriers appeared to be diagnosed at an earlier age in later generations. Accordingly, BRCA mutations might provide some explanation for the younger age at diagnosis observed in Arab population. Nevertheless, much larger cohort studies are needed to assess the spectrum of BRCA mutations in Arab women. Further evaluation of these studies is vital to suggest the appropriate interventions and timing for initiating screening programmes (Hall et al., 2009, Litton et al., 2012, Chouchane et al., 2013, Mahfoudh et al., 2012). The National Comprehensive Cancer Network guideline stated that carriers of BRCA mutation should be educated and trained in Breast Self-Examination (BSE) by the age of 18 and should undergo semi-annual Clinical Breast Examination (CBE) by the age of 25 years (Daly et al., 2010). Also it recommended that women should begin having annual mammography or MRI

performed by the age of 25 years or otherwise an individualized timetable based on the earliest age of cancer onset in family members should be developed.

Single Nucleotide Polymorphism (SNPs) contributes to genetic predisposition of breast cancer (Shan et al., 2012, Alawadi et al., 2011). Though SNPs are of low penetrance susceptibility, together with nutritional and environmental factors, they can affect breast cancer risk (Chouchane et al., 2013). Common SNPs occurs in TP53 gene. TP53 is a tumour suppressor gene that is regulated by MDM2 gene and polymorphism in both genes may be associated with increased risk for breast cancer. A case-control study of 100 Saudi breast cancer patients reported a statistically significant association between TP53-72 Pro/Pro and MDM2 309 GG genotypes with increased risk (Alshatwi et al., 2012). Moreover, carriers of both genotypes had a much higher risk for breast neoplasms. However, different results were concluded in another genotyping study of 288 patients and 188 controls from Kuwait and Syria (Alawadi et al., 2011). Data showed that frequency of TP53-72 Pro/Pro allele was higher in controls than in cases, meaning that it is a protective factor.

These findings suggest that the Arab population presents with different genetic susceptibility patterns compared to other populations and that differences in biological and clinical characteristics of tumours may be due to the high frequency of pertinent genetic risk factors that are unique to Arab.

Consanguinity

Acquiring two copies of the gene (homozygosity) is associated with increased risk for many cancers. Homozygosity increases among children of consanguineous parents and therefore they have higher risk of cancers (Denic et al., 2007). In Arab countries, the prevalence of consanguinity is about 40-68%, with marriage predominantly between first cousins (Bener and Alali, 2004). Studies undertaken to examine the effect of consanguinity on breast cancer have yield contrasting results. For example, the population of Pakistan has been reported to have the highest rate of breast cancer of any Asian population and the overall frequency of consanguineous marriage is 60-76% among Pakistani (Gilani and Kamal, 2004). On the other hand, other results show a high rate of consanguinity was associated with a decreased risk of breast cancer(Denic et al.,

2005, Denic and Bener, 2001). Similarly, parental consanguinity was higher in controls than in cancer patients residing in Qatar (Bener et al., 2010). It is suggested that offspring of consanguineous parents will have acquired two copies of deleterious genes that are important in both development of breast cancer and at the same time development of normal embryo (Denic and Bener, 2001). Accordingly, these genes impair embryogenesis, perinatal or postnatal development resulting in abortions or stillbirths, which are noticed to be high among consanguineous parents. Some of these lost embryos are actually 'lost breast cancer patients' and therefore the long-term practice of consanguinity may decrease the frequency of such deleterious genes.

Infections

Viruses have been reported to be associated with development of several cancers (Serraino et al., 2001). Epstein-Barr Virus (EBV) has been detected in neoplastic tissues of breast cancer patients. A case-control study was conducted with 40 Egyptian and 50 Iraqi patients to assess the association between EBV and breast cancer (Zekri et al., 2012). Interestingly, EBV was detected in 45% of Egyptian and 28% of Iraqi patients, while it was absent in the control groups of both populations. These findings suggest that EBV might have a role in the development of breast cancer.

Obesity

Obesity is an established important prognostic risk factor for breast cancer particularly in postmenopausal women (Sharma and Davidson, 2013, Henderson et al., 2010). Usually, obese patients exhibit more aggressive tumours with higher tendency to metastasis (Alokail et al., 2013). Metabolic Syndrome (MS) is defined by the presence of obesity together with Diabetes Mellitus Type 2. MS prevalence is reported to be increasing in the Arab world. Prevalence of MS in men residing in GCC areas ranged from 20.7%-37.2% while it ranged from 32%-42.7% for women (Mabry et al., 2010). It is 10-15% higher than in most developed countries with the difference being higher for women. Alokail et al. (2013), (2009) demonstrated in two published studies from Saudi Arabia that patients with MS have a higher risk of developing breast cancer. Altered expression of inflammatory markers (such as Angiotensin II, C reactive protein and Leptin) observed in those patients may enhance

tumorigenic activity leading to breast cancer aetiology (Alokail et al., 2009). The magnitude of the effect of MS on breast cancer risk in other Arab countries should be considered because intervention programmes for MS may contribute to reduction in breast cancer incidence.

Reproductive factors

With regards to reproductive factors and their contribution to breast cancer risk, a study carried out in the GCC concluded that difference in incidence rate in GCC countries reflects the history of reproductive factors of each country (Ravichandran and Al-Zahrani, 2009). Reproductive patterns in the GCC countries are characterised by an early start of childbearing, short birth intervals and ultimately high parity. Fertility rates in high incidence countries were low compared to those in low incidence countries. Moreover, there was a steady rise in the age at first birth over time and this decline in early childbearing age was more rapid in high incidence areas than in low incidence.

2.3 Women's perception of breast cancer risk

Perceived risk refers to an individual's belief about the probability or likelihood of developing some specified illness (McQueen et al., 2008). For example, a sample of 41 women recruited from Atlanta described breast cancer as a uniformly progressive disease, which is curable if found at an early stage, but deadly if found late (Silverman et al., 2001). Although "benign" disease of the breast is biologically classified as a separate entity from breast cancer, there were those who believed that "benign condition" of the breast is a stage in progression to malignancy (Silverman et al., 2001). More specifically, breast cancer is perceived to convey a substantial and real threat to women's health, their bodies, and their sense of future self (d'Agincourt-Canning, 2006). McGregor et al. (2004) found that when a sample of women from US were asked, '*compared to most women, what do you think the chances are that you will get breast cancer someday?*' their mean response was a little higher than the average women. When asked, '*What do you think the chances are that the average woman will have breast cancer some day?*' their mean response was 30%-40%. However their response lowered to 20%-30% when they were asked, '*What do you think the chances are that you will have breast cancer someday?*'

When using the Gail model to estimate the actual risk, it has been found that the mean estimated absolute risk for this sample was 10.5%, which implies that this sample of women has overestimated the risk. In another study Grunfeld et al. (2002) looked closely at the age and perceived risk. His study demonstrated a relationship between age and the perception of risk with 35% of over 65-year-olds and 30% of over 75-years-olds reporting reduced personal risk.

It appears there are two distinct groups of women in relation to their perceived breast cancer risk; those who believe that they are at a high risk of getting breast cancer and overly stressed about it and those who think that they will never get it and so they ignore it (d'Agincourt-Canning, 2006, Bryan, 2002). These perceived estimates of risk have a relationship with experience. Researchers have found that women who have a family history of the disease usually overestimate their risk and this is demonstrated in many genetic counselling clinics and family history clinics (Absetz et al., 2000, Vernon et al., 1993, McQueen et al., 2008, Anderson et al., 2002, Katapodi et al., 2004, MacDonald, 2002). Familial breast cancer accounts for approximately 15% to 20% of overall breast cancer cases (Saadatmand et al., 2013). Indeed there is a high risk of developing breast cancer among those who have an affected first degree relative compared to the general population, especially if diagnosed at younger age. The risk of breast cancer for women with one, two, and three or more affected first-degree relatives, when compared with women not having a first-degree relative with a history of breast cancer, were 1.8, 2.9, and 3.9 respectively in a large UK cohort (Beral et al., 2001). Therefore, it is not surprising that woman with a family history have perceived a high risk.

Risk perception is created within the mind of the individual based on many factors (Slovic, 1999). Rothman et al. (1996) indicated that both psychological and contextual factors could affect perception of risk. Psychological factors related to breast cancer risk perception might include breast cancer worry and anxiety. Contextual factors related to breast cancer might include such things as family history/genetics, one's own health behaviours, the history of benign breast disease, and beliefs about risk factors. Findings have indicated that the majority of women have poor understanding and lack knowledge about the disease risk factors (Grunfeld et al., 2002, Williams et al., 2002). A significant

number of studies demonstrate that many of the risk factors identified were modifiable factors that are weakly, if at all, associated with breast cancer (Buxton et al., 2003, Silverman et al., 2001). Most recognized the importance of “uncontrollable” factors for breast cancer such as age, sex, family history, and genetics. Family history was the most recognizable risk factor across the literature (Buxton et al., 2003, Grunfeld et al., 2002, Williams et al., 2002). However, other “controllable” factors (e.g., smoking, diet) were given equal or greater importance, which suggests that many women feel responsible for their level of breast cancer risk (Silverman et al., 2001).

Although advanced age is the most important risk factor for developing breast cancer, several studies revealed that it was poorly understood by the vast majority of women (Vernon et al., 1993, McQueen et al., 2008, Katapodi et al., 2004). This belief often acquired by women over the age of 60 years who provided an explanation that they are too old to develop breast cancer, *‘I think if I was going to develop it, I would have by now’* (Grunfeld et al., 2002). In the UK, women aged 50-64 are usually offered breast cancer screening and this might contribute to high-risk perception among this group. However, it sends the wrong message to women over the age of 64 years who think they are no longer at risk, *‘At my age I think the danger has passed’, ‘[Because] they stop mammograms at 65’ and ‘I think older people are less likely to have breast cancer problems’* (Grunfeld et al., 2002).

Understanding the actual risk of developing breast cancer is important for women because it influences their decisions to adopt preventive actions such as engaging in healthy lifestyle behaviours including regular physical activity, increasing fruit and vegetable intake and consumption of a low-fat diet for weight control, and limiting alcohol intake and health care such as genetic counselling and hormonal replacement therapy (Katapodi et al., 2004, Bottorff et al., 2004, Haas et al., 2005, Lemon et al., 2004). Also risk perception has a role in enhancing appropriate participation in recommended screening (Absetz et al., 2000, Buxton et al., 2003, Hailey et al., 2000). In addition, such knowledge is important in improving one’s quality of life because misperception of personal risk, especially among those who overestimate their risk, has been linked with excessive worry, anxiety, neglecting the importance

of other high-risk diseases, and causing psychological distress (Buxton et al., 2003, McGregor et al., 2004, Bottorff et al., 2004, Hailey et al., 2000, Williams et al., 2002). In contrast, women who underestimate their risk are susceptible to the threat of ill health as a result of deferring screening and not involving themselves in risk reducing behaviours (Haas et al., 2005, Williams et al., 2002). A study in the UK found that women who perceived a high risk of developing breast cancer (such women with family history) experienced heightened levels of worry and stress leading to increased performance of BSE and other reducing techniques (Norman and Brain, 2005). On the other hand, women with no experience or limited knowledge of breast cancer and who perceived themselves of having low risk of developing the disease are highly unlikely to undertake any early detection or knowledge/awareness raising techniques (Williams et al., 2002, Haas et al., 2005, Norman and Brain, 2005). Nevertheless, it was demonstrated that women with the highest objective risk for breast cancer do not report healthier lifestyle behaviours suggesting other important factors that might play a role in motivating behavioural changes (Madlensky et al., 2005, Spector et al., 2009). Such factors include inadequate knowledge about known risk factors, lack of personal control, lack of motivation and additional roadblocks towards healthy behaviours (Spector et al., 2009).

In summary, woman's perception of her risk for developing breast cancer influences her decision to undertake health actions such as seeking evaluation of new breast symptoms and also to involve in preventive actions such as screening programs.

2.4 Delay in seeking medical care in patient with breast cancer

The period of time between a woman's first noticing a breast cancer symptom and receiving treatment for this can be referred to as 'delay' or 'total delay' (Unger-Saldaña and Infante-Castañeda, 2009). Delay in seeking medical help contributes to advanced-stage presentation (Unger-Saldaña and Infante-Castañeda, 2009). Patient delay has been associated with increased tumour size, increased involvement of the lymph nodes, more advanced stages of the disease and poor long-term survival (Unger-Saldaña and Infante-Castañeda, 2009). A

systemic review of 87 studies with direct data linking delay and survival concluded that patients with a delay of three months or more had 12% lower five-year survival than those with a shorter delay (Richards et al., 1999b). A patient with a significant delay may have worse prognosis simply because she is further from the onset of disease and not necessarily because treatment has not been initiated. Patients with a delay of 3-6 months had 7% lower survival rate than those who sought medical help earlier (Richards et al., 1999b). This finding of delay associated with worse survival rate is strongly supported by another meta-analysis of 21 studies on patient delay (Bish et al., 2005). In addition, the review found an association between longer duration of symptoms and advanced tumour stage, which has been documented in several countries like Iran (Montazeri et al., 2003), Egypt (Stapleton et al., 2011), Germany (Arndt et al., 2002), Malaysia (Norsa'adah et al., 2011) and Thailand. In Thailand, for example, a study reported that patients with TNM stage III disease had a median delay of presentation of two months compared to seven months for those in stage IV (Thongsuksai et al., 2000). Similarly, a cross sectional study carried in Egypt found that while 26.3% (88/335) of women with < 3 months delay were at stage III and IV, the corresponding proportion among women with >3 months delay was 72.1% (Abdel-Fattah et al., 1999).

Traditionally, breast cancer delay has been classified into two types: patient delay and provider delay. The term 'patient delay' was first introduced by Pack and Gallo in 1938 and it is defined as "the period between an individual's first awareness of a sign or a symptom of illness and initial medical consultation" (Pack and Gallo, 1938). Terms like 'help seeking delay', 'help-seeking behaviour', 'late presentation' and 'consultation delay' are frequently used synonyms for 'patient delay' in the literature.

'Provider delay' refers to the period of time between the initial medical consultation and definitive treatment of cancer (Unger-Saldaña and Infante-Castañeda, 2011). This includes the time between visiting the general practitioner and referral to the hospital, between first hospital visit and cancer diagnosis and the period between diagnosis and treatment (Bish et al., 2005). Based on the meta-analysis carried by Richards et al in (1999b) which found a significant association between delay of longer than three months and worse

rates of survival, the most accepted threshold for patient delay is three months and one month for 'provider delay'.

Several studies have been conducted to explore breast cancer delay in developed and developing countries. For instance, a study conducted in Iran reported that 68% (136/200) of cases had delayed their first visit by ≥ 1 month and 42.5% by ≥ 3 months with median patient delay of 12 weeks (Harirchi et al., 2005). Likewise patient-related delay of more than three months was found in 38.1% of Egyptian patients (Abdel-Fattah et al., 1999). The median interval between the discovery of the first symptom and the first visit among all patients was five weeks (ranging from 1 to 192 weeks). Thongsuksai et al. (2000) from Thailand reported a median delay of eight weeks in patients with stage III disease and 28 weeks in patients with stage IV disease. Similar figures come from a study conducted at five large medical centres in Malaysia where the frequency of diagnosis delay of more than three months was 72.6% and delay of more than six months occurred in 45.5% of the cases (Norsa'adah et al., 2011).

Patient delay of three months was reported to range from 14% to 19% in developed countries (Pineros et al., 2009). In a large study from the UK, Richards et al (1999a) reported a prevalence of patient delay (>12 weeks) of 55.5% in women with locally advanced breast cancer. This percentage rose to 67.3% in metastatic cases. In Germany, the median patient delay was 16 days but one out of six women (17.4%) waited more than three months before seeking professional health care (Arndt et al., 2002). In New Zealand, out of a total sample of 85 women, 40% had seen their doctor within seven days, 52% within 14 days, 69% within 30 days, and 14% had waited over 90 days (Meechan et al., 2002).

Many studies have been conducted to identify the factors that contribute to delay in seeking treatment and a variety of socio-demographic, clinical and psychosocial factors have been examined in relation to patient delay in seeking treatment (Rastad et al., 2012). These studies have, however, presented varying and contradictory results. A systematic review was undertaken to identify the explanatory factors and assess the strength of the evidence for the determination of late or delayed presentation for breast cancer in the Middle East. It included

six studies from Iran and Egypt and found strong evidence in the association between older age and patient delay (Alhurishi et al., 2011). This was because there were three studies (Abdel-Fattah et al., 1999, Elzawawy, 1999, El-Zawawy, 1991) which demonstrated a positive association between older age and patient delay with a large study population (a total of 827 patients) compared to two studies (Stapleton et al., 2011, Montazeri et al., 2003) showing negative association with 533 patients. The review also found that lower education levels were strongly associated with longer delay where in Egypt delayed presentation was 13 times greater for illiterate women compared with university graduates (Abdel-Fattah et al., 1999). Ramirez et al. (1999) concluded that there was strong evidence that patient delay was associated with older age but moderate evidence that patient delay was associated with fewer years of education in a systematic review of 23 studies on patient delay and breast cancer. Several reasons might explain patient delay in older women. Older women may attribute their symptoms to existing chronic conditions or to aging (Arndt et al., 2002). Grunfeld et al. (2002) stated that older women were less likely to perceive changes in breast skin and change in breast shape or size as symptoms of breast cancer. In addition, it has been argued that older adults, who suffer from other illnesses, are less likely to seek medical help for symptoms that are not causing them pain or that have a minor impact on their daily function (Grunfeld et al., 2002). Failure to identify breast cancer symptoms and poor knowledge about breast cancer risk factors have been demonstrated among older women (Grunfeld et al., 2002) (Bish et al., 2005).

Similar findings to Ramirez et al. (1999) were found in a systematic review of patient delay in developing countries, which included 13 studies from Thailand, Egypt, Pakistan, Iran, Nigeria, Tunisia, Malaysia, Colombia, India and Ghana (Sharma et al., 2012). While some studies found no association between patient delay and marital status (Abdel-Fattah et al., 1999, Elzawawy, 1999, Ramirez et al., 1999, Bish et al., 2005) other studies found that being married (Harirchi et al., 2005), or being divorced or widowed (Montazeri et al., 2003, Ali et al., 2008) resulted in longer delays. With respect to income status, Sharma et al. (2012) concluded in their systemic review in developing countries that “the predominant theme emerging from the results of this review emphasizes how

poverty constitutes the underlying common denominator and (was the) most important barrier contributing to delayed patient presentation in these settings.” The causal conditions of poverty are supported by evidence from both “good” and “fair” studies and are chiefly manifested economically via lower income status, lower education levels, rural residency, and lack of access to healthcare systems”. It is easy to see how lack of financial resources to use health services is significantly associated with longer delay, as one Mexican patient described it: *“Money is everything, isn’t it? For transportation, for medication, for everything that you need to pay at the hospital”* (Unger-Saldaña and Infante-Castañeda, 2011).

Lack of knowledge regarding breast cancer has been linked with patient delay in several studies (Stapleton et al., 2011, Abdel-Fattah et al., 1999, Harirchi et al., 2005, Rastad et al., 2012). Failure to identify and label the initial symptoms influences a woman’s decision to seek medical help immediately (Norsa’adah et al., 2011, Burgess et al., 2001). Interpretation of breast symptoms is based on the pre-existing knowledge, experience, self-education and observation of individuals (Norsa’adah et al., 2011). If the woman has knowledge regarding the variation of symptoms in breast cancer, she will be able to interpret and assess her symptoms more correctly and decide to seek medical attention. Patients are more likely to attribute new symptoms to less serious conditions instead of to a life-threatening disease (Bish et al., 2005). A study reported that considering symptoms to be harmless was the most important reason for delaying consultation for more than half of the patients (Nosarti et al., 2000). Similar results come from the UK where *‘I didn’t realise it was serious’*, was a frequently comment among patients who delayed (Burgess et al., 2001). Perception of the seriousness of a symptom is dependent upon the first symptom and how fast the symptom changes and multiplies. Burgess et al. (2001) stated that women monitored the situation, keeping their symptoms under review: *‘I mentally kept an eye on it and I thought that has got bigger. So I made an appointment to go to the doctor’s’*

False interpretation of the initial symptom was a prevalent and a common issue expressed as a main reason for delay in seeking treatment (Rastad et al., 2012). Mexican women talked about not knowing the initial symptom they discovered

might be a sign of breast cancer (Unger-Saldaña and Infante-Castañeda, 2011). Some women confessed that they did not know that inward retraction of the nipple, an axillary mass, a painless mass, etc. could be an early sign of breast cancer: *'My breast had no problem at all! Just a little hard lump under my arm...'* *'I went to take a bath... the brown areola was pulled in and a large piece ... of this side of my breast was very hard... Because it didn't have any pain, I did not think that it was serious'*. (Rastad et al., 2012)

In fact, the nature of presenting symptoms influenced whether or not to delay seeking medical help. This fact is demonstrated in the finding that women with non-lump symptoms tended to delay consultations compared to those with a lump (Burgess et al., 2001, Burgess et al., 1998, Abdel-Fattah et al., 1999, Montazeri et al., 2003). It is suggested that symptoms which fail to match the expectations of breast cancer presenting as a discrete breast lump may contribute to the delay in seeking treatment and that the public perception of the presenting symptoms of breast cancer may need to be broadened (Burgess et al., 2001). In other studies, the absence of pain has been associated with longer delay and late stage diagnosis (Burgess et al., 2001, Stapleton et al., 2011). Pain is a common symptom of any disease that draws attention to the site of the disease. In case of breast cancer, pain is most likely to occur in case of large tumours or ulceration both of which are indicative of late-stage disease (Stapleton et al., 2011).

