Multiple Symptoms and Their Influences on Health-Related Quality of Life in Adolescents with Hematologic Malignancies Undergoing Chemotherapy

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Abstract: An understanding of symptom experiences is essential to improve patient outcomes. This cross-sectional, predictive correlation study investigated the symptom experiences and predictive abilities on health-related quality of life in 94 Thai adolescents with hematologic malignancies undergoing chemotherapy at the Division of Pediatric Hematology and Oncology at three tertiary care hospitals in Bangkok. The Theory of Unpleasant Symptoms was used as the conceptual framework. Data were collected through a Demographic and Medical Record Form, the Modified Memorial Symptom Assessment Scale, and the Pediatric Quality of Life Inventory.

The findings demonstrated that participants experienced several symptoms. The most prevalent were pain, nausea/vomiting, lack of appetite, worrying and hair loss. In addition, feeling sad, hair loss, and sleeping difficulty significantly influenced health-related quality of life and explained 33.2% of variances. The findings support the evidence of concurrent multiple symptoms. The implications for nursing practice are that nurses should attend to the symptoms of sadness, hair loss and sleeping difficulty in this patient group, and design interventions to manage these symptoms to improve their quality of life during chemotherapy treatment.

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Introduction

Hematologic malignancies (HM) consisting of acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic myeloid leukemia (CML), Non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL) represent a significant proportion of pediatric malignancies.[1-3] International patterns of cancer among adolescents (15-19 years) demonstrate that HM incidence comprises approximately one-third of all cancers, with a slightly higher prevalence among males

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than females, ranging from 27-42 per million in males and 18-41.5 per million in females.[2] In Thailand, the incidence of HM in adolescents (10-19 years) during 2010 and 2012 was 84 (37.8%),and 73 (30.4%) cases per million in male and female respectively.[3] Leukemia and lymphoma are usually treated with a combination of chemotherapy agents administered in cycles, which may last for months or even years.[4-5] Although success in the refinement of chemotherapy agents has improved survival rates for most childhood HM to above 80%,[5] adolescents report numerous symptoms during treatment.[6-8]

Adolescence is a transitional period that includes immense physical, cognitive and psychosocial changes. Receiving a diagnosis and treatment of cancer interrupts the normative developmental process, with impaired physical function[9], which increases dependence on parents and restrictions on social activity[10], having uncertainty in illness[11], disruptions in education and employment[10], and lack of peer or sexual relationships.[9-10] Regardless of cancer diagnoses, adolescents undergoing chemotherapy have significantly poorer health-related quality of life (HRQoL) than their peers.[12-13] The inconsistent findings[6-8,] in terms of the most prevalent, severe, frequent or distressing symptoms were results of heterogeneous samples with mixed developmental age groups and types of cancer diagnoses.[14-15] To date the literature on symptom experience[16-21] and HRQoL[22-23] in adolescents with HM is limited. In addition, the participants do not represent a homogeneous sample in terms of age group,[16-20] thus the appraisal of symptom experiences may differ.[24-25] In addition, there is limited knowledge regarding the key symptoms that influence HRQoL of adolescents with HM[.26-28] Thus, this study aimed to describe the occurrence, severity and distress dimensions of symptoms, and determine the predictive ability of symptoms to explain HRQoL in Thai adolescents with HM receiving treatment.

Conceptual Framework and Review of Literature

The Theory of Unpleasant Symptoms (TOUS)[14] was used as a conceptual framework to guide this study. This theory focuses on symptoms experience, with multiple symptoms occurring together. Symptoms can vary in intensity, timing, level of distress perceived and quality. The antecedents of symptoms experience are physiological, psychological and situational factors.[14] In the TOUS, symptoms experience is hypothesized to affect performance, including functional and cognitive activities.[15] Activities of daily living, social interaction and role performance are categorized as functional performance, while knowledge and ability to learn, problem solving, and abstract and logical thinking are categorized as cognitive performance.[15] Since quality of life (QoL) incorporates both functional and cognitive ability, it can be considered to be an indicator of both types of performance.[15]

The TOUS depicts the nature of symptoms experience and the influences of these symptoms on the above-mentioned patient outcomes, including QoL. However, the effects of symptoms on performance are just beginning to be identified.[15] In the current study, the physiological factor was controlled by including participants in a specific developmental stage, with similar cancer diagnoses, undergoing the same treatment (adolescents diagnosed with blood cell tumors undergoing chemotherapy). In the study framework, symptoms experience was hypothesized to occur concurrently, with each symptom described in terms of severity, frequency and distress. In addition, symptoms experience was hypothesized to affect HRQoL.

The symptoms experienced by patients with HM have not been well documented in existing literature.[16-21, 29-31] Few studies included adults undergoing chemotherapy,[29-31] and only one was conducted in Thailand.[31] However, adolescents' illness appraisal is different from that of adults in terms of specific concerns, including the impact of the illness on body image, fear, loss of control and reluctance to disclose pain.[24] The symptoms that disturb this unique group may be not the same as in adults. For adolescents with HM, the existing evidence also reveals a limited number of studies investigating symptoms in this group.

