Original Article

Impact of Chemotherapy Side Effects on Quality of Life of Thai Cancers Patients Assessed by Dermatology Life Quality Index [DLQI] and Chemotherapy induced Alopecia Distress Scale [CADS]

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Objective: To evaluate the quality of life [QoL] in dermatology aspect among Thai cancer patients who were treated with chemotherapy and had cutaneous side effects.

Materials and Methods: This was a cross-sectional descriptive study of Thai cancer patients aged >18 years old who were treated with chemotherapy at the out-patient Oncology Clinic at Vajira Hospital. All patients had complete physical examinations by a dermatologist who recorded the cutaneous manifestations. The patients who gave consent to participate were requested to do the Dermatologic Life Quality index [DLQI] and Chemotherapy-induced Alopecia Distress Scale [CADS].

Results: From 89 enrolled patients, 58 (65.2%) were female and 31 (34.8%) were male. Skin xerosis was the main cutaneous side effects. One-third of the patients reported hair abnormalities. The average DLQI score was 3.55±6.94. Twenty-seven patients (30.3%) reported small to extremely large effects of chemotherapy on their QoL. Symptoms of itching, sore, pain and embarrassment were their most common concerns whereas the personal relationship was least affected. Female patients had significant higher mean CADS than male patients ($p<0.05$). Most patients perceived that shielding hair loss affected their daily activities. We did not find a significant relationship between DLQI and CAD scores ($r = 0.089$, $p = 0.406$).

Conclusion: Cutaneous side effects of chemotherapy are very important concern in cancer patients. Skin xerosis was common problem and should not be neglected. Itching, sore, pain and embarrassment were most commonly found. Female patients were significantly affected than male in chemotherapy inducing hair loss. Knowledge sharing and counselling are needed in such patients to minimize their distress and refusal of treatment completion.

Keywords: Cancer, Chemotherapy, Quality of life, DLQI, CADS

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Cancer has become a significant health problem in Thailand, and is the leading cause of death among Thai[1,2]. Chemotherapy plays a major role in various types of cancer. Its main mechanism of action is to prevent or impede tumor growth by inhibiting cellular proliferation. Unfortunately, the chemotherapy also exerts its activity on normal cells especially rapid growing or replicating cells e.g. hair, mucosa, etc. This results in various types of side effects from chemotherapy[3,4]. Hence, the cancer patients are not only suffering from cancer itself but also from the side effects of chemotherapy. Chemotherapy with dermatologic side effects were, for example, cisplatin, cyclophosphamide, 5-fluorouracil, carboplatin, paclitaxel and doxorubicin. These side effects include any lesions of skin, hair, nail and mucosa[4].

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Cutaneous side effects of chemotherapy can be presented in various forms, such as, alopecia, pruritus, xerosis cutis, nail discolorations and mucosal hyperpigmentation. These signs and symptoms can add psychological distress to the patients aside from cancer, and sometimes are underestimated by physicians[5,6]. The psychological distress may present with a spectrum of disorders ranging from anxiety, low self–esteem, and depression. The noticeable alopecia certainly makes patients aware of their vulnerability[7,8]. Among female patients, one third of them no longer felt like woman after hair loss[5].

A lack of reliable measurement is one of the reasons why psychological assessment is frequently underestimated. At present, there are several self-reporting questionnaires that were developed and validated for measuring quality of life [QoL] in patients with skin diseases. Nevertheless, data for dermatology-specific, health-related QoL in Thai cancer patients treated with chemotherapy are still lacking.

The purpose of this study was to evaluate the QoL related to dermatologic system using Dermatology Life Quality Index [DLQI] questionnaires[9,10] and distress from alopecia using Chemotherapy induced Alopecia distress Scale [CADS][11] among Thai cancer patients who were treated with chemotherapy and have cutaneous side effects.

Materials and Methods

This study was approved by Vajira Hospital Institutional Ethical Committees. This cross-sectional descriptive study included Thai cancer patients aged ≥18 years old who were treated with chemotherapy at the out-patient Oncology Clinic at Vajira Hospital. Patients with cancers of breast, lung, liver and colon were included in the study. The participants must be able to read Thai.