Moreover, knowledge of breast self-examination (BSE) increased the likelihood of women presenting in early stages in some studies (Abdel-Fattah et al., 1999, Stapleton et al., 2011, Rastad et al., 2012). Lack of knowledge about BSE and not having a previous clinical breast examination (CBE) or a mammogram were also associated with late stage at presentation (Stapleton et al., 2011). A qualitative study carried in Iran noted that the majority of the participants said they didn't practice BSE, while the rest of them pointed out that they did not always follow the instructions consistently (Rastad et al., 2012). Another study also showed that the knowledge and attitude of Iranian women about breast cancer screening and the signs of breast cancer are not enough (Khanjani et al., 2012). Some did not do breast cancer screening examinations such as BSE because they did not believe it was necessary, but most of them did not do it

because they did not know how to perform the examination. Similar findings come from Egypt where patients who did not practice BSE had nearly 18 times higher risk of diagnostic delay as compared to those who practiced it, regardless of its regularity (Abdel-Fattah et al., 1999). The benefit of BSE is being debated across the literature. Several observational studies, including case-control and cohort studies, have examined the effects of BSE in various women populations (Muscat and Huncharek, 1991, Newcomb et al., 1991, Holmberg et al., 1997). These studies have yielded conflicting conclusions, but the majority have shown that BSE failed to detect cancer at earlier stages or improve survival. Nevertheless, the results of these studies have been questioned as being unreliable because observational studies have several limitations when they are used to examine screening techniques (Corbex et al., 2012). Further, BSE has been questioned in view of two randomized trials: one from Russia (Semiglazov et al., 2003) and the other from Shanghai (Thomas et al., 2002). The result of both trials discredited BSE as a screening tool and showed that it greatly increases the number of benign lumps detected. This, too, is the official position of health authorities like the US Preventive Services Task Force and the Canadian Task Force on Preventive Health Care to issue recommendations against teaching BSE, stating, “For the teaching of BSE, there is moderate certainty that the harms outweigh the benefits” (Corbex et al., 2012). However, some have suggested that enhanced breast health awareness may motivate women to seek treatment for breast-related symptoms earlier than women who did not know about BSE (Stapleton et al., 2011)

The association between family history and patient delay among breast cancer patients showed contradictory results from different studies. While some studies conducted in India (Ali et al., 2008) and New Zealand (Meechan et al., 2002) reported positive correlation between family history and patient delay, others have reported negative correlation (Harirchi et al., 2005, Montazeri et al., 2003) or did not find any significant associations in this regard (Burgess et al., 1998, Nosarti et al., 2000). Harirchi et al. (2005) explained that woman with a family history perceived a high risk; this might have led to more immediate actions upon discovery of a mass. Being familiar with breast cancer through the experience of a family member is associated with shorter delays: *‘I never had*

seen anyone with this problem...if it was so, maybe I would come sooner.’ ‘I knew nothing [about breast cancer]... since we did not have it in our family.’ (Rastad et al., 2012)

Other reason for patient delay is what could broadly be defined as the social relations of care seeking. Studies have shown that social relations are important mediators in care seeking decisions. As Facione (1993) suggested that role demands such as devoting time and attention to the needs of someone else and taking time to make domestic arrangements prior to having a biopsy taken may delay care seeking. Family engagement and career commitments were among the common reasons for delay mentioned by Iranian patients (Rastad et al., 2012). Harirchi et al. (2005) explains that traditionally with respect to women's role in the Iranian families, women do not usually have much time for themselves as they have to deal with household chores, children's needs and outdoor activities such as shopping. Though some women knew that the present signs could be serious, they thought that visiting a doctor and the subsequent workup would take too much time, and they would have to sacrifice their family responsibilities and job commitments (Rastad et al., 2012): *‘I was scared that if I visit a doctor, I may need an operation. My children were too young and I was working...’* Likewise in the UK, Burgess et al. (2000) reported that patients who delayed did not prioritize their health over competing demands. Others have shown that social networks are central triggers for care seeking. Studies show that breast cancer patients who do not disclose their symptoms to someone else within a week have longer patient delay (Burgess et al., 2006, Burgess et al., 1998). Disclosing symptom discovery to another person could facilitate recognition of the potential seriousness of the situation and the decision to seek medical advice, as one patient said: *‘I happened to speak to a friend who had breast symptoms in the past ... and she said, ‘You must go straight away’.* (Burgess et al., 2001)

Fear appears to be an important psychological factor in delay, and its intensity may influence magnitude of delay (Dubayova et al., 2010a). Dubayova et al. (2010a) explained that feelings, such as worry, fear and anxiety, could be elicited by several factors. Such factors include symptoms which induce pain or discomfort, presumed diagnosis and anticipated consequences of treatment, as

well as by coping failures and reinterpretations of the illness condition. Across the literature on breast cancer and patient delay, fear is a major barrier to early medical help (Stapleton et al., 2011, Harirchi et al., 2005, Rastad et al., 2012, Burgess et al., 1998, Unger-Saldaña and Infante-Castañeda, 2011).

Different reasons in different cultural contexts explained this fear. For example, African and Afro-Caribbean patients with breast cancer feared they might end up having a mastectomy and were concerned about their fertility and ability to keep their sexual partners (Rastad et al., 2012). Other patients recognised their symptoms to be serious and might be cancerous yet they delayed seeing a doctor because they feared the consequences of therapeutic intervention (Norsa'adah et al., 2011, Burgess et al., 2001, Rastad et al., 2012). It seems as if the patient was convinced that cancer could not be cured or that it would necessitate invasive treatments.

Similar studies reported that some of the participants confessed that because of their fear about being diagnosed with cancer, they postponed their medical consultation (Rastad et al., 2012). It seems as if they felt safer not knowing that they had cancer, even if they suspected it. In patients with different types of carcinoma, 17% of the delayers reported fear of discovering the cause of their symptoms was the reason for their delay (Dubayova et al., 2010b). These fears had often been influenced by past experiences of cancer in relatives or friends (Burgess et al., 2001, Rastad et al., 2012). Because of this evidence, some have suggested that there may be some benefit in reassuring women of the benefits of early treatment on prognosis (Rastad et al., 2012). They should be assured that surgery is minimal if the cancer is diagnosed early enough, and that there have been advances in the management of the side effects of chemotherapy. Such education would need to be informed by more data on current beliefs and attitudes about breast cancer and its treatments in the general population. Fear of hospitals, operations, and medical tests has been linked to patient's delay (Burgess et al., 2001).

Negative perception of breast cancer treatment and the use of alternative therapy are also explanations as to why women with breast cancer delay seeking medical help (Norsa'adah et al., 2011). A negative perception of breast cancer

treatment prevented patients from receiving early diagnoses has been documented in studies from Malaysia (Norsa'adah et al., 2011), Iran and Nigeria (Ajekigbe, 1991). Negative perception of the side effects of chemotherapy might induce fear in some patients causing them to refuse treatment. Some women hold the belief that treatment would affect their ability to perform their role and thus they would have to rely on others to care for them (Norsa'adah et al., 2011). Fear of divorce or the husband remarrying could lead some women to decide not to get their symptoms diagnosed if they suspected breast cancer (Norsa'adah et al., 2011). Others believed that breast cancer could not be cured, so there was no point in having it diagnosed and treated (Andersen et al., 2009).

Diagnosis delay was also related to a belief that mastectomy causes disfigurement and disability (Grinfeld et al., 2003). Sharma et al (2012) concluded in a systematic review of patient delay in developing countries that alternative treatment use including use of other practitioners and use of prayer was associated with longer delays. Malaysian patients, for example, used alternative therapy as a way to avoid surgery or took it when the prognosis was fatal and disease caused suffering (Norsa'adah et al., 2011). It is clear from this evidence that women who delay seeking help for symptoms of breast cancer have a reduced chance of survival. It is, therefore, extremely important in a programme of primary research into understanding the factors that lead to increased risk of delay, that it is vital to determine effective approaches to shortening of delay and thereby improving women's survival and quality of life.

In summary, 'patient delay' is defined as the time between the initial presentation of symptoms and first medical consultation. The most accepted cut off for patient delay is three months. Older age and lower educational levels are shown to be associated with longer delay. There were inconsistent results on the association between marital status and family history with patient delay. Other factors that were identified to be associated with patient delay included lower income, rural residency, access to health care services and nature of presenting symptoms. Studies also have identified other reasons for longer delay including lack of knowledge regarding breast cancer symptoms, knowledge and practice of BSE, negative perception of breast cancer treatment, competing demands in terms of family and work commitments and finally, fear and embarrassment.

Exploring the literature on breast cancer and patient delay helps to identify the common factors that are likely to be associated with longer delay. These factors will be used in the design of the questionnaire used in this study to assess patient delay among a sample of Omani women with breast cancer.

Chapter Three: Delay in Seeking Medical Care for Self-Detected Breast Cancer Symptoms in Omani Women

3.1 Introduction

The extent of patient delay in Oman with self-detected breast symptoms and the factors influencing this delay time have not been investigated. Published studies from Oman found that more than half of the patients presented with advanced disease (stage III and IV) (Al-Moundhri et al., 2004, Al-Moundhri et al., 2011). So the aim of this study is to address this gap by assessing the magnitude of the delay among Omani women presenting with breast cancer and to evaluate possible factors causing this delay in order to recommend strategies and programs to prevent patient delay in breast cancer diagnosis.

3.2 Aims

- To identify the magnitude of the delay in breast cancer diagnosis in Oman.
- To assess the relationship between delay and socio-demographic characteristics, medical and obstetric history, nature of presenting symptoms and women's knowledge about breast cancer.
- To identify reasons for delay in seeking medical help for self-detected breast cancer symptoms in Omani women.

3.3 Methodology

3.3.1 Sample and sample recruitment

The population of interest for this research study was women diagnosed with breast cancer in Oman. Participants were recruited from two tertiary hospitals in Oman, Royal Hospital (RH) and Sultan Qaboos University Hospital (SQUH). These two hospitals were chosen because there are the only two main hospitals in the country that provide cancer treatment especially chemotherapy. RH has the National Oncology Centre, which is the only place in the country that provides radiotherapy treatment. Nevertheless, some of the eligible participants

for the study might be missed due to the following reasons. First, Eligible patients were included after the diagnosis of breast cancer was made and did not include those patients who had died before the study was conducted. Second, other patients may have stopped attending the follow-up clinics and hence were not seen in the clinics at the time of the study. Third, some patients from other regions in the country required treatment of conservative surgeries only which are sometimes carried out in the regional hospitals and therefore are not seen in RH or SQUH.

Sample size was determined by pragmatic considerations. It was anticipated that over four months of data collection in the two hospitals, I would be able to interview at least 150 women of whom at least 100 would have been diagnosed with later stage disease. In a study of 200 women with stage IIB and above breast cancer in Iran, Harirchi et al. (2005) found that 68% had waited for more than a month after their first symptom to seek medical care. Of those with delay, 98% were married compared with 87% of those without delay ($p=0.002$), and 52% of those with delay were illiterate compared with 31% of those without delay ($p=0.04$). If my findings were found to be similar to those of Harirchi et al. (2005), I would have 68% power to detect the higher proportion married and 63% to detect the higher proportion illiterate in the delayed group, with 5% significance.

At RH patients attended the oncology outpatient clinic within the National Cancer Centre every Tuesday and were approached in the waiting room from 27th April till 15th July 2013. Also additional patients were approached at the chemotherapy day-care unit at the centre every Sunday and Wednesday. At SQUH patients attending the oncology outpatient clinic every Monday from 13th May to 20th July 2013, were approached and all Thursday patients from the chemotherapy day-care room within SQUH were asked to participate in the study.

The initial plan was to get the nurses at the clinics' reception in both hospitals to provide the patients with the information sheet and I was to answer any questions from the participants and ask for consent. However, because they were very busy clinics and nurses were not always present at the reception, a list

with names of attending breast cancer patients was given to me and I approached them where they were sitting at the waiting room and asked them to take part in the study. Other patients were referred to me after their consultation with the doctor. At the chemotherapy unit, I approached patients while they were waiting for their blood results before starting the chemotherapy.

3.3.2 Data collection

Participants were provided with an information sheet in Arabic and were given the opportunity to ask questions if there was anything that they did not understand or wanted to clarify. For those who were illiterate, I read and explained the information sheet for them. Then a consent form, which was also in Arabic, was completed. There was an emphasis placed on ensuring that the participants' involvement in the research was voluntary and that they were free to withdraw at any stage. In addition, patients were asked for permission to access their medical notes using their hospital number to confirm any medical information like date of diagnosis, if necessary. However they had the option to consent to the interview only (if they consented at all). The interview was carried out in a private room within the two hospitals.

Face-to-face interviews were conducted using standardized questionnaires. The content of the questionnaire used (see appendix 1) was derived from the existing literature on delayed presentation. Each interview took around 15-20 minutes. The questionnaire was filled in by me during the interviews.

The questionnaire consisted of 34 questions. Most of the questions were closed questions except for few open questions that used to enquire about reasons for delay. It covered four themes, which were:

- Socio-demographic characteristic which included age, educational level, occupation, family guardian, occupation, house-hold income, place of living, travel time to the nearest medical centre and marital status.
- Obstetric and medical histories, which included number of children, age at first childbirth, number of children who are breastfed, breastfeeding duration, phase of menopause, weight, height, history of chronic disease, family history of breast cancer.

- Symptoms and healthcare seeking behaviour which included date of diagnosis, stage at diagnosis, detected breast cancer symptoms, date when first noticed these symptoms, number of weeks between noticing the symptoms and visiting a doctor, reasons to visit the doctor at time of diagnosis, reasons for delaying seeing a doctor after discovering the symptoms and whether the participant talked about her symptoms to any one before she visited a doctor.
- Knowledge and attitude toward breast cancer which included knowledge about breast cancer symptoms, incidence of breast cancer in Oman, main method of diagnosing breast cancer, early detection methods, familiarity and performance of breast self-examination before and after the diagnosis, and beliefs about prevention and cure of breast cancer.

After the interviews, the supervising doctors at each hospital completed the missing information from the patients' medical records using the hospital numbers they provided during the interviews. Such information included, patient's BMI, menopausal stage, date of diagnosis and stage of disease.

3.4 Variable definition for analysis

A number of variables were derived from the data collected in the questionnaire for use in data analysis:

- **Patient delay:** Patient delay was defined as “the period between an individual's first awareness of a sign or a symptom of illness and initial medical consultation” (Pack and Gallo, 1938). In this study and in line with other published studies on patient delay (see section 2.4), patient delay was categorised into periods of non-delay (<3 months) and delay (≥ 3 months). To reduce recall error, the participants were reminded of events in the calendar such as school holidays, religious/national occasions and birth dates, to help them remember important dates relative to their medical history.
- **Age groups:** Age was collected from patients and then confirmed using medical record of each patient. As mentioned earlier (section 2.1), 78% of the Arab population diagnosed are below 50 years compared to only

25-30% in the western population (Chouchane et al., 2013). Age was categorised into four groups: 27-35 years, 36-49 years, 50-64 years and >65 years in order to compare percentage of women below 50 years to the rest of Arab populations and western population and also to allow comparison with frequency of cases published in the Omani National Cancer Registry.

- **Occupation:** occupations were classified according to the “Australian and New Zealand Standard Classification of Occupations” available at Statistics New Zealand website:
http://www.stats.govt.nz/surveys_and_methods/methods/classifications-and-standards/classification-related-stats-standards/occupation.aspx
- **Phase of menopause:** participants were asked about their stage of menopause. Some women were under chemotherapy treatment causing them to have irregular menstrual cycles and so their actual phase of menopause was confirmed from their medical notes.
- **Breastfeeding duration:** women were asked how many children they had breastfed and for how long, then that time was added for all children together to calculate the total lifetime breastfeeding duration.
- **Body Mass Index (BMI):** BMI for each patient was calculated using weight and height obtained from patients’ medical notes.
- **Chronic diseases:** women were considered to have a chronic disease if they reported hypertension, diabetes, heart diseases, asthma and other diseases that require lifelong monitoring.
- **A family history of breast cancer:** was defined as having a first-degree relative, i.e. sister, mother or daughter who had breast cancer.
- **Stage at diagnosis:** T, N, and M categories of the tumours were recorded from patients’ medical notes. These were grouped to determine the breast cancer stage using the staging system of breast cancer published by the American Joint Committee on Cancer (Compton et al., 2012).

3.5 Data analysis

The data was entered into an Excel spread sheet and the Statistical Package for the Social Science (SPSS) version 20 was used to analyse data. Frequencies of

the socio-demographic characteristics of the participants, their medical history and their clinical characteristics were calculated.

To identify the most influential and important characteristics associated with patient delay, women in the two categories, no delay (< 3 month) and delayed (≥ 3 months), were compared using cross-tabulation analysis. The Chi-square test, or Fisher's exact test (where there were cell counts less than 5) were used to assess the significance of the association between potential patient characteristics and patient delay. In all tests, $p \leq 0.05$ was regarded statistically significant.

Answers to the open questions that were used to enquire reasons for delay were categorised to different themes, some of which were similar to those identified from the literature review as qualitative analysis is beyond the scope of this research.

3.6 Ethical considerations

Ethical approval was obtained from the Ministry of Health in Oman in order to recruit participants from the RH. In addition, another approval was obtained from the SQUH Research Committee to include patients from the SQUH. Finally, as a student of the University of Otago, ethical approval was obtained from the University of Otago Human Ethics Committee.

3.7 Results

3.7.1 Study population

The study sample consisted of 150 patients with 94 patients recruited from the RH and 56 patients recruited from SQUH. Four eligible patients declined to participate in the study. Table 3-1 shows the socio-demographic characteristics of participants. Their age ranged from 27 to 71 years with a mean of 46.3 years (SD 10.4). The majority (60.7%) of patients were < 50 years old, 35.3% between 50-65 and only 4% of patients were 65 years or over. The majority (75.3%) of the participants were married. Academically, 31.3% of the patients were illiterate, while 45.3% of patients had a high school or less education level and 23.3% had higher (university) education. 81.3% of participants resided in an urban city compared to 18.7% coming from rural places and the majority of

them had access to a near medical centre within 15 minutes or less (mean=10.8 minutes SD 10.8).

Table 3-1: Socio-demographic characteristics of participants

Socio-demography	Frequency N=150	%
Age group		
27-34 years	25	16.7
35-49 years	66	44.0
50-64 years	53	35.3
≥ 65 years	6	4.0
Marital Status		
Married	113	75.3
Never Married (single)	9	6.0
Widowed	17	11.3
Divorced	11	7.3
Education level		
Illiterate	47	31.3
Secondary school or less	39	26.0
High school certificate	29	19.3
Higher education (university)	35	23.3
Place of residence		
Urban (large city)	60	40.0
Urban (small city)	62	41.3
Rural (Village)	28	18.7
Travel time to nearest medical centre		
>15	130	86.7
16-30	17	11.3
31-60	2	1.3
>60	1	0.7
Occupation		
Retired	6	4.0
Housewives	111	74.0
Education professionals	15	10.0
Health professional	5	3.3
Marketing professional	2	1.3
Personal service worker	1	.7
Clerical and administrative worker	10	6.7
Household income		
200-500	82	54.7
600-900	38	25.3
1000+	30	20.0

Table 3-2 shows the medical history of the participants. 52% of patients were premenopausal with a mean age of 38.3 years (SD 5.6) and only 4 patients were going through menopause. Only 29 patients (19.3%) had a family history of breast cancer and 57 (38%) had co-morbid chronic disease. 45.3 % of patients were obese with BMI >30, 29.3% were overweight with BMI of 25-30 and 25.3% had a BMI \leq 25 with three patients being underweight.

Table 3-2: Medical histories of the participants

Medical history	Frequency N=150	%
Phase of menopause		
Pre-menopause	78	52.0
Going through menopause	4	2.7
Postmenopausal	68	45.3
History of chronic disease		
No	93	62.0
Yes	57	38.0
Family History of Breast Cancer		
No	121	80.7
Yes	29	19.3
BMI		
\leq 25	38	25.3
25.1-30	44	29.3
>30	68	45.3

The reproductive history of participants who have had children (N=136) is shown in Table 3-3. The majority of respondents (90.7%) had children. 70.6% of patients with children had more than three children. 61% of women with children had their first child at the age of 21 years or less and the mean age of patient at first pregnancy was 20.6 (SD 5.8). Just over two-thirds of patients who had children had breastfed for a total of 18-36 months, but few had breastfed for more than 36 months.

