QUALITY OF LIFE AMONG BREAST CANCER PATIENTS UNDERGOING CHEMOTHERAPY IN ONCOLOGY UNIT AT HOSPITAL UNIVERSITI SAINS MALAYSIA

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by

WAN NUR ATIRAH WAN AZMAN

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requirements for the degree of
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DECLARATION

I certify that this thesis does not incorporate without acknowledgement any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

CERTIFICATE

This is to certify that the dissertation entitled "Quality of Life among Breast Cancer Patients undergoing Chemotherapy in Oncology Unit at Hospital Universiti Sains Malaysia" is the bonafide record of research work done by Wan Nur Atirah Wan Azman, Matric Number 106756 during the period of December 2012 to June 2013 under my supervision. This dissertation is submitted in partial fulfillment for the degree of Bachelor of Health Sciences (Nursing). Research work and collection of data belong to Universiti Sains Malaysia.

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LIST OF ABBREVIATIONS

1TD		1 Timur Depan
CIA	-	Chemotherapy-Induced Alopecia
CIAA	-	Chemotherapy-Induced Appetite Alteration
CIC	-	Chemotherapy-Induced Constipation
CID	-	Chemotherapy-Induced Diarrhea
CIF	-	Chemotherapy-Induced Fatigue
CINV	-	Chemotherapy-Induced Nausea and Vomiting),
DV	-	Dependent Variables
EORTC QLQ-C30	-	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30
FACT-G		Functional Assessment of Cancer Therapy-General
FEC	-	5-fluoroacil + epirubicin + cyclophosphamide
FILE	-	Functional Index Living Emesis
Hospital USM	-	Hospital Universiti Sains Malaysia
IDV	-	Independent Variables
NCCN	-	National Comprehensive Cancer Network
NROD	-	Nuclear Medicine, Radiotherapy and Oncology Department
QOL	-	Quality of Life
WHO	-	World Health Organization

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ABSTRACT

Breast cancer is among the top cancer in women with chemotherapy as an important treatment in curing it. But, the side effects of chemotherapy are always suffered by most cancer patients that could reduce the quality of life (QOL). The goal of this quantitative cross-sectional study was to evaluate the QOL of breast cancer patients undergoing chemotherapy in Oncology Unit at Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. This study also determine the most common side effects for breast cancer patients undergoing chemotherapy, the level of QOL of breast cancer patients undergoing chemotherapy and to identify the relationship between the domains of QOL (physical, mental and social) with the most common side effects among breast cancer patients undergoing chemotherapy. A total of 52 breast cancer patients were involved using non-probability purposive sampling. Data were collected using a self-administered questionnaire which was the Bahasa Malaysia modified version of The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30) version 3.0. The data were gathered and analyzed using SPSS version 20 for frequency, percentage, mean, standard deviation and p-value. Majority of the breast cancer experienced alopecia (mean = 3.75, SD = 0.556), fatigue (mean = 3.65, SD = 0.653) and appetite alteration (mean = 3.62, SD = 0.599) during chemotherapy. Overall, the level of QOL for majority of breast cancer patients undergoing chemotherapy at Hospital USM was at satisfactory level (78.8%). The study found that, there was a significant relationship between social domain and alopecia ($r = 0.309$, $p = 0.026$), social domain and fatigue ($r =$

0.280, $p = 0.045$) and as well as physical domain and appetite alteration ($r = 0.422$, $p = 0.002$). Besides, there was no significant relationship between physical and mental domains on alopecia, physical and mental domains on fatigue and mental and social domains on appetite alteration (p value > 0.05). Since there are negative effects of breast cancer and chemotherapy on patients' QOL, health care providers, especially nurses, should support the patients throughout their illness and chemotherapy.

KUALITI KEHIDUPAN PESAKIT KANSER PAYUDARA YANG SEDANG MENJALANI RAWATAN KEMOTERAPI DI UNIT ONKOLOGI, HOSPITAL UNIVERSITI SAINS MALAYSIA