Four studies focused on few certain symptoms including pain,[16] difficulty sleeping[16-19] and lack of energy[16-19] experienced by adolescents undergoing chemotherapy for ALL. Adolescents reported pain, difficulty sleeping, and lack of energy over a three-day course of vincristine.[16] Difficulty sleeping and lack of energy were investigated in adolescents undergoing chemotherapy for ALL in three studies.[17-19] Adolescents reported difficulty sleeping[17-19] with an average 12 times or more nocturnal awakenings per night.[17] Lack of energy increased when dexamethasone was given.[17-19] In addition, families viewed sleep as a problem for their child (22-42%), and many more (43-53%) felt that a lack of energy was a problem.[18] Combining both child and parent reports indicated that dexamethasone disrupted sleep quality and exacerbated a lack of energy.[18-19]

One study conducted in Thailand investigated the occurrence of multiple symptoms in adolescents undergoing chemotherapy for ALL.[20] Most participants reported hair loss, nausea/vomiting, lack of energy, mouth sores and itching (71.9-90.6%).[20] However, the current evidence examined symptoms experience in a mixed group of adolescents that included younger children.[16-20] Children's developmental stage influences their illness appraisal, affecting their ability to recall and rate symptoms using traditional self-reported instruments;[24-25] hence, the findings cannot represent the symptom experience among adolescents with HM undergoing chemotherapy.

To date, there is a dearth of literature investigating symptoms experience in relation to a specific developmental stage of adolescents with HM. In addition, a small amount of literature described the negative relationship between symptoms experience and HRQoL in adolescents with variety of cancer diagnoses.[12,26-28] However, the key predicting symptoms for HRQoL in this unique group is underestimated. Discovering the most influencing symptoms can guide nurses to develop integrative interventions for improving patients' HRQoL during chemotherapy treatment.

Research Questions

1. What is the symptoms experience of adolescents with HM undergoing chemotherapy in terms of occurrence, severity and distress of symptoms?
2. What symptom experiences influence HRQoL of Thai adolescents with HM receiving chemotherapy?

Methods

Design

A cross-sectional predictive correlation design was used for this study.

Sample and Setting

The sample comprised participants being treated with HM at three tertiary care hospitals in Bangkok. All settings provide treatment and care services based on the national protocol for the treatment of childhood cancers,[4] which means that the types and doses of chemotherapy regimens used for cancer treatment were similar across settings. The criteria for inclusion in the study were: 1) 10-18 years of age, 2) diagnosed with HM (including ALL, AML, CML, APL, HL and NHL), 3) receiving chemotherapy, and 4) able to speak and read Thai. The exclusion criteria included cognitive disabilities, too weak to answer the questionnaires, and if they were being treated with oxygen.

The sample size was estimated using G*Power program version 3.1.9. Based on the squared multiple correlation (R^2) from a previous study by Johnson[28] ($R^2 = 0.14$). Using the F test (linear multiple regression), the effect size calculated from R^2 equals 0.16, $\alpha = 0.05$, b = 0.80 and 11 independent variables; therefore, the calculated sample size was 114 cases. Over seven months of the data collection period, 96 adolescents were approached, of whom two refused to participate due to one girl perceiving too much fatigue and a boy not wanting to participate. Therefore, a total of 94 participants was recruited. The post-hoc calculated power (1-b) equals 0.996, given an alpha of 0.05 with an effect size (d = 0.44) calculated from the multiple regression analysis ($R^2 = 0.33$). Thus, our sample size of 94 was considered appropriate for the planned analysis.

Ethical Considerations

Prior to conducting fieldwork, the study was approved by the Institutional Review Boards of Faculty of Medicine at Siriraj Hospital, Mahidol University and each setting (COA no.Si740/2015, IRB/RTA 1808/2558, REC.043/2559). Each potential participant and their parents were informed about the purposes of the study, confidentiality and anonymity issues, and the right to withdraw at any point in the study with no effect on their treatment or hospital services. The adolescents were required to give their own consent and to have parental permission to participate.

Instruments:

The Demographic and Medical Record form was used to assess participants' personal characteristics (in terms of age, sex, education, school leave for treatment, living arrangement, and source of support) and disease characteristics including type of HM, stage of illness (only lymphoma), week/month diagnosed, diagnosis status (first diagnosis, relapsed disease), status of disease (completed remission or not), present treatment, daily medications and type of chemotherapy regimens. The questionnaire was developed by the researchers based on the previous studies.[32]

The Modified Memorial Symptom Assessment Scale (MSAS7-12) was used to measure both physical and psychological symptoms.[33] It consists of eight symptoms to specify the presence of particular symptom in the last 48 hours. The following are examples of questions: "Did you feel more tired yesterday or today than you usually do?" (occurrence), "How tired did you feel?" (intensity), "How long did it last?" (duration/frequency), and "How much did being tired bother you or trouble you?" (distress).

