Symptoms and symptom clusters in adolescents with cancer

Remziye Semerci[a], Trakya University, Faculty of Health Sciences,22030 Edirne, Turkey.
remziyesemerci@gmail.com https://orcid.org/0000-0003-1999-9179

Melahat Akgunmela Kostak [b], Trakya University,Department of Child Health and Disease Nursing , Edirne, Turkey. akgunmel@yahoo.com https://orcid.org/0000-0003-0507-9638

Tuba Eren [c], Faculty of Medicine, Department of Pediatric Hematolog /Oncology, Trakya University, Edirne, Turkey. Tubagurleyen@yahoo.co.uk https://orcid.org/0000-0001-5471-0663

Filiz Savran[d], Trakya University Hospital, Department at paediatric haematology/oncology, Edirne, Turkey. filiz.savran22@hotmail.com https://orcid.org/0000-0003-0296-1705

Gulcan Avci[e], Trakya University Hospital, Department at paediatric haematology/oncology, Edirne, Turkey. gulcanavci22@hotmail.com https://orcid.org/0000-0002-1454-5111

Abstract

Clinical specialists have suggested that adolescents with cancer experience multiple problems including physical, psychological, and emotional symptoms. This study aimed to identify symptoms and symptoms clusters among adolescent inpatients and outpatients receiving cancer treatment. The study's sample consisted of 26 adolescents who were selected with the purposeful sampling method in a paediatric oncology unit in Edirne, Turkey. Data were collected using the Memorial Symptom Assessment Scale (MSAS). From the results of the research, in terms of symptoms, outpatients reported a greater lack of concentration than inpatients did. Inpatients reported more hair loss and weight loss symptoms than outpatients. Adolescent inpatients and outpatients experienced the most symptoms during the treatment. Inpatient adolescents experienced more acute treatment-related symptoms than did outpatients. The study recommends regular monitoring and screening for nurses to identify symptom and symptom clusters.

Keywords: Adolescent; nursing; symptom cluster; symptom assessment; cancer;

* ADDRESS FOR CORRESPONDENCE: **Remziye Semerci**[a], Trakya University, Faculty of Health Sciences,22030 Edirne, Turkey
E-mail address: . remziyesemerci@gmail.com

1. Introduction

Clinical specialists have suggested that adolescents with cancer experience multiple problems including physical, psychological, and emotional symptoms (Atay, Conk, & Bahar, 2012; Cheng, Wong, Ling, Chan, & Thompson, 2009). Adolescents with cancer experience physical, psychological, and emotional symptoms not only because of the disease process but also because of the side effects of cancer treatment (Atay et al., 2012; Cheng et al., 2009). These symptoms include pain, loss of appetite, cachexia, alterations in taste, alopecia, nausea, vomiting, mucositis, fatigue, dyspnoea, sleep disorders, depression and anxiety (Kurt Sadırlı, 2008; Seven, Akyüz, Sever, & Dinçer, 2013; Tranmer et al., 2003). These symptoms negatively affect their quality of life (Linder et al., 2015; Rodgers, Hooke, Ward, & Linder, 2016).

A symptom assessment can play an important role in improving the quality of life of adolescents with cancer (Chang, Hwang, Feuerman, Kasimis, & Thaler, 2000). Symptom clusters refer to two or more symptoms that occur together. An analysis of symptom clusters can shed light on the relationship between symptoms (Kim, McGuire, Tulman, & Barsevick, 2005; Macpherson et al., 2014). Although some nursing research has focused on symptom clusters related to cancer (Atay et al., 2012; Kim et al., 2005), the data in the literature are insufficient to understand this framework, especially for paediatric patients (Atay et al., 2012; Kim et al., 2005; Rodgers et al., 2016).

Nurses need to be aware of symptoms and symptom clusters associated with cancer treatment in adolescents (Lopes-Júnior, Bomfim, Nascimento, Pereira-da-Silva, & Lima, 2015). By understanding symptom relationships, nurses can focus on major symptoms and minimize the occurrence of these symptoms (Rodgers et al., 2016). Paying attention to symptom clusters, in addition to single symptoms, can promote a more comprehensive assessment and effective symptom management (Macpherson et al., 2014).