ABSTRAK

Kanser payudara merupakan penyakit kanser yang teratas dalam kalangan wanita dengan kemoterapi sebagai sesuatu rawatan yang penting untuk memulihkannya. Namun, kesan-kesan sampingan kemoterapi sentiasa dialami oleh kebanyakan pesakit kanser dan ianya boleh mengurangkan kualiti kehidupan (KK). Matlamat utama kajian kuantitatif ini adalah untuk menilai KK pesakit kanser payudara yang sedang menjalani kemoterapi di Unit Onkologi, Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. Kajian ini turut menentukan kesan-kesan sampingan kemoterapi yang paling kerap dialami oleh pesakit kanser payudara., tahap KK pesakit kanser payudara yang sedang menjalani kemoterapi, dan untuk mengenalpasti hubungan antara domain KK (fizikal, mental dan sosial) bersama kesan sampingan paling kerap di antara pesakit kanser payudara yang sedang menjalani kemoterapi. Sejumlah 52 pesakit kanser payudara telah terlibat dalam kajian ini dengan menggunakan pensampelan bertujuan 'non-probability'. Pengumpulan data telah dilakukan dengan menggunakan soalan kaji selidik yang telah diubah kepada Bahasa Melayu iaitu 'The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30) version 3.0'. Data telah dikumpul dan dianalisis dengan mengugunakan SPPS versi 20 untuk melihat frekuensi, peratus, min, sisihan piawaian dan nilai p. Kebanyakan pesakit kanser payudara mengalami keguguran rambut (min = 3.75, SD = 0.556), keletihan (min = 3.65, SD = 0.653) dan gangguan selera makan (min = 3.62, SD = 0.599) ketika menjalani kemoterapi. Keseluruhannya, tahap KK buat majoriti pesakit kanser payudara yang sedang menjalani kemoterapi di Hospital USM adalah di tahap yang memuaskan (78.8%). Kajian ini mendapati bahawa terdapat hubungan di antara domain social dan keguguran rambut ($r = 0.309$, $p = 0.026$), domain sosial dan keletihan ($r = 0.280$, $p = 0.045$) dan turut juga domain fizikal dan gangguan selera ($r = 0.422$, $p = 0.002$). Sebaliknya, tiada hubungkait antara domain fizikal dan mental dengan kegururan rambut, domain fizikal dan mental dengan keletihan dan domain mental dan social dengan gangguan selera makan (nilai $p > 0.05$). Oleh sebab adanya kesan negatif penyakit kanser payudara dan kemoterapi terhadap KK pesakit, pembekal penjagaan kesihatan, terutamanya jururawat-jururawat, harus menyokong para pesakit melalui penyakit mereka dan kemoterapi.

CHAPTER 1 : INTRODUCTION

1.1 Background of the Study

Cancer is one of the most significant health concerns of today. According to the 2001 statistics of World Health Organization (WHO), 10 million people are diagnosed with cancer – most of which are in developing countries – and about 6 million people die of cancer every year around the world (Pinar et al. 2003). In 2008, WHO reported a total of 7.6 million people worldwide died from cancer, and it is currently, cancer had become one of the common health problems in Malaysia.

One of the most common cancers in the world is breast cancer. Breast cancer is among the top cancer in women in both developed and developing world (WHO, 2012). Statistics shows that each year there is over 1.1 million newly diagnosed women with breast cancer worldwide and 410,000 women die from the disease (Steward and Paul Kleihues, 2003). National Cancer Institute defined breast cancer as cancer cells that form in tissues of the breast, usually the ducts and lobules. Breast cancer also affects men, but it rarely happens.

In Malaysia, breast cancer is the number one of most frequent cancer affecting the residence of Malaysia. In the Second Report of National Cancer Registry of Malaysia, there were 3242 breast cancer cases that were diagnosed in 2007. Based on this report, it is reported that breast cancer has accounted for 18.1% of all cancer cases and 32.1% of all cases are female. Besides that, it is the common cancer affecting Malaysian women especially Malay and Chinese women (Omar and Ibrahim Tamin, 2011).

Chemotherapy is one of the most common treatments for breast cancer patients, besides radiation therapy, surgery, and hormonal therapy (Salonen et al. 2011b). Chemotherapy is used to reduce the risk of breast cancer recurrence by preventing the replication of cancer cells and their attack on other tissues. There are two types of chemotherapy; neo adjuvant and adjuvant chemotherapy. Neo adjuvant therapy is chemotherapy before surgery or radiotherapy. Adjuvant therapy is chemotherapy after surgery or radiotherapy. Adjuvant chemotherapy had shown improvement for disease-free survival and overall survival in women with early breast cancer (Rotonda et al. 2011).

Essentially, chemotherapy is an important treatment in cancer care, but this modality is well known to be liable to a range of dose-related toxic effects (Pei et al. 2012). These toxic effects or side effects of chemotherapy are always suffered by most cancer patients that reduce the quality of life.

Quality of Life (QOL) has been an increasingly important issue in oncology discipline. According to the World Health Organization (WHO 1997), QOL is defined as individual perception of life, values, objectives, standards, and interests in the framework of culture. QOL is increasingly being used as a primary outcome measure in studies to evaluate the effectiveness of treatment and the well-being of cancer patients undergoing chemotherapy. The common side effects of chemotherapy are nausea, vomiting, hair loss, cognitive dysfunction, fatigue and changes in sexual functioning (Kayl and Meyers, 2006). Furthermore, Kayl and Meyers also stated that chemotherapy affects body image, psychosocial distress and consequently reduces QOL ratings or level. Meanwhile, decreased QOL as a result of chemotherapy side effects may predict early treatment discontinuation in patients (Richardson et al. 2007). Thus it is very important to measure the QOL of breast cancer patients undergoing chemotherapy. This is because the side effects of chemotherapy could affect the QOL of breast cancer patients negatively.