Table 3-3: Reproductive histories of participants who had children

Reproductive history	Frequency N=136	%
Do you have any children?		
No	14	9.3
Yes	136	90.7
Age at first child birth		
≤ 15 years	26	19.1
16-20 years	57	41.9
21-25 years	25	18.4
26-30 years	22	16.2
>30 years	6	4.4
Number of children		
1	12	8.8
2-3	28	20.6
>3	96	70.6
Number of children who were breastfed		
0	3	2.2
1	12	8.8
2-3	26	19.1
>3	95	69.9
Total life time breastfeeding duration		
0 months	3	2.2
1-6 months	12	8.8
7-17 months	26	19.1
18-36 months	95	69.9
>36 months	3	2.2

Table 3-4 shows the clinical characteristics of the participants. A palpable breast lump was by far the most common symptom, being present in 78.7% of patients. These included 87 (58%) who noticed a lump alone and a further 31 (20.7%) who noticed a lump in association with at least one other symptom. Nipple symptoms (without a breast lump) including nipple discharges, retracted nipple and change in appearance of the nipple were reported by seven patients. Other symptoms of the breast such as heavy breast, breast pain, change in breast skin and axillary lump were reported less frequently (12.7%).

With regards to stage at presentation 44% of patients had early stage disease (stage I/stage II) compared to 56% of patients with late stage disease (stage III/stage IV).

Table 3-4: Clinical presentations of the participants

	Frequency N=150	%
Presenting symptoms		
Breast lump only	87	58.0
Lump with others	31	20.7
Breast lump AND pain	12	8.0
Breast AND Axillary mass	5	3.3
Breast lump AND nipple changes	6	4.0
Breast lump AND change in breast size	1	0.7
Breast lump AND change in breast skin	2	1.3
Breast lump AND arm Or shoulder Or back pain	5	3.3
Nipple symptoms	7	4.7
Nipple changes	2	1.3
Nipple discharges	3	2.0
Retracted nipple AND pain	1	0.7
Nipple discharges AND pain	1	0.7
Others	19	12.7
Breast pain	2	1.3
Heavy breast	1	.7
Change in breast size	2	1.3
Change in breast skin	4	2.7
Breast AND Axillary mass	5	3.3
Heavy breast AND arm pain	1	0.7
Others (abdominal pain, coughing, shoulder pain)	3	2.0
Nothing noticed (symptoms discovered during mammography screening or general check-up)	6	4.0
Stage at presentation		
I	11	7.3
IA	11	7.3
II	55	36.6
IIA	23	15.3
IIB	32	21.3
III	58	38.6
IIIA	36	24.0
IIIB	17	11.3
IIIC	5	3.3
IV	26	17.3

3.7.2 Knowledge and attitude toward breast cancer

Patients were presented with a list of possible breast cancer symptoms and were asked to select the relevant symptoms. Almost all patients agreed that breast or axillary mass is a symptom of breast cancer while 67.3% believed that breast pain could be a symptom. Only 56.0% of patients knew that nipple retraction is a sign of breast cancer (Table 3-5).

When participants were asked about the prevalence of breast cancer, the majority of them (92.7%) said that it is the most common female cancer. 5.3% declared ignorance about breast cancer prevalence. 64.7% of patients believed that breast cancer is preventable and curable. With regards to potential ways of early detection of breast cancer, 84.0% of patients believed that BSE is a way of early detection, 92.7% believed clinical breast examination (CBE) can detect breast cancer early, 95.3% reported that mammography is an early detection method and 64.7% of patients said that blood test cannot be used for early detection. Almost four out of five participants identified mammography as the main way of diagnosis for breast cancer.

3.7.3 Breast self-examination (BSE)

Only 37 participants (24.7%) performed BSE before their diagnosis of breast cancer though the majority 137 (91.3%) declared importance of BSE. However, out of 113 (75.3%) patients who were not performing BSE before diagnosis, 71 (62.8%) patients were aware with the technique of BSE. In fact, 41 out of 113 started performing BSE after diagnosis.

Table 3-5: Patients' knowledge and attitude toward breast cancer

Variable	Frequency N =150	%
<u>Knowledge about symptoms</u>		
Breast/axillary mass		
Yes	149	99.3
No	1	0.7
Breast pain		
Yes	101	67.3
No	49	32.7
Nipple retraction		
Yes	84	56.0
No	66	44.0
Declare ignorance "I don't know"		
	2	1.3
<u>Knowledge about prevalence</u>		
Breast cancer is the most common female cancer	139	92.7
Another cancer is the most common cancer	3	2.0
Declare ignorance "I don't know"	8	5.3
<u>Attitude about prevention and treatment</u>		
Breast cancer is preventable and curable	97	64.7
Breast cancer is incurable and fatal	1	0.7
Breast cancer is in one's fate	52	34.7
<u>Knowledge about ways for early detection of breast cancer</u>		
Breast self-examination		
Yes	126	84.0
No	24	16.0
Clinical breast examination		
Yes	139	92.7
No	11	7.3
Mammography		
Yes	143	95.3
No	7	4.7
Blood test		
Yes	53	35.3
No	97	64.7
Declare ignorance "I don't know"		
	1	0.7
<u>Knowledge about main way of diagnosis</u>		
Breast self-examination	6	4.0
Clinical breast examination	9	6.0
Mammography	124	82.7
Blood tests	2	1.3
Others	9	6.0

Performing BSE before diagnosis		
Yes	37	24.7
No	113	75.3
Familiarity of BSE now for people not performing it already (n=113)		
Yes	71	62.8
No	42	37.2
Importance of BSE		
Not important	13	8.7
Important	137	91.3
Performing BSE now		
Yes	76	50.7
No	74	49.3

3.7.4 Extent of delay

In the analysis for patient delay, only 144 patients were included and the other six patients were excluded because they did not discover their symptoms; rather, they were first discovered by health professionals. Three patients were diagnosed after having a mammography in the Mobile Mammography Unit provided by National Association for Cancer Awareness (non-governmental organisation). All three patients had early stage diagnosis (two patients with stage IA and one with stage IIB). A further one patient was diagnosed after an admission for hip fracture and she was discovered to have a breast lump, which she did not notice before, and was diagnosed with breast cancer at stage I. The final two patients were diagnosis after having a general check-up including, imaging and CBE and diagnosed with breast cancer stage IA.

The median time taken by women in this sample between discovering the breast symptoms and seeing a doctor was 14 days. 56.9% of patients had a medical consultation in less than a month after detecting symptoms; in fact 48.6% of patients had their first visit within a week. 33 patients of the 144 (22.9%) met the definition of delay. Of those with delay, 27.3% delayed consultation for more than a year after the onset of symptoms. The frequency distribution of patients according to the time between onset of symptoms and initial medical consultation is shown in table 3-6.

Table 3-6: Frequency distribution of patients presenting with breast cancer according to duration of patient delay

Duration of patient delay (months)	Frequency	%
< 1	82	56.9
1-2	29	20.1
3-5	8	5.6
6-12	16	11.1
13-24	3	2.1
25-36	1	0.7
37+	5	3.5
Total	144	100.0

3.7.5 Influence of socio-demographic factors on delay

Table 3-7 shows patient delay and socio-demographic factors, and the result of the chi squared test. Delay was significantly associated with age ($p=0.004$). In general older women waited longer than younger women before seeking medical help. Educational level was also found to be significantly associated with delay ($p= 0.047$). Patient delay was 2.8 times more likely to be reported by illiterate women (32.6%) compared to women with higher education (11.8%). When looking at the influence of occupation on the magnitude of delay, results showed that women who were housewives (27.8%) waited longer than employed women (8.6%). Delay was not significantly associated with other socio-demographic factors including marital status ($p =0.536$), place of living ($p=0.275$), travel time to the nearest medical centre ($p=0.294$) and household income ($p = 0.174$).

Table 3-7: Patient delay in breast cancer patient by socio-demographic factors

Variable	Patient delay		P
	< 3 months	≥ 3 months	
	N=111 [n (% of raw)]	N=33 [n (% of raw)]	
Age group			
27-34 years	24 (100)	0 (0.0)	0.004
35-49 years	48 (75.0)	16 (25.0)	
50-64 years	36 (72.0)	14 (28.0)	
≥ 65 years	3 (50.0)	3 (50.0)	
Educational level			
Illiterate	31 (67.4)	15 (32.6)	0.047
Secondary school or less	26 (70.3)	11 (29.7)	
High school certificate	24 (88.9)	3 (11.1)	
Higher (university) education	30 (88.2)	4 (11.8)	
Marital status			
Married	88 (79.3)	23 (20.7)	0.536
Never Married (single)	6 (66.7)	3 (33.3)	
Widowed	10 (66.7)	5 (33.3)	
Divorced	7 (77.8)	2 (22.2)	
Place of residency			
Urban (large city)	47 (81.0)	11 (19.0)	0.275
Urban (small city)	47 (78.3)	13 (21.7)	
Rural (Village)	17 (65.4)	9 (34.6)	
Travel time to nearest medical centre			
>15	97 (78.2)	27 (21.8)	0.294
16-30	12 (70.6)	5 (29.4)	
31-60	2 (100)	0 (0.0)	
>60	0 (0.0)	1 (100)	
Occupation			
Employed	33 (91.7)	3 (8.3)	0.021
Housewife	78 (72.2)	30 (27.8)	
Household income (OR)			
200-500	57 (73.1)	21 (26.9)	0.174
600-900	27 (75.0)	9 (25.0)	
1000+	27 (90.0)	3 (10.0)	

3.7.6 Influence of health characteristics, medical presentation and health behaviours on delay

Table 3-8 shows patient delay and health characteristics, medical presentation and health behaviours. No significant association was found between delay and family history of breast cancer (p=0.983). In contrast, a history of chronic

disease showed a significant association with delay where patients with comorbid chronic disease presented later than those without chronic disease ($p=0.012$), with 33.9% of patients with chronic disease delaying presentation for ≥ 3 months compared to 15.9% without a history of chronic disease. Whether or not the patients had children was not associated with delay ($p=1.000$). Similarly, no statistically significant association was found between delay and BMI, or the nature of presenting symptom, or stage of disease.

There was no statistically significant association between delay and the patient's attitude about prevention and the treatment of breast cancer. The majority in the delay and non-delay groups believed that breast cancer is preventable and curable. Likewise, factors like disclosing discovered symptoms and knowledge about the prevalence of breast cancer among females did not show an association with patient delay.

3.7.7 BSE and patient delay

Patient delay tended to be less common among women who reported performing BSE before diagnosis ($p= 0.001$). Almost all patients (32 patients) who delayed ≥ 3 months did not practise BSE. Also patient delay was observed to be less common among patients who acknowledged the importance of BSE but the association was not statistically significant ($p =0.162$).

Table 3-8: Patient delay by health characteristics, presenting symptoms and health behaviour

Variable	Patient delay		P
	< 3 months	≥ 3 months	
	N=111 [n (%)]	N=33 [n (%)]	
Family history of breast cancer			
Yes	20 (76.9)	6 (23.1)	0.983
No	91 (77.1)	27 (22.9)	
History of chronic disease			
Yes	37 (66.1)	19 (33.9)	0.012
No	74 (84.1)	14 (15.9)	
BMI			
<25	28 (75.7)	9 (24.3)	0.905
25.1-30	31 (75.6)	10 (24.4)	
>30	52 (78.8)	14 (21.2)	
Phase of menopause			
Premenopausal	65 (84.4)	12 (15.6)	0.059
Going through menopause	2 (66.7)	1 (33.3)	
Postmenopausal	44 (68.8)	20 (31.3)	
Do you have any children?			
Yes	101 (77.1)	33 (22.9)	1.000
No	10 (76.9)	3 (23.1)	
Nature of presenting symptoms			
Breast lump (with or without other symptoms)	90 (76.9)	27 (23.1)	0.924
Symptoms other than a lump	21 (77.8)	6 (22.2)	
Stage at diagnosis			
Early stage disease (I/II)	48 (78.7)	13 (21.3)	0.694
Late stage disease (III/IV)	63 (75.9)	20 (24.1)	
Disclosed symptoms			
No	15 (75.0)	5 (25.0)	0.811
Yes	96 (77.4)	28 (22.6)	
Prevalence of breast cancer			
Breast cancer is the most common female cancer	103 (76.9)	31 (23.1)	0.412
Another cancer is the most common cancer	1 (50.0)	1 (50.0)	
Declare ignorance "I don't know"	7 (87.5)	1 (12.5)	
Attitude about prevention and treatment			
Breast cancer is preventable and curable	76 (81.7)	17 (18.3)	0.074
Breast cancer is in one's fate	35 (68.6)	16 (31.4)	
Performing BSE before diagnosis			
Yes	32 (97.0)	1 (3.0)	0.001
No	78 (70.3)	33 (29.7)	
Importance of BSE			
Not important	8 (61.5)	5 (38.5)	0.162
Important	103 (78.6)	28 (21.4)	

3.7.8 Reasons for patient delay

Patients who delayed their consultation for three months or more were asked to provide reasons for delaying. There were 33 patients with delay of ≥ 3 month and reasons are summarised in Table 3-9. Two themes emerged to explain patient delay, patient individual characteristics and socio-cultural context characteristics. With regard to patient individual characteristics, 7 out of 33 patients thought that their symptoms were normal and would resolve by themselves, while six patients recognised their symptoms to be abnormal but never thought it might be cancer. The majority of patients who thought their symptoms were abnormal were breastfeeding at the time they discovered the lump and almost all of them interpreted it as plugged milk ducts. Four patients thought that their symptoms were not worrying because no other symptoms were present or the lump was painless. Not seeing oneself at risk was a major reason reported by four patients. Being afraid of cancer treatment and embarrassment from being examined by a doctor arose as a reason for delay for four of the patients. Two patients reported using alternative medicine before seeking medical help. Family and work commitments were the two main reasons in socio-cultural context characteristics and were the main reasons for four patients.

Table 3-9: Reported main reasons for patient delay ≥ 3 months

	Specific reason	Example of participants responses	Frequency N=33
Patient individual characteristics	Patient thought that her symptoms were normal	<ul style="list-style-type: none"> • <i>"I thought it is a normal thing and will go with time and I didn't think it will be cancer...it started to get bigger with time and then I told my daughter about It"</i> • <i>"I thought the lump is part of normal physiology of breast that comes during menstrual cycle and I never thought it could be cancer"</i> • <i>"I didn't think of it as cancer and therefore ignored it"</i> • <i>"I thought it was normal and didn't put in mind that it would be cancer"</i> • <i>"I thought of it as a normal lump due to change in hormonal cycle and will disappear by time"</i> 	7
	Patient thought that her symptom was abnormal but it was not cancer.	<ul style="list-style-type: none"> • <i>"I thought the lump was due to obstructed milk ducts and will disappear with time but I noticed it to become bigger and then I just went to the hospital"</i> • <i>"I was breastfeeding at that time and I thought it was due to milk collection till I noticed it didn't disappear and visited a doctor"</i> • <i>"I heard that breast cancer patients usually have discharges but the lump wasn't ... and when it got bigger I thought I should go to the hospital"</i> • <i>"I thought it is an allergy and will go with time, but it got redder and then saw the doctor"</i> 	6
	Not Worrisome symptoms	<ul style="list-style-type: none"> • <i>"I had the lump for about 15 years [ago] and didn't trigger my attention because it didn't have any other symptoms or pain"</i> • <i>"It was painless and so I thought it is nothing serious"</i> • <i>"Before 7 months I had pain but because there was nothing visible in the breast I thought it might be normal"</i> • <i>"There was no pain associated with the lump so I wasn't worrying about it"</i> 	4

	Did not see oneself at risk	<ul style="list-style-type: none"> • <i>"I didn't regard myself as being at risk and so I ignored the symptoms"</i> • <i>"I didn't regard myself as being at risk and so I didn't think of it as serious"</i> • <i>"I didn't regard myself as being at risk and I never linked the symptoms to be cancer"</i> 	4
	Lack of knowledge	<i>"I didn't know the signs of breast cancer and one day I saw a poster in the clinic about signs of breast cancer that triggered my attention and thought it might be cancer and visited the doctor immediately"</i>	2
	Fear of treatment (surgery and chemotherapy)	<ul style="list-style-type: none"> • <i>"I saw the experience of breast cancer and its treatment on my friend and I was afraid of having surgery and chemotherapy"</i> • <i>"I was afraid that it is cancer and I will have to have surgery"</i> 	2
	Embarrassment	<i>"I was embarrassed by being examined by a male doctor"</i>	2
	Using alternative medicine	<i>Patient used alternative medicine (likes herbs and natural oils) before seeking medical help.</i>	2
Sociocultural context characteristics	Family commitments	<ul style="list-style-type: none"> • <i>"I was busy with the housework and I didn't think it could be cancer"</i> • <i>"I had children and no one to take care of them while I am a way, so I had to travel to my family place so I can leave the children there and go for treatment"</i> • <i>"My husband just passed away and I didn't care about it at that time and I didn't want to bother my children to take me to the hospital"</i> 	3
	Work commitments	<i>"I had lot of things going with my work at that time and I just ignored it"</i>	1

3.8 Discussion

Breast cancer is the most common cancer in Oman constituting 24.8% of total cancer. The incidence rate of breast cancer increased from 13.8 per 100,000 women in 1999 to 25.5 per 100,000 women in 2011 (Al Lawati et al., 2013). This study is the first in Oman to determine the extent of patient delay for women with self-discovered breast symptoms and to investigate the specific reasons influencing this delay time. In this section, the strengths and limitations of this cross-sectional study of women with breast cancer are discussed. Then the major findings are discussed and compared with other similar studies. Recommendations are made for future research and policy makers.

3.8.1 Strengths and limitations

A major strength of this study was the careful and detailed collection of information on patient delay using face-to-face interviews using standardized questionnaires with content from the existing literature on delayed presentation in breast cancer. All questionnaires were filled in by the same interviewer during a direct interview with the participants. In addition, patients' clinical information was collected from the medical records with the help of the consultants who usually see these patients in the clinics. Further, the participants were recruited from the two major hospitals in Oman that provide breast cancer treatment.

A number of limitations should be kept in mind when considering the findings of this study. One limitation is the possibility of recall error as an issue for some women who may have wrongly recalled the date of their first symptoms as well as their first visit to the clinician. We tried to minimize this by reminding the participants of events in the calendar such as school holidays, religious/national occasions and birth dates, to help them remember important dates relative to their medical history. In addition collecting information regarding data about the onset of symptoms and of first consultations is probably more reliable than asking the patients about length of delay. The problem of selection bias is another limitation due to that fact that participants were only those who finally saw a doctor and excluded those who did not present to doctor for symptom

evaluation and so magnitude of delay might be bigger in reality. Additionally, selection bias might be present due the fact that participants were included after the diagnosis of breast cancer was made and did not include the patients who have died before the study was conducted, nor does it include those who had stopped attending follow-up clinics. Nevertheless, if it is assumed that those who died early had advanced disease and had longer delay that would suggest that patient delay was under-estimated in this study. Although this study has developed initial information regarding the magnitude of delay and factors associated with delay, future studies could conduct more qualitative, in- depth analysis in order to obtain a deeper understanding of the problem and to provide additional data for designing breast health promotion strategies that are culturally sensitive in Oman.

3.8.2 Patient delay in Omani women with breast cancer

In Oman, women present with breast cancer at a younger age than their counterparts in the West. The mean age of 46.3 years at diagnosis in this study is a clear contrast to the older age at diagnosis (mean age of 63 years) in industrial western nations (Chouchane et al., 2013). However, it is relatively consistent with other developing countries including neighbouring Arab countries where the majority of patients are under 50 years (Najjar and Easson, 2010). 60.7% of our sample is under 50 years of age, compared with data from other Arab countries such as KSA where 78% of patients diagnosed are under the age of 50 (Ezzat et al., 1999).

The median time taken by women in this sample between discovering the symptoms and seeing a doctor was 14 days. This result is in line with other published studies on patient delay from developed countries such as in the UK (13 days) (Nosarti et al., 2000) Germany (16 days) (Arndt et al., 2002) and NZ (14 days) (Meechan et al., 2002). However, it is much shorter than those reported from developing countries including Malaysia (2 months) (Norsa'adah et al., 2011), Libya (4 months) (Ermiah et al., 2012b) and Egypt (5 weeks) (Abdel-Fattah et al., 1999).

Most estimates of patient delay use the definition proposed in 1935 by Pack and Gallo, a time period of three months or more from symptoms discovery to the initial seeking of diagnosis (Pack and Gallo, 1938). By this criterion, 22.9% of women in the current study report delayed presentation of breast cancer symptoms. The majority of women in this sample presented to health professionals within one month after they discovered the symptoms. These findings are comparable to a study conducted in Iran where 25% of patients delayed >3 months but it is higher than those reported in developed countries such as Germany (Arndt et al., 2002), Ireland (O'Mahony et al., 2013a), UK (Burgess et al., 1998) and NZ (Meechan et al., 2002) where they reported a range of 14-19%.

3.8.3 Participants' characteristics and patient delay

In consideration of previous research, I investigated the role of socio-demographic factors on patient delay. In the current study it was observed that patients' characteristics associated with delay included older age, low educational level and employment status. The study demonstrates an association between age and patient delay where older women tend to present later compared to younger patients. According to the systematic review by Ramirez et al. (1999), there is strong evidence that advanced age is a predictor of patient delay. Similar findings come from another systematic reviews done in six studies from the Middle East (Alhurishi et al., 2011). Nevertheless, a few studies showed no association between age and patient delay (Montazeri et al., 2003).

