

# Depression and health-related quality of life after discharge and associated factors in childhood cancer patients in Japan

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## Summary

We identified the prevalence of depression and quality of life (QOL) of Japanese children with childhood cancer after discharge using the Birleson Depression Self-rating Scale for Children (DSRS-C) and the Pediatric Quality of Life Inventory (PedsQL). Subjects were 118 caregivers who raised children ages 2-18 with childhood cancer; subjects resided in suburban districts of Japan and completed instruments after their children were discharged. Multiple regression analysis of data collected from 105 respondents revealed that lower PedsQL scores correlated with more problems in life at school and at home, an increased frequency of hospital visits, less cooperation within the family, and higher DSRS-C scores. To ensure the QOL of children with childhood cancer, outpatient nurses need to encourage children to psychosocially adapt after discharge, periodically screen children during outpatient treatment using instruments such as the DSRS-C, and conduct preventive interventions for children who meet screening criteria and their families before they suffer from adaptation disorders and offer multilateral psychosocial assistance in cooperation with a multidisciplinary care team.

**Keywords:** Childhood cancer, health-related quality of life (HRQOL), depression, family cohesion, Japan

## 1. Introduction

Childhood cancer is a generic term for malignant neoplasms that occur in childhood, with hematopoietic malignant tumors such as leukemia and malignant lymphoma accounting for approximately half of childhood cancers, followed by other solid tumors, such as a brain tumor, neuroblastoma, Wilms' tumor, and rhabdomyosarcoma (1). The recent development of new treatment strategies has greatly improved clinical

outcomes, with a 5-year disease-free survival rate of approximately 80% for patients with acute lymphoid leukemia (ALL), 50% for those with acute myeloid leukemia (AML), 85-100% for those with malignant lymphoma (non-Hodgkin's disease), 92-100% for those with neuroblastoma (Stages 1 and 2), 80-96% for those with Wilms' tumor, and 75% for those with rhabdomyosarcoma; this survival rate differs, however, depending on the stage and the status of metastasis and recurrence of disease (2). The number of individuals who have experienced childhood cancer has increased in recent years.

The treatment of childhood cancer requires long-term hospitalization and imposes physical and psychological burdens on children with childhood cancer (3). The treatment of leukemia involves four stages: *i*) induction therapy to achieve a response (a reduction in leukemia cells to less than 5% in the bone marrow), *ii*) intensification therapy, *iii*) CNS

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prophylaxis, and *iv*) maintenance therapy. Generally, childhood cancer patients in Japan require nearly one year of hospitalization and two to three years of outpatient treatment (2). In the event of a solid tumor, surgical excision of the primary tumor is frequently performed before the chemotherapy mentioned earlier and is often combined with radiotherapy. A lumbar puncture and bone marrow aspiration performed at each stage of treatment and intense side effects of therapeutic agents (*e.g.* nausea, fatigue, and headaches) place a physical burden on the children. Changes in body image such as hair and weight loss and living apart from one's family and friends impose a psychological burden on the children. The families of such children also have physical burdens (*e.g.* going back and forth between home and the hospital, housekeeping, caring for siblings, nursing of the ill child in the hospital) and psychological burdens (the child's fear of having cancer and caring about other family members, especially siblings) and fatigue (4,5).

Many children who have completed painful anti-cancer treatment may suffer direct or indirect damage (late effects), such as treatment-related damage to the cranial nerves and the heart, functional deficits following tumor resection, post-transfusion hepatitis, and failure to grow; these children may also have various psychosocial problems (6-8). As a result, various studies have been conducted regarding the quality of life (QOL) and psychosocial adaptation of childhood cancer survivors (9).