1.2 Problem Statements

Breast cancer is one of the prevailing chronic conditions which adversely affects the QOL in the patients and has been the subject of many studies (Perry et al. 2007). It is also stated that the diagnosis of breast cancer and its treatments, including types of axillary surgery, chemotherapy, radiotherapy and hormonal therapy, have an impact on patient's QOL in various ways during the treatment period (Browall et al. 2008). Moreover, there has been a study found that the time of diagnosis, initial stages of the treatment course and the months following the end of the treatment are stressful events for patients both physically and emotionally. During these periods poor adjustment and decreased QOL in breast cancer patients can easily occur (Hanson Frost et al. 2000).

Besides that, most of health care providers (example: nurses and doctors) dealing with breast cancer patients with chemotherapy, often underestimated the side effects of chemotherapy towards the patients. Parsaie et al. (2000) found that nurses tend to overestimate the effects of the physical and psychosocial stressors associated with chemotherapy and the cancer itself. In a review by Lampic and Sjödén (2000), health care providers are surveyed to express their thoughts about the needs of cancer patients in general, which resulted in poor estimations of the concerns that are most important to patients. It was revealed that most of health care providers were given limited and inconsistent knowledge regarding the side effects of chemotherapy. They were lacking in estimating cancer patient's experienced burden associated with chemotherapy. Thus, in reality their overall well-being and QOL were not prioritized during their course of chemotherapy treatment.

Thus, just focusing on breast cancer patients receiving chemotherapy, a better view regarding their QOL and side effects of chemotherapy could be explored. It was revealed that their experience on several side-effects and symptoms of chemotherapy, could give a negative effect on their QOL. The QOL has many aspects. King et al. (1996) defined QOL as the patient's perception of his or her health described in terms of his or her ability to function physically, mentally, and socially, and the extent of both disease symptoms and treatment side effects. Thus, the main aspects of QOL are the physical, mental and social domain. This is because these three domains are related to each other.

Despite of the increasing number of breast cancer patients in Malaysia, there are not so many studies that investigate the relation of QOL and the side effects of chemotherapy among breast cancer patients. In Hospital Universiti Sains Malaysia (Hospital USM), a significant number of breast cancer patients undergoing chemotherapy in the Oncology Unit. In Nuclear Medicine, Radiotherapy and Oncology Department (NROD) of Hospital USM, cancer patients that undergone chemotherapy there is mostly breast cancer patients. With the increasing number of breast cancer patients undergoing chemotherapy in Hospital USM, it is useful to measure the QOL of breast cancer patients in order to improve their lives. Figure 1.1 below shows the statistics of number of breast cancer patients undergoing chemotherapy in NROD from January 2012 until June 2012.

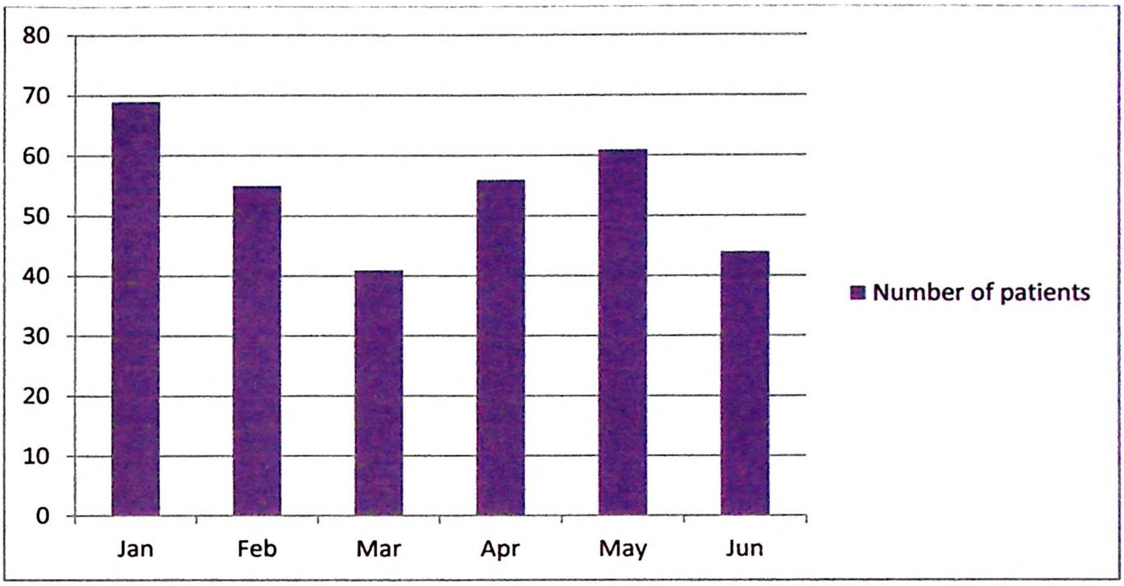

Figure 1.1: Number of breast cancer patients undergoing chemotherapy in NROD, Hospital USM from January until Jun 2012 (Nuclear, Radiology and Oncology Department of Hospital Universiti Sains Malaysia, 2012).

To describe the phenomena of QOL and the most common side effects of chemotherapy, a theoretical framework from the Integrative Theory of QOL by Danish Quality of Life Survey (Ventegodt, Merrick and Andersen, 2003) was used in this study. The theoretical framework describes how the subjective QOL of well-being which were composed of the three domains of QOL; physical, mental and social domains were interrelated with the side effects of chemotherapy. It will be further explained in Chapter 2.