The Thai version of MSAS 7-12 translated by Pongsing et al.[32] was used with the addition of three symptoms: hair loss, fever and diarrhea/constipation, therefore the modified MSAS 7-12 included 11 symptoms. Symptom occurence was coded as present (1) and absent (0). Symptom severity and frequency were coded as 1 (a little or a very short time) to 3 (very much or almost all the time). Symptom distress was coded as 0 (not at all) to 3 (very much). The scoring of each symptom is achieved by averaging the scores of all dimensions.[34] The symptom score for each symptom ranged between 0-3, with higher scores indicating greater symptom experience. The Cronbach's alpha coefficients for the pilot and main study were 0.91 and 0.87 respectively

Pediatric QoL Inventory Generic Core Scale (PedsQL 4.0) was used to measure HRQoL.[13] It consists of 23 items that evaluate four dimensions of HRQoL: physical functioning (eight items), emotional functioning (five items), social functioning (five items), and school functioning (five items). The developmentally appropriate forms for children aged 8-12 and 13-18 years were used in this study. The initial question asked adolescents about how much of a problem this been for them in the past month. The following are examples of questions in each domain: "It is hard for me to take a bath or shower by myself" (physical functioning), "I feel sad or blue" (emotional functioning),"Other teens do not want to be my friend" (social functioning), and "It is hard to pay attention in class" (school functioning)

A translated Thai version of PedsQL 4.0 exists in Thailand.[35] The response scale for each item ranged from 0 "never a problem" to 4 "almost always a problem". The scores for each item were linearly transformed to a numerical scale of 0-100 as follows: 0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0. The total score or overall HRQoL is the sum of all of the items in the four dimensions of HRQoL, with higher scores indicating better HRQoL. The Cronbach's alpha coefficients for the pilot and main study were 0.831 and 0.808 respectively. Before starting the study, permission to use the scales was obtained from all developers.[13, 32-33, 35]

Data Collection

Data were collected at both pediatric oncology wards and outpatient chemotherapy units by the primary investigator (PI). All participants who met the inclusion criteria were approached by the staff nurses at each setting. When the participants and their parents agreed to participate in the study, the PI provided information regarding study purposes and procedures to the participants. Subsequently formal written assent and consent forms were obtained from the adolescents and their parents. Most adolescents completed three questionnaires by answering each item read to them by the PI during 15-20 minutes.

Data Analysis

Descriptive statistics were used to analyze participants' demographic and clinical characteristics, symptoms experience as well as HRQoL. Stepwise multiple regression analysis was used to examine the predictability of the symptom experience of 11 symptoms on HRQoL. The assumptions of normality, linearity, homoscedasticity and multi-collinearity were met for this multiple regression analysis.

Results

Participant Characteristics

Of the 94 adolescents with HM undergoing chemotherapy, the majority was male (76.6%), with a mean age of 13 years, attending primary school (59.6%). Approximately half of participants did not attend school during their treatments (52.1%). The majority of the participants were living with parents in their own homes (73.4%). Nearly all participants had a caregiver (98.9%), with a small majority (52.1%) identifying their mothers as their primary support while receiving chemotherapy. Nearly half (48.9%) described the support they received from their caregiver in terms of preparing meals, providing tepid sponge baths, administering home medication, and giving assistance to walk when they were too fatigued. The participants' disease characteristics are presented in **Table 1**.

Table 1 Disease Characteristic of the Participants (n = 94)

Characteristics		N	%
Type of cancer			
Leukemia	ALL	57	60.6
	AML	7	7.4
	APL	1	1.1
	CML	8	8.5
Lymphoma	HL	4	4.3
	NHL	17	18.1
Diagnosis status			
First diagnosis		74	78.7
Relapsed Disease		20	21.3
Months following diagnosis (months)			
1-6 months		30	31.9
7-12 months		15	16.0
13-18 months		12	12.8
19-24 months		9	9.6
More than 24 months		28	29.8
Status of disease			
Completed remission		78	83.0
Not completed remission		14	14.9
Not identified		2	2.1

Symptoms Experience

The results showed that the participants reported 4.7 symptoms (SD = 2.35). According to **Table 2**, the five most common symptoms that occurred during treatment in the past two days were pain (69.1%), nausea/vomiting (51.1%), lack of appetite (47.9%), worrying (42.6%), and hair loss (41.5%). The mean symptom severity scores ranged from 1.39-2.00 of a possible score of 1-3. The mean symptom frequency scores ranged from 1.28-1.83 of a possible score 1-3. The mean symptom distress scores ranged from 0.42-1.27 of a possible score of 0-3. Lack of appetite (mean = 2.00 ±0.79) was the most severe symptoms, while diarrhea/constipation was most frequent symptoms (mean = 1.83 ±0.69). Lastly, nausea/vomiting was the most distressing symptom (mean 1.27 ±1.04).

Table 2 Mean and standard deviations for each symptom scores, and total number of symptoms.

Symptom	N	Occurrence (%)	Frequency (1-3)	Severity (1-3)	Distress (0-3)	symptom scores
			Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Pain	65	69.1	1.46 (0.59)	1.75 (0.64)	0.88 (1.02)	1.36 (0.59)
Nausea/vomiting	48	51.1	N/A	1.62 (0.67)	1.27 (1.04)	1.45 (0.81)
Lack of appetite	45	47.9	N/A	2.00 (0.79)	0.82 (0.98)	1.41 (0.72)
Worrying	40	42.6	1.55 (0.72)	1.50 (0.59)	0.85 (0.83)	1.30 (0.61)
Hair loss	39	41.5	N/A	1.95 (0.88)	0.90 (1.27)	1.42 (0.81)
Sleeping difficulty	36	38.3	N/A	N/A	1.17 (1.02)	1.17 (1.03)
Itching	36	38.3	1.28 (0.56)	1.39 (0.64)	0.42 (0.77)	1.03 (0.53)
Lack of energy	35	37.2	1.69 (0.72)	1.86 (0.69)	1.26 (1.01)	1.60 (0.66)
Diarrhea/ constipation	30	31.9	1.83 (0.69)	1.73 (0.69)	0.70 (.95)	1.39 (0.52)
Fever	29	30.9	1.76 (0.69)	1.69 (0.66)	0.97 (1.11)	1.47 (0.55)
Feeling sad	24	25.5	1.46 (0.59)	1.54 (0.59)	0.96 (0.95)	1.32 (0.46)
Total Number of symptoms	1-10					4.7 (2.35)

Note: N/A: not applicable.