In Japan, investigations of the QOL of childhood cancer survivors/children have just started. A Japanese version of the Pediatric Quality of Life Inventory (PedsQL) was developed in 2010; PedsQL assesses health-related QOL (HRQOL), and the reliability and validity of the Japanese version have been tested (10). The background for the treatment of childhood cancer and the cultural background of the parent-child relationship/family relationship in Japan differ from those in other countries. In Japan, for example, a child is often informed of his or her illness, but many parents still hesitate to inform children of the fact that they are ill (11). Children are often poorly and improperly informed of their illness. In fact, children are informed of their illness at the age of 15, on average, and in many instances younger children are not informed of the fact that they have cancer. Previous studies conducted in Japan on the same topic have reported on the mental health, anxiety, and adaptive process of children after discharge (12,13). The reality of outcomes has been determined, but relevant factors that will guide interventions and assistance have not been analyzed.

This study looked at family cohesion (the degree of cooperation and family functioning) during hospitalization and after discharge from the viewpoint of "a child living with his or her family". This study sought to assess the prevalence of depression and

HRQOL of the children and associated factors by focusing on the psychosocial adaptation of children with childhood cancer after discharge.

## 2. Methods

### 2.1. Subjects

Subjects were children who made periodic visits to the Pediatric Department of A University Hospital and the Hematology and Oncology Department of B Pediatric Hospital and their primary family caregivers. The inclusion criteria were: *i*) being a child from primary school age to age 18 who had been hospitalized for childhood cancer or being a family caregiver who primarily provided care to a child over 2 years of age during the child's hospitalization for cancer and *ii*) being able to complete a physical and psychological questionnaire (in about 20 minutes) administered by the child's primary physician.

### 2.2. Data collection

Potential subjects were recruited by primary physicians using the inclusion criteria. Subjects who consented to participate in the study were provided with detailed information about the study and asked to complete a questionnaire. The subjects could answer the questionnaire either at the hospital while waiting for consultation or payment or at home. Subjects who chose to fill in the questionnaire at the hospital were asked to submit it to the Outpatient Department, and subjects who completed the questionnaire at home were asked to return it by mail using the nearest post office.

The questionnaire included items on *i*) the characteristics of the children and their families, *ii*) the prevalence of depression and the QOL of the children after discharge, and *iii*) possible factors related to *ii*).

Subject characteristics of children and their families were determined by asking family caregivers about their child's current age and about "the number of family members" and "siblings".

The prevalence of depression and the QOL of the children were determined by administering the Japanese version of the Birlson Depression Self-rating Scale for Children (DSRS-C) to the children and the Japanese version of the Pediatric Quality of Life Inventory™ (PedsQL™) to the family caregivers. The DSRS-C is an 18-item self-rating scale that was developed by Birlson to screen for the presence of depression in children (14) and was translated in Japanese by Murata *et al.* (15) (*ex.* 'I sleep very well' – item 2; 'I feel like crying' – item 3; 'I have horrible dreams' – item 14; 'I feel very lonely' – item 15). The children are asked to rate their own state during the last week on a 3-point scale. The answers are scored from 0 to 2 with a total score of 36 points. The cut-off score is set at 16 points.

The PedsQL is a 23-item measure that was designed for parents by Varni *et al.* (16) to evaluate the HRQOL of children (*ex.* 'lifting something heavy' – item 4; 'feeling sad or blue' – item 11; 'getting along with other children' – item 14; 'missing school because of not feeling well' – item 22). The Japanese version has been tested for reliability and validity by Kobayashi & Kamibeppu (10). The current study used the overall score on the PedsQL, which includes the following sub-constructs: physical, emotional, social, and school functioning. The higher the total score, the better the HRQOL.

Family caregivers were asked about their child's "age of onset", "illness (type of cancer)", "type of treatment given", "status of recurrence", "frequency of hospital visits", "whether or not [the] child has been informed of his or her illness", the "frequency of visits by family caregivers", the "sense of burden felt by family caregivers while providing care", the "degree of cooperation within the family", "support from outside the family" during the child's hospital stay, and "sequelae in [the] child". Caregivers were also asked "whether or not [the] child will be able to return to school", "problems encountered by [the] child in daily life", "limitations imposed on [the] child's daily life", "whether or not [the] child has been informed of his or her illness", the "sense of burden felt by family caregivers while providing care", the "degree of cooperation within the family", and "support from outside the family" after discharge. The sense of burden and the degree of cooperation were assessed using a Likert five-point scale. Furthermore, the caregivers were asked to complete the FACES SKGIV to assess family functioning (17).