1.3 Research Objectives

The general objective of this study is to evaluate the QOL of breast cancer patients undergoing chemotherapy in Oncology Unit at Hospital USM, Kubang Kerian, Kelantan.

1.3.1 Specific Objectives

- To determine the most common side effects for breast cancer patients undergoing chemotherapy treatment.
- To determine the level of QOL of breast cancer patients undergoing chemotherapy.
- To identify the relationship between the domains of QOL (physical, mental and social) and the most common side effects among breast cancer patients undergoing chemotherapy.

1.4 Research Questions

- What are the most common side effects for breast cancer patients undergoing chemotherapy treatment?
- What is the level of QOL of breast cancer patients undergoing chemotherapy?
- Is there a relationship between the domains of QOL (physical, mental and social) and the most common side effects among breast cancer patients undergoing chemotherapy?

1.5 Research Hypothesis

- H_O: There is no significant relationship between the domains of QOL (physical, mental and social) and the most common side effects among breast cancer patients undergoing chemotherapy.

- H_A: There is a significant relationship between the domains of QOL (physical, mental and social) and the most common side effects among breast cancer patients undergoing chemotherapy.

1.6 Definition of Terms

- Breast cancer

  Breast cancer is caused by the development of malignant cells in the breast. The malignant cells originate in the lining of the milk glands or ducts of the breast (ductal epithelium), defining this malignancy as a cancer. Cancer cells are characterized by uncontrolled division leading to abnormal growth and the ability of these cells to invade normal tissue locally or to spread throughout the body, in a process called metastasis (The Free Dictionary, 2012a).

- Quality of Life (QOL)

  Patient's perception of his or her health described in terms of his or her ability to function physically, mentally, and socially, and the extent of both disease symptoms and treatment side effects (King et al. 1996).

- Chemotherapy

  Chemotherapy is a treatment of cancer using anticancer drugs. The main purpose of chemotherapy is to kill cancer cells (The Free Dictionary, 2012b).

1.7 Significance of the Study

With the findings of this study, this study could benefit both health care providers and breast cancer patients. In terms of health care providers, especially doctors and nurses, this study could provide a lot of information about the most common side effects when breast cancer patients undergoing chemotherapy and how it affects the QOL of breast cancer patients. Thus, this is very beneficial for breast cancer patients. The implementation of QOL assessments into clinical practice for breast cancer treatment has a high potential to benefit patients. Health-related QOL has increasingly been an important factor to consider in the holistic treatment of breast cancer patients, and by providing accurate insights into QOL through self-reported questionnaires; doctors will be better able to make treatment decisions. Technologies can provide a highly efficient and accurate means of implementing QOL assessments so that they can help a wider range of breast cancer patients (Perry et al. 2007). Not only doctors could give better treatment decisions for the patients, nurses could also give more holistic nursing management towards patients who are undergoing chemotherapy by focusing on the side effects of chemotherapy. Adherence to chemotherapy is highly related with the QOL of patients. Thus, symptom management is very important to ensure patient is fully adhering to the treatment.

Besides that, with the findings of this study, a systematic intervention protocol for breast cancer patients to help them manage with breast cancer, support their functioning and emotional well-being and prevent limiting disabilities (Salonen et al., 2011b).

An educational program could also be created through findings of this study in order to improve breast cancer patients' QOL and be better breast cancer survivors. In addition, health care providers should be focusing the factors that most undermine the QOL of women with breast cancer and therefore should be given closest attention when supporting women during their treatments especially chemotherapy (Salonen et al. 2011b).

CHAPTER 2 : LITERATURE REVIEW

2.1 Introduction

This literature review provides some selected literatures on previous studies in relation with this study. A further aim was to gain a clearer picture of the support available and the QOL of breast cancer patients undergoing chemotherapy. Several literature searches were done to review the latest findings on chemotherapy and the QOL of breast cancer patients. This literature review also provides information on the theory, research design, instrumentation, data collection method and previous study findings.

Literature searches by using these key words:

- Breast cancer
- Chemotherapy
- Quality of life
- Side effects of chemotherapy

2.2 Review of Literature

2.2.1 Breast cancer

Breast cancer is a malignant (cancerous) growth that begins in the tissues of the breast. Cancer is a disease in which abnormal cells grow in an uncontrolled way (Stephan, 2012). In Malaysia, it is the commonest cancer among Malaysian women, regardless of their ethnicity (Lim et al. 2002; Lim and Yahaya, 2004). Lim et al. (2002) also stated that a woman in Malaysia has a 1 in 19 chance of getting breast cancer in her lifetime and out of 100 women who are afflicted with cancer, 30 will be breast cancer patients.

Based on the Second Report of National Cancer Registry: Cancer Incidence in Malaysia, in the year of 2003, there were 3738 breast cancer cases that were reported, making it the most commonly diagnosed cancer in women. It accounted for 31.0% of newly diagnosed female cases (Lim and Yahaya, 2004).