HRQoL in Adolescents with HM undergoing chemotherapy

The average total scores of HRQoL was 72.24 (SD = 13.65). Considering four dimensions of HRQoL, social functioning of participants demonstrated the highest score (77.87, SD = 17.80), while school functioning demonstrated the lowest (mean = 66.98, SD = 15.7).

The Influence of Symptoms Experience on HRQoL

Associations between symptoms experience and HRQoL are illustrated in **Table 3**. Bivariate correlation analysis between each symptom scores and HRQoL revealed that feeling sad and difficulty sleeping were negatively correlated to HRQoL at a moderate level ($r = -.458$, $p < 0.01$; $r = -.339$, $p < 0.01$). The remaining symptoms were negatively correlated to HRQoL of participants at a low level. **Table 4** presents multivariate analysis data for the symptoms experience of three symptoms predicting HRQoL. Using stepwise regression analysis, feeling sad (ß = -0.395, $p < 0.001$), hair loss (ß = -0.246, $p < 0.05$), and sleeping difficulty (ß = -0.235, $p < 0.05$) demonstrated significant effects on the HRQoL. Together they explained 33.2% of variance in HRQoL of adolescents with HM undergoing chemotherapy.

Table 3 Intercorrelations for HRQoL and 11 symptoms

Measure	1	2	3	4	5	6	7	8	9	10	11	12
1. HRQoL	_											
2. Feeling sad	-.458**	_										
3. Sleeping difficulty	-.339**	.207*	_									
4. Hair loss	-.290**	.058	.089	_								
5. Worry	-.275**	.201	.325**	.135	_							
6. Nausea/Vomiting	-.247*	.237*	.156	.248*	.152	_						
7. Lack of energy	-.244*	.386**	.178	.067	.253*	.348**	_					
8. Itching	-.212*	.342**	.200	.007	.239*	.180	.218*	_				
9. Pain	-.209*	.112	.169	.152	-.034	.165	.281**	.069	_			
10. Lack of appetite	-.160	-.014	.222*	.313**	-.008	.226*	.047	.045	.332**	_		
11. Diarrhea/ Constipation	-.148	.010	-.06	.08	-.016	.258*	.118	.096	.173	.163	_	
12. Fever	.008	.084	-.018	.153	-.159	.297**	.303**	-.054	.224*	.247*	.200	_

Note * Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.001 level (2-tailed).

Table 4 Regression Analysis Summary for the overall HRQoL of adolescents with HM receiving treatment

Predictor	R	R^2	R^2 change	F change	B	Beta	t	p value
Feeling sad	0.458	0.210	0.21	24.443	-8.659	-0.395	-4.48	0.000
Hair loss	0.529	0.280	0.07	8.807	-0.383	-0.246	-2.84	0.006
Sleeping difficulty	0.576	0.332	0.05	7.104	-3.780	-0.235	-2.66	0.009

Discussion

Symptom Experiences of Adolescents with HM Undergoing Chemotherapy

Adolescents with HM reported experiencing multiple, multidimensional symptoms, the most prevalent of which was pain experienced over the previous two days. Young patients with chronic illness tend to be more bothered by intrusive procedures.[24] More than half of participants (69%) in this study reported pain, with approximately half of them (46%) identifying bone marrow aspiration or injection/venous puncture as **the** major source of their pain. In addition, headache, eye pain, neuropathic pain, abdominal pain and muscle/joint pain were mentioned. Side effects of chemotherapy regimens resulted pain as well; for example, vincristine contributes to neuropathic pain and jaw pain, while methotrexate contributes to abdominal pain.[4] Previous investigation of HM in Thailand did not include pain in the symptom assessment tool.[20] However, these findings were similar to previous abroad studies, pain was most commonly occurring symptoms during chemotherapy among adolescents with ALL[16] and those with mixed diagnoses of cancer.[6-8] Compared with adolescents with HM,[16] more variety types of pain were found in this study; as a result of samples recruited in any phase of chemotherapy treatment, of whom 26.6% were in the induction or consolidation phase, in which high doses and combinations of chemotherapy regimens were used. Therefore oncology nurses must be knowledgeable about the basic pathophysiology of cancer pain and treatment side effects. In addition, the World Health Organization's Pain Relief Ladder[36] as well as non-pharmacological interventions should be incorporated into pain management strategies for every adolescent with cancer.