Data collected were demographic features of the patients, underlying diseases, details of cancer (stage and chemotherapy regimens) were obtained from the patients' chart. Cutaneous manifestations were noted during a complete physical examination by the dermatologist (M.B.). The cutaneous manifestations assessed in this study included hair loss, and skin abnormalities of xerosis cutis, pruritus, wound, and nail abnormalities (Beau's line and nail's discolorations).

Dermatology life quality index[9,10]

The Thai version of the DLQI questionnaire, which had been tested with high validity and good reliability, was used with permission[10]. DLQI is a specific scale assessing the impact of dermatological diseases on patients' quality of life. It is self-explanatory with short and easily understood question. It is composed of 10 questions and 6 domains in the previous 7 days. The 6 domains include symptoms and feelings (2 questions), daily activities (2 questions), leisure (2 questions), work and school (1 question), personal relationships (2 questions) and treatments (1 question). The patients were instructed before answering in the self-administered questionnaires. Assistance or question clarification was available upon request.

The total DLQI score was calculated by summing the score of each question resulting in a score range of 0 to 30. The score was reversely associated with the quality of life (the higher score, the worse quality of life). The DLQI scores were categorized as follows: 0 to 1 = no effect at all, 2 to 5 = small effect, 6 to

Table 1. DLQI Questionnaires[9]

Feelings	1) Over the last week, how itchy, sore, painful or stinging has your skin been?
	2) Over the last week, how embarrassed or self conscious have you been because of your skin?
Daily activities	3) Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?
	4) Over the last week, how much has your skin influenced the clothes you wear?
Leisure	5) Over the last week, how much has your skin affected any social or leisure activities?
	6) Over the last week, how much has your skin made it difficult for you to do any sport?
Work and School	7) Over the last week, has your skin prevented you from working or studying? If "No", over the last week how much has your skin been a problem at work or studying?
Personal relationship	8) Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives?
	9) Over the last week, how much has your skin caused any sexual difficulties?
Treatment	10) Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time?

10 = moderate effect, 11 to 20 = very large effect, 21 to 30 = extremely large effect[9]. Table 1 shows DLQI record form.

Chemotherapy-induced alopecia distress scale [CADS][11]

CADS is a reliable and valid instrument for measuring distress due to chemotherapy-induced alopecia in cancer patients. It was first developed and validated for assessing the distress breast cancer patients experienced from chemotherapy induced alopecia. The 4 factors analyzed reflected the 4 subdomains of physical, emotional, activity, and relationship[11].

Concurrent and discriminant validities were tested for correlations among body image, overall QoL, and self-esteem. Total of 17 items in 5 domains were measured: physical (2), emotional (6), daily activity (6), relationship (3). CADS was self-administered by the patients who were instructed to indicate on a four-point Likert scale on each statement (1 = not at all, 2 = a little, 3 = quite a bit, and 4 = very much). Total scores were calculated by summing responses of all items. The score was reversely associated with distress due to Chemotherapy-induced alopecia (the higher score, the higher level of distress). Table 2 shows CADS record form.

Statistical analysis

All analyses were performed using SPSS software version 22.0 (IBM Corp, Armonk, NY). Continuous data were described as mean and standard deviation or number with percentage. The statistical comparisons of the DLQI and CADS between gender were performed using Fisher's exact test or Mann-Whitney U test as appropriate. Correlation analysis between DLQI and CADS was performed using Spearman's Rank Correlation Coefficient. The *p*-value <0.05 was considered to be statistically significant.

Results

From a total of 89 patients participated in the study, 58 were female (65.2%). Table 3 shows demographic data of the patients. Fifty-six patients (63%) were unemployed, half of them were married and lived together with their couple. Eight-six (76%) have underlying diseases; most of which was hypertension. More than half of the patients in this study had breast cancer (53 patients or 59.6%). More than half (53.9%) had no available data of stage. Table 4 shows cancer information of the patients studied. The duration of cancer diagnosis was 3.06 ± 1.97 years. Treatment for cancer patients may be only chemotherapy (40 patients or 44.9%) or together with surgical treatment (49 patients or 55%). Chemotherapeutic agents varied from doxorubicin, cyclophosphamide, pacitaxel, docetaxel, carboplatin, gemcitabine, etoposide, capecitabine, or oxaliplatin.