Several explanations why patient delay is more often found among older women have been suggested (see section 2.4). They might attribute their symptoms to existing chronic conditions or to aging (Arndt et al., 2002) or fail to identify breast cancer symptoms or have poor knowledge about breast cancer risk factors (Grunfeld et al., 2002, Bish et al., 2005). Other studies showed that older women held a negative attitude toward breast cancer treatment (Burgess et al., 2006, Bish et al., 2005). This poor level of knowledge regarding breast cancer could potentially contribute to delaying seeking medical help for cancer symptoms among this group. It is also possible that effect of age on delay is

affected by level of education among older patients as it is likely that older Omani women are illiterate or have low educational level. Therefore, older women, in particular, may require further information regarding the potential seriousness of breast changes and recommendations for action if they identify some symptoms. Since older age is a risk factor for both developing breast cancer and subsequent delayed presentation, any intervention strategies should target older women in particular (Montazeri et al., 2003, Grunfeld et al., 2002).

The annual report on cancer incidence published by the Omani National Cancer Registry in 2011 showed there were 14.3% of women with breast cancer aged \geq 65years, a percentage that is bigger than the percentage reported in this study (4.0%). This finding suggests that older women might be under-represented in this study and the observed magnitude of delay among older women may be bigger if all older patients with breast cancer were included. All of the older women presented at the follow-up clinics in both hospitals at the time of this study agreed to participate and so this leave the possibility that some older women do not attend the follow-up appointments after the diagnosis for various reasons. It might be that older patients have co-morbidities or were diagnosed at advanced stage so breast cancer treatment would not improve their prognosis. Or it could be that due to travel distances to these two main hospitals, older women might find this a barrier, and thus prefer to attend the follow-up appointments at other closer regional hospitals.

Being less educated and being housewives are significant predictors of patient delay in this sample of women. Alhurishi et al. (2011) reported that there is strong evidence of an association between low educational level and longer delay, while Ramirez et al. (1999) has provided moderate evidence for this association where three studies comprising 11174 patients showed positive associations compared to two non-supportive studies including 351 patients. On the other hand, Alhurishi et al. (2011) provided strong evidence that employment status was not related to patient delay in four studies conducted in Egypt comprising 1170 patients and so did studies from Germany (Arndt et al., 2002) and NZ (Meechan et al., 2002). Women in their traditional roles as housewives do not usually have time for themselves as they have to deal with household chores, children's needs and outdoor activities (Harirchi et al., 2005).

This study has found that marital status was unrelated to patient delay. The association between marital status and patient delay remains unclear (see section 2.4). Women with chronic disease are more likely to delay seeking help after discovery of breast symptoms. This finding is in agreement with previous studies. It is suggested that those women may attribute their symptoms to comorbid conditions.

Neither family history of breast cancer nor the nature of presenting symptoms is related to patient delay in the current study. It is argued that women with a first-degree relative with breast cancer are less likely to present late (Montazeri et al., 2003, Meechan et al., 2002) (Ali et al., 2008). This might be due to high breast cancer awareness, which makes them more susceptible to promptly seek help after symptom discovery (Harirchi et al., 2005). Similarly, the discovery of breast lumps has been shown to reduce patient delay (Burgess et al., 2001, Abdel-Fattah et al., 1999, Montazeri et al., 2003, Bish et al., 2005). It is proposed that those with non-lump symptoms are less likely to attribute their symptoms to definite causes, are less likely to consider breast cancer (Burgess et al., 1998) and are more likely to believe that their symptom is harmless and does not require action (Nosarti et al., 2000, Arndt et al., 2002). In my study, there was no difference in delay between those who discovered a lump and those who discovered non-lump symptoms. Breast lump was by far the most frequent discovered breast symptoms in this sample and these findings suggest that those women failed to recognise the significance of a breast lump. Hence, Omani women need to be educated about the different types of breast cancer symptoms and be educated in symptom recognition as well as encouraged to seek medical advice if symptoms are ambiguous.

3.8.4 Patient delay and breast self-examination

Practice of BSE was associated with shorter delay in this study. This finding is in line with other published studies on BSE and patient delay (Rastad et al., 2012, Abdel-Fattah et al., 2000, Stapleton et al., 2011) (see section 2.4). In NZ, for example, women who discover their symptoms during regular BSE had shorter delay (Meechan et al., 2002). BSE is still scarce and inconsistent among

Omani women, which is similar to the case in other Arab countries (see appendix 3 for screening practice in the Arab women) (Donnelly et al., 2013).

The benefit of BSE is being debated across the literature as discussed previously (see section 2.4). Majority of studies have shown that BSE failed to detect cancer at earlier stages or improve survival (Muscat and Huncharek, 1991, Newcomb et al., 1991, Holmberg et al., 1997). BSE has been questioned in view of two randomized trials: one from Russia and the other from Shanghai. The Russian trial recruited 122,471 women aged 40-64 between 1985 and 1989 (Semiglazov et al., 2003). After nine years of follow-up, there were more breast cancer deaths in the group performing BSE than in the control group but the results were not statistically significant. The Shanghai trial started in 1989 and follow 266,064 women aged 31 to 65 for 10 years (Thomas et al., 2002). Results showed no difference in breast cancer mortality between the control group and intervention group. The result of both trials discredited BSE as a screening tool and showed that it greatly increases the number of benign lumps detected. Correspondingly, the official position of health authorities like the US Preventive Services Task Force and the Canadian Task Force on Preventive Health Care to issue recommendations against teaching BSE (Corbex et al., 2012).

However, several points are worth clarifying regarding both the randomized trials. Smith et al. (2006) pointed out that the evidence of these trials does not mean that BSE instructions is ineffective and that it would not be effective in any setting. In both trials there was limited room for BSE screening to achieve mortality reduction since breast cancer awareness in the population was already high and clinical stage at diagnosis was relatively good (Abdalla et al., 2012, Corbex et al., 2012). In the Shanghai trial, for example, approximately half of the tumours among the control group were stage T1 or better, suggesting the trial does not carry benefits in down-staging breast cancer cases in Shanghai compared to other populations. Some authors suggest that BSE examination could be beneficial in increasing awareness and decreasing tumour size and stage at diagnosis in countries where mean tumour size is above 3-4 cm and most women present with stage III and IV (Corbex et al., 2012, Shulman et al., 2010). Since this is the case in Oman, Oman could consider educational

programmes to increase female awareness about BSE and encourage it to determine whether it leads to early detection of breast lumps.

3.8.5 Stage at diagnosis and patient delay

More than half of the sample (56%) was diagnosed with late stage disease (III and IV). This percentage is in line with previous reports from Oman (Al-Moundhri et al., 2004, Al-Moundhri et al., 2011, Al-Moundhri et al., 2003). One possible explanation for the high proportion of advanced disease is that those women may delay longer after they have discovered a breast symptom. Most studies have found the longer the delay, the more likely the women is diagnosed in advanced stages (Abdel-Fattah et al., 1999, Arndt et al., 2002, Montazeri et al., 2003, Ermiah et al., 2012a). Surprisingly, however, this study found no association between delay and stage of disease. This finding suggests that in addition to patient delay, system or provider delay may play a role in advanced stage presentation among Omani women, an issue that merits further investigation.

Early stage at diagnosis is a key determinant of breast cancer outcome, because earlier stage disease has lower cancer mortality and requires fewer resources to provide effective treatment (Anderson et al., 2008). There is an urgent need to adopt a screening program in Oman to downstage the symptomatic patients and to detect cancer in asymptomatic at-risk populations. Screening by mammography has been accepted as the gold standard for early detection of breast cancer (Corbex et al., 2012). Due to the low level of overall incidence in Oman and similar developing countries, the younger age of the target population (40s and 50s) and because the high rate of false positive mammographic results, especially among young women, some authors have suggested that combination of mammography and clinical breast examination (CBE), (implementation of CBE for younger women aged <45 years and mammography for women 45 years onward), would be more promising and cost effective (Corbex et al., 2012, Asadzadeh et al., 2011, Al-Foheidi et al., 2013). The results from the Egyptian and Taiwanese control programmes indicate that using a two- phase screening, starting with CBE and continuing with mammography in case of suspected findings, could increase the overall

effectiveness of the programme in countries with low to medium risk of breast cancer (Asadzadeh et al., 2011).

CBE is considered a valid screening tool for breast cancer. The Canadian National Breast Screening Study carried a trial where women aged 50–59 years were randomized to receiving CBE or CBE plus mammography. The trial showed no difference in mortality between the two groups (Al-Foheidi et al., 2013). Another study was conducted in Jakarta, Indonesia to compare the effectiveness of CBE screening with mammography in an unscreened population of 1,179 women (Kardinah et al., 2014). Of the fourteen breast cancers that were diagnosed, all but one were detected by both CBE and mammogram; in only one did an abnormal mammogram detect a cancer that CBE failed to uncover concluding that CBE is nearly as effective as mammography in detecting prevalent breast cancers. Two other randomized trials designed to compare CBE with no screening in countries without screening mammography programs are still in progress (Kardinah et al., 2014). Thereupon, the training of healthcare providers in performing effective CBE is a key program component. Breast Health Global Initiative has recommended when initiating mammography screening, it should first target a selective group of high-risk women and gradually expand to involve the entire population (Anderson et al., 2008).

Breast cancer will continue to increase “predictably” in Oman and developing countries in coming years due mainly to two reasons: increasing life expectancy and adoption of western life-style particularly decreased parity, delaying age of childbirth, shorter duration of lactation and dietary habits associated with earlier menarche, all of which associated with increased risk for postmenopausal breast cancer (Anderson et al., 2008, Shulman et al., 2010).

Cancer prevention through risk factor modifications should be advertised. It is evident from this study that obesity is prevalent in Oman as there were 45.3 % of participants who were obese with BMI >30 and 29.3% were overweight with BMI of 25-30. Health behaviours including maintenance of ideal body weight, regular physical activity, and avoidance of prolonged use of exogenous hormone therapy can have an important impact on breast cancer risk (Shulman

et al., 2010). Besides, these health behaviours will reduce risk for other chronic diseases, so they may be of high interest for general public health (Anderson et al., 2008).

3.8.6 Reasons for patient delay

There were 33 patients who delayed visiting a medical consultant for three months or more. Several reasons for the delay were provided by those patients. Women falsely interpreted their initial symptoms as not cancer. Some women attributed their symptoms to be “normal” and tried to provide normal logical explanations for them. Initial interpretation of symptoms as “normal” is a frequent finding among participants from other studies (Unger-Saldana and Infante-Castaneda, 2011, Burgess et al., 2001, Arndt et al., 2002). Other women recognized that their symptoms were not normal but they were not of cancer. It has been demonstrated that women tend to attribute their symptoms to less serious conditions instead of life-threatening disease (Bish et al., 2005) and that the interpretations of their symptoms to be ‘not serious’ is documented to be strongly associated with longer delay (Nosarti et al., 2000, Burgess et al., 2001). This was evident in this sample of women where they attributed their symptoms to allergies or plugged milk ducts or hormonal changes. It was also evident that those women monitored their symptoms and persistence of these symptoms led them to seek help. Continuous monitoring and reviewing of symptoms was also demonstrated in a study of British women (Burgess et al., 2001).

Persistence of breast cancer symptoms was one of the factors, which triggered help seeking amongst Mexican participants with self-discovered breast symptoms (Unger-Saldana and Infante-Castaneda, 2011). Additionally, it has been shown that pain and visibility of symptoms trigger the seeking of medical help (Unger-Saldana and Infante-Castaneda, 2011). In this sample, it was the absence of pain and non- visible symptoms, which was associated with delay. In a study from Egypt, women whose initial symptoms were not associated with pain, were 2.68 times more likely to delay compared with those who presented with pain (Stapleton et al., 2011). Symptoms appraisal to identify and label the initial symptoms is always the important first step in seeking medical evaluation (Bish et al., 2005). Ayers et al. (2007) stated that symptoms appraisal

constitutes approximately 60 % of total patient delay. Women will continue to apprise and decide whether a symptom means something is “wrong” and this doubt is the factor which will drive her decision to whether to seek medical evaluation. The way in which patients interpret and label their symptoms has been shown to influence help-seeking behaviour with a range of other illnesses like heart attack (Burgess et al., 2001). Norsa'adah et al. (2011) have stated that interpretation of initial breast symptoms is based on the pre-existing knowledge, experience, self-education and observation of individuals. If the woman has the knowledge regarding the variation of breast cancer symptoms, she will interpret the symptoms correctly and this will influence her assessment of symptoms as well her decision to seek medical attention. A study done on British women with breast cancer demonstrated that women who were likely to delay scored significantly lower on the breast cancer knowledge scale than women who are not likely to delay (Facione et al., 2002).

Feeling safe from breast cancer and perceiving oneself as not being in the risk zone for breast cancer was another reason for delay in this sample. Perceived risk has an important role in determining and motivating one's health behaviour and has been incorporated into many health behaviour models such as the 'health belief' model (McQueen et al., 2008, Norman and Brain, 2005, Buxton et al., 2003). A willingness to undertake a health action after symptoms discovery is affected by woman's perceived risk. One of many factors that influence perceived risk is the beliefs and knowledge about risk factors (Rothman et al., 1996). As discussed earlier in the literature review (see section 2.3), findings indicate that women have a poor understanding and knowledge regarding breast cancer risk factors (Grunfeld et al., 2002, Williams et al., 2002). Family history and its contribution to breast cancer risk was the most recognizable factor (Buxton et al., 2003, Grunfeld et al., 2002, Williams et al., 2002). On the other hand, age, which is considered an important risk factor for breast cancer development, is poorly understood (McQueen et al., 2008, Vernon et al., 1993, Katapodi et al., 2004). Therefore, women with no experience or limited knowledge about breast cancer who perceive low risk of developing the disease are highly unlikely to undertake any early detection or awareness raising methods.

Fear has been recognized as an important psychological factor in breast cancer delay across many studies (Rastad et al., 2012, Dubayova et al., 2010b, Stapleton et al., 2011, Norsa'adah et al., 2011). Fear is stimulated by many factors including symptoms of pain or discomfort, presumed diagnosis and anticipated consequences of treatment (Dubayova et al., 2010b). Fear usually provokes one of two opposite actions in the women that experienced it: either to delay or to prompt help seeking (Unger-Saldana and Infante-Castaneda, 2011). It seems women in this sample were provoked to delay as a result of fear from the therapeutic interventions of breast cancer as discussed earlier (see section 2.4). Rastad et al. (2012) pointed out that fear is influenced by past experience of cancer in family or friends. Breast cancer treatment is believed to interfere with a woman's ability to perform their role as a caregiver for their families and they have to rely on others to care for them (Norsa'adah et al., 2011). A sample of women from Jordan associated breast cancer with fear of distorted body image and loss of femininity, as it affects a body organ that symbolizes femininity and motherhood (Taha et al., 2012). Fear from medical interventions for breast cancer has led some women to seek alternative therapy as a way to escape surgery. The use of alternative therapies could lead sometimes to worsening of symptoms and progressing to advanced stage of the disease (Ermiah et al., 2012b, Norsa'adah et al., 2011)

Indeed, emotions such as fear are complex and multidimensional psychological factors which evidently influence the decision-making process in patient on help seeking behaviours (Dubayova et al., 2010a). Emotions and emotion regulatory styles differ systematically across nations and each culture has its own system of beliefs, perceptions, and ideas about health and illness which affect people's perception to illness (Iskandarsyah et al., 2014). Interaction between fear and perceived risk of breast cancer and their effect on patient delay is complex (Lipkus et al., 2000) and beyond the scope of this thesis. However, it is worth noting that fear is an important factor and should be taken into account when facilitating help seeking by patients. It was observed that health education about cancer mostly tells people how to identify cancer symptoms but provides little about the consequences of a cancer diagnosis (Burgess et al., 2001). As Nosarti et al. (2000) pointed out "there is a delicate balance between scaring

women away from their doctors on the one hand (especially when they suspect the worst), and adding to a false sense of reassurance, thus taking away any motivation to come forward. Women should be encouraged to think of their breast symptom as ‘urgent but not necessarily serious’ and should be prompted to present to their doctor as soon as possible”. Therefore, information about clinical variables could be included in the content of health programmes for early help seeking (Dubayova et al., 2010a). Women should be informed of the benefits of early treatment on prognosis and that surgery is minimal if the cancer is diagnosed early enough.

Embarrassment and shyness were another reasons for delay that were conveyed by only two participants in this study. They expressed feeling uncomfortable and shy about having their CBE done by a male doctor. In a sample 1002 Qatari women, 53.3% of them revealed that they were embarrassed by the performing of the CBE (Bener et al., 2009). A preference for female physicians in breast clinics was expressed by women from Egypt (Ismail, 2013), Jordan (Taha et al., 2012), Saudi Arabia (Bener et al., 2001) and UAE (Bener et al., 2001). Ahmad et al. (2001) indicated that physician’s gender plays a role in sex sensitive examinations such as Pap test and CBE. This was reflected in male physicians reporting more frequent requests by female patients for another physician to do Pap tests and CBE.

Further, there is evidence from this study that competing social demands in terms of family and work commitments acted as barriers to help seeking. Role demands such as devoting time and attention to the needs of someone else and taking time to make domestic arrangements prior to having biopsy may account for longer delay (Facione, 1993) (O’Mahony et al., 2011). Women’s prioritization of family and work demands over their own health has been recognized in many other studies. For example, a study from the UK identified practical issues (being too busy, having other things to worry about) as barriers to seek medical help for breast cancer examinations (O’Mahony et al., 2013b).

After discussing the reasons for delay reported by women in this sample, it became clear that those women might have low awareness and knowledge about breast cancer. Particularly, they showed low knowledge regarding breast cancer

symptoms and signs, personal risk and risk factors, treatment modalities, and importance of early detection. Therefore, there is an urgent need to improve and raise level of awareness of breast cancer among Omani women. The Breast Health Global Initiative has emphasized that public education is the key first step in implementing breast health programmes (Anderson et al., 2008). Education should aim to raise women's awareness of all potential breast cancer symptoms and encourage prompt help seeking for self-discovered breast symptoms. Such education programmes must convey the importance of early detection of cancer. In fact raising public education regarding early detection should be the first key step in implementing cancer prevention programmes because early detection programmes will not be successfully utilized if the public are unaware of the value of early detection (Yip et al., 2008).

In addition, correcting the misconceptions around breast cancer treatment has to be included in educational campaigns. Women should be taught the scientific facts that early breast cancer can be treated and that mastectomy might not be necessary. It should be highlighted that the surgery may be minimal and there is the potential for breast conservation surgery. There have also been advances in the management of side effects of chemotherapy (Burgess et al., 2001).

Religious beliefs can influence how women think about cancer. Figures from this study indicate that 34.7% of our sample believes that breast cancer is one's fate. This comes from the religious view of Muslim women that onset of illness is the will of God and it is not a matter of chance. This finding has also been documented in similar breast cancer studies (Taha et al., 2012, Lamyian et al., 2007, Mitchell et al., 2002) (Cohen and Azaiza, 2008, Cohen, 2013), which have implications for the role of religious authority figures and for medical personnel in women's decisions about breast health. Hence, collaboration is needed among medical professionals, policy makers, and religious leaders to persuade women that their religion can complement their (breast) health behaviour (Mitchell et al., 2002, Donnelly et al., 2013). Hatefnia et al. (2010) stated that religious leaders should communicate the fact that even though illness is the will of God, Islam also holds individuals responsible for their personal wellness, health and physical wellbeing, and "failing to take responsibility for one's health is a serious sin". So women should educate

themselves regarding breast cancer as well as participating in early detection programs. Equally healthcare practitioners should be aware of the role of religious belief in breast cancer help-seeking decisions and so they should enlist women's religious beliefs as a supportive influence in women's decision to pursue breast cancer preventive measures and treatment (Mitchell et al., 2002).

More attention needs to be paid to designing material for breast cancer awareness, in particular for women who are illiterate or less educated because this group would be reluctant to seek help if they were unaware of the meaning of breast mass and whether breast cancer is a curable disease or not (El-Shinawi et al., 2013). So the use of vivid images in health communication intervention should be incorporated through the use of narrative and visual illustrations (Yip et al., 2008). There is the suggestion that involving women living with breast cancer who would promote the perception that breast cancer is curable and "not a death sentence" could give women hope and encourage them to accept educational messages (Donnelly et al., 2013, Heisey et al., 2011). Furthermore, a woman help seeking behaviour is shown to be influenced by the social networks around her (including family, friends, colleague at workplace) and the opinions of the significant other is often sought prior to seeking help from healthcare professionals (O'Mahony et al., 2011, Ayers et al., 2007). So it will be advantageous if appropriate health education programmes are directed at social support networks, which should encourage women to accept health education messages and enrol in early detection programs (Rastad et al., 2012, Yip et al., 2008).