In Malaysia Cancer Statistics: Data and Figure 2007, there were 3242 female breast cancer cases diagnosed in 2007, and reported to the National Cancer Registry. It accounted for 18.1% of all cancer cases reported and 32.1% of all female cases (Omar and Ibrahim Tamin, 2011).

2.2.2 Chemotherapy

Chemotherapy is used to reduce the risk of breast cancer recurrence by preventing the replication of cancer cells and their attack on other issues. Chemotherapy is almost always recommended if there is cancer in the lymph nodes, regardless of tumour size or menopausal status. Breast cancer tends to be more aggressive in premenopausal women, and therefore chemotherapy is often part of the treatment plan. In inflammatory breast cancer chemotherapy is given as a neoadjuvant treatment to improve the prognosis (Salonen, 2011a). Neoadjuvant therapy is chemotherapy before surgery or radiotherapy. Adjuvant therapy is chemotherapy after surgery or radiotherapy. Adjuvant chemotherapy had shown improvement for disease-free survival and overall survival in women with early breast cancer (Rotonda et al., 2011).

2.2.3 Quality of life (QOL)

World Health Organization (WHO) defines QOL as individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns (World Health Organization, 1997). It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment (World Health Organization, 1997). In other worlds, QOL is a person's subjective evaluation of his functioning in a wide range of area.

Meanwhile King et al. (1996) stated that QOL is the patient's perception of his or her health described in terms of his or her ability to function physically, mentally, and socially, and the extent of both disease symptoms and treatment side effects.

In a review by Hughes et al. (1995), the 14 frequently mentioned QOL domains: social relationships and interaction; psychological well-being and personal satisfaction; employment; self-determination, autonomy, and personal choice; recreation and leisure; personal competence, community adjustment and independent living skills; residential environment; community integration; support services received; individual and social demographic indicators; personal development and fulfillment; social acceptance, social status, and ecological fit; physical and material well-being; and civic responsibility.

2.2.4 QOL and breast cancer

A breast cancer diagnosis is one of the most shocking experiences a woman can undergo. Breast cancer is potentially life threatening, and the diagnosis and the treatment can have dramatic effects on physical, psychological, social and economic aspects of life (Albert et al. 2004). Patients with breast cancer experience physical and emotional problems as well as problems in their family, social and work lives from the disease itself, surgery, radiotherapy, chemotherapy and hormone therapy. Meanwhile, Spagnola et al. (2003) stated that uncontrolled nausea, vomiting and weight gain have a negative effect on the quality of life of women with breast cancer who are receiving chemotherapy.

Montazeri et al. (2008) provides a several reason why QOL studies in breast cancer patients has received most attention. First, the number of women with breast cancer is increasing. It has been reported that each year over 1.1 million women worldwide are diagnosed with breast cancer and 410,000 die from the disease (Boyle and Levin, 2008). Secondly, early detection and treatment of breast cancer have improved and survivors now live longer, so studying QOL in this context is important. Thirdly, breast cancer affects women's identities and therefore studying QOL for those who lose their breasts is vital. In addition, it is believed that females play important roles as partners, wives, and mothers within any family. Thus, when a woman develops breast cancer, all members of family might develop some sort of illness.

In a study conducted by Aliasghar Ahmad Kiadaliri et al. (2012), a double blind cohort study was done to evaluate the effects of adjuvant chemotherapies on health related QOL in patients with node-positive breast cancer in Iran. Result showed that health related QOL were deteriorated during chemotherapy and improved later on. One possible explanation for the deterioration of QOL in this study is the severe side effects that incurred during treatment period.

Besides that, it was revealed that women who experienced severe neurosensory toxicity and nausea were more likely to drop out of chemotherapy treatment (Richardson et al. 2007). This is based on a study entitled 'The Role of Health-Related Quality of Life in Early Discontinuation of Chemotherapy for Breast Cancer'. This study focuses on the impact of changes in health-related QOL on early discontinuation of prescribed treatment, using data of adjuvant clinical trial that compared an intensive 16 week regimen with six cycles of cytoxan (cyclophosphamide), adriamycin (doxorubicin), and 5-flurouricil (5-FU) (CAF). Thus, they hypothesized that declines in health-related QOL during therapy would be associated with early discontinuation of chemotherapy. 164 women participated in this study and 29 of them did not complete planned treatment for the following reasons: refusal because of complication or toxicity, treatment complication, withdraw or refusal for reasons other than complications or toxicity, progression, refusal because of other disease and unknown reasons. Thus, it is obvious that complications of chemotherapy could affect breast cancer patients' choice to discontinue chemotherapy.

2.2.5 Side effects of chemotherapy

Many patients diagnosed with breast cancer receive chemotherapy treatment. Sitzia and Dikken (1997) reported that there were 71 side effects of chemotherapy and the most commonly happened are; nausea, fatigue, alopecia, difficulty in sleeping, feeling depressed, feeling physically weak, constipation and diarrhea. Literature review below describes specifically each side effects of chemotherapy that are chosen, which are; chemotherapy-induced nausea and vomiting (CINV), chemotherapy-induced appetite alteration (CIAA), chemotherapy-induced constipation (CIC), chemotherapy-induced fatigue (CIF), chemotherapy-induced alopecia (CIA), and chemotherapy-induced diarrhea (CID).