Table 5 shows cutaneous manifestations of the patients. Among 28 patients (31%) who concerned about their hair abnormalities, 14 patients (16%) had total baldness with the other 10 (12%) experienced some

Table 2. CADS questionnaires[10]

Physical	1) The area is itching.
	2) The area is burning or prickling resulting pain.
Emotional	3) I feel different from others.
	4) I am dissatisfied with my appearance.
	5) I lose confidence about the future.
	6) I am easily irritated and stressed.
	7) I feel depressed.
	8) I feel lonely.
Activity	9) I have difficulty doing personal care such as bath and make-up.
	10) I experience limitations doing leisure activities.
	11) I feel sicker because of my hair loss.
	12) I do not like it when people find that I have cancer because of my hair loss.
	13) I have problems going out shopping and to restaurants.
	14) I always wear a wig or scarf to hide hair loss.
Relationship	15) I am worried about relationships with family and friends.
	16) I am worried about my relationship with my spouse or partner.
	17) I am worried about my sexual relationship with spouse or partner.

Table 3. Demographic data of subjects

	n (%)
Gender	
Male	31 (34.8)
Female	58 (65.2)
Occupation	
No occupation	56 (62.9)
Employee	15 (16.9)
Officer	2 (2.2)
State enterprise staff	1 (1.1)
Private business	8 (9.0)
Others	7 (7.9)
Education	
No education	2 (2.2)
Primary school	44 (49.4)
Secondary school	21 (23.6)
Bachelor or above	16 (18.0)
Unknown	6 (6.7)
Marriage status	
Married and live together	48 (53.9)
Married with no live together	3 (3.4)
Single	19 (21.3)
Divorced	9 (10.1)
Widow	10 (11.2)
Medical illness	
Diabetes mellitus	14 (15.7)
Hypertension	32 (36.0)
Hyperlipidemia	19 (21.3)
Heart disease	10 (11.2)
Cerebrovascular disease	5 (5.6)
Others	16 (18.0)

Table 4. Cancer data of subjects

	n (%)
Type of cancer	
Lung	21 (23.6)
Colon	10 (11.2)
Liver	5 (5.6)
Breast	53 (59.6)
Stage of cancer	
I	4 (4.5)
II	6 (6.7)
III	13 (14.6)
IV	18 (20.20)
Unknown	48 (53.9)
Duration of cancer (year)	3.06±1.97
Number of chemotherapy (times)	6.07±6.98
Surgical intervention	
No	40 (44.9)
Yes	49 (55.1)

degree of hair loss. Approximately one third of the patients who had skin xerosis over body, face and leg had associating pruritus. Nail abnormalities were found in 19 patients (21%). Only few had chronic cutaneous ulcers. Mucosal hyperpigmentation were not found.

This study found 62 patients stated that the cutaneous involvements had no effect on their DLQI score while 27 reported some effects. Table 6 shows quality of life of the patients according to their gender. More female had impact on QoL from chemotherapy than male (34.5% vs. 22.6%). However, the difference was not statistical significant. Very large and extremely large DLQI scores cutaneous side effects were found in 12 patients: more common with female (n = 9) and with breast cancer (n = 7).

Regarding the CADS, female had higher mean score of CADS than male (more affected): 18.5 (range, 17 to 22) vs. 17.5 (17 to 18), $p = 0.035$. Figure 1 presents that feeling issue (question#1, 2) was the most affected whereas personal relationship issue (question# 8, 9) was least affected. Sixteen people who felt that hair loss affected working and studying had the lowest mean score (score = 1).