Public education and awareness about breast cancer is an important step towards improving breast cancer outcome. Mortality rates for breast cancer have been decreasing in the United States and many other western countries over the past 25 years, due to improved treatment and early detection via mammography, which has been shown to increase treatment options and survival (Kardinah et al., 2014). Nevertheless, in the US and prior to the routine use of mammography or adjuvant therapy, which was commenced in the 1975, significant improvements were made in breast cancer survival. Between 1950 and 1975 incidence nearly doubled but mortality remained constant (Shulman et al., 2010). So during this period the ratio of mortality over incidence (an

approximation of the case-fatality rate) fell from 0.42 to 0.27 representing a 36% decline, which suggests that more women were surviving their cancers in 1975 as compared to 1950. This reduction in case-fatality rates is at least as large as the improvement evidenced since the introduction of mammography. Authors who analysed data prior to 1974 explain that the improvements seen in breast cancer survival result from more effective breast education programs, increased breast cancer awareness and detection of tumours palpable with self or clinical breast examination (Shulman et al., 2010). Similarly, in the UK, in the 1980s before the National Breast Screening Program began, the rate of advanced breast cancer fell dramatically and it is believed that this down-staging was due to growing awareness that resulted from the greater presence of public education messages about early detection (Smith et al., 2006).

Finally, a delivery of an organised and successful breast healthcare programme can be best accomplished if multiple sectors acted in collaboration (Anderson et al., 2008). Thus, improvement is most likely to be achieved when healthcare ministries and government organisations, national cancer institutes, education ministries and public and patients groups work together.

3.8.7 Conclusion

In conclusion, this is a cross-sectional study conducted to examine delay in seeking medical help for self-discovered breast cancer symptoms among a sample of Omani women. The median time taken by women in this study between discovering the symptoms and seeing a doctor was 14 days and 22.9% of women delayed for three months or more. Socio-demographic characteristics associated with patient's delay included older age, low educational level, and being a housewife. Delay was not associated with marital status, or with household income. Neither it was associated with presenting symptoms nor with having a family history of breast cancer. Women who had chronic diseases seemed to wait longer. Although the majority of the sample was diagnosed at later stages (stage III and IV), there was no association between duration of delay and stage at diagnosis. Additionally, women who practised BSE presented earlier than those who did not practice it. Looking closely at reasons for delay reported by women who delayed for a month or more, it was evident that Omani

women have a low level of awareness regarding breast cancer including signs and symptoms, personal risk, available breast cancer treatment and the importance of early detection. Competing social demands in term of family and work commitment were also a reported reason for delay.

To summarise the implication of this study: programmes aiming to improve public health knowledge and awareness regarding breast cancer are needed in Oman. Efforts should be made to educate women about the variety of breast cancer symptoms and to prompt medical consultation for any changes noticed. There is a necessity for Omani women to be breast aware and to continually practice BSE and CBE. Training healthcare providers need to correctly carry out CBE and educating women on BSE is an important step in breast cancer controlling programmes. Additionally, educational campaigns must convey the idea that breast cancer is curable if detected earlier and that a mastectomy might not be required. The potential for breast conservative surgery must also be advocated. Educating the public to adapt a healthier lifestyle by increasing physical activity and paying more attention to diet and usage of external hormonal therapy might impact the incidence of breast cancer as well as other chronic diseases in Omani women. Importantly, more attention should be paid to raising the awareness of older women and those who are illiterate by designing materials that are easily understood and which might include images and illustrations. Finally, initiating a screening programme, possibly CBE for women aged < 45 years and mammography for women aged >45 years, should be considered in Oman to decrease late stage presentation of breast cancer and hence improve survival taking into consideration the WHO guidelines to assess the feasibility and appropriateness of such a programme (World Health Organization, 2002).

Chapter Four - Mortality and Survival of Omani Breast Cancer Patients

4.1 Introduction

The Omani National Cancer Registry (NCR) provides continuous information on the incidence of breast cancer among Omani women including frequency of cancer case, age-specific rates and morphology of cancer. Other data that the NCR routinely collects is all the information recorded on the Oman National Cancer Registry Form (see appendix 2). Information regarding mortality from breast cancer in Oman is still lacking which leaves a big gap in understanding the extent of its burden. The only mortality information available is aggregate hospital-based deaths, which are reported in the Omani cancer incidence reports (Figure 4-1). However, these are not representative of the whole population because many do not die in hospitals.

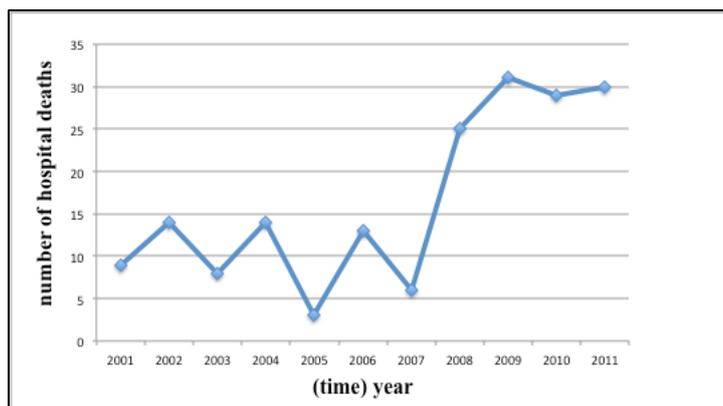


Figure 4-1: Hospital-based breast cancer deaths

Note: Figure generated by accumulating figures reported in the Omani cancer incidence reports

Up-to-date, studies on breast cancer survival among Omani patients are all hospital-based that are conducted to assess the outcome of cancer treatments in these hospitals [see (Al-Moundhri et al., 2004, Al-Moundhri et al., 2011, Burney et al., 2008)]. Results of these studies are institution-based and not population-based which means they do not representative of the whole population beside patient who did not dies in hospital and were lost to follow up where censored. Therefore, there is a great need in Oman for population-based statistics concerning the mortality and survival cancer rates. These statistics

would provide information that is comparable with other populations and would uncover gaps in systemic policy and program delivery and help in planning cancer control systems.

This chapter presents the research undertaken to provide data on survival rate among Omani women with breast cancer.

4.2 Aim

To calculate the population-based survival rate from breast cancer in Oman

4.3 Methodology

Cancer mortality is defined as the number of deaths occurring due to cancer, and the cancer mortality rate is the number of deaths due to cancer per 100,000 persons per year in a defined population. Survival statistics describe the percentage of people with a certain type of cancer who will continue to live for a certain time after the cancer is detected. It was decided to calculate the population –based survival rates instead of mortality rates because the Omani NCR does not consistently record all cases of cancers and causes of deaths. There are two mortality databases in Oman which are the Directorate General of Civil Status (DGCS) located in the police IT network, which records deaths occurring outside the Ministry of Health (MOH) institutions (at home, in private health institutions or outside the country) and the Parallel Mortality Database (PMD) within the MOH which records deaths occurring in the MOH institutions. The DGCS lacks the capability to record all causes of death, and cause-of-death might be incomplete or inaccurate at the PMD. Therefore, it is not possible to calculate population-based mortality rates.

The first stage in survival analysis is to define clearly the group of patients registered for whom calculations are to be made. Population-based cancer registries collect information on all cancer cases in defined areas. The survival rates for different cancers calculated from such data will therefore represent the average prognosis in the population. The Omani NCR is a population-based registry, which was established in 1996, although cancer notification did not become mandatory until 2001. Because the DGCS was only established by May 2004 and because this study proposed to calculate 5-year survival rate, the linking was limited to patients diagnosed with breast cancer from 2005 to 2009.

Therefore, records of Omani breast cancer patients diagnosed from the beginning of 2005 to the end of December 2009 were sought.

The second stage of calculating survival rates is to identify deaths among the group of women with breast cancer. Women with breast cancer who are registered on the NCR were sought in Oman's mortality data to determine whether there is a record of their death. They were intended to be linked, firstly, to the DGCS (primarily to identify deaths outside MOH institutions) and, secondly, to the PMD (primarily to identify deaths in MOH institutions).

The original plan was to follow a procedure developed by Al-Mahrouqi (2010) in his thesis "The Epidemiology of Stomach Cancer in Oman" which was to link records from NCR with records from the DGCS and PMD using specific identifiers to link cases. One identifier was the civil number, which is a unique number code given to every citizen in Oman. Al-Mahrouqi (2010) found that although the mortality databases (DGCS and PMD) in Oman recorded the civil number, the NCR did not record the civil number despite the fact that there is an allocated field for it in the Omani NCR form. This is because the civil number is missing in the medical records from which the cancer registry mainly obtains demographic information. Therefore, other personal details like full name, age, address had to be used to try to match information from the different data sources.

4.4 Data collection and ethical approval

A letter of support from the supervisors and a research proposal was submitted to the DGCS and they approved my obtaining data from their registry.

To obtain the needed information there were several documents required which included a letter from University Supervisors in Oman and in New Zealand, confidentiality declaration and a study proposal. After these documents were provided and the research proposal was approved by the under-secretary of health affairs within the NCR, another ethical approval was required by Research and Ethical Review and Approve Committee within the MOH. An initial approval was given on 6th April 2014. However they required another proposal regarding obtaining raw data from the MOH. Final approval came on

9th July 2013 with a request to meet Director General of Planning and Chairman of the Ethical committee who explained to me that there were changes in the MOH policy regarding giving names of patients and names of diagnosed patients would not be made available.

Consequently, without the names, an accurate linkage could not be carried out because address and dates of birth are insufficient for linkage with records of the PMD and DGCS. Therefore, the linking procedure was limited to those who had their civil number written down.

4.5 Results

I obtained addresses and date of birth for 547 patients from the NCR. However, only 93 patients had civil number. Only ten patients were identified to be dead through linkage with civil number and therefore survival analysis was not practicable for this small number.

4.6 Discussion

Policies and programmes to address health problems in a population require an understanding of the nature and extent of the problems, their causes and changes over time (Mathers et al., 2005). Equally, priorities for health research should be based on assessment of the relative importance of various diseases affecting the population of the health. The most commonly used data for meeting these needs and related needs for development of health policies includes incidence, mortality and survival (Parkin and Fernandez, 2006). Incidence data are annually reported by Omani NCR, but this study was aiming to provide population-based survival data for breast cancer in Oman.

Mortality and information on deaths from cancer in any population is usually collected by civil registration system (recording vital events; birth, marriage, and deaths) (World Health Organization, 2002). Mortality data are normally derived from death certificates on which information about the death of the person and cause of death are certified, usually by a medical practitioner. Over the years, United Nations, WHO and International Institutes for Vital Registration and Statistics have intensified efforts to support the collection of vital information and mortality data (Sibai, 2004). The WHO stated that one of

its priorities is the strengthening of vital statistics registration systems (Mathers et al., 2005). It has developed the International statistical classification of diseases and related health problems (known as ICD) that provides a uniform system to codify cause of death allowing comparability between populations (World Health Organization, 2002). Almost all countries have legalisations that establish vital registration systems to collect and organise statistics on mortality. Nevertheless, for many countries of the world, vital statistics on cause of deaths are unavailable, cover very restricted population, are incomplete, or are inaccurate, especially if cause of deaths is certified by non-medical personnel (Mathers et al., 2005, Parkin, 2008). National-level mortality statistics are collected and made available online by the WHO which also provides tables of estimated coverage and completeness of data from different countries (Parkin and Fernandez, 2006). In Oman, the DGCS, a population-based registry, was established in 2004 as the body where all vital registrations (births, deaths, marriages, divorces) are recorded. However, the DGCS lacks the capability of documenting all deaths and cause-of-deaths. Consequently death notifications from the DGCS were sent to MOH where the PMD was established primary to record cause of deaths. It was noticed that also cause of death in the PMD was far from being accurate. Because cause of death was not documented in the DGCS and was inaccurate in the records of the PMD, the calculation of population-based mortality rate was not possible, given that it requires accurate and complete documentation of cause of death data.

Many cancer registries aim to follow up their cases in order to produce survival statistics (World Health Organization, 2002). Many studies conduct survival analysis using population-based registry data and many population-based figures have been published (Parkin, 2008). For example, the Surveillance, Epidemiology and End Results program comprising 14 cancer registries covering 26% of US population and the EUOCARE project covering 12 countries of Europe (Parkin, 2008). Unfortunately, the Omani NCR does not routinely collect data on the status of patients, so this study aimed to link the NCR records with the mortality database in Oman to assess the vital status of the breast cancer patients. Linkage was proposed to be done using different identifiers which includes civil number, and in case it was missing, the full

name, year of birth, address were to be used collectively to accurately identify cases. However, the documentation of civil number in the obtained records from the NCR was poor, and without the name of patients from the NCR, linkage between the records of NCR and mortality databases was not feasible.

Cancer statistics are important in order to prioritize and allocate resources to combat the projected rise in cancer including the planning for cancer related health care (Parkin and Fernandez, 2006). Additionally, mortality data are widely used in evaluation and comparison of cancer rates between different populations and overtime to study differences in cancer risk (Parkin and Fernandez, 2006). Mortality statistics play a crucial role in demonstrating the effects which screening programmes have on burden of cancer. For example, a screening programme aimed at detection of pre-invasive cancer, as the case in breast cancer, reduction in mortality is the ultimate measure of its effectiveness (Jensen, 1991, Parkin, 2008). So it is important for any country planning a screening programme to have baseline mortality statistics prior to initiation of the programme, as well as to the continuing of monitoring mortality trends after that.

Survival is one of the major outcome measurement and key criteria for assessing the quality of cancer control related to both prevention through early detection and therapeutic level (Seedhom and Kamal, 2011). Survival following a diagnosis of cancer is used to evaluate the impact of the extent to which new or improved cancer treatments are incorporated into clinical practice (World Health Organization, 2002). Such rates are also increasingly used to compare the effectiveness of cancer treatment in subsections of the country population or in different countries (World Health Organization, 2002). Survival rates vary greatly across countries due to different factors, such as difference in quality of cancer treatment facilities, in screening programmes, evidence-based best-practice guidelines and in accessibility to new anti-cancer drugs (Verdecchia et al., 2007). Recognition of the differences in survival rates among population could assist the uncovering of failure in systemic policies and inappropriate programmes and further support the planning of system enhanced cancer control (Seedhom and Kamal, 2011, Parkin, 2008). The international comparisons of survival coordinated by the EUROCARE group, for example, have had a

profound influence in policy-making for cancer treatment services in several European countries.

The improvement in the quality and completeness of mortality registration in Oman is essential for appreciating the burden of diseases and reforming health policies. Although survival and mortality analysis could not be carried out in this study, several recommendations for future references should be noted. Efforts to complete registration of patients' civil numbers by the NCR are encouraged. Correct and complete recording of this number will facilitate fast and accurate linkage of NCR cases with the mortality databases to identify status of patients. Additionally, civil number will aid in NCR identifying duplicate entries from multiple primaries and also be helpful to be used by other bodies. Pharmacies, for example, could assess the effect of prescription drugs on the development or course of a disease (Al-Mahrouqi, 2010).

An additional problem noted was the NCR's lack of complete documentation of treatment and stage at diagnosis. Obtaining good quality data on cancer stages and treatment is urgently needed so that future studies examining survival differences could be explained in the light of prognostic factors, and for evaluating an appropriate cancer control programme such as breast cancer screening programme, where decrease in incidence of advanced stage reflects effectiveness of the programme. It is important to note that NCR primarily obtained their data from patients' medical records, which are incomplete. Therefore, full documentation of NCR cases is dependent on completeness of medical records. Hence, accurate and full records of patient medical notes should be the goal among clinicians. Equally important is the availability of trained personnel to ensure that information about medical conditions leading to death is coded appropriately so the underlying cause of each death is easily identified. Moreover, The DGCS may need to make cause of death data available in their system to achieve a complete mortality registry where a single body contains all the relevant information.

Chapter Five - Conclusion

Breast cancer is the most common cancer among women. In 2008, there were around 1.38 million new female breast cancer cases diagnosed worldwide (Ferlay et al., 2010). Breast cancer estimated to be responsible for around 458,500 female deaths in 2008 or nearly one in seven (around 14%) of all cancer deaths in women (Ferley et al., 2010). In Oman too, breast cancer has been constantly topping the list every year. Age standardized incidence rate increased from 13.8 per 100,000 women in 1999 to 25.5 per 100,000 women in 2011. In 2011, breast cancer accounted for 24.8% of all cancer diagnosed among Omani women (Al Lawati et al., 2013). Previous researches on breast cancer from Oman have found that majority of Omani females present with late stage of the disease (stage III and IV) (Al-Moundhri et al., 2004, Al-Moundhri et al., 2011, Burney et al., 2008). It is well documented that prognosis of breast cancer depends on stage at diagnosis and those diagnosed at earlier stage show a better survival rate (Kumar et al., 2007). Therefore, this project aimed to examine the epidemiology of breast cancer in Oman. This was done by conducting two small studies. The first study was aiming to explore the reasons for delaying seeking medical help for self-detected breast cancer symptoms in Omani women to help recommend solutions to shorten this delay. The second study was aiming to provide survival rate and mortality data from breast cancer in Oman.

5.1 Main findings

The median time taken by women in this study between discovering the symptoms and seeing a doctor was 14 days where 22.9% of women delayed for 3 months or more.

- Socio-demographic characteristics that was associated with patient's delay included older age, low educational level, and being a housewife. Delay was not associated with marital status, and household income
- Women who had a chronic disease seemed to wait longer. However, delay was not associated with family history of breast cancer, nature of presenting symptoms, and stage at diagnosis. Further, women who practised BSE presented earlier than those who did not practice it.

- From this study, it was evident that Omani women have low level of awareness regarding breast cancer in particular sign and symptoms, personal risk, available breast cancer treatment and the importance of early detection, all of which has been associated with longer patient delay. Competing social demand in term of family and work commitment was also reported as a reason for delay.
- Due to incomplete documentation of civil number by the Omani NCR, and inability to obtain names of breast cancer patients from the NCR, linkage of NCR records to Omani mortality database was not possible.

5.2 Implications

Many of the implications of this project are relevant to health policy makers in Oman as cancer burden as general and breast cancer specifically will continue to rise in Oman and similar developing countries. The most important implications of this study are:

- There is a need for educational programmes which aim to increase awareness and knowledge around breast cancer among Omani women. Educational campaigns should focus on educating women about various breast cancer systems, important to prompt medical attention for any changes noticed, and convey the idea that breast cancer is curable especially if discovered early. Omani women should also be taught to practice BSE and CBE and efforts should be made to train physician to appropriately carry CBE and encourage women to practice BSE. More attention should be paid to older and illiterate women, as those appear to be more likely to delay. This could be done by designing materials that are easy to be understood, which might include images and illustrations.
- Patient delay is associated with advanced stage at diagnosis. This study did not show an association between patient delay and stage of disease which suggest, in addition to patient delay, system or provider delay may play a role in advanced stage presentation among Omani women. Further studies to investigate provider delay and breast cancer is needed in Oman.

- Early stage at diagnosis is a key determinant of breast cancer outcome, because earlier stage disease has lower breast cancer mortality and requires fewer resources to provide effective treatment. Breast cancer screening is the best strategy to obtain this goal and screening by mammography has been accepted as the gold standard for early detection of breast cancer. Some authors have suggested that in countries like Oman, where the target population is young (40s and 50s), it might be more efficient and cost-effective to start screening by CBE for women aged <45 years and screening mammography for women aged >45 years. Nevertheless, WHO guidelines should be used to assess the feasibility and appropriateness of a population-based screening programme for breast cancer in Oman (World Health Organization, 2002).
- For the Omani National Cancer Registry, the quality and completion of cancer data collected must be encouraged. It will be important to follow-up of patients registered at the cancer registry especially for survival studies. The availability of treatment and the status (dead or alive) of the patients are important for understanding the burden of cancer in Oman. Complete collection of civil number should be a priority for the NCR as complete documentation of it will greatly facilitate regular collection of mortality data for cancer patients. Efforts should also be made to complete medical notes of cancer patients that will eventually be used to register them at the NCR. Oman should consider training personnel to ensure that information about medical condition leading to death is coded appropriately so the underlying cause of each death is easily identified.
- The DGCS may need to make cause-of-death data available in their system to help in shaping a complete mortality registry where a single body contains all the relevant information. The improvement in the quality and completeness of mortality registration in Oman is essential for appreciating the burden of diseases and reforming health policies.