The most severe symptom experienced by adolescents with HM in this study was lack of appetite. All-Trans-Retinoic-Acid and bleomycin, commonly used in HM treatment, resulted in dry mouth and oral mucositis,[4] which can decrease patient appetite.[37] Contrary to a previous study in the HM group, a lack of appetite was not reported among most severe symptoms during ALL chemotherapy.[20] Most researchers omitted "lack of appetite" when measuring symptoms in adolescents with HM.[16-21] However, the findings of this study are congruent with a qualitative study of patients' HM experiences, which found that adolescents with ALL focused on "being able to eat", which was among common themes they raised when asked "what makes a good day for you during treatment?"[23] This finding suggests that lack of appetite was the most severe symptom, which must be considered in nursing intervention strategies. Reduced food intake in cancer patients commonly results from treatment-associated with nausea and/or vomiting, gastrointestinal dysfunction and changes in the way food tastes.[37] During rapid growing and changes in growth and biologic development of adolescents, the aspect of energy balance should be maintained to ensure adequate growth and their tolerance for cancer treatments.

The most frequent symptom reported by adolescents in this study was diarrhea/constipation. This finding cannot compared to previous studies, since these symptoms were not included in symptom assessment among adolescents with HM.[16-21] For childhood cancer patients, diarrhea is mostly caused by infections, drug reactions, dietary alterations, inflammatory bowel, or graft versus host disease.[37] Chemotherapy-induced diarrhea can be potential side effect of cytarabine, cyclophosphamide and methotrexate.[4,37] Causes of constipation can be due to decreases in gastric motility secondary to vinca alkaloids and opioid analgesics, tumor compression, decreased mobility, anorexia and changes in toileting patterns during hospitalization.[4,37] The explanation for intermittent of constipation among participants in this study might be a result of vincristine, which was primarily used in treatment phase of most participants during the data collection period. This finding suggests that assessment of diarrhea/constipation is needed when caring for this cancer population during chemotherapy.

The most distressing symptom was nausea/vomiting. This finding was inconsistent with a previous study by Kuntana et al.,[20] which found that adolescents reported oral mucositis as the most distressing symptom, and that fewer participants (17.2%) perceived that nausea/vomiting distressed them. The possible explanation for this inconsistent finding may be related to a greater variety of chemotherapy regimens being used for HM in the current study, whereas only chemotherapy regimens for ALL were used in the previous study.[20] For adolescents, more than half of their chemotherapy regimens were judged to be moderately to severely emetogenic. In spite of receiving antimetic regimens, uncontrolled nausea was reported among half of participants.[38] Various factors, can contribute to nausea and vomiting in pediatric oncology patients, including the disease process, constipation, abdominal obstruction, infections and medications.[37] The findings of this study identify adolescent patients' need for both pharmacological and non-pharmacological interventions to alleviate this symptom.

In conclusion, these findings revealed the multidimensional characteristic of symptom experiences and confirm previous studies on HM groups[20,30] and heterogenous types of cancer,[6-8] which found that the patients perceived symptoms differently and in varying degrees across dimensions. The symptoms identified as the most prevalent were not necessarily the most severe, frequent or distressing. The findings of multiple symptoms experienced by adolescents with HM undergoing chemotherapy in this study can add up to the evidence support of the TOUS.[14]

The Influence of Symptoms Experience on HRQoL

Eight symptoms were negatively correlated with HRQoL; however, only three were found to be the main predicting factors of HRQoL, accounting for 33.2% of the variance in HRQoL in adolescents with HM undergoing chemotherapy: feeling sad, hair loss and sleeping difficulty.

Feeling sad was found to be the strongest predictor of HRQoL ($\beta = -0.395$, $p < .001$). The adolescents who reported greater feelings of sadness were more likely to have poorer HRQoL. Our findings are similar to those reported in adolescent ALL survivors[22] and adolescents receiving chemotherapy for various types of cancer.[26] Feeling sad was one of symptoms that occurred frequently during chemotherapy cycles for HM,[20, 30] it is a potential symptom of depression if experiencing it with anxiety, empty mood, feeling hopeless, irritability, decreased energy, or lack of appetite most of the day, nearly every day, for at least two weeks.[39] Mood disturbances (including feeling sad together with worry and anxiety) have been limited to descriptive studies, with a dearth of intervention studies.[7] This finding signals the urgent need for focused study on symptoms management in this unique population.

Hair loss was found to be another predictor of HRQoL ($\beta = -0.246$, $p < .05$). The adolescents who reported greater hair loss were more likely to have poorer HRQoL. These findings are congruent with adolescents diagnosed with cancer in Sweden, those who reported hair loss were more likely to have a less satisfying life.[40] Hair loss was one apparent change during chemotherapy which adolescents were particularly concerned with, because it made them feel "ugly", "different", and "less normal" than before treatment.[7] Hair loss was one of the significant impacts whereby cancer interfered in their lives.[7,40] At this age, the adolescents pay more specific concern to the impact of illness on body image.[24-25] This may help explain the deteriorative effect of this symptom on HRQoL in adolescents.