The children were asked about "the hardest and most distressing time and event that [they] experienced while ill", and their "bounce back" to the present was assessed on a six-point face scale. Data were collected from June 2010 to March 2011.

### 2.3. Data analysis

Questionnaires with more than 90% of the questions completed were defined as valid responses and were subjected to analysis.

Descriptive statistics were determined by calculating distributions, means, and standard deviations of responses for each variable regarding subject characteristics, the child's depression and QOL, and possible factors associated with the child's QOL. Next, univariate analysis of PedsQL scores and each possible associated factor was performed prior to multivariate analysis for factors associated with each outcome. Spearman rank-correlation coefficients were used for continuous variables, a *t*-test for dichotomous variables, and analysis of variance for polychotomous variables. If no multicollinearity was found among related factors, then multiple regression analysis was performed with

PedsQL scores as objective variables and possible associated factors as explanatory variables.

A statistical analysis package, PASW Statistics 18.0 for Windows (SPSS Japan Inc.), was used for analysis. The significance level was set at 5%.

### 2.4. Ethical considerations

Potential subjects were informed verbally and in writing that: *i*) the subject's cooperation with the study was entirely voluntary, *ii*) a child would not be penalized in terms of medical care or treatment if the caregiver did not cooperate with the study, *iii*) consent to participate in the study could be withdrawn at any time during the study; and *iv*) when the study results were published the privacy of subjects would be strictly protected.

The study was approved by the medical ethics review board of the University of Tsukuba and Ibaraki Children's Hospital.

## 3. Results

### 3.1. Summary of subject characteristics

Of 118 family caregivers who consented to participate in the study, 105 completed more than 90% of the questionnaire. Of 100 children with childhood cancer, 90 completed more than 90% of the questionnaire; the remaining children were preschool age or severely ill.

Table 1 shows the characteristics of children and their caregivers and families. The most common "illness (type of cancer)" was acute lymphoblastic leukemia (40 patients), followed by acute myeloid leukemia (12 patients) and neuroblastoma (7 patients). "The age of onset" was  $5.5 \pm 3.7$  (mean  $\pm$  S.D.) years and the "current age" was  $11.5 \pm 8.2$  (mean  $\pm$  S.D.) years. The "length of hospital stay" was  $11.2 \pm 6.9$  (mean  $\pm$  S.D.) months, and 15 patients experienced "recurrence" and 3 had repeated recurrence. All of the children received chemotherapy, 39 underwent surgery, 33 underwent radiotherapy, and 17 underwent transplantation. After admission, the children lived with  $3.7 \pm 1.4$  (mean  $\pm$  S.D.) family members and had  $1.2 \pm 0.9$  (mean  $\pm$  S.D.) siblings.

### 3.2. Current status of depression and HRQOL of children with childhood cancer

Table 2 shows the mean scores, S.D., and the range of DSRS-C and PedsQL scores.

### 3.3. Factors associated with the HRQOL of children with childhood cancer

The original plan was to conduct two sets of multiple regression analyses using the DSRS-C scores and the PedsQL scores shown in Table 2 as objective variables,