Although accurate symptom evaluation is crucial for the provision of high-quality supportive care and treatment assessments, only a few published studies have examined symptom clusters in adolescents with cancer (Given et al., 2006; Linder et al., 2015; Macpherson et al., 2014). In recent years, most research has focused on symptoms and symptom clusters in adolescents while receiving cancer treatment in the hospital (Given et al., 2006; Linder et al., 2015; Macpherson et al., 2014). However, not all treatment takes place in the hospital, and side effects of some treatments may occur at a later stage. To understand and eliminate factors that have a negative impact on cancer treatment, information is needed on the symptoms of outpatients (i.e., at home).

1.1. Purpose of study

Children could have various, disturbing, and interrelated symptoms throughout cancer therapy. Investigation of symptom interrelationships and how changes during therapy might produce clinically appropriate patient profiles for guiding patient care is needed (Wang et al., 2018). Approximately 80% of cancer children are suffering a minimum of one symptom throughout therapy, most often with several symptoms in therapy (Hockenberry et al., 2017; Rodgers et al., 2019). Most cancer symptom research focused on individual symptoms at a single point. But more recently, symptoms clusters have received popularity for their potential contribution to cancer-related symptoms identified as multiple concurrent symptoms (Rodgers et al., 2019). Based on a literature search, there is a gap in studies on symptoms and symptoms clusters for cancer inpatients and outpatients. Therefore, this study aimed to assess symptoms and symptom clusters among inpatient and outpatient adolescents receiving cancer treatment.

2. Methods

2.1. Sample and setting

This study adopted a descriptive design. The study was conducted between December 2016 and February 2017 at Trakya University Hospital, Turkey. This is the only hospital in the Trakya region with a paediatric oncology unit. Adolescents with various types of cancers were included in the study, as were all sorts of treatment regimens. The sample included 31 adolescents aged between 10 and 18 years who were receiving cancer treatment and who were followed up by the paediatric oncology unit.

The purposive sampling method was used to determine the sample size. Children who met the inclusion criteria of the study were included in the study. The inclusion criteria were as follows: receiving chemotherapy, a cancer diagnosis at least 1 month previously and no neurodevelopmental disorders, verbal difficulties, or hearing or visual impairments. Literacy, voluntary participation in the study and stable health status were additional inclusion criteria. The exclusion criteria were terminal-stage cancer, severe pain or other severe symptoms and sedation. Five adolescents with terminal-stage disease and severe pain were excluded from the study. Thus, the final study comprised 26 adolescents**.**

2.2. Data collection instruments

The data were collected using a survey form and Memorial Symptom Assessment Scale (MSAS) (Atay, Conk, Bahar, & Kantar, 2007). The form included 14 questions on the socio-demographic characteristics of the study population, including age, sex, parental education status, number of siblings, family structure, family income level, school attendance status, time of diagnosis, kind of treatment received and number of chemotherapy cycles.

The MSAS was developed by Collins et al. to identify the symptoms of adolescents aged 10–18 y with cancer (Collins et al., 2002). An assessment of the validity and reliability of the scale for use in a Turkish population was conducted by Atay et al. (Atay et al., 2007). In the validity and reliability study, the Cronbach alpha values of physical, psychological, and global distress index subscales were 0.83, 0.87 and 0.85, respectively. The scale, which consists of 30 items in total, has three sub-dimensions: a psychological subscale, physical subscale, and global distress scale.

The psychological subscale consists of six items: feeling sad, worried, or nervous and difficulty sleeping or concentrating. The physical subscale consists of 11 items: lack of appetite, lack of energy, pain, feeling drowsy, constipation, a dry mouth, nausea, vomiting, change in taste, weight loss and dizziness. The global distress scale consists of 10 items: feeling sad, worried, restless, or nervous and anorexia, weakness, pain, drowsiness, constipation, and sort of oral problems/dysfunction. When the frequency of eight symptoms cannot be determined, two dimensions are assessed, including the severity of the symptoms (e.g., mouth sores, changes in food taste, weight loss, hair loss, swelling of hands and feet, self-alienation, skin changes and irritability due to constipation). The total MSAS score was computed as the average of the symptom scores for all the items.