Sleeping difficulty was also found to be a predictor of HRQoL ($\beta = -0.235$, $p < .05$). The adolescents who reported greater sleeping difficulty were more likely to have poorer HRQoL. Our finding was consistent with the previous study by Gordijn et al.[22] In addition, difficulty sleeping was among the most prevalent symptoms in adolescents receiving chemotherapy for mixed cancer diagnoses.[6-7] Adolescents reported more severe sleep problems during chemotherapy when compared to healthy adolescents or to themselves before their cancer diagnoses, and receiving chemotherapy made them have a worse sleep pattern.[7] Besides, there is less attention exploring interventions to prevent or manage this interfering symptom in adolescents receiving cancer chemotherapy;[7] therefore, this finding addresses the recognized need for integrated nursing interventions.

In spite of worrying, nausea/vomiting, lack of energy, itching, and pain were negatively correlated to HRQoL, and they were not found to be the predicting factors of HRQoL. A possible explanation is that, most of these symptoms (worrying, nausea/vomiting, itching, lack of energy) are correlated with predicting symptoms already in the equation or some of them correlated with each other (pain and lack of energy), consequently, they are not selected into the regression equation of HRQoL. (see Table 3). These findings were consistent with the previous study by Arslan,[26] which found that experience of pain, and lack of energy, and constipation were not associated with HRQoL.

In conclusion, the results of this study demonstate that multiple symptoms have negatively accumulated effects on HRQoL in adolescents with HM undergoing chemotherapy, which supported the proposition of the TOUS in that the experience of multiple symptoms can have an impact on the individual's HRQoL. The influences of feeling sad, hair loss, and sleeping difficulties had major impacts on the HRQoL of adolescents with HM undergoing chemotherapy, which can enhance health professionals' understandings when evaluating and providing care for this specific cancer population. This may challenge nurses to initiate multidisciplinary collaborating programs to manage this group of symptoms in order to increase patients' HRQoL during treatment.

Strengths and Limitations

To the author's knowledge, this is the first reported study determining the symptoms experience and their predictive power on HRQoL in adolescents with HM undergoing chemotherapy in Thailand. However, the researcher recognizes some limitations of this study. The effect of confounding variables in influences of multiple symptoms on HRQoL including chemotherapy regimens and drugs used for symptom management, were not controlled in this study. In addition, the cross-sectional study may limit understanding of the patterns of symptoms over the illness trajectory.

Conclusions and Implications for Nursing Practice

The findings of this study have provided evidence on the symptoms experience of adolescents with HM undergoing chemotherapy. Individual symptoms were perceived in varying degrees regarding severity, frequency and distress dimension. In addition, feeling sad, hair loss, and sleeping difficulty were found to significantly influence HRQoL among this population. This study's results can guide nurses to deliberate on nursing interventions designed holistically to alleviate these multiple symptoms and improve adolescents' HRQoL during treatment.

Since feeling sad was the strongest predictor of HRQoL in adolescents with HM undergoing chemotherapy, psychological interventions should address nursing care guidelines during chemotherapy cycles. Future research should employ a longitudinal design to investigate the pattern of multiple symptoms over time during treatment trajectory, and to develop the intervention program based on the predicting symptoms on HRQoL to test its effectiveness for improving HRQoL in adolescents with HM undergoing chemotherapy.

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References

1. Burkhamer J, Kriebel D, Clapp R. The increasing toll of adolescent cancer incidence in the US. PLoS ONE. 2017;12(2):e0172986. PubMed PMID: PMC5325567.
2. Stiller CA. International patterns of cancer incidence in adolescents. Cancer Treatment Reviews. 2007;33 (7):631-45.
3. Imsamran W, Chaiwerawattana A, Wiangnon S, Pongnikorn D, Suwanrungrung K, Sangrajrang S, Buasom R. Cancer in Thailand Vol.VIII, 2010-2012. Thailand: National Cancer Institute; 2015.
4. The Thai Pediatric Oncology Group, The Thai Society of Hematology, The Thai National Health Security office. National protocol for the treatment of childhood cancers 2014. Bangkok: M Print Cooperation; 2014.
5. Place AE, Frederick NN, Sallan SE. Therapeutic approaches to haematological malignancies in adolescents and young adults. British Journal of Haematology. 2014;164 (1):3-14.
6. Baggott C, Dodd M, Kennedy C, Marina N, Miaskowski C. Multiple symptoms in pediatric oncology patients: A systematic review. Journal of Pediatric Oncology Nursing: Official Journal of the Association of Pediatric Oncology Nurses. 2009;26(6):325-39.
7. Erickson JM, MacPherson CF, Ameringer S, Baggott C, Linder L, Stegenga K. Symptoms and symptom clusters in adolescents receiving cancer treatment: A review of the literature. International Journal of Nursing Studies.; 2013; 50(6): 847-69