Figure 2 demonstrates the results of each question in CADS. From 28 patients whose QoL were affected by hair loss, 20 patients (71%) reported that wearing wig or scarf disturbed their daily activity most. Of note, only 1 patient reported that her hair loss affected the relationship with partner. However, this study did not find significant correlation between DLQI and CADS ($r = 0.089$, $p = 0.406$) (Figure 3).

Discussion

The use of chemotherapeutic agents is increasing in frequency and varieties of drugs or regimens to treat cancer patients. Cutaneous side effects of these agents could range from common

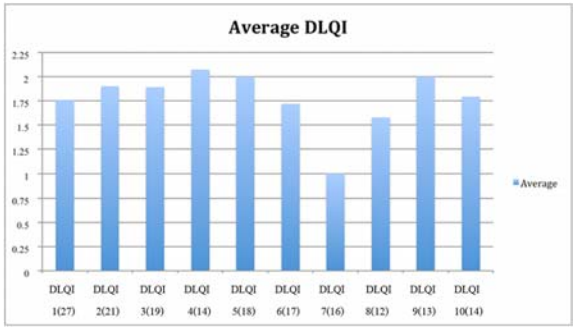
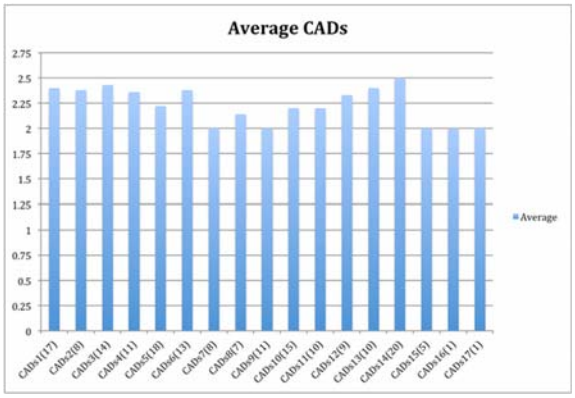


Figure 1. Average DLQI score in affected patients studied.



* Datas presented on parenthesis shows affected patients studied

Figure 2. Average CADS in affected patients studied.

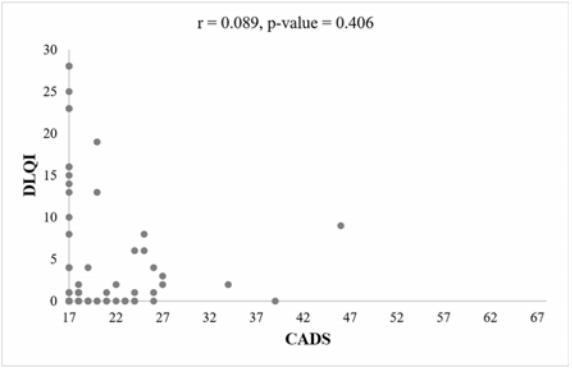


Figure 3. Relationship between DLQI and CADs

events, such as, hair loss, skin xerosis, skin hyperpigmentation, folliculitis, or other unusual abnormalities[4,8]. The present study found that xerosis was the main problems in the patients. Skin hyperpigmentation and folliculitis were not found. Xerosis as a common skin lesion in Thai cancer patients in this study was similar to that found in the study of Menon et al[4]. However, the rate was much higher in the present study, 92% compared to only 26% in their study. The difference might lie on the percentage calculation because the authors' study assessed each part of the body (leg, body and face) whereas their study presented figures of the whole body. Moreover, their study found 22% of skin hyperpigment which was not evidenced in this study. This might lie on the concern and recognition of the hyperpigmentation in the patients in each study.