**Table 1. Subject Characteristics (n = 105)**

Variables	n/mean ± S.D.	%/range
Children		
Current age	11.5 ± 8.2	2-18
Age of onset	5.5 ± 3.7	0-17
Illness (type of cancer) [multiple answers permitted]		
ALL	40	38.1%
Ph+ALL	5	4.8%
ALL with Down syndrome	1	1.0%
AML	12	11.4%
Neuroblastoma	7	6.7%
Rhabdomyosarcoma	6	5.7%
ML	6	5.7%
LCH	4	3.8%
Hodgkin's lymphoma	3	2.9%
Medulloblastoma	3	2.9%
APL	2	1.9%
AL	2	1.9%
Non-Hodgkin's lymphoma	2	1.9%
Burkitt lymphoma	2	1.9%
Embryoma	2	1.9%
Germ cell tumor	2	1.9%
Wilms' tumor	1	1.0%
T-cell lymphoma	1	1.0%
Retinoblastoma	1	1.0%
Rimitive neuroectodermal tumor	1	1.0%
Pineoblastoma	1	1.0%
Osteoblastoma	1	1.0%
Lymphocytic leukemia	1	1.0%
Germinoma	1	1.0%
Brain tumor	1	1.0%
Type of treatment given		
Chemotherapy	105	100.0%
Radiotherapy	33	31.4%
Surgery	39	37.1%
Transplantation	17	16.2%
Other	2	1.9%
Status of recurrence		
Yes	15	14.3%
No	90	85.7%
Frequency of hospital visits per year	9.1 ± 7.3	1-48
Return to school		
Yes	92	87.6%
No	13	12.4%
Sequelae		
Yes	37	35.2%
No	68	64.8%
Problems in daily life		
Currently	33	31.4%
Temporarily in the past	44	41.9%
No	26	24.8%
Limitations on daily life		
Yes	15	14.3%
No	90	85.7%
Bounce back from the most distressing time (1-6)	5.1 ± 1.0	2-6
Family caregivers		
During hospitalization		
Frequency of visits		
Stayed for 24 hours	17	16.2%
All the time while the child was awake	28	26.7%
Almost the entire time during the day	30	28.6%
A few hours during the day	29	27.6%
Was the child informed of his/her illness		
Yes	47	44.8%
Somewhat (but not that he/she had cancer)	35	33.3%
No	21	20.0%

*To be continued*

Continued

Variables	n/mean ± S.D.	%/range
Sense of burden while providing care		
Yes, very much so	18	17.1%
Yes	33	31.4%
Somewhat	39	37.1%
No	13	12.4%
No, none at all	1	1.0%
Cooperation within the family		
Frequent	66	62.9%
Sometimes	26	24.8%
On occasion	8	7.6%
Not much	3	2.9%
None at all	2	1.9%
Support from outside the family		
Frequent	58	55.2%
Sometimes	20	19.0%
On occasion	10	9.5%
Not much	13	12.4%
None at all	4	3.8%
After discharge to present		
Was the child informed of his/her illness		
Yes	61	58.1%
Somewhat (but not that he/she had cancer )	19	18.1%
No	21	20.0%
Sense of burden while providing care		
Yes, very much so	2	1.9%
Yes	8	7.6%
Somewhat	26	24.8%
No	39	37.1%
No, none at all	30	28.6%
Cooperation within the family		
Frequent	39	37.1%
Sometimes	44	41.9%
On occasion	18	17.1%
Not much	3	2.9%
None at all	1	1.0%
Support from outside the family		
Frequent	40	38.1%
Sometimes	19	18.1%
On occasion	20	19.0%
Not much	17	16.2%
None at all	8	7.6%
Family members		
Number of family members living with the child	3.7 ± 1.4	1-7
Number of siblings	1.2 ± 0.9	0-4
FACES-cohesion		
Enmeshed	55	52.4%
Connected	40	38.1%
Separated	10	9.5%
Disengaged	0	0.0%
FACES-adaptability		
Rigid	8	7.6%
Structured	75	71.4%
Flexible	18	17.1%
Chaotic	4	3.8%

Abbreviations: ALL, acute lymphatic leukemia; AML, acute myelogenous leukemia; ML, malignant lymphoma; LCH, Langerhans cell histiocytosis; APL, acute promyelocytic leukemia; AL, acute leukemia.

but multiple regression analysis was performed once using the scores of PedsQL as objective variables and subject characteristics and other possible relevant factors as explanatory variables since there was a significant negative correlation between PedsQL scores and DSRS-C scores ( $r = -0.29, p < 0.01$ ).