8. Kestler SA, LoBiondo-Wood G. Review of symptom experiences in children and adolescents with cancer. Cancer Nursing. 2012;35(2):E31-49. PubMed PMID: 21760492. Epub 2011/07/16. eng.
9. Buckner TW, Wang J, DeWalt DA, Jacobs S, Reeve BB, Hinds PS. Patterns of symptoms and functional impairments in children with cancer. Pediatric Blood Cancer. 2014; 61(7):1282-8.
10. Taylor RM, Pearce S, Gibson F, Fern L, Whelan J. Developing a conceptual model of teenage and young adult experiences of cancer through meta-synthesis. Int J Nurs Stud. 2013; 50(6): 832-46
11. Tiwaree C, Kantawng S, Wonghongkul T, Lertwatthanawilat W. Predicting Factors of Uncertainty in Illness Among Children with Leukemia Undergoing Chemotherapy [Internet]. Pacific Rim International Journal of Nursing Research. 2016;20(1):33-4. Available from: //www.tci-thaijo.org/index.php/PRIJNR/article/view/24453
12. Baggott CR, Dodd M, Kennedy C, Marina N, Matthay KK, Cooper B, et al. An evaluation of the factors that affect the health-related quality of life of children following myelosuppressive chemotherapy. Supportive Care in Cancer. 2011; (3):353-61.
13. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P. The PedsQL in pediatric cancer: Reliability and validity of the Pediatric Quality of Life Inventory Generic Core Scales, multidimensional Fatigue Scale, and Cancer Module. Cancer. 2002;94(7):2090-106.
14. Lenz ER, Pugh LC, Milligan RA, Gift A, Suppe F. The middle-range theory of unpleasant symptoms: An update. Advances in Nursing Science. 1997; 19(3):14-27.
15. Lenz R, Gift A, Pugh C, & Milligan A. Unpleasant symptoms. In Peterson J, Bredow S, **editors.** Middle range theories: Application to nursing research Philadelphia: Lippincott Williams & Wilkins; 2013., pp. 69-81.
16. Gedaly-Duff V, Lee KA, Nail LM, Nicholson HS, Johnson KP. Pain, sleep disturbance, and fatigue in children with leukemia and their parents: A pilot study. Oncology Nursing Forum. 2006;33(3):641-6.
17. Sanford SD, Okuma JO, Jianmin PAN, Deo Kumar S, West N, Farr L, et al. Gender differences in sleep, fatigue, and daytime activity in a pediatric oncology sample receiving dexamethasone. Journal of Pediatric Psychology. 2008;33(3):298-306.
18. Zupanec S, Jones H, Stremler R. Sleep habits and fatigue of children receiving maintenance chemotherapy for ALL and their parents. Journal of Pediatric Oncology Nursing. 2010;27(4):217-28.
19. Hinds PS, Hockenberry MJ, Gattuso JS, Srivastava DK, Tong X, Jones H, et al. Dexamethasone alters sleep and fatigue in pediatric patients with acute lymphoblastic leukemia. Cancer. 2007;15 110(10):2321-30.
20. Kuntana K, Soomlek S, Treevanich A. Unpleasant symptoms and symptom management among children with acute lymphoblastic leukemia undergoing chemotherapy. Journal of Nursing and Health Care. 2005;23(2):17-27 [in Thai].
21. Docherty SL, Sandelowski M, Preisser JS. Three months in the symptom life of a teenage girl undergoing treatment for cancer (English). Research in nursing & health. 2006 01/2006;29(4):294-310.
22. Gordijn MS, van Litsenburg RR, Gemke RJ, Huisman J, Bierings MB, Hoogerbrugge PM, et al. Sleep, fatigue, depression, and quality of life in survivors of childhood acute lymphoblastic leukemia. Pediatric Blood & Cancer. 2013;60(3):479-85.
23. Momani TeG, Mandrell BN, Gattuso JS, West NK, Taylor SL, Hinds PS. Children's Perspective on Health-Related Quality of Life During Active Treatment for Acute Lymphoblastic Leukemia. Cancer Nursing. 2015;38(1): 50-9.
24. Algren C. Family-centered care of the child during illness and hospitalization. In Hockenberry MJ, Wilson D. , Wong's nursing care of infants and children (10th ed.). St. Louis: Mosby Elsevier;2015, pp. 1046-1082.
25. Linder LA. Developmental diversity in symptom research involving children and adolescents with cancer. J Pediatr Nurs. 2008;23(4):296-309.
26. Arslan FT, Basbakkal Z, Kantar M. Quality of life and chemotherapy-related symptoms of Turkish cancer children undergoing chemotherapy. Asian Pacific journal of cancer prevention : APJCP. 2013;14(3):1761-8. PubMed PMID: 23679270. Epub 2013/05/18. eng.
27. Williams PD, Williams AR, Kelly KP, Dobos C, Gieseking A, Connor R, et al. A symptom checklist for children with cancer: the therapy-related symptom checklist -- children. Cancer Nursing. 2012;35(2):89-98.