Chemotherapy inducing alopecia [CIA] is a common side effect of several chemotherapeutic regimens[8,12]. Certain cancer drugs especially taxane compound can suppress new hair growth, so the patients frequently have hair loss or even baldness. Most patients especially female found that their images were important and perceived that baldness as a pitiful condition[13]. Several studies reported that hair loss was one of the most traumatizing and distressing experiences for both cancer patients and their family[14-16]. Previous studies from other countries reported moderate to severe distress among patients with cancer and alopecia that the conditions significantly deteriorated their body image, well-being and depression[16-18]. One study reported that the large majority of patients considered alopecia from chemotherapy to be among the most distressing problems[16]. The duration of stress could last from 3 weeks to 6 months after treatment[16]. The long duration of stress may also have impact on, aside from their physical and psychological effects, their social engagement[17]. Previous studies reported that alopecia was an indicator of their sickness exposed to public or other non-acquaintance, so loss of their privacy[13,15]. Some of the patients had strategies to cope their stress with social withdrawal and isolation[17]. Most of the patients with hair loss (71%) coped their problems with various methods to improve their confidence such as cap or scarf. Nevertheless, very little body change was preferred to make them confident to do the daily activity.

Generally, CADS is directly associated with body image and should be related to overall QoL[11]. However, the present study showed minimal emotional impact with CIA and CIA inducing distress was poorly correlated with DLQI of the patients. To our knowledge, there were no previous study about correlation between DLQI and CADS before. This study is consistent with other previous report in term of no differences of dermatological QoL between men and women[14].

Dermatologic quality of life of individuals in each study may vary due to socioeconomic, educational status, the type or regimens of chemotherapy provoking the side effects[18,19]. This study collected data in a governmental hospital which serves various socioeconomic classes of patients. Most of the patients in this study had education of mid level (under bachelor) and were unemployed, so the issues of cutaneous manifestation or alteration of images may not have high impact especially when the affected parts were not severe. Another different issue from previous studies was this study yielded data from Thai patients. The race and cultural difference were also possible factors

influencing on outcomes.

The authors were aware of few limitations in this study. Data in this study collected from the out-patient oncology clinic, hence, the extent of impact may not be as severe as those who sought for consultation in dermatology clinic. Heterogeneous features of cancer types, stage of disease, chemotherapeutic regimens may also influence the overall results. Nevertheless, the present study was the first study which evaluated the impact of chemotherapy on dermatologic system using DLQI and CADS among cancer patients in Thailand. Detailed subgroup analysis to control possible confounding factors would be explored in our further study.

Table 5. Cutaneous manifestation of subjects

Hair	
Baldness	14
Hair loss	10
Androgenic alopecia	1
Telogen effuvium	1
Alopecia areata	2
Skin	
Body	
Xerosis	28
Pruritus	15
Ulceration	1
Leg	
Xerosis	27
Pruritus	13
Ulceration	1
Face	
Xerosis	27
Pruritus	7
Ulceration	1
Nail	
Beau'sline	7
Nail discoloration	12

Conclusion

The present study found modest impact of chemotherapeutic dermatologic side effects on QoL of the Thai cancer patients. Skin xerosis was a common problem lesion whereas ichting, sore, pain and embarrassment were common symptoms or complaints. Female patients were significantly distress than male in aspects of hair loss, but not QoL. The physician and caregiver should be cautious of dermatologic side effects in order to improve the patient's quality of life. This might eventually increase the adherence of cancer treatment with chemotherapeutic agents.

What is already known on this topic?

Cutaneous manifestations of cancer patients treated with chemotherapy can be presented in various forms. These alterations are usually associated with psychological distress. Although there are several available instruments to evaluate the impact of dermatologic side effects of chemotherapy, a lack of reliable measurement is one of the reasons that psychological assessment is not seriously undertaken.

What this study adds?

Xerosis was a common skin problem among cancer patients having chemotherapy. Feeling and embarrassment were most affected issues. Female patients were more significantly affected than male regarding hair loss. These data should be incorporated

Table 6. Quality of life of subjects

	Total (n = 89)		Male (n = 31)		Female (n = 58)		*p*-value*
DLQI							0.836
No effect	62	69.7	24	77.4	38	65.5	
Effect							
Small effect	9	10.1	3	9.7	6	10.3	
Moderate effect	6	6.7	1	3.2	5	8.6	
Very large effect	7	7.9	2	6.5	5	8.6	
Extremely large effect	5	5.6	1	3.2	4	6.9	
CADS score			17.5 (17 to 18)		18.5 (17 to 22)		0.035