2.2.5.1 Chemotherapy-induced nausea and vomiting (CINV)

Among of all the side effects of chemotherapy, chemotherapy-induced nausea and vomiting have been commonly rated as the most unpleasant and distressing side effect. CINV may occur within hours of the administration of chemotherapy drugs (acute), or their appearance may be delayed until after the first 24 hour (delayed), and may persist for several days (Cohen et al. 2007). A learned or conditioned response known as anticipatory CINV could additionally occur prior to patients' past experience of poor controlled CINV.

Pei et al. (2012) conducted a study regarding 'Health-Related Quality Of Life Profile In Relation To Chemotherapy-Induced Nausea and Vomiting among Breast Cancer Patients' which aimed to evaluate health-related QOL status in relation to incidence and severity of CINV. This cross-sectional preliminary study using convenient sampling was conducted in two government hospitals located in the East Coast of Peninsular Malaysia. Using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30) instrument, 41 female respondents participated in this study and 90.2% of them experienced nausea even though anti emetic has been administered. 12.0% of them also reported of vomiting. Almost half of those to have reported nausea rated the intensity as 'severe' during its worst with no time more severe as any other. In terms of health-related QOL, patients with 'a lot' and 'moderate' nausea reported significantly more fatigue compared to those with little nausea. Patients with little nausea displayed better health-related QOL mainly in role, emotional, and cognitive functioning meanwhile patients who experienced vomiting reported lower health-related QOL. The researchers of this study concluded that nausea and vomiting could be one possible stressor in which their presence and severity could weaken patients' concentration and may influence their individual role and function, and could affect their overall QOL.

A study of 'Chemotherapy-Induced Nausea and Vomiting—Incidence and Impact on Patient Quality of Life at Community Oncology Settings' conducted by Cohen et al. (2007) consisted of 151 patients. The findings of this study were during cycle 1 of chemotherapy, only 33% had neither acute nor delayed CINV, of the 36% patients who developed acute CINV, 8% developed acute CINV only. Of the 59% who developed delayed CINV, 53% reported delayed only and 47% reported acute and delayed CINV. A similar pattern was seen at cycles 2 and 3 of chemotherapy. It is figured that experience of CINV at cycle 1 of chemotherapy was associated with the development of CINV at cycles 2 and 3. Meanwhile, occurrence of CINV significantly interfered with patient QOL as assessed by the Functional Index Living Emesis (FILE). Both acute and delayed CINV had a significant impact on patients' daily functioning as patients who developed both acute and delayed CINV reported that CINV significantly interfered with daily functioning. It is reported that by 6 days after treatment, patients who developed just delayed CINV reported that CINV significantly interfered with their QOL to a greater extent than did patients who did not have CINV. They concluded that better anti emetics are still needed for the control of both acute and delayed CINV, a common side effect of chemotherapy that remains a significant problem in the community oncology setting.

2.2.5.2 Chemotherapy-induced appetite alteration (CIAA)

Chemotherapy also could affect patients' appetite due to taste changes. It is revealed that food liking and appetite are adversely affected by chemotherapy (Boltong and Keast, 2012). Both of them reviewed that chemotherapy related taste changes are linked to altered number or structure of taste cell receptors, interruption of neural coding, neurotoxicity from systemic chemotherapy or detection of drug secretion in saliva. Besides that, altered flavour perception has profound effects on nutritional status, QOL and morbidity and mortality due to an association with reduced appetite; inadequate energy and nutrient intake; weight loss; malnutrition; reduced compliance with treatment regimens; reduced immunity; impaired ability or desire to procure food; diminished food appreciation; altered food relationships; changed patterns of food intake, rituals and social activities linked to eating and drinking; and emotional distress and interference with daily life (Boltong and Keast, 2012).

CIAA is also associated with oral mucositis. Oral mucositis is an acute inflammation of the oral cavity characterized by redness, swelling, and ulceration. Oral mucositis represents a major non hematologic complication of cytotoxic chemotherapy and radiotherapy associated with significant morbidity; pain, odynodysphagia, dysgeusia, and subsequent dehydration and malnutrition reduce the QOL of affected patients (Köstler *et al.*, 2001). Up to 40% of cancer patients undergoing chemotherapy will experience oral treatment-related complications. Thus, patient with oral mucositis will experience appetite alteration because of this condition. With loss of appetite, patients will experience physical weakness and weight loss, which will affect QOL.

2.2.5.3 Chemotherapy-induced constipation (CIC)

In a review regarding chemotherapy-induced constipation (CIC) by Gibson and Keefe (2006), CIC is recognized as being a mixture of reduced frequency of bowel action and increased stool consistency. Both of them stated that constipation is associated with decreased frequency and increased consistency of bowel motions, which may also be accompanied with blood and pain. Chemotherapy changes the bowel contents and it increased transit time results in bowel contents being in communication with the bowel wall for a longer time, leading to increased fluid absorption, resulting in constipation. The chemotherapeutic agents that could cause constipation are vinca alkaloids, platinums, thalidomide and hormonal agents. With constipation, QOL of breast cancer patients could be affected because of increased in physical, social and psychological distress. Constipation could affect QOL because of abdominal distention, painful cramping, flatus and excessive straining to relieve hard stool.