Table 3 shows factors associated with the HRQOL

of children with childhood cancer. More problems in life at school and at home (standard partial regression coefficient [sb] =  $-0.298, p = 0.009$ ), an increased frequency of hospital visits (sb =  $-0.281, p = 0.017$ ), less cooperation within the family (sb =  $0.247, p = 0.034$ ), and higher DSRS-C scores ( $\beta = -0.221, p = 0.025$ ) were correlated with lower PedsQL scores (F =

**Table 2. Scores on the Japanese versions of PedsQL™ and DSRS-C**

	No. of items	Score range	Mean ± S.D.	Range
Scores on the Japanese version of PedsQL™	34	0-100	79.32 ± 18.14	(n = 105) 38.1-100
Scores on the Japanese version of DSRS-C	18	0-36	6.98 ± 4.17	(n = 90) 0-18

PedsQL™: Higher scores indicate better HRQOL; DSRS-C: Higher scores indicate worse depression.

**Table 3. Factors related to the HRQOL<sup>1)</sup> of childhood cancer survivors (n = 105)**

Factors	sb	p-value
<b>Children</b>		
Current age	0.11	0.28
Age of onset	-0.01	0.96
Illness (type of cancer)	--	--
Type of treatment given (Radiotherapy/surgery/transplantation/other <sup>#</sup> )	0.12	0.31
Status of recurrence (Yes/No <sup>#</sup> )	0.05	0.65
Frequency of hospital visits per year	-0.28	0.02*
Return to school (Yes/No <sup>#</sup> )	0.07	0.50
Sequelae (Yes/No <sup>#</sup> )	-0.01	0.92
Problems in daily life (1: No, none at all, 2: Sometimes, 3: Consistently)	-0.3	< 0.01**
Limitations on daily life (Yes/No <sup>#</sup> )	0.01	0.93
Bounce back from the most distressing time (1-6)	-0.14	0.23
Status of depression <sup>2)</sup>	-0.22	0.03*
<b>Family caregivers</b>		
During hospitalization		
Frequency of visits (1: A few hours during the day, 2: Almost the entire time during the day, 3: All the time while the child was awake, 4: Stayed for 24 hours)	-0.06	0.58
Was the child informed of his/her illness (1: No, 2: Somewhat, 3: Yes)	0.02	0.84
Sense of burden while providing care (1: No, none at all, 2: No, 3: Somewhat, 4: Yes, 5: Yes, very much so)	-0.09	0.41
Cooperation within the family (1: None at all, 2: Not much, 3: On occasion, 4: Sometimes, 5: Frequent)	0.11	0.35
Support from outside the family (1: None at all, 2: Not much, 3: On occasion, 4: Sometimes, 5: Frequent)	-0.08	0.42
After discharge to present		
Was the child informed of his/her illness (1: No, 2: Somewhat, 3: Yes)	0.05	0.63
Sense of burden while providing care (1: No, none at all, 2: No, 3: Somewhat, 4: Yes, 5: Yes, very much so)	-0.13	0.25
Cooperation within the family (1: None at all, 2: Not much, 3: On occasion, 4: Sometimes, 5: Frequent)	0.25	0.03*
Support from outside the family (1: None at all, 2: Not much, 3: On occasion, 4: Sometimes, 5: Frequent)	-0.1	0.35
<b>Family members</b>		
Number of family members living with the child	-0.06	0.58
Number of siblings	0.03	0.78
Cohesion (1. Disengaged, 2. Separated, 3. Connected, 4. Enmeshed)	-0.11	0.30
Adaptability (1. Chaotic, 2. Flexible, 3. Structured, 4. Rigid)	0.008	0.94
R <sup>2</sup>	0.4	
Adjusted R <sup>2</sup>	0.31	

sb: the values are standardized partial regression coefficients; \*  $p < 0.05$ , \*\*  $p < 0.01$ ; # reference category; -- Variables that were not selected as model variables as a result of variable selection; <sup>1)</sup> Assessed using the Japanese version of PedsQL™; <sup>2)</sup> Assessed using the Japanese version of DSRS-C.