2.3. Procedure

Before the data collection from adolescent inpatients and outpatients who received cancer treatment at Trakya University Hospital, the adolescents and their parents were informed about the purpose and content of the study. All the adolescents were receiving a chemotherapy protocol. Before administering the survey, the adolescents were given 15–20 min to recollect the symptoms they had experienced during the previous week. They then filled out the forms in the presence of a researcher.

They completed the forms in a quiet environment at a time when there was no pain or other symptoms that would prevent communication with the adolescent and outside of treatment hours. The adolescents were encouraged to ask the researcher if they did not understand any of the survey items.

2.4. Data analysis

The data were analysed using the Statistical Package for the Social Sciences (SPSS), version 23.0 program (IBM Corp. in Chicago). In evaluating the socio-demographic characteristics of the adolescents, the data were presented as the number, percentage, mean and standard deviation. The Mann–Whitney *U* test was used to compare the symptom scores of the inpatients and outpatients. A cluster analysis of the symptoms was performed to identify symptoms that tended to occur together. This type of analysis of multiple cancer-related symptoms and treatment aims to understand the effects of symptoms on each other and patient outcomes. There is no consensus in the literature on identifying symptom clusters. In the present study, each symptom was graded as absent or present.

Symptom clusters were analysed using SPSS, version 23 (IBM Corp.) Symptoms, where the prevalence was less than 20%, were not included in the symptom cluster analysis because of the small sample size. The cluster analysis was based on 18 symptoms. (Atay et al., 2012). In the cluster analysis, hierarchical clustering methods were applied, and a dendrogram showing the symptom affinity was generated. In accordance with the literature, to identify symptom clusters in dendrograms, a cut-off point was determined (Atay et al., 2012; Erdem, 2016). Similar to the study by Erdem Pearson's coefficient value of ≥ 0.25 denoted a strong correlation (Erdem, 2016). The results, together with their 95% confidence intervals, are presented. A value of $p < 0.05$ was accepted as statistically significant.

2.5. Ethical considerations

The ethics committee of the Faculty of Medicine of Trakya University approved the study. Written permission was also obtained from the Paediatric Oncology-Haematology Department of Trakya University Hospital where the research took place. Prior to the administration of the survey form and scale, written consent was obtained from the parents, and verbal assent was obtained from the adolescents. All the participants were advised that they could withdraw from the study at any time if they wished. All the parents and adolescents were also advised that the information obtained would be used only for scientific study.

3. Results

The mean age of the adolescents was 15.04 ± 2.18 (min: 10 y, max: 18 y), 53.8% were males, and 46.2% were females. The mean time since the diagnosis was 2.52 ± 2.76 y (min:1 mo, max: 12 y). The majority of the adolescents (79.8%) had a nuclear family structure, 84.6% had a moderate family income, and 50% were attending school. The sample was heterogeneous in terms of the disease diagnosis and treatment regimen but homogeneous in terms of disease stage (second stage). All the adolescents received chemotherapy, 38.5% received radiotherapy, 30.8% had undergone surgery, and 57.7% continued their treatment at home. In terms of the type of diagnosis, 23% had osteosarcomas, 19% had acute lymphoblastic leukemia (ALL), 19% had medulloblastoma, and 15% had lymphoma (Fig. 1).
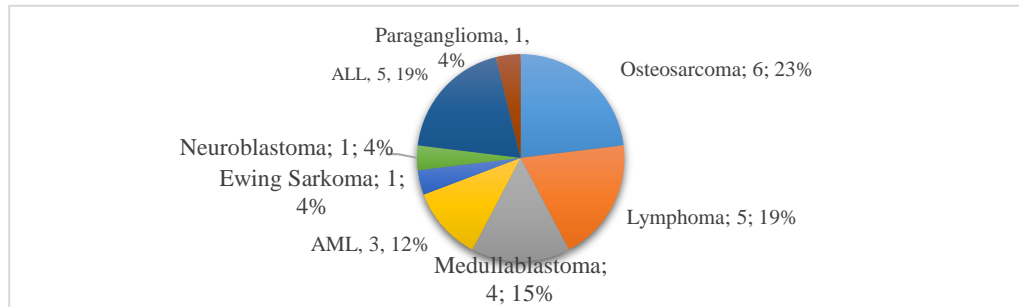
Figure 1.