2.2.5.4 Chemotherapy-induced fatigue (CIF)

Chemotherapy also contributes to fatigue. But fatigue is already associated with the cancer itself. The most commonly reported symptom among cancer sufferers is fatigue. The National Comprehensive Cancer Network (NCCN) has defined cancer related fatigue as an ''unusual, persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning.'' Cancer related fatigue is thought to affect more than 70% of cancer patients with some assessments as high as 80–99% for those who are currently undergoing treatment (Jean-Pierrea et al. 2007). It can affect patients on multiple levels of psychosocial and physical functioning and usually causes a noticeable decrease in patients' QOL.

In a study conducted by Jacobsen et al. (1999), characteristics, course, and correlates of fatigue in women receiving adjuvant chemotherapy for breast cancer are investigated. They compared fatigue between women in chemotherapy group and non-cancer women (women with no history of cancer). It was revealed that changes in fatigue following the start of treatment were evident mostly on ratings that encompassed the interval between treatments. Analysis of these ratings indicated that fatigue increased in prevalence, severity, and disruptiveness after the start of treatment. More severe fatigue before the start of treatment was associated with poorer performance status and with the presence of several fatigue-related symptoms (e.g. sleep problems and muscle weakness). Increases in fatigue severity following the start of chemotherapy were associated with the continued presence of fatigue-related symptoms and the development of treatment side effects (e.g. nausea and mouth sores). This study also provides strong evidence that fatigue is a significant clinical problem during adjuvant chemotherapy for breast cancer. As predicted, the fatigue experienced by women undergoing adjuvant chemotherapy was considerably more severe than the fatigue experienced by women of similar age with no cancer history.

CIF are also associated with anemia. Mock and Olsen (2003) stated, anemia that accompanies cancer and its treatment is considered one of the most common clinical conditions associated with cancer-related fatigue.

Meanwhile, Mills et al. (2005) examined the relationship between inflammatory markers and fatigue, depressed mood and functional outcomes during chemotherapy for breast cancer. Outcomes of interest were assessed prior to the start of chemotherapy and approximately 2.5 months later at the start of cycle 4 of chemotherapy. To summarized, the study showed that chemotherapy for breast cancer leads to increased fatigue, poor mood, and reduced QOL.

2.2.5.5 Chemotherapy-induced alopecia (CIA)

Chemotherapy-induced alopecia is considered one of the most traumatic factors in cancer patient care and occurs with an estimated incidence of 65%. In Sitzia and Dikken (1997) study of the incidence and severity of side effects reported by patients receiving six cycles of 5-fluorouracil + epirubicin + cyclophosphamide (FEC) chemotherapy, hair loss was the most common side effect experienced by patients with mean incidence of 98%.

Hair loss negatively affects a patient's perception of appearance, body image, sexuality, and self-esteem. Moreover, patients feel deprived of their privacy because the hair loss is readily interpreted by the lay public as associated with having cancer especially women (Trüeb, 2009).

Trüeb (2009) also explained that the three major and most frequent toxicities of cytotoxic cancer therapy (chemotherapy) are bone marrow suppression, gastrointestinal disturbances, and alopecia, which are a consequence of direct toxic insult to the rapidly dividing cells of the bone marrow, gastrointestinal tract, and hair follicle, respectively. It is a major characteristic of the hair follicle that the epithelial compartment undergoes proliferation, with the bulb matrix cells showing the greatest proliferative activity in building up the hair shaft. The abrupt cessation of mitotic activity leads to the weakening of the partially keratinized, proximal portion of the hair shaft, a narrowing, and a subsequent breakage within the hair canal. Thus, the consequence is hair shedding that usually begins at 1 to 3 weeks and is complete at 1 to 2 months after initiation of chemotherapy (Batchelor, 2001).

CIA has a negative impact on the QOL of most cancer patients, especially breast cancer patients. In a study conducted by Richardson et al. (2007) about the role of QOL in early discontinuation of chemotherapy, they found out that there was inverse association between hair loss and early discontinuation of treatment among women who have already begun therapy. Alopecia was one of the reasons why participants decided to discontinue chemotherapy in the study. In their qualitative literature, they found out that there are multiple reports indicating that hair is a powerful defining characteristic for women's self-identity and that alopecia causes a great deal of distress. Besides that, patients with early stage cancer and a good prognosis with therapy, the anticipation of side effects and their impact on QOL was more important than the possible benefits of prolonged life with chemotherapy. They concluded that stopping treatment early may be an attempt to interrupt the process of hair loss. Women who have lost most of their hair may be more willing to pay the price for possibly prolonging survival with treatment. Thus, it could be concluded that CIA affects the QOL of breast cancer patients.