References

- ABDALLA, F. B. E., MARKUS, R., BUHMEIDA, A., BODER, J., SYRJÄNEN, K. & COLLAN, Y. 2012. Estrogen receptor, progesterone receptor, and nuclear size features in female breast cancer in Libya: Correlation with clinical features and survival. *Anticancer Research*, 32, 3485-3493.
- ABDEL-FATTAH, M., ZAKI, A., BASSILI, A., EL-SHAZLY, M. & TOGNONI, G. 2000. Breast self-examination practice and its impact on breast cancer diagnosis in Alexandria, Egypt. *Eastern Mediterranean Health Journal*, 6, 34-40.
- ABDEL-FATTAH, M. M., ANWAR, M. A., MARI, E., EL-SHAZLY, M. K., ZAKI, A. A., BEDWANI, R. N. & NICOLUCCI, A. 1999. Patient- and system-related diagnostic delay in breast cancer: Evidence from Alexandria, Egypt. *European Journal of Public Health*, 9, 15-19.
- ABSETZ, P., ARO, A. R., REHNBERG, G. & SUTTON, S. R. 2000. Comparative optimism in breast cancer risk perception: Effects of experience and risk factor knowledge. *Psychology, Health and Medicine*, 5, 367-376.
- AGARWAL, G., RAMAKANT, P., SÁNCHEZ FORGACH, E. R., RENDÓN, J. C., CHAPARRO, J. M., BASURTO, C. S. & MARGARITONI, M. 2009. Breast cancer care in developing countries. *World Journal of Surgery*, 33, 2069-2076.
- AHMAD, F., STEWART, D. E., CAMERON, J. I. & HYMAN, I. 2001. Rural physicians' perspectives on cervical and breast cancer screening: a gender-based analysis. *J Womens Health Gend Based Med*, 10, 201-8.
- AJEKIGBE, A. T. 1991. Fear of mastectomy: The most common factor responsible for late presentation of carcinoma of the breast in Nigeria. *Clinical Oncology*, 3, 78-80.
- AKHTAR, S. S., NADRAH, H. M., AL-HABDAN, M. A., EL GABBANI, S. A., EL FAROUK, G. M. K., ABDELGADIR, M. H. & AL-SAIGUL, A. M. 2010. First organized screening mammography programme in Saudi Arabia: Preliminary analysis of pilot round. *Premier programme de mammographie de dépistage en Arabie saoudite: Rapport préliminaire de l'opération pilote*, 16, 1025-1031.
- AL KHAJA, M. A. W. & CREEDON, P. 2010. Evaluating the effectiveness of the first breast cancer awareness campaign in the United Arab Emirates: Lessons learned and next steps. *Public Relations Review*, 36, 386-388.
- AL LAWATI, J. A., AL LAWATI, N. A., AL SIYABI, N. H., AL GHARBI, D. O. & AL WEHAIBI, S. 2013. Cancer incidence in Oman, 2011. Muscat: Ministry of Health.
- AL-AJMI, K., GANGULY, S. S., AL-AJMI, A., AL MANDHARI, Z. & AL-MOUNDHRI, M. S. 2012. Insulin-like growth factor 1 gene polymorphism and breast cancer risk among Arab Omani women: A case-control study. *Breast Cancer: Basic and Clinical Research*, 6, 103-112.
- AL-ANSARI, A., AL-MAWALI, K., AL-BAHRANI, B. & AL-MOUNDHRI, M. 2013. BRCA1 gene Molecular Alterations in Omani Breast Cancer Patients. *G. J. O.*

- AL-FOHEIDI, M., AL-MANSOUR, M. M. & IBRAHIM, E. M. 2013. Breast cancer screening: review of benefits and harms, and recommendations for developing and low-income countries. *Med Oncol*, 30, 471.
- AL-HAMDAN, N., RAVICHANDRAN, K., AL-SAYYAD, J., AL-LAWATI, J., KHAZAL, Z., AL-KHATEEB, F., ABDULWAHAB, A. & AL-ASFOUR, A. 2009. Incidence of cancer in Gulf Cooperation Council countries, 1998-2001. *Eastern Mediterranean Health Journal*, 15, 600-611.
- AL-IDRISSI, H. Y., IBRAHIM, E. M., KURASHI, N. Y. & SOWAYAN, S. A. 1992. Breast cancer in a low-risk population. The influence of age and menstrual status on disease pattern and survival in Saudi Arabia. *Int J Cancer*, 52, 48-51.
- AL-KURAYA, K., SCHRAML, P., SHEIKH, S., AMR, S., TORHORST, J., TAPIA, C., NOVOTNY, H., SPICHTIN, H., MAURER, R., MIRLACHER, M., SIMON, R. & SAUTER, G. 2005. Predominance of high-grade pathway in breast cancer development of Middle East women. *Mod Pathol*, 18, 891-7.
- AL-MADOUJ, A. M., ELDALI, A. M. & AL-ZAHRANI, A. S. 2011. 10-Year Cancer Incidence Among Nationals of the GCC States, 1998-2007. Riyadh, Saudi Arabia.: Gulf Center for Cancer Control and Prevention.
- AL-MAHROUQI, H. 2010. *The epidemiology of stomach cancer in Oman*. University of Otago.
- AL-MAHROUQI, H., PARKIN, L. & SHARPLES, K. 2011. Incidence of stomach cancer in oman and the other gulf cooperation council countries. *Oman Med J*, 26, 258-62.
- AL-MOUNDHRI, A., AL-BAHRANI, B., PERVEZ, I., GANGULY, S. S., NIRMALA, V., AL-MADHANI, A., AL-MAWALAY, K. & GRANT, C. 2004. The outcome of treatment of breast cancer in a developing country - Oman. *Breast*, 13, 139-145.
- AL-MOUNDHRI, M., NIRMALA, V., AL-MAWALAY, K., GANGULY, S., BURNEY, I., RIZVI, A. & GRANT, C. 2003. Significance of p53, Bcl-2, and HER-2/neu Protein Expression in Omani Arab Females with Breast Cancer. *Pathology and Oncology Research*, 9, 226-231.
- AL-MOUNDHRI, M. S., KUMAR, S., BURNEY, I. A. & AL-AJMI, A. 2011. Changing trends of breast cancer survival in sultanate of Oman. *Journal of Oncology*.
- AL-NAGGAR, R. A., ISA, Z. M., SHAH, S. A., CHEN, R. & KADIR, S. Y. A. 2009. Mammography screening: Female doctors' attitude and practice in sana'a, yemen. *Asian Pacific Journal of Cancer Prevention*, 10, 743-746.
- AL-QATTAN, M. M., AL SALEH, K. A., AL-MUSALLAM, S. S. & MAZOUZ, G. M. 2008. Knowledge and factors affecting breast self-examination among Kuwaiti women. *Kuwait Medical Journal*, 40, 103-110.
- AL-TAMIMI, D. M., BERNARD, P. S., SHAWARBY, M. A., AL-AMRI, A. M. & HADI, M. A. 2009. Distribution of molecular breast cancer subtypes in middle eastern-saudi arabian women: a pilot study. *Ultrastruct Pathol*, 33, 141-50.
- ALAWADI, S., GHABREAU, L., ALSALEH, M., ABDULAZIZ, Z., RAFEEK, M., AKIL, N. & ALKHALAF, M. 2011. P53 gene

- polymorphisms and breast cancer risk in Arab women. *Med Oncol*, 28, 709-15.
- ALBAIN, K. S., ALLRED, D. C. & CLARK, G. M. 1994. Breast cancer outcome and predictors of outcome: are there age differentials? *J Natl Cancer Inst Monogr*, 35-42.
- ALHURISHI, S., LIM, J. N. W., POTRATA, B. & WEST, R. 2011. Factors influencing late presentation for breast cancer in the middle east: A systematic review. *Asian Pacific Journal of Cancer Prevention*, 12, 1597-1600.
- ALI, R., MATHEW, A. & RAJAN, B. 2008. Effects of socio-economic and demographic factors in delayed reporting and late-stage presentation among patients with breast cancer in a major cancer Hospital in South India. *Asian Pacific Journal of Cancer Prevention*, 9, 703-707.
- ALOKAIL, M. S., AL-DAGHRI, N., ABDULKAREEM, A., DRAZ, H. M., YAKOUT, S. M., ALNAAMI, A. M., SABICO, S., ALENAD, A. M. & CHROUSOS, G. P. 2013. Metabolic syndrome biomarkers and early breast cancer in Saudi women: Evidence for the presence of a systemic stress response and/or a pre-existing metabolic syndrome-related neoplasia risk? *BMC Cancer*, 13.
- ALOKAIL, M. S., AL-DAGHRI, N. M., AL-ATTAS, O. S. & HUSSAIN, T. 2009. Combined effects of obesity and type 2 diabetes contribute to increased breast cancer risk in premenopausal women. *Cardiovascular Diabetology*, 8.
- ALSHATWI, A. A., HASAN, T. N., SHAFI, G., ALSAIF, M. A., ALHAZZANI, A. A. & ALSAIF, A. A. 2012. A single-nucleotide polymorphism in the TP53 and MDM-2 gene modifies breast cancer risk in an ethnic Arab population. *Fundam Clin Pharmacol*, 26, 438-43.
- ALTHUIS, M. D., DOZIER, J. M., ANDERSON, W. F., DEVESA, S. S. & BRINTON, L. A. 2005. Global trends in breast cancer incidence and mortality 1973-1997. *International Journal of Epidemiology*, 34, 405-412.
- AMERICAN CANCER SOCIETY 2010. Breast cancer facts & figures 2009-2010. Atlanta: American Cancer Society.
- ANDERSEN, R. S., VEDSTED, P., OLESEN, F., BRO, F. & SØNDERGAARD, J. 2009. Patient delay in cancer studies: A discussion of methods and measures. *BMC Health Services Research*, 9.
- ANDERSON, B. O., YIP, C. H., SMITH, R. A., SHYYAN, R., SENER, S. F., ENIU, A., CARLSON, R. W., AZAVEDO, E. & HARFORD, J. 2008. Guideline implementation for breast healthcare in low-income and middle-income countries: overview of the Breast Health Global Initiative Global Summit 2007. *Cancer*, 113, 2221-43.
- ANDERSON, W. F., CHATTERJEE, N., ERSHLER, W. B. & BRAWLEY, O. W. 2002. Estrogen receptor breast cancer phenotypes in the Surveillance, Epidemiology, and End Results database. *Breast Cancer Research and Treatment*, 76, 27-36.
- ARNDT, V., STÜRMER, T., STEGMAIER, C., ZIEGLER, H., DHOM, G. & BRENNER, H. 2002. Patient delay and stage of diagnosis among breast cancer patients in Germany - A population based study. *British Journal of Cancer*, 86, 1034-1040.

- ASADZADEH, V. F., BROEDERS, M. J., KIEMENEY, L. A. & VERBEEK, A. L. 2011. Opportunity for breast cancer screening in limited resource countries: a literature review and implications for Iran. *Asian Pac J Cancer Prev*, 12, 2467-75.
- ATOUM, M. F. & AL-KAYED, S. A. 2004. Mutation analysis of the breast cancer gene BRCA1 among breast cancer Jordanian females. *Saudi Medical Journal*, 25, 60-63.
- AYERS, S., BAUM, A., MCMANUS, C., NEWMAN, S., WALLSTON, K., WEINMAN, J. & WEST, R. 2007. Cambridge Handbook of Psychology, Health and Medicine. 2 ed. Cambridge: Cambridge University Press.
- AZAIZA, F. & COHEN, M. 2008. Between traditional and modern perceptions of breast and cervical cancer screenings: A qualitative study of Arab women in Israel. *Psycho-Oncology*, 17, 34-41.
- AZAIZA, F., COHEN, M., AWAD, M. & DAOUD, F. 2010. Factors associated with low screening for breast cancer in the Palestinian authority: Relations of availability, environmental barriers, and cancer-related fatalism. *Cancer*, 116, 4646-4655.
- BARON-EPEL, O., GRANOT, M., BADARNA, S. & AVRAMI, S. 2004. Perceptions of breast cancer among Arab Israeli women. *Women and Health*, 40, 101-116.
- BATEMAN, A. C. 2006. Pathology of breast cancer. *Women's Health Medicine*, 3, 18-21.
- BENER, A. & ALALI, K. A. 2004. Consanguineous marriages in the new developed country: Qatari population. *J. Biosoc. Sci.*
- BENER, A., ALWASH, R., MILLER, C. J., DENIC, S. & DUNN, E. V. 2001. Knowledge, attitudes, and practices related to breast cancer screening: A survey of Arabic women. *Journal of Cancer Education*, 16, 215-220.
- BENER, A., AYOUBI, H. R. E., ALI, A. I., AL-KUBAISI, A. & AL-SULAITI, H. 2010. Does consanguinity lead to decreased incidence of breast cancer? *Cancer Epidemiology*, 34, 413-418.
- BENER, A., EL AYOUBI, H. R., MOORE, M. A., BASHA, B., JOSEPH, S. & CHOUCANE, L. 2009. Do we need to maximise the breast cancer screening awareness?: Experience with an endogamous society with high fertility. *Asian Pacific Journal of Cancer Prevention*, 10, 599-604.
- BENER, A., HONEIN, G., CARTER, A. O., DA'AR, Z., MILLER, C. & DUNN, E. V. 2002. The determinants of breast cancer screening behavior: a focus group study of women in the United Arab Emirates. *Oncology nursing forum*, 29, E91-98.
- BERAL, V., BULL, D., DOLL, R., PETO, R. & REEVES, G. 2001. Familial breast cancer: Collaborative reanalysis of individual data from 52 epidemiological studies including 58 209 women with breast cancer and 101 986 women without the disease. *Lancet*, 358, 1389-1399.
- BISH, A., RAMIREZ, A., BURGESS, C. & HUNTER, M. 2005. Understanding why women delay in seeking help for breast cancer symptoms. *Journal of Psychosomatic Research*, 58, 321-326.
- BOTTORFF, J. L., RICHARDSON, C., BALNEAVES, L. G., MCCULLUM, M., BUXTON, J. A., RATNER, P. A. & HACK, T. 2004. Unraveling women's perceptions of risk for breast cancer. *Health Education Research*, 19, 469-475.

- BRAY, F., MCCARRON, P. & PARKIN, D. M. 2004. The changing global patterns of female breast cancer incidence and mortality. *Breast Cancer Research*, 6, 229-239.
- BRYAN, A. D. 2002. Performance of breast self-exam: An interaction with age. *Journal of Prevention and Intervention in the Community*, 22, 7-22.
- BURGESS, C., HUNTER, M. S. & RAMIREZ, A. J. 2001. A qualitative study of delay among women reporting symptoms of breast cancer. *British Journal of General Practice*, 51, 967-971.
- BURGESS, C. C., POTTS, H. W., HAMED, H., BISH, A. M., HUNTER, M. S., RICHARDS, M. A. & RAMIREZ, A. J. 2006. Why do older women delay presentation with breast cancer symptoms? *Psychooncology*, 15, 962-8.
- BURGESS, C. C., RAMIREZ, A. J., RICHARDS, M. & LOVE, S. B. 1998. Who and what influences delayed presentation in breast cancer? *British Journal of Cancer*, 77, 1343-1348.
- BURGESS, C. C., RAMIREZ, A. J., SMITH, P. & RICHARDS, M. A. 2000. Do adverse life events and mood disorders influence delayed presentation of breast cancer? *J Psychosom Res*, 48, 171-5.
- BURNEY, I. A., AL MOUNDHRI, M. S., RIZVI, A. J., GANGULY, S. S., AL ABRI, R. & ASHRAFI, R. A. 2008. Outcome as a measure of quality of care in oncology: experience at sultan qaboos university hospital, oman. *Sultan Qaboos Univ Med J*, 8, 27-36.
- BUXTON, J. A., BOTTORFF, J. L., BALNEAVES, L. G., RICHARDSON, C., MCCULLUM, M., RATNER, P. A. & HACK, T. 2003. Women's perceptions of breast cancer risk: Are they accurate? *Canadian Journal of Public Health*, 94, 422-426.
- CHALABI, N., BERNARD-GALLON, D. J., BIGNON, Y. J., KWIATKOWSKI, F., AGIER, M., VIDAL, V., LAPLACE-CHABAUD, V., SYLVAIN-VIDAL, V., BERTHOLET, V., DE LONGUEVILLE, F., LACROIX, M., LECLERCQ, G., REMACLE, J., SIBILLE, C., ZAMMATEO, N., BEN JAAFAR, N., SEFIANI, A., OULDIM, K., MEGARBANE, K., JALKH, N., MAHFOUDH, W., TROUDI, W., BEN AMMAR-EL GAIED, A. & CHOUCANE, L. 2008. Comparative clinical and transcriptomal profiles of breast cancer between French and South Mediterranean patients show minor but significant biological differences. *Cancer Genomics Proteomics*, 5, 253-61.
- CHIA, K. S., DU, W. B., SANKARANARAYANAN, R., SANKILA, R., WANG, H., LEE, J., SEOW, A. & LEE, H. P. 2004. Do younger female breast cancer patients have a poorer prognosis? Results from a population-based survival analysis. *Int J Cancer*, 108, 761-5.
- CHOUCANE, L., BOUSSEN, H. & SASTRY, K. S. R. 2013. Breast cancer in arab populations: Molecular characteristics and disease management implications. *The Lancet Oncology*, 14, e417-e424.
- COHEN, M. 2013. An integrated view of cultural perceptions of cancer among Arab people in Israel. *Health Psychology Review*, 1-19.
- COHEN, M. & AZAIZA, F. 2008. Developing and testing an instrument for identifying culture-specific barriers to breast cancer screening in Israeli Arab women. *Acta Oncologica*, 47, 1570-1577.

- COMPTON, C., BYRD, D., GARCIA-AGUILAR, J., KURTZMAN, S., OLAWAIYE, A. & WASHINGTON, M. 2012. Breast. In: COMPTON, C. C., BYRD, D. R., GARCIA-AGUILAR, J., KURTZMAN, S. H., OLAWAIYE, A. & WASHINGTON, M. K. (eds.) *AJCC Cancer Staging Atlas*. Springer New York.
- CORBEX, M., BURTON, R. & SANCHO-GARNIER, H. 2012. Breast cancer early detection methods for low and middle income countries, a review of the evidence. *Breast*, 21, 428-34.
- COUGHLIN, S. S. & EKWUEME, D. U. 2009. Breast cancer as a global health concern. *Cancer Epidemiology*, 33, 315-318.
- CURADO, M. P., EDWARDS, B. & SINHA, H. R. 2008. Cancer incidence in five continents. Volume IX. *IARC Sci Publ*, 1-837.
- D'AGINCOURT-CANNING, L. 2006. Genetic testing for hereditary breast and ovarian cancer: Responsibility and choice. *Qualitative Health Research*, 16, 97-118.
- DALY, M. B., AXILBUND, J. E., BUYS, S., CRAWFORD, B., FARRELL, C. D., FRIEDMAN, S., GARBER, J. E., GOORHA, S., GRUBER, S. B. & HAMPEL, H. 2010. Genetic/familial high-risk assessment: breast and ovarian. *Journal of the National Comprehensive Cancer Network*, 8, 562-594.
- DENIC, S. & BENER, A. 2001. Consanguinity decreases risk of breast cancer - Cervical cancer unaffected. *British Journal of Cancer*, 85, 1675-1679.
- DENIC, S., BENER, A., SABRI, S., KHATIB, F. & MILENKOVIC, J. 2005. Parental consanguinity and risk of breast cancer: A population-based case-control study. *Medical Science Monitor*, 11, CR415-CR419.
- DENIC, S., FRAMPTON, C. & NICHOLLS, M. G. 2007. Risk of cancer in an inbred population. *Cancer Detect Prev*, 31, 263-9.
- DONNELLY, T. T., AL KHATER, A., AL-BADER, S. B., AL KUWARI, M. G., AL-MEER, N., MALIK, M., SINGH, R. & JONG, F. C. 2013. Arab women's breast cancer screening practices: A literature review. *Asian Pacific Journal of Cancer Prevention*, 14, 4519-4528.
- DONNELLY, T. T., AL-KHATER, A.-H., AL-KUWARI, M., AL-MEER, N., AL-BADER, S. B., MALIK, M., SINGH, R. & JONG, F. C.-D. 2011a. Study exploring breast cancer screening practices amongst Arabic women living in the State of Qatar. *Avicenna*, 1.
- DONNELLY, T. T., AL-KHATER, A. H. & AL-KUWARI, M. 2011b. Study exploring breast cancer screening practices amongst Arabic women living in the state of Qatar. *Avicenna*.
- DUBAYOVA, T., VAN DIJK, J. P., NAGYOVA, I., ROSENBERGER, J., HAVLIKOVA, E., GDOVINOVA, Z., MIDDEL, B. & GROOTHOFF, J. W. 2010a. The impact of the intensity of fear on patient's delay regarding health care seeking behavior: A systematic review. *International Journal of Public Health*, 55, 459-468.
- DUBAYOVA, T., VAN DIJK, J. P., NAGYOVA, I., ROSENBERGER, J., HAVLIKOVA, E., GDOVINOVA, Z., MIDDEL, B. & GROOTHOFF, J. W. 2010b. The impact of the intensity of fear on patient's delay regarding health care seeking behavior: a systematic review. *Int J Public Health*, 55, 459-68.
- EL SAGHIR, N. S., KHALIL, M. K., EID, T., EL KINGE, A. R., CHARAFEDDINE, M., GEARA, F., SEOUD, M. & SHAMSEDDINE,

- A. I. 2007. Trends in epidemiology and management of breast cancer in developing Arab countries: A literature and registry analysis. *International Journal of Surgery*, 5, 225-233.
- EL SAGHIR, N. S., SEOUD, M., KHALIL, M. K., CHARAFEDDINE, M., SALEM, Z. K., GEARA, F. B. & SHAMSEDDINE, A. I. 2006. Effects of young age at presentation on survival in breast cancer. *BMC Cancer*, 6, 194.
- EL-HARITH, E. H. A., ABDEL-HADI, M. S., STEINMANN, D. & DORK, T. 2002. BRCA1 and BRCA2 mutations in breast cancer patients from Saudi Arabia. *Saudi Medical Journal*, 23, 700-704.
- EL-SHINAWI, M., YOUSSEF, A., ALSARA, M., ALY, M. K., MOSTAFA, M., YEHIA, A., HURLBERT, M., EL-TAWAB, R. A. & MOHAMED, M. M. 2013. Assessing the level of breast cancer awareness among recently diagnosed patients in Ain Shams University Hospital. *Breast*, 22, 1210-4.
- EL-ZAWAWY, A. 1991. Delay in seeking medical advice by breast cancer patients presenting with a breast lump. *International Atomic Energy Authority/TECDOC*, 614, 35-42.
- ELLISON-LOSCHMANN, L., MCKENZIE, F., HIGHNAM, R., CAVE, A., WALKER, J. & JEFFREYS, M. 2013. Age and Ethnic Differences in Volumetric Breast Density in New Zealand Women: A Cross-Sectional Study. *PLoS ONE*, 8.
- ELZAWAWY, A. 1999. Delay in seeking medical advice by breast cancer patients presenting with breast lump. *Cancer Strategy*, 1, 16-19.
- ERMIAH, E., ABDALLA, F., BUHMEIDA, A., LARBESH, E., PYRHONEN, S. & COLLAN, Y. 2012a. Diagnosis delay in Libyan female breast cancer. *BMC Res Notes*, 5, 452.
- ERMIAH, E., ABDALLA, F., BUHMEIDA, A., LARBESH, E., PYRHÖNEN, S. & COLLAN, Y. 2012b. Diagnosis delay in Libyan female breast cancer. *BMC Research Notes*, 5, 452.
- EZZAT, A. A., IBRAHIM, E. M., RAJA, M. A., AL-SOBHI, S., ROSTOM, A. & STUART, R. K. 1999. Locally advanced breast cancer in Saudi Arabia: High frequency of stage III in a young population. *Medical Oncology*, 16, 95-103.
- FABBRI, A., CARCANGIU, M. & CARBONE, A. 2008. Histological Classification of Breast Cancer. In: BOMBARDIERI, E., GIANNI, L. & BONADONNA, G. (eds.) *Breast Cancer*. Springer Berlin Heidelberg.
- FACIONE, N. C. 1993. Delay versus help seeking for breast cancer symptoms: A critical review of the literature on patient and provider delay. *Social Science and Medicine*, 36, 1521-1534.
- FACIONE, N. C., MIASKOWSKI, C., DODD, M. J. & PAUL, S. M. 2002. The self-reported likelihood of patient delay in breast cancer: new thoughts for early detection. *Prev Med*, 34, 397-407.
- FAN, F. & THOMAS, P. 2011. Common Benign Conditions of Low Concern. In: THOMAS, P. A. (ed.) *Breast Cancer and its Precursor Lesions*. Humana Press.
- FERLAY, J., HÉRY, C., AUTIER, P. & SANKARANARAYANAN, R. 2010. Global Burden of Breast Cancer. In: LI, C. (ed.) *Breast Cancer Epidemiology*. Springer New York.