Type of diagnosis

Table 1 presents data on the findings of the MSAS and subscales of the inpatients and outpatients. There were no differences in the psychological and global distress subscales of the MSAS according to hospitalization status, but there was a significant difference in the physical subscale scores among those in the hospital setting, with adolescent inpatients having a higher physical score (0.86 ± 0.74) than adolescent outpatients (0.39 ± 0.54) (*p* = 0.026, Table 1).

Table 1

Distribution of Memorial Symptom Assessment Scale and subscales according to the hospital setting

	Outpatient Setting (n=15)	Inpatient Setting (n=11)	Z	P
	M±SD	**M**±SD		
MSAS (total score)	0.57±0.77	0.68±0.59	58.000	0.298
Psychological subscales	0.67±0.49	0.73±0.91	68.500	0.639
Physical subscales	0.39±0.54	0.86±0.74	36.500	**0.026**
Global distress index	0.84±0.65	0.88±0.92	71.500	0.762

Z; Mann Whitney U Test

Table 2 presents data on the comparison of the symptom scores according to the treatment setting. There was a significant difference in the symptom scores according to the treatment setting (*p* < 0.05). The mean score for lack of concentration of the outpatients was higher (1.07 ± 0.92) than that of the inpatients (0.6 ± 0.62). Adolescent inpatients had a higher weight loss score (0.90 ± 1.07) as compared with that of outpatients (0.07 ± 0.27). The score of adolescent inpatients for hair loss was higher than that of outpatients (1.50 ± 1.75 vs. 0.36 ± 1.08). Adolescent inpatients experienced swelling of arms/legs symptoms when outpatient did not experience.

Table 2
*Comparison of treatment setting with symptoms scores (n=26)*

	Outpatient setting (n=15)	Inpatient (n=11)	Z	p
Lack of concentration	1.07±0.92	0.6±0.62	41.000	**0.033**
Pain	0.40±0.69	0.97±1.35	60.500	0.293

Lack of energy	0.76±1.30	1.12±1.30	62.000	0.353
Cough	0.67±0.88	0.70±1.07	74.500	0.877
Feeling nervous	1.29±1.06	1.18±1.25	71.500	0.757
Dry mouth	0.14±0.39	0.70±1.06	57.000	0.143
Nausea	0.74±1.08	0.84±1.11	74.000	0.853
Feeling drowsy	0.29±0.57	0.64±0.90	61.000	0.267
Numbness/tingling	0.24±0.50	0.49±0.85	69.000	0.558
Insomnia	0.17±0.47	0.94±1.31	50.000	0.062
Problems with urination	0.14±2.99	0.27±0.65	69.500	0.467
Vomiting	0.36±0.72	0.91±1.11	56.00	0.164
Dyspnea	0.17±0.62	0.33±0.75	69.500	0.467
Diarrhea	-	0.21±0.48	63.00	0.103
Feeling sad	0.80±1.04	0.82±1.30	73.500	0.828
Sweating	0.14±0.53	0.30±0.53	63.000	0.230
Worrying	0.52±0.79	0.30±1.00	59.000	0.188
Itching	0.20±0.52	0.55±1.01	65.500	0.368
Lack of appetite	0.71±0.97	1.42±1.25	52.500	0.154
Dizziness	0.29±0.74	0.40±0.88	73.500	0.764
Difficulty swallowing	-	0.27±0.65	63.000	0.103
Feeling irritable	0.14±0.53	0.76±1.38	60.500	0.157
Mouth sores	0.14±0.53	0.40±0.63	56.500	0.108
Change in the way food tastes	0.39±0.88	1.23±1.21	48.000	0.064
Weight loss	0.07±0.27	0.90±1.07	39.000	**0.009**
Hair loss	0.36±1.08	1.50±1.75	45.000	**0.034**
Constipation	0.14±0.53	0.36±0.71	62.500	0.214
Swelling of arms/legs	-	0.32±0.56	56.000	**0.042**
''Don't look like myself''	0.46±1.18	0.55±1.21	75.000	0.864
Skin changes	0.39±0.68	0.64±0.84	63.500	0.389