4.155,  $p < 0.001$ ).

The problems frequently encountered by the children in their daily life included feeling fatigued and a sense of isolation because of "feeling weak", loss of confidence and difficulty with social interaction due

to "changes in body image", and underachievement, feeling lonely, or feeling anxious due to "inconsistent school attendance when being treated to prevent infection". In some instances, "underachievement" and "feeling left out by friends" discouraged the

child's school attendance. Some children had physical complaints caused by social stress, such as headaches or abdominal pain, or psychological instability, such as a temper and melancholy, at home.

#### 4. Discussion

This is the first study in Japan to assess the prevalence of depression and HRQOL of children and associated factors from the viewpoint of "a child living with his or her family". Results of this cross-sectional questionnaire-based study offer suggestions for the support needed by caregivers and families raising children with childhood cancer.

##### 4.1. Actual depression and HRQOL of children with childhood cancer

The current subjects had DSRS-C scores, which indicate one's level of depression, that were comparable to those reported in previous studies [ $8.79 \pm 4.57$  (mean  $\pm$  S.D.) as reported by Uchida & Fujimori (18) and  $12.55 \pm 6.42$  (mean  $\pm$  S.D.) as reported by Nagai (19)]. Only 3 subjects had scores above the cut-off. Based on these results, factors including cancer morbidity and treatment may affect depressive tendencies in individual children, but they had little effect on subjects as a whole in this study.

A previous study found that the Japanese version of the PedsQL was applicable to community and school health settings and useful in clinical settings (10). That study involved healthy children, including those with chronic health needs and mental conditions. In that study, toddlers and young children had a total PedsQL score of  $83.1 \pm 13.8$  (mean  $\pm$  S.D.) (range: 33.3-100), school children and adolescents had one of  $84.1 \pm 13.3$  (mean  $\pm$  S.D.) (range: 42.4-100), and subjects overall had one of  $83.91 \pm 13.4$  (mean  $\pm$  S.D.) (range: 33-100). These scores are higher than the PedsQL score of  $79.3 \pm 18.1$  (mean  $\pm$  S.D.) (range: 38.1-100) for children ages 2 to 18 with childhood cancer in the current study. Hao *et al.* also noted that healthy children reported higher scores than pediatric leukemia patients ( $p < 0.001$ ) although the children were in a different country; healthy children had a total score of PedsQL of  $82.38 \pm 13.29$  (mean  $\pm$  S.D.) while children with leukemia had one of  $56.72 \pm 20.35$  (mean  $\pm$  S.D.) (20). Whether children with cancer have high or low scores will depend on the differences in medical care and cultural background of the country in question. In either instance, the factors of cancer morbidity and treatment may have a major impact on the HRQOL of children.

##### 4.2. Factors associated with the HRQOL of children with childhood cancer

Results of multivariate analysis suggested that having

problems in daily life, an increased frequency of hospital visits, less cooperation within the family after the child's discharge, and an increased tendency for the child to experience depression were correlated with a low HRQOL for the child.

This study showed that children with childhood cancer encountered problems in daily life after discharge, including feeling fatigued and a sense of isolation because of "feeling weak", loss of confidence and difficulty with social interaction due to "changes in body image", and underachievement, feeling lonely, or feeling anxious due to "inconsistent school attendance when being treated to prevent infection". Suzuki *et al.* also reported four categories of characteristic problems encountered by Japanese children with childhood cancer after discharge: "physical difficulties", "behavioral difficulties", "interpersonal difficulties" and "fear of the future"; they also suggested that physical and behavioral problems may develop into social problems such as problems with interpersonal relationships and view of the future over time (21). In cooperation with a multidisciplinary care team consisting of physicians, social workers, psychological specialists, school teachers, and other members, nurses are expected to provide long-term support that takes into account both the status of outpatient treatment and the life stage of their patients.