Data are presented as n (%) or median (interquatile range)
*Comparison between male and female. Mann-Whitney U test for DLQI score and CADS score and Fisher's exact test for DLQI

to routine clinical practices to focus on the chemotherapy side effects and to provide appropriate counseling and treatment.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Imsamran W, Chaiwarawattana A, Wiangnon S, Pongnikorn D, Suwanrungrung K, Sangrajrang S, et al. Cancer incidence in Thailand. In: Cancer incidence in Thailand. Cancer in Thailand. Vol. VIII, 2010-2012. Bagkok: Cancer Registry Unit, National Cancer Institute Thailand; 2015. p. 5-72.
2. Khunaprema T, Attasara P, Sriplung H, Wiangnon S, Sangrajrang S. Cancer incidence in Thailand. In: Cancer in Thailand. Volume VII, 2007-2009. Bagkok: Cancer Registry Unit, National Cancer Institute Thailand; 2013. p. 8-76.
3. Trueb RM. Chemotherapy-induced alopecia. Semin Cutan Med Surg 2009;28:11-4.
4. Menon A, Handattu S, Shetty J, Girisha BS. Study of cutaneous adverse effects of cancer chemotherapy. Clin Dermatol Rev 2018;2:19-24.
5. Macquart-Moulin G, Viens P, Bouscary ML, Genre D, Resbeut M, Gravis G, et al. Discordance between physicians' estimations and breast cancer patients' self-assessment of side-effects of chemotherapy: an issue for quality of care. Br J Cancer 1997;76:1640-5.
6. Meyerowitz BE, Sparks FC, Spears IK. Adjuvant chemotherapy for breast carcinoma: psychosocial implications. Cancer 1979;43:1613-8.
7. Remlinger KA. Cutaneous reactions to chemotherapy drugs: the art of consultation. Arch Dermatol 2003;139:77-81.
8. Susser WS, Whitaker-Worth DL, Grant-Kels JM. Mucocutaneous reactions to chemotherapy. J Am Acad Dermatol 1999;40:367-98.
9. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)-a simple practical measure for routine clinical use. Clin Exp Dermatol 1994;19:210-6.
10. Kulthanan K, Jiamton S, Wanitpahakdeedecha R, Chantharujikaphong S. The validity and reliability of the Dermatology Life Quality Index (DLQI) in Thais. Thai J Dermatol 2004;20:113-23.
11. Cho J, Choi EK, Kim IR, Im YH, Park YH, Lee S, et al. Development and validation of Chemotherapy-induced Alopecia Distress Scale (CADS) for breast cancer patients. Ann Oncol 2014;25:346-51.
12. Can G, Yildiz M, EmelEmine □zdemir RN. Supportive care for chemotherapy induced alopecia: challenges and solutions. Clin Res Infect Dis 2017;4:1048.
13. Villasante AC, Herskovitz I, Mauro LM, Jimenez JJ. Chemotherapy-induced alopecia. J Clin Investigat Dermatol 2014;2:8.
14. Can G, Demir M, Erol O, Aydiner A. A comparison of men and women's experiences of chemotherapy-induced alopecia. Eur J Oncol Nurs 2013;17:255-60.
15. Lemieux J, Maunsell E, Provencher L. Chemotherapy-induced alopecia and effects on quality of life among women with breast cancer: a literature review. Psychooncology 2008;17:317-28.
16. Luoma ML, Hakamies-Blomqvist L. The meaning of quality of life in patients being treated for advanced breast cancer: a qualitative study. Psychooncology 2004;13:729-39.
17. van den Hurk CJ, Mols F, Vingerhoets AJ, Breed WP. Impact of alopecia and scalp cooling on the well-being of breast cancer patients. Psychooncology 2010;19:701-9.
18. Freedman TG. Social and cultural dimensions of hair loss in women treated for breast cancer. Cancer Nurs 1994;17:334-41.
19. Rosman S. Cancer and stigma: experience of patients with chemotherapy-induced alopecia. Patient Educ Couns 2004;52:333-9.