- FERLEY, J., SHIN, H. R. & BRAY, F. 2010. GLOBOCAN 2008 , Cancer incidence and mortality worldwide: IARC CancerBase No. 10 [Internet]. *International Agency for Research on Cancer*.
- FOWBLE, B. L., SCHULTZ, D. J., OVERMOYER, B., SOLIN, L. J., FOX, K., JARDINES, L., OREL, S. & GLICK, J. H. 1994. The influence of young age on outcome in early stage breast cancer. *International Journal of Radiation Oncology Biology Physics*, 30, 23-33.
- GILANI, G. M. & KAMAL, S. 2004. Risk factors for breast cancer in Pakistani women aged less than 45 years. *Annals of Human Biology*, 31, 398-407.
- GRUNFELD, E. A., HUNTER, M. S., RAMIREZ, A. J. & RICHARDS, M. A. 2003. Perceptions of breast cancer across the lifespan. *Journal of Psychosomatic Research*, 54, 141-146.
- GRUNFELD, E. A., RAMIREZ, A. J., HUNTER, M. S. & RICHARDS, M. A. 2002. Women's knowledge and beliefs regarding breast cancer. *British Journal of Cancer*, 86, 1373-1378.
- GURAY, M. & SAHIN, A. A. 2006. Benign breast diseases: Classification, diagnosis, and management. *Oncologist*, 11, 435-449.
- HAAS, J. S., KAPLAN, C. P., DES JARLAIS, G., GILDENGOIN, V., PÉREZ-STABLE, E. J. & KERLIKOWSKA, K. 2005. Perceived risk of breast cancer among women at average and increased risk. *Journal of Women's Health*, 14, 845-851.
- HAILEY, B. J., CARTER, C. L. & BURNETT, D. R. 2000. Breast cancer attitudes, knowledge, and screening behavior in women with and without a family history of breast cancer. *Health Care for Women International*, 21, 701-715.
- HALL, M. J., REID, J. E., BURBIDGE, L. A., PRUSS, D., DEFFENBAUGH, A. M., FRYE, C., WENSTRUP, R. J., WARD, B. E., SCHOLL, T. A. & NOLL, W. W. 2009. BRCA1 and BRCA2 mutations in women of different ethnicities undergoing testing for hereditary breast-ovarian cancer. *Cancer*, 115, 2222-2233.
- HARIRCHI, I., GHAEMMAGHAMI, F., KARBAKHSH, M., MOGHIMI, R. & MAZAHERIE, H. 2005. Patient delay in women presenting with advanced breast cancer: An Iranian study. *Public Health*, 119, 885-891.
- HATEFNIA, E., NIKNAMI, S., BAZARGAN, M., MAHMOODI, M., LAMYIANM, M. & ALAVI, N. 2010. Correlates of mammography utilization among working Muslim Iranian women. *Health Care Women Int*, 31, 499-514.
- HEISEY, R., CLEMONS, M., GRANER, L., FERGUS, K., HUM, S., LORD, B., MCCREADY, D. R. & FITZGERALD, B. 2011. Health care strategies to promote earlier presentation of symptomatic breast cancer: perspectives of women and family physicians. *Curr Oncol*, 18, e227-37.
- HEMMINKI, K., MOUSAVI, S. M., SUNDQUIST, J. & BRANDT, A. 2011. Does the breast cancer age at diagnosis differ by ethnicity? A study on immigrants to Sweden. *Oncologist*, 16, 146-154.
- HENDERSON, K., PRESCOTT, J. & BERNSTEIN, L. 2010. Physical Activity and Anthropometric Factors. In: LI, C. (ed.) *Breast Cancer Epidemiology*. Springer New York.
- HÉRY, C., FERLAY, J., BONIOL, M. & AUTIER, P. 2008. Quantification of changes in breast cancer incidence and mortality since 1990 in 35

- countries with Caucasian-majority populations. *Annals of Oncology*, 19, 1187-1194.
- HOLMBERG, L., EKBOM, A., CALLE, E., MOKDAD, A. & BYERS, T. 1997. Breast cancer mortality in relation to self-reported use of breast self-examination. A cohort study of 450,000 women. *Breast Cancer Res Treat*, 43, 137-40.
- ISKANDARSYAH, A., DE KLERK, C., SUARDI, D. R., SOEMITRO, M. P., SADARJOEN, S. S. & PASSCHIER, J. 2014. Psychosocial and cultural reasons for delay in seeking help and nonadherence to treatment in Indonesian women with breast cancer: A qualitative study. *Health Psychology*, 33, 214-221.
- ISMAIL, G. M. 2013. Assessment of Factors that Hinder Early Detection of Breast Cancer among Females at Cairo University Hospital. *World Applied Sciences Journal*, 23, 99-108.
- ISMAIL, G. M., ABD EL HAMID, A. A. & ABD ELNABY, A. G. 2013. Assessment of factors that hinder early detection of breast cancer among females at Cairo university hospital. *World Applied Sciences Journal*, 23, 99-108.
- JALKH, N., NASSAR-SLABA, J., CHOUERY, E., SALEM, N., UHRCHAMMER, N., GOLMARD, L., STOPPA-LYONNET, D., BIGNON, Y. J. & MEGARBANE, A. 2012. <Prevalance of BRCA1 and BRCA2 mutations in familial breast cancer patients in Lebanon.pdf>. *hereditary Cancer in Clinical Practice*, 10, 7.
- JAN, M., MATTOO, J. A., SALROO, N. A. & AHANGAR, S. 2010. Triple assessment in the diagnosis of breast cancer in Kashmir. *Indian Journal of Surgery*, 72, 97-103.
- JATOI, I. 2010. Surgical Considerations in the Management of Primary Invasive Breast Cancer. In: JATOI, I. & KAUFMANN, M. (eds.) *Management of Breast Diseases*. Springer Berlin Heidelberg.
- JEMAL, A., BRAY, F., CENTER, M. M., FERLAY, J., WARD, E. & FORMAN, D. 2011. Global cancer statistics. *CA Cancer Journal for Clinicians*, 61, 69-90.
- JENSEN, O. M. 1991. *Cancer registration: principles and methods*, IARC.
- KAMANGAR, F., DORES, G. M. & ANDERSON, W. F. 2006. Patterns of cancer incidence, mortality, and prevalence across five continents: Defining priorities to reduce cancer disparities in different geographic regions of the world. *Journal of Clinical Oncology*, 24, 2137-2150.
- KARDINAH, D., ANDERSON, B. O., DUGGAN, C., ALI, I. A. & THOMAS, D. B. 2014. Short report: Limited effectiveness of screening mammography in addition to clinical breast examination by trained nurse midwives in rural Jakarta, Indonesia. *International Journal of Cancer*, 134, 1250-1255.
- KATAPODI, M. C., LEE, K. A., FACIONE, N. C. & DODD, M. J. 2004. Predictors of perceived breast cancer risk and the relation between perceived risk and breast cancer screening: A meta-analytic review. *Preventive Medicine*, 38, 388-402.
- KHANJANI, N., NOORI, A. & ROSTAMI, F. 2012. The Knowledge and Practice of Breast Cancer Screening Among Women in Kerman, Iran. *Al Ameen J Med Sci*, 5, 221-226.

- KHATIB, O. M. & MODJTABAI, A. 2006. *Guidelines for the early detection and screening of breast cancer*, World Health Organization, Regional Office for the Eastern Mediterranean.
- KUMAR, V., ABBAS, A. K. & MITCHELL, R. N. 2007. *Robbins basic pathology*, Philadelphia, PA, Saunders/Elsevier.
- KURIAN, A. & CARLSON, R. 2010. Principles of Breast Cancer Therapy. In: LI, C. (ed.) *Breast Cancer Epidemiology*. Springer New York.
- LAMYIAN, M., HYDARNIA, A., AHMADI, F., FAGHIHZADEH, S. & AGUILAR-VAFAIE, M. E. 2007. Barriers to and factors facilitating breast cancer screening among Iranian women: A qualitative study. *Eastern Mediterranean Health Journal*, 13, 1160-1169.
- LEMON, S. C., ZAPKA, J. G. & CLEMOW, L. 2004. Health behavior change among women with recent familial diagnosis of breast cancer. *Preventive Medicine*, 39, 253-262.
- LI, C. 2010. *Breast Cancer Epidemiology*, Springer New York.
- LIOE, T. & CAMERON, R. I. 2013. Breast. In: ALLEN, D. C. & CAMERON, R. I. (eds.) *Histopathology Specimens*. Springer London.
- LIPKUS, I. M., KUCHIBHATLA, M., MCBRIDE, C. M., BOSWORTH, H. B., POLLAK, K. I., SIEGLER, I. C. & RIMER, B. K. 2000. Relationships among breast cancer perceived absolute risk, comparative risk, and worries. *Cancer Epidemiology Biomarkers and Prevention*, 9, 973-975.
- LITTON, J. K., READY, K., CHEN, H., GUTIERREZ-BARRERA, A., ETZEL, C. J., MERIC-BERNSTAM, F., GONZALEZ-ANGULO, A. M., LE-PETROSS, H., LU, K., HORTOBAGYI, G. N. & ARUN, B. K. 2012. Earlier age of onset of BRCA mutation-related cancers in subsequent generations. *Cancer*, 118, 321-325.
- LY, D., FORMAN, D., FERLAY, J., BRINTON, L. A. & COOK, M. B. 2013. An international comparison of male and female breast cancer incidence rates. *International Journal of Cancer*, 132, 1918-1926.
- MABRY, R. M., REEVES, M. M., EAKIN, E. G. & OWEN, N. 2010. Gender differences in prevalence of the metabolic syndrome in Gulf Cooperation Council Countries: A systematic review. *Diabetic Medicine*, 27, 593-597.
- MACDONALD, D. J. 2002. Women's decisions regarding management of breast cancer risk. *Medsurg nursing : official journal of the Academy of Medical-Surgical Nurses*, 11, 183-186.
- MADLENSKY, L., VIERKANT, R. A., VACHON, C. M., PANKRATZ, V. S., CERHAN, J. R., VADAPARAMPIL, S. T. & SELLERS, T. A. 2005. Preventive health behaviors and familial breast cancer. *Cancer Epidemiology Biomarkers and Prevention*, 14, 2340-2345.
- MAHFOUDH, W., BOUAOUINA, N., AHMED, S. B., GABBOUJ, S., SHAN, J., MATHEW, R., UHRHAMMER, N., BIGNON, Y. J., TROUDI, W., ELGAAIED, A. B., HASSEN, E. & CHOUCANE, L. 2012. Hereditary breast cancer in Middle Eastern and North African (MENA) populations: identification of novel, recurrent and founder BRCA1 mutations in the Tunisian population. *Mol Biol Rep*, 39, 1037-46.
- MARIANI, P. & GIANNI, L. 2008. The Choice of the Correct Imaging Modality in Breast Cancer Management. In: BOMBARDIERI, E., GIANNI, L. & BONADONNA, G. (eds.) *Breast Cancer*. Springer Berlin Heidelberg.

- MATHERS, C. D., FAT, D. M., INOUE, M., RAO, C. & LOPEZ, A. D. 2005. Counting the dead and what they died from: an assessment of the global status of cause of death data. *Bull World Health Organ*, 83, 171-7.
- MCGREGOR, B. A., BOWEN, D. J., ANKERST, D. P., ANDERSEN, M. R., YASUI, Y. & MCTIERNAN, A. 2004. Optimism, perceived risk of breast cancer, and cancer worry among a community-based sample of women. *Health Psychology*, 23, 339-344.
- MCQUEEN, A., SWANK, P. R., BASTIAN, L. A. & VERNON, S. W. 2008. Predictors of Perceived Susceptibility of Breast Cancer and Changes Over Time: A Mixed Modeling Approach. *Health Psychology*, 27, 68-77.
- MEECHAN, G., COLLINS, J. & PETRIE, K. J. 2002. Delay in seeking medical care for self-detected breast symptoms in New Zealand women. *New Zealand Medical Journal*, 115.
- MIAO, H., VERKOOIJEN, H. M., CHIA, K. S., BOUCHARDY, C., PUKKALA, E., LARØNNINGEN, S., MELLEMKJÆR, L., CZENE, K. & HARTMAN, M. 2011. Incidence and outcome of male breast cancer: An international population-based study. *Journal of Clinical Oncology*, 29, 4381-4386.
- MISSAOUI, N., JAIDENE, L., ABDELKRIM, S. B., ABDELKADER, A. B., BEIZIG, N., YAACOUB, L. B., YAACOUBI, M. T. & HMISSA, S. 2011. Breast cancer in Tunisia: Clinical and pathological findings. *Asian Pacific Journal of Cancer Prevention*, 12, 169-172.
- MITCHELL, J., LANNIN, D. R., MATHEWS, H. F. & SWANSON, M. S. 2002. Religious beliefs and breast cancer screening. *J Womens Health (Larchmt)*, 11, 907-15.
- MONTAZERI, A., EBRAHIMI, M., MEHRDAD, N., ANSARI, M. & SAJADIAN, A. 2003. Delayed presentation in breast cancer: A study in Iranian women. *BMC Women's Health*, 3.
- MUSCAT, J. E. & HUNCHAREK, M. S. 1991. Breast self-examination and extent of disease: a population-based study. *Cancer Detect Prev*, 15, 155-9.
- NAJJAR, H. & EASSON, A. 2010. Age at diagnosis of breast cancer in Arab nations. *International Journal of Surgery*, 8, 448-452.
- NEWCOMB, P. A., WEISS, N. S., STORER, B. E., SCHOLLES, D., YOUNG, B. E. & VOIGT, L. F. 1991. Breast self-examination in relation to the occurrence of advanced breast cancer. *J Natl Cancer Inst*, 83, 260-5.
- NOOYI, S. C. & AL-LAWATI, J. A. 2011. Cancer incidence in Oman, 1998-2006. *Asian Pac J Cancer Prev*, 12, 1735-8.
- NORMAN, P. & BRAIN, K. 2005. An application of an extended health belief model to the prediction of breast self-examination among women with a family history of breast cancer. *British Journal of Health Psychology*, 10, 1-16.
- NORSA'ADAH, B., RAMPAL, K. G., RAHMAH, M. A., NAING, N. N. & BISWAL, B. M. 2011. Diagnosis delay of breast cancer and its associated factors in Malaysian women. *BMC Cancer*, 11.
- NOSARTI, C., CRAYFORD, T., ROBERTS, J. V., ELIAS, E., MCKENZIE, K. & DAVID, A. S. 2000. Delay in presentation of symptomatic referrals to a breast clinic: Patient and system factors. *British Journal of Cancer*, 82, 742-748.

- O'MAHONY, M., HEGARTY, J. & MCCARTHY, G. 2011. Women's help seeking behaviour for self discovered breast cancer symptoms. *Eur J Oncol Nurs*, 15, 410-8.
- O'MAHONY, M., MCCARTHY, G., CORCORAN, P. & HEGARTY, J. 2013a. Shedding light on women's help seeking behaviour for self discovered breast symptoms. *European Journal of Oncology Nursing*, 17, 632-639.
- O'MAHONY, M., MCCARTHY, G., CORCORAN, P. & HEGARTY, J. 2013b. Shedding light on women's help seeking behaviour for self discovered breast symptoms. *Eur J Oncol Nurs*, 17, 632-9.
- PACK, G. T. & GALLO, J. S. 1938. The culpability for delay in the treatment of cancer. *Am J Cancer*, 33, 443-462.
- PARKIN, D. 2008. The role of cancer registries in cancer control. *International Journal of Clinical Oncology*, 13, 102-111.
- PARKIN, D. M., FERLAY, J., HAMDI-CHERIF, M., SITAS, F., THOMAS, J. & WHELAN, S. 2003. Cancer in Africa: epidemiology and prevention. *IARC scientific Publications*.
- PARKIN, D. M. & FERNANDEZ, L. M. 2006. Use of statistics to assess the global burden of breast cancer. *Breast J*, 12 Suppl 1, S70-80.
- PARKIN, D. M., WHELAN, S. L. & FERLAY, J. 2002. Cancer incidence in five continents. Volume VIII. *IARC Sci Publ*, 1-781.
- PERRY, N., BROEDERS, M., DE WOLF, C., TORNBERG, S., HOLLAND, R. & VON KARSA, L. 2008. European guidelines for quality assurance in breast cancer screening and diagnosis. Fourth edition--summary document. *Ann Oncol*, 19, 614-22.
- PETRO-NUSTAS, W. I. 2001. Factors associated with mammography utilization among Jordanian women. *Journal of Transcultural Nursing*, 12, 284-291.
- PETRO-NUSTAS, W. & MIKHAIL, B. I. 2002. Factors associated with breast self-examination among Jordanian women. *Public Health Nursing*, 19, 263-271.
- PHIPPS, A. & LI, C. 2010. Breast Cancer Biology and Clinical Characteristics. In: LI, C. (ed.) *Breast Cancer Epidemiology*. Springer New York.
- PINEROS, M., SANCHEZ, R., CENDALES, R., PERRY, F. & OCAMPO, R. 2009. Patient delay among Colombian women with breast cancer. *Salud Publica Mex*, 51, 372-80.
- RAMIREZ, A. J., WESTCOMBE, A. M., BURGESS, C. C., SUTTON, S., LITTLEJOHNS, P. & RICHARDS, M. A. 1999. Factors predicting delayed presentation of symptomatic breast cancer: A systematic review. *Lancet*, 353, 1127-1131.
- RASTAD, H., KHANJANI, N. & KHANDANI, B. K. 2012. Causes of delay in seeking treatment in patients with breast cancer in Iran: A qualitative content analysis study. *Asian Pacific Journal of Cancer Prevention*, 13, 4511-4515.
- RAVICHANDRAN, K. & AL-ZAHRANI, A. S. 2009. Association of reproductive factors with the incidence of breast cancer in Gulf Cooperation Council countries. *Eastern Mediterranean Health Journal*, 15, 612-621.
- RECHT, A., EDGE, S. B., SOLIN, L. J., ROBINSON, D. S., ESTABROOK, A., FINE, R. E., FLEMING, G. F., FORMENTI, S., HUDIS, C., KIRSHNER, J. J., KRAUSE, D. A., KUSKE, R. R., LANGER, A. S.,