Meeting and talking with the attending physician during hospital visits can reduce the fear felt by parents. A study of families of children with chronic diseases reported that an increased frequency of patients' hospital visits is associated with greater family empowerment. In the current study of children with childhood cancer, an increased frequency of hospital visits indicated that "little time had passed since treatment started", "[the] child's condition was not stable", or "a high risk of recurrence". That is, children with childhood cancer who have an increased health risk and require professional supervision will visit the hospital more frequently. Redaelli *et al.* noted a positive correlation between the HRQOL of children with childhood cancer after discharge and the "time since treatment" (22), but the current study is the first to demonstrate a significant correlation between the HRQOL after admission and the frequency of hospital visits. Maurice-Stam *et al.* noted that a better HRQOL was associated particularly with more positive expectations of the further course of the disease and less frequent parental asking after disease-related emotions of the child (23). Children who visit the hospital more frequently are presumed to have more difficulty being hopeful about the future and such children and their parents are both presumed to be more prone to fear of disease because of their health risks. Thus, children visiting the hospital more frequently need more psychosocial support from a multidisciplinary care team of childhood cancer specialists.

Data on the degree of cooperation within the family were collected during hospitalization and after discharge. The HRQOL of the child was found to be significantly correlated with the degree of cooperation within the family "after discharge". The families of children with childhood cancer have more things to do on their own after discharge than during hospitalization. The family is responsible for escorting the child to the hospital for a couple of years, managing medication, coordinating school attendance (while monitoring of the potential for infection), solving various problems at school, and careful care of the child. If all of these responsibilities are borne by one family member (e.g. the mother), that family member will be under considerable psychological pressure and feel fatigued. Previous studies noted that the anxiety and emotional fluctuations experienced by parents will be transmitted to their children (24,25). The HRQOL of the child may be negatively affected. Outpatient nurses are expected to communicate with parents accompanying their children to the hospital in order to assess the child's family life, including the system of family cooperation and, if necessary, share information with medical social workers, local public health nurses, and school nurses and intervene in the family.

The negative correlation between the level of depression (DSRS-C scores) and HRQOL (total PedsQL score) has also been described by Kobayashi & Kamibepu (10). Maurice-Stam *et al.* have indicated that many childhood cancer survivors who have remained in remission may have several psychosocial problems in addition to treatment-related physical problems (3). The problems experienced by the children include depression, emotional disturbance, PTSD, and withdrawal. Family issues include prolonged parental anxiety, PTSD, and maladjustment of siblings. In the present study, some children had adaptation disorders, e.g. loss of voice after being bullied by friends, and fell behind in schoolwork or had difficulty developing friendships due to frequent absences from school because of the fear of infection. These issues led to inconsistent school attendance. However, overall levels of depression (DSRS-C scores) were not high as those reported in previous studies. Schultz *et al.* noted that "having cancer of the central nervous system" and "undergoing cancer therapy involving the central nervous system" (such as brain radiation or chemotherapy injected into the spinal fluid) are factors that contribute to depression in children (26). However, the current study found no significant differences in levels of depression (DSRS-C scores) for patients with "cancer of the central nervous system" and patients with another form of cancer. Since high levels of depression are associated with a low HRQOL in children with cancer after their discharge, results suggested that outpatient staff members need to prevent and address both depression and a low HRQOL in

children with childhood cancer. In particular, outpatient nurses should: *i)* periodically screen children during outpatient treatment using instruments such as the DSRS-C and *ii)* conduct preventive interventions for children who meet screening criteria and their families before they suffer from adaptation disorders and offer multilateral psychosocial assistance in cooperation with a multidisciplinary care team of childhood cancer specialists.

#### 4.3. Study limitations or directions for future research

This study advanced the hypothesis that family functioning may influence HRQOL or depression of children with childhood cancer, but the hypothesis was not tested because most families rearing children with childhood cancer had stylized family functioning, *i.e.*, "enmeshed cohesion" and "structured adaptability". In future research, the authors wish to focus on a stylized family functioning and parental care of children who have cancer after discharge and discuss the role of outpatient nurses and the multidisciplinary care team.

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