2.2.5.6 Chemotherapy-induced diarrhea (CID)

Patients undergoing chemotherapy may also experience diarrhea. Diarrhea is the passage of more than three unformed stools in 24 hours. Severe diarrhea can be debilitating and, at times, even life threatening. It contributes to dehydration, electrolyte imbalance, malnutrition, declining immune function, and pressure ulcer formation (Cherny, 2008).

Diarrhea is a well-documented side effect of many cancer treatments and has serious consequences that can include malnutrition, electrolyte imbalance, and immune attenuation. An overview of CID by Viele (2003) stated that diarrhea may involve impaired absorption in the intestine or excessive secretion of fluid and electrolytes throughout the gastrointestinal tract. These impairments generally result from direct biochemical toxicity and cell death of the rapidly dividing crypt cells of the gastrointestinal tract which is from chemotherapy. This leads to an increased proportion of immature crypt cells, which are secretory. Corresponding damage to intestinal villi, whose role is normally to absorb fluid, results in an imbalance between absorption and secretion of fluid. In addition, inflammation leads to the secretion of factors, such as prostaglandins, leukotrienes, and cytokines, which stimulate additional fluid secretion. Thus, CID is primarily a secretory diarrhea that typically occurs within 24 to 96 hours after infusion of the chemotherapy drug.

Viele (2003) also stated that chemotherapeutic agents commonly associated with diarrhea include the following types of drugs5-12: the fluoropyrimidines (eg, 5-fluorouracil and prodrugs of this compound, such as capecitabine), topoisomerase I inhibitors (eg, irinotecan, topotecan), and other agents (eg, cisplatin, docetaxel, oxaliplatin, cytarabine [ara-C]).

With CID, patients' QOL are negatively affected because of discomfort and limitation of social activities. In addition, severe diarrhea has significant physical effects on the patient, including pain, weakness, lethargy, dehydration, weight loss, electrolyte imbalance, and renal insufficiency. All of these problems, if serious enough, will require hospitalization and lead to decreased QOL for patients (Arbuckle et al. 2005).

2.3 Instruments to measure QOL

QOL assessment is gaining importance in health care and medicine. The European Organization for Research and Treatment of Cancer (EORTC) made an approach towards the QOL of cancer patients. This is because both cancer and its treatment are severely debilitating and the need to consider their impact upon health-related QOL when making patient management or treatment decisions is nowadays well accepted. The first generation of EORTC of QOL questionnaire was done on 1987. It was designed to be; cancer specific, multidimensional in nature, appropriate for self-administration, applicable for a range of cross cultural settings, and suitable for use with additional site- or treatment specific models. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30) incorporated of five functional scales, (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), a global health status/QOL scale, and a number of single items assessing additional symptoms commonly reported by cancer patients (dyspnea, loss of appetite, insomnia, constipation and diarrhea) and perceived financial impact of the disease. Subsequent versions were built upon the same basic principles, culminating in the 'core' 30-item EORTC QLQ-C30 (version 3.0) questionnaire, representing over 20 years of continuous development, refinement and validation (Fayers and Bottomley, 2002).

Besides EORTC QLQ-C30 instrument, there are also other instruments that could be used to measure the QOL especially for cancer patients. According to Kemmler et al. (1999), among the QOL instruments for cancer patients, the EORTC QLQ-C30 and the Functional Assessment of Cancer Therapy-General (FACT-G) are probably the most commonly used. Both instruments consists several subscales for specific QOL domains, which are labeled similarly; physical functioning (EORTC QLQ-C30) and physical well-being (FACT-G), social functioning (EORTC QLQ-C30) and social/family well-being (FACT-G), emotional functioning (EORTC QLQ-C30) and emotional well-being (FACT-G), and role functioning (EORTC QLQ-C30) and functional well-being (FACT-G). Kemmler et al. (1999) compare both instruments and it was found out that the items of EORTC QLQ-C30 seem to concentrate largely on physical domain which is physical functioning and clinical symptoms. Meanwhile the social functioning of EORTC QLQ-C30 focuses on the social role implication of the physical state. In contrast, the social/family well-being subscale of the FACT-G focuses on social support and emotional closeness. As a conclusion, EORTC QLQ-C30 is more closely related to physical aspects.

A study conducted by Montazeri et al. (2008) which was about the QOL of breast cancer patients before and after diagnosis uses two types of instruments. QOL was measured using the EORTC QLQ-C30 and its supplementary breast cancer questionnaire (EORTC QLQ-BR23). The EORTC QLQ-C30 is a well-known instrument for measuring quality of life in cancer patients and contains 30 items that measures five functional scales, global quality of life and several cancer related symptoms. The EORTC QLQ-BR23 is a specific questionnaire containing 23 items measuring functioning and symptoms related to breast cancer. The questionnaires were administered at three points in time: baseline, after initial treatment and one year after completion of treatment. In this study, subjects' physical functioning, global QOL and symptoms are measured by the EORTC QLQ-C30 meanwhile subjects' arm symptoms and body image are measured by EORTC QLQ-BR23.