28. Johnson, A. Adolescents receiving chemotherapy: Sleep, symptoms, and quality of Life [Doctoral Dissertation]. Portland: Oregon Health & Science University; 2008. [cited 2017 June 30]. Available from http://digitalcommons.ohsu.edu/etd.
29. Manitta V, Zordan R, Cole-Sinclair M, Nandurkar H, Philip J. The symptom burden of patients with hematological malignancy: A cross-sectional observational study. Journal of Pain & Symptom Management. 2011; 42(3):432-42.
30. Suedee N., Pongthavornkamol, K. , Sriyuktasuth, A., & Siritanaratkul, N. Symptom experiences and their influences on functional status in hematological malignancy patients receiving chemotherapy. Journal of Nursing Science. 2015; 33(2):29-40[in Thai].
31. Zimmermann C, Yuen D, Mischitelle A, Minden MD, Brandwein JM, Schimmer A, et al. Symptom burden and supportive care in patients with acute leukemia. Leukemia research. 2013;37(7):10.1016/j.leukres.2013.02.009. PubMed PMID: PMC3808347.
32. Pongsing Y, Thai mothers' reports of symptoms in young children receiving chemotherapy. [Dissertation]. Portland: Oregon Health & Science University. 2010. [cited 2017 June 30]. Available from http://digitalcommons.ohsu.edu/etd.
33. Collins JJ, Devine TD, Dick GS, Johnson EA, Kilham HA, Pinkerton CR, et al. The measurement of symptoms in young children with cancer: The validation of the Memorial Symptom Assessment Scale in children aged 7-12. Journal of Pain & Symptom Management. 2002;23(1):10-6.
34. Portenoy RK, Thaler HT, Kornblith AB, Lepore JM, Friedlander-Klar H, Kiyasu E, et al. The Memorial Symptom Assessment Scale: An instrument for the evaluation of symptom prevalence, characteristics and distress. European Journal of Cancer. 1994;30(9):1326-36.
35. Sritipsukho P, Wisai M, Thavorncharoensap M. Reliability and validity of the Thai version of the Pediatric Quality of Life Inventory 4.0. Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation. 2013;22(3):551-7.
36. World Health Organization. Persisting pain in children package: WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses. [Switzerland]: World Health Organization; 2012 [cited 2018 Jan 28]. Available from: http://apps.who.int/iris/bitstream/10665/44540/1/9789241548120_Guidelines.pdf
37. Maloney AM. Gastrointestinal tract. In: Tomlinson D, Kline N. Pediatric oncology nursing: Advanced clinical handbook. New York: Springer; 2010, pp. 354-375.
38. Holdsworth MT, Raisch DW, Frost J. Acute and delayed nausea and emesis control in pediatric oncology patients. Cancer. 2006;106(4):931-40. PubMed PMID: 16404740. Epub 2006/01/13. eng.
39. National Institute of Mental Health. Depression. 2016 [updated 2016 October; cited 2018 Jan 20]. Available from https://www.nimh.nih.gov/health/topics/depression/index.shtml
40. Enskar K, von Essen L. Physical problems and psychosocial function in children with cancer. Paediatric Nursing. 2008;20(3):37-41.

ประสบการณ์ด้านอาการและอิทธิพลของอาการต่อคุณภาพชีวิตในผู้ป่วยวัยรุ่นโรคมะเร็งระบบโลหิตวิทยาระหว่างได้รับยาเคมีบำบัด

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บทคัดย่อ: การทำความเข้าใจในประสบการณ์ด้านอาการเป็นสิ่งสำคัญยิ่งในการพัฒนาผลลัพธ์ด้านผู้ป่วย การวิจัยภาคตัดขวางวิเคราะห์ความสัมพันธ์เชิงทำนายครั้งนี้มีวัตถุประสงค์เพื่อศึกษาประสบการณ์ด้านอาการและอิทธิพลของอาการต่อคุณภาพชีวิต ซึ่งรับรู้โดยผู้ป่วยวัยรุ่นโรคมะเร็งระบบโลหิตวิทยา 94 ราย ที่กำลังได้รับการรักษาด้วยยาเคมีบำบัด ณ แผนกกุมารเวชศาสตร์โลหิตวิทยาและมะเร็งในโรงพยาบาลระดับตติยภูมิ 3 แห่งในกรุงเทพฯ โดยใช้แนวคิดอาการที่ไม่พึงประสงค์ของเลนซ์และคณะ เป็นกรอบในการศึกษา เก็บข้อมูลโดยให้ผู้ป่วยตอบแบบสอบถามประกอบด้วย แบบบันทึกข้อมูลส่วนบุคคล โรคและการรักษา แบบบันทึกอาการจากโรคและการรักษา และแบบสอบถามคุณภาพชีวิตสำหรับเด็ก

ผลการศึกษาพบว่า กลุ่มตัวอย่างเกิดอาการหลายอาการระหว่างการรักษา อาการที่พบบ่อยที่สุดได้แก่ อาการเจ็บปวด คลื่นไส้/อาเจียน ไม่อยากอาหาร รู้สึกวิตกกังวล และอาการผมร่วง นอกจากนี้พบว่า อาการรู้สึกเศร้า ผมร่วง และนอนหลับยาก มีอิทธิพลต่อคุณภาพชีวิตโดยรวมอย่างมีนัยสำคัญทางสถิติ โดยอธิบายร้อยละ 33.2 ของความผันแปรของคุณภาพชีวิต ผลการศึกษายืนยันหลักฐานเชิงประจักษ์ของการเกิดอาการหลายอาการ และโดยเฉพาะอย่างยิ่งได้เสนอแนะบทบาทของพยาบาลในการเอาใจใส่ต่ออาการรู้สึกเศร้า ผมร่วง และนอนหลับยากในผู้ป่วยวัยรุ่นโรคมะเร็งระบบโลหิตวิทยาเพื่อเพิ่มคุณภาพชีวิตของผู้ป่วยกลุ่มนี้ระหว่างได้รับยาเคมีบำบัด

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คำสำคัญ: เคมีบำบัด คุณภาพชีวิต โรคมะเร็งระบบโลหิตวิทยา ประสบการณ์ด้านอาการ

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