- SLEDGE, G. W., JR., WHELAN, T. J. & PFISTER, D. G. 2001. Postmastectomy radiotherapy: clinical practice guidelines of the American Society of Clinical Oncology. *J Clin Oncol*, 19, 1539-69.
- RICHARDS, M. A., SMITH, P., RAMIREZ, A. J., FENTIMAN, I. S. & RUBENS, R. D. 1999a. The influence on survival of delay in the presentation and treatment of symptomatic breast cancer. *British Journal of Cancer*, 79, 858-864.
- RICHARDS, M. A., WESTCOMBE, A. M., LOVE, S. B., LITTLEJOHNS, P. & RAMIREZ, A. J. 1999b. Influence of delay on survival in patients with breast cancer: A systematic review. *Lancet*, 353, 1119-1126.
- ROTHMAN, A. J., KLEIN, W. M. & WEINSTEIN, N. D. 1996. Absolute and Relative Biases in Estimations of Personal Risk. *Journal of Applied Social Psychology*, 26, 1213-1236.
- ROUBA, A., KAISI, N., AL-CHATY, E., BADIN, R., PALS, G., YOUNG, C. & WORSHAM, M. J. 2000. Patterns of allelic loss at the BRCA1 locus in Arabic women with breast cancer. *International journal of molecular medicine*, 6, 565-569.
- SAADATMAND, S., TILANUS-LINTHORST, M. M. A., RUTGERS, E. J. T., HOOGERBRUGGE, N., OOSTERWIJK, J. C., TOLLENAAR, R. A. E. M., HOONING, M., LOO, C. E., OBDEIJN, I. M., HEIJNSDIJK, E. A. M. & DE KONING, H. J. 2013. Cost-effectiveness of screening women with familial risk for breast cancer with magnetic resonance imaging. *Journal of the National Cancer Institute*, 105, 1314-1321.
- SAINSBURY, J. R. C., ANDERSON, T. J. & MORGAN, D. A. L. 2000. ABC of breast diseases: Breast cancer. *British Medical Journal*, 321, 745-50.
- SALIM, E. I., MOORE, M. A., AL-LAWATI, J. A., AL-SAYYAD, J., BAWAZIR, A., BAZARBASHI, S., BENER, A., CORBEX, M., EL-SAGHIR, N., HABIB, O. S., MAZIAK, W., SEIF-ELDIN, I. A. & SOBUE, T. 2009. Cancer epidemiology and control in the Arab world - past, present and future. *Asian Pacific Journal of Cancer Prevention*, 10, 3-16.
- SEEDHOM, A. E. & KAMAL, N. N. 2011. Factors affecting survival of women diagnosed with breast cancer in El-Minia Governorate, Egypt. *Int J Prev Med*, 2, 131-8.
- SEMIGLAZOV, V. F., MANIKHAS, A. G., MOISEENKO, V. M., PROTSENKO, S. A., KHARIKOVA, R. S., SELEZNEV, I. K., POPOVA, R. T., MIGMANOVA, N., ORLOV, A. A., BARASH, N., IVANOVA, O. A. & IVANOV, V. G. 2003. [Results of a prospective randomized investigation [Russia (St.Petersburg)/WHO] to evaluate the significance of self-examination for the early detection of breast cancer]. *Vopr Onkol*, 49, 434-41.
- SERRAINO, D., PISELLI, P. & SCOGNAMIGLIO, P. 2001. Viral infections and cancer: Epidemiological aspects. *Journal of Biological Regulators and Homeostatic Agents*, 15, 224-228.
- SHAHEEN, R., SLANETZ, P. J., RAZA, S. & ROSEN, M. P. 2011. Barriers and opportunities for early detection of breast cancer in Gaza women. *Breast*, 20, S30-S34.
- SHAN, J., MAHFOUDH, W., DSOUZA, S. P., HASSEN, E., BOUAOUINA, N., ABDELHAK, S., BENHADJAYED, A., MEMMI, H., MATHEW, R. A., AIGHA, II, GABBOUJ, S., REMADI, Y. & CHOUCANE, L.

2012. Genome-Wide Association Studies (GWAS) breast cancer susceptibility loci in Arabs: susceptibility and prognostic implications in Tunisians. *Breast Cancer Res Treat*, 135, 715-24.
- SHARMA, D. & DAVIDSON, N. E. 2013. Obesity and Breast Cancer: A Multipartite Connection. *Journal of Mammary Gland Biology and Neoplasia*, 1-3.
- SHARMA, K., COSTAS, A., SHULMAN, L. N. & MEARA, J. G. 2012. A systematic review of barriers to breast cancer care in developing countries resulting in delayed patient presentation. *Journal of Oncology*.
- SHULMAN, L. N., WILLETT, W., SIEVERS, A. & KNAUL, F. M. 2010. Breast cancer in developing countries: opportunities for improved survival. *J Oncol*, 2010, 595167.
- SIBAI, A. M. 2004. Mortality certification and cause-of-death reporting in developing countries. *Bulletin of the World Health Organization*, 82, 83-83.
- SILVERMAN, E., WOLOSHIN, S., SCHWARTZ, L. M., BYRAM, S. J., WELCH, H. G. & FISCHHOFF, B. 2001. Women's views on breast cancer risk and screening mammography: A qualitative interview study. *Medical Decision Making*, 21, 231-240.
- SINGLETERY, S. E. & CONNOLLY, J. L. 2006. Breast cancer staging: Working with the sixth edition of the AJCC Cancer Staging Manual. *Ca-A Cancer Journal for Clinicians*, 56, 37-47.
- SLOVIC, P. 1999. Trust, emotion, sex, politics, and science: surveying the risk-assessment battlefield. *Risk Anal*, 19, 689-701.
- SMIGAL, C., JEMAL, A., WARD, E., COKKINIDES, V., SMITH, R., HOWE, H. L. & THUN, M. 2006. Trends in breast cancer by race and ethnicity: Update 2006. *Ca-A Cancer Journal for Clinicians*, 56, 168-183.
- SMITH, R. A., CALEFFI, M., ALBERT, U. S., CHEN, T. H., DUFFY, S. W., FRANCESCHI, D. & NYSTROM, L. 2006. Breast cancer in limited-resource countries: early detection and access to care. *Breast J*, 12 Suppl 1, S16-26.
- SOSKOLNE, V., MARIE, S. & MANOR, O. 2007. Beliefs, recommendations and intentions are important explanatory factors of mammography screening behavior among Muslim Arab women in Israel. *Health Education Research*, 22, 665-676.
- SPECTOR, D., MISHEL, M., SKINNER, C. S., DEROO, L. A., VANRIPER, M. & SANDLER, D. P. 2009. Breast cancer risk perception and lifestyle behaviors among White and Black women with a family history of the disease. *Cancer Nurs*, 32, 299-308.
- STAPLETON, J. M., MULLAN, P. B., DEY, S., HABLAS, A., GAAFAR, R., SEIFELDIN, I. A., BANERJEE, M. & SOLIMAN, A. S. 2011. Patient-mediated factors predicting early- and late-stage presentation of breast cancer in Egypt. *Psycho-Oncology*, 20, 532-537.
- TAHA, H., AL-QUTOB, R., NYSTROM, L., WAHLSTROM, R. & BERGGREN, V. 2012. "Voices of fear and safety" women's ambivalence towards breast cancer and breast health: a qualitative study from Jordan. *BMC Womens Health*, 12, 21.
- THOMAS, D. B., GAO, D. L., RAY, R. M., WANG, W. W., ALLISON, C. J., CHEN, F. L., PORTER, P., HU, Y. W., ZHAO, G. L., PAN, L. D., LI, W., WU, C., CORIATY, Z., EVANS, I., LIN, M. G., STALSBERG, H.

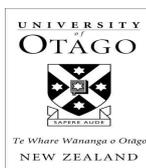
- & SELF, S. G. 2002. Randomized trial of breast self-examination in Shanghai: final results. *J Natl Cancer Inst*, 94, 1445-57.
- THOMAS, P. 2011. Benign Conditions Associated with a Risk for the Subsequent Development of Cancer. In: THOMAS, P. A. (ed.) *Breast Cancer and its Precursor Lesions*. Humana Press.
- THONGSUKSAI, P., CHONGSUVIVATWONG, V. & SRIPLUNG, H. 2000. Delay in breast cancer care: A study in Thai women. *Medical Care*, 38, 108-114.
- TOMMASI, S., CRAPOLICCHIO, A., LACALAMITA, R., BRUNO, M., MONACO, A., PETRONI, S., SCHITTULLI, F., LONGO, S., DIGENNARO, M., CALISTRI, D., MANGIA, A. & PARADISO, A. 2005. BRCA1 mutations and polymorphisms in a hospital-based consecutive series of breast cancer patients from Apulia, Italy. *Mutation Research - Fundamental and Molecular Mechanisms of Mutagenesis*, 578, 395-405.
- UNGER-SALDAÑA, K. & INFANTE-CASTAÑEDA, C. 2009. Delay of medical care for symptomatic breast cancer: a literature review. *Salud pública de México*, 51 Suppl 2, s270-285.
- UNGER-SALDAÑA, K. & INFANTE-CASTAÑEDA, C. 2011. Is Breast Cancer Delay really the patient's fault. *Relational Concepts in Medicine*.
- UNGER-SALDANA, K. & INFANTE-CASTANEDA, C. B. 2011. Breast cancer delay: a grounded model of help-seeking behaviour. *Soc Sci Med*, 72, 1096-104.
- VERDECCHIA, A., FRANCISCI, S., BRENNER, H., GATTA, G., MICHELI, A., MANGONE, L. & KUNKLER, I. 2007. Recent cancer survival in Europe: a 2000-02 period analysis of EURO CARE-4 data. *Lancet Oncol*, 8, 784-96.
- VERNON, S. W., VOGEL, V. G., HALABI, S. & BONDY, M. L. 1993. Factors associated with perceived risk of breast cancer among women attending a screening program. *Breast Cancer Research and Treatment*, 28, 137-144.
- VOROBIOF, D. A., SITAS, F. & VOROBIOF, G. 2001. Breast cancer incidence in South Africa. *J Clin Oncol*, 19, 125s-127s.
- WILLIAMS, T., CLARKE, V. A. & SAVAGE, S. 2002. Women's perceptions of familial aspects of breast cancer. *Health Education*, 102, 50-59.
- WORLD HEALTH ORGANIZATION 2002. *National Cancer Control Programmes: Policies & Managerial Guidelines*, WHO.
- YIP, C. H., SMITH, R. A., ANDERSON, B. O., MILLER, A. B., THOMAS, D. B., ANG, E. S., CAFFARELLA, R. S., CORBEX, M., KREPS, G. L. & MCTIERNAN, A. 2008. Guideline implementation for breast healthcare in low- and middle-income countries: early detection resource allocation. *Cancer*, 113, 2244-56.
- YOULDEN, D. R., CRAMB, S. M., DUNN, N. A. M., MULLER, J. M., PYKE, C. M. & BAADE, P. D. 2012. The descriptive epidemiology of female breast cancer: An international comparison of screening, incidence, survival and mortality. *Cancer Epidemiology*, 36, 237-248.
- ZEKRI, A. R. N., BAHNASSY, A. A., MOHAMED, W. S., EL-KASSEM, F. A., EL-KHALIDI, S. J., HAFEZ, M. M. & HASSAN, Z. K. 2012. Epstein-Barr virus and breast cancer: Epidemiological and Molecular

study on Egyptian and Iraqi women. *Journal of the Egyptian National Cancer Institute*, 24, 123-131.

ZIDAN, J., SIKORSKY, N., BASHER, W., SHARABI, A., FRIEDMAN, E. & STEINER, M. 2012. Differences in pathological and clinical features of breast cancer in Arab as compared to Jewish women in Northern Israel. *Int J Cancer*, 131, 924-9.

Appendices

Appendix 1: Questionnaire



The Epidemiology of Breast Cancer in Oman Questionnaire

a) Socio-demographic characteristics

1. How old are you?
2. What is your educational level?
 - Illiterate
 - High school and less
 - High school certificate
 - Higher (university) education
3. What is your occupation?
4. What is your family guardian's occupation?
5. What is your income and your total household income?
6. Where do you live?
 - Urban (large city)
 - Urban (small city)
 - Rural (village)
7. How far are you from the nearest medical centre? What is your travel time in minutes?
.....

b) Reproductive and Medical History

1. Are you
 - Married
 - Never married (single)
 - Widowed
 - Divorced

Do you have any children?

- No
- Yes. How many children do you have?

2. How old were you when you had your first child?

3. How many of your children did you breast feed?

4. How long in total have you spent breastfeeding (add time for all children together)?(months/years)

5. Are you

- Premenopausal
- Going through menopause at the moment
- Postmenopausal

6. What is your weight?

7. What is your height?

8. Do you have any history of chronic disease?

- Yes – please specify:
- No

9. Do you have any family members with breast cancer?

- Yes – please say which relative(s) (ie mother, sister, mother’s sister, etc):
.....
- No

c) Symptoms and healthcare seeking behaviour

1. When were you diagnosed with breast cancer? (month /year)

.....

2. What was the stage of disease at the time of diagnosis?

.....

3. What was the first symptom(s) you noticed?

.....
.....

4. Could you remember the date when you first noticed this symptom(s)
(approximate month and year)?

.....

5. How many weeks was it between when you first noticed this symptom(s) and
when you went to see a doctor?

.....

6. Please remember back to how your breast cancer was diagnosed, which may
have included X-rays and biopsy tests. At the doctor's appointment when this
process *first* started, what was your reason for seeing the doctor? (*ie was it for
the symptoms, and if so which symptoms, or for something else and the doctor
did a breast check or noticed something which led them to do investigations?*)

.....
.....
.....

7. If you waited for 3 months or more between first noticing breast symptoms
and seeing a doctor, what was your reason(s) for waiting to see the doctor?

.....
.....
.....
.....

8. Did you disclose the discovery of symptom(s) to someone else, before going
to the doctor?

- Yes, please specify who
- No

d) Knowledge and attitude toward breast cancer

1. What symptoms do you know of that breast cancer can cause? (*tick all mentioned*)
 - Breast or axillary mass
 - Breast pain
 - Nipple retraction ('pulled in' nipple)
 - Other symptoms: specify:
 - 'I don't know'

2. How common would you say breast cancer is compared with other cancers for Omani women?
 - Breast cancer is the most common female cancer
 - Another cancer is the most common cancer
 - 'I don't know'

3. Are you aware of any ways that breast cancer can be found in its early stages?
 - Self-examination
 - Doctor's examination
 - Mammography
 - Blood test
 - 'I don't know'
 - Other (specify):

4. What is the main way of diagnosing breast cancer?
 - Self-examination
 - Doctor's examination
 - Mammography
 - Blood test
 - 'I don't know'
 - Other (specify):

5. Do you believe that :
- Breast cancer is preventable and curable
 - Breast cancer is incurable and fatal
 - Breast cancer is in one's fate
 - Don't know
6. Before you were diagnosed with breast cancer, had you ever done Breast Self Examination?
- Yes – how often?
 - No
7. Are you familiar with Breast Self-Examination now?
- Yes
 - No
8. How important would you say Breast Self-Examination is?
- Important
 - Not important
9. Do you regularly perform Breast Self-Examination?
- Yes specify how often:
 - No

That is the end of my questions. Thank you very much for answering them, and being part of this research project. Please keep the information sheet in case you have any questions about this project in the future.

Appendix 3: Arab Women's Breast Cancer Screening Practices

In most Arab countries breast cancer patients present with late stage disease and therefore survival rates are reported to be low among these patients (Donnelly et al., 2011b). Late diagnosis of breast cancer is shown to have an impact on the individual, society and government's health resource expenditure (Ismail et al., 2013). Early detection of breast cancer cases is linked to reduce morbidity and mortality. For example, mammography screening reduces mortality by 25% in women aged 40-74 years (Ismail et al., 2013). Consequently, decreasing incidence and mortality associated with breast cancer can be achieved through implementing early detection programs. Because of the lack of population-based screening programs in the majority of Arab countries, participation in Breast Cancer Screening (BCS) is reported to be low (Donnelly et al., 2013, Akhtar et al., 2010). In Saudi Arabia, a pilot-screening programme was organised and results showed that only 18% of the total population in the target area participated (Akhtar et al., 2010). This percentage was lower compared to similar conducted pilot programmes in Europe and also than the recommended international standard of more than 70% (Perry et al., 2008). Similarly in Qatar, Bener et al. (2009) reported that only 22.5% of 1200 Qatari women aged 30-55 years have ever attended mammography, and only 2.9% practiced BSE and 13.8% had CBE. Similarly low participation rates were reported in UAE (Bener et al., 2001), Egypt (Abdel-Fattah et al., 2000), Palestine (Azaiza et al., 2010) and Jordan (Petro-Nustus and Mikhail, 2002).

Individual health behaviour is determined by social and cultural context. Likewise, women's beliefs, knowledge and practice of BCS are influenced by social and cultural frameworks (Donnelly et al., 2011a). Accordingly, investigating barriers and facilitators that influence women participation in BCS is vital in order to implement effective intervention programmes that are culturally and socially appropriate.

Across the literature several barriers and facilitators of BCS have been identified in Arab countries. Lack of knowledge and awareness about breast cancer, and especially the benefits of screening, has been found as a major barrier (Bener et al., 2002, Soskolne et al., 2007). Poor knowledge seems to be

associated with under-utilisation of screening in low-income, poorly educated minorities and the elderly (Bener et al., 2002). Women who were aware of breast cancer causes were more likely to seek prevention. Ismail et al (2013) reported in a study on Egyptian women that more than half of the participants lacked knowledge about BSE.

Fear is a well-recognised psychological barrier to BCS (Donnelly et al., 2013, Lamyian et al., 2007). Fear is believed to be associated with negative attitudes toward prevention. Fear of breast cancer being detected has been related to underuse of screening activities (Lamyian et al., 2007, Bener et al., 2002). In Kuwait, women revealed that they did not want to know if they had breast cancer (Al-Qattan et al., 2008). Equally, others never practiced BSE because they feared finding a lump or other abnormalities. On the other hand, some women stated that early detection was important to provide assurance that they did not have cancer. Additionally, fear of pain from mammography and CBE were reported in several studies (Cohen, 2013, Bener et al., 2009). In UAE, about a third of 367 women surveyed thought that mammography was painful (Bener et al., 2001, Azaiza et al., 2010). Others feared that diagnosis of breast cancer would affect their family relationship and marriage prospects (Chouchane et al., 2013). In particular, some women held the belief that screening could lead to the diagnosis of breast cancer and that this would interfere with their traditional duties in taking care of their houses and children (Baron-Epel et al., 2004, Azaiza and Cohen, 2008). In contrast, this has been recognised as a motivator for women to seek early detection because their family depended on their continued health (Lamyian et al., 2007). Moreover, competing priorities, insufficient time to attend screening centres and forgetfulness were identified as significant barriers (Lamyian et al., 2007, Al-Qattan et al., 2008). Easy accessibility of breast screening services is a well-recognised facilitating factor (Chouchane et al., 2013, Ismail et al., 2013, Lamyian et al., 2007). Another barrier to access screening services is lack of transportation (Azaiza et al., 2010, Ismail et al., 2013). In some countries, there is inadequate distribution of screening centres (Donnelly et al., 2013). In some Arab countries where women are not allowed to drive or travel without a male, they are dependent on a male family member for transporting them to breast

screening facilities (Donnelly et al., 2011a). Cost and availability of health insurance might act as hindrances to screening services (Petro-Nustas, 2001).

Another major barrier identified across the literature is lack of healthcare providers' involvement in educating and offering screening. In Yemen, 36.5% of physicians referred asymptomatic patients for mammography, 26.9% referred those with breast cancer family history and 24.7% referred everyone regardless of symptoms status (Al-Naggar et al., 2009). In the UAE, while 80% of women were willing to undergo CBE, only 33% were offered CBE by physicians (Bener et al., 2001). A recommendation from health care providers has been found to motivate women to practice screening activities. "*The doctor told me that when you turned 40, you should have a mammography every year and I have been doing it ever since*" (Lamyian et al., 2007). Equally, a recommendation from a family member or friend has a positive impact on women attitude toward screening (Soskolne et al., 2007, Lamyian et al., 2007).

Embarrassment and shyness are other psychological barriers (Cohen, 2013, Donnelly et al., 2013). Bener et al (2009) interviewed 1,002 Qatari women and revealed that 53.3% of women were embarrassed from performing CBE. Arab women tended to refuse to be examined by doctors especially for sensitive feminine places due to embarrassment and the influence of culture (Ismail et al., 2013). Also unavailability of female doctors is conveyed as a barrier to BCS in Saudi Arabia (Bener et al., 2001). 97% of 1367 surveyed Emirati women showed a preference for female physician (Bener et al., 2001). Israeli Arab women state that they were uncomfortable with male examination but it was not seriously to be considered a barrier (Azaiza and Cohen, 2008). They believed that Islam would support medical examination by male doctor if a female was not available. Religion is found to act as an enabler for screening because women believe that religion is encouraging them to take responsibility for their own health. One woman said, "*We have responsibility for our bodies. We should go to the doctor because it is a divine responsibility based on the divine teaching that humans should act and only then the help of God will come*" (Lamyian et al., 2007). In contrast, fatalism expressed by some women who believe that cancer is deadly and that only limited influence on the course of the

disease was possible has been associated with low participation in BCS (Donnelly et al., 2013, Donnelly et al., 2011a).

Therefore, each Arab country is recommended to identify and measure the magnitude of barrier to screening before developing effective prevention strategies that are socially appropriate, socially accepted and address each population's unique needs (Donnelly et al., 2013).