Z; Mann Whitney U Test

Three symptom clusters were identified: a change in the way food tastes, hair loss and weight loss (cluster 1); vomiting, lack of appetite and nausea (cluster 2); and pain, insomnia and feeling drowsy (cluster 3) (Fig. 2).

Figure 2
Symptom clusters
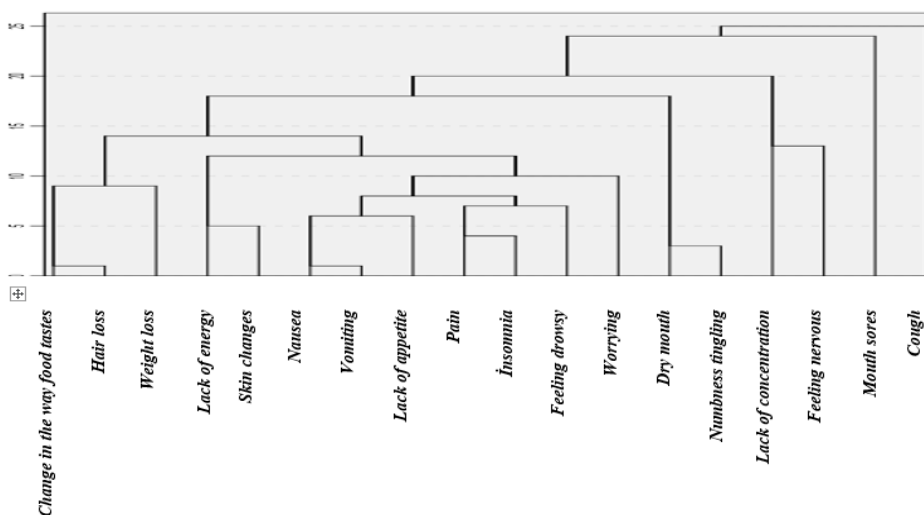
4. Discussion

This study aimed to identify symptoms and symptom clusters among adolescent inpatients and outpatients receiving cancer treatment for symptom management. The adolescent inpatients

experienced more physical symptoms than did the adolescent outpatients in accordance with findings in the literature (Chang et al., 2000; Collins et al., 2000). Wolfe et al. concluded that adolescents with cancer mostly experienced physical symptoms (Wolfe et al., 2015), which generally occur during the early stages of treatment and hospitalization (Atay et al., 2012). Among cancer treatments, chemotherapy, in particular, is associated with multiple symptoms, with physical symptoms followed by the emergence of other symptoms at a later stage. In our hospital, adolescent inpatients are frequently discharged after receiving chemotherapy, assuming they are in reasonably good health (i.e., no physical symptoms). As adolescent inpatients generally have physical symptoms, the findings of the study were expected.

In this study, adolescent inpatients experienced more weight loss, hair loss and swelling of arms/legs than did outpatients. This result was in accordance with that of Yeh et al., who reported that adolescents receiving cancer treatment experienced more weight loss and hair loss than those of treatment (Yeh, Wang, Chiang, Lin, & Chien, 2009). Hair loss was the most common symptom of paediatric in patients with cancer in a study by Bal Yılmaz et al. (Bal Yılmaz, Karayağız Muslu, Taş, Başbakkal, & Kantar, 2009). Baggott et al. reported a similar finding among paediatric oncology patients during chemotherapy (Baggott, Cooper, Marina, Matthay, & Miaskowski, 2012), as did Gonzalez Mercado et al. with 72.31% of paediatric cancer patients experiencing hair loss (Gonzalez-Mercado, Williams, Williams, Pedro, & Colon, 2017).

Symptoms, such as hair loss, usually occur in adolescents during intensive and mixed treatments (Linder, Al-Qaaydeh, & Donaldson, 2018), with the manifestation of acute and delayed side effects throughout this treatment period (Miller, Jacob, & Hockenberry, 2011). In previous research, lack of energy, nausea, vomiting, weight change, hair loss, loss of appetite and swelling of arms/legs were most frequently reported by paediatric oncology inpatients (Atay et al., 2012; Miller et al., 2011; Yeh et al., 2009). According to the results of these studies, adolescent outpatients might experience less hair loss, weight loss and swelling of arms/legs than inpatients because the aforementioned symptoms are acute side effects of the treatment.

In the present study, adolescent outpatients experienced a greater lack of concentration as compared with that of inpatients. This finding was in accordance with that of several studies (Miller et al., 2011; Rodgers et al., 2016; Williams et al., 2012; Yeh et al., 2009). In a study by Atay et al., the prevalence of lack of concentration increased according to the duration of cancer treatment, suggesting that a lack of concentration is a delayed side effect of cancer treatment (Atay et al., 2012). If a lack of concentration is a delayed symptom of cancer treatment, it should be greater among outpatients than inpatients.

Identifying symptom clusters among paediatric cancer patients can aid nurses in the understanding of symptom-relationship (Rodgers et al., 2016). Symptom clusters comprise co-occurring and associated symptoms. In our study, symptom clusters were identified by cluster analysis (Fig. 2). According to the cluster analysis, changes in the way food tastes, hair loss and weight loss formed one cluster. This result differed from that found in a study on paediatric cancer patients by Ameringer et al., who reported that changes in visual appearance, changes in how food tastes, skin changes and hair loss formed one cluster and that weight loss, lack of appetite and nausea formed another cluster (Ameringer, Erickson, Macpherson, Stegenga, & Linder, 2015). Altay et al. reported that changes in the way food tastes, mouth sores and lack of appetite formed one cluster among in pediatric cancer patients (Atay et al., 2012)]. Other studies found that hair loss and weight loss formed one cluster (Ameringer et al., 2015; Atay et al., 2012; Erdem, 2016). In the present study, changes in the way food tastes may explain the observed weight loss.

In the present study, vomiting, nausea and lack of appetite formed another cluster. This finding was in accordance with that of many studies in the literature (Atay et al., 2012; Erickson et al., 2013; Rodgers et al., 2016). In a study on paediatric cancer patients by Atay et al. (2012), vomiting, nausea and lack of energy formed one symptom cluster. Gastrointestinal irritation symptoms in the form of nausea and vomiting are common side effects of chemotherapy (Rodgers et al., 2016), and most adolescents with cancer experience these symptoms during the early stage of chemotherapy (Miller et al., 2011; Yeh et al., 2009). Hongo et al. (2003) reported that all adolescents with cancer experienced poor appetite. Lack of appetite may be due to nausea and vomiting. The latter may impair how food tastes, causing further lack of appetite.

In this study pain, insomnia and drowsiness formed the third cluster. This result was similar to that found in previous research (Kim et al., 2005; Rodgers et al., 2016). Atay et al. (2012) reported that irritability, lack of concentration, dizziness and pain formed one cluster in adolescents with cancer. Yeh et al., (2009) found that difficulty concentrating or paying attention; insomnia; lack of energy; drowsiness; feelings of sadness, worry and irritability; and sweating formed one symptom cluster. Pain, drowsiness and insomnia are known neuropsychological discomfort clusters (Rodgers et al., 2016). Many adolescents with cancer experience pain as a result of the disease and treatment (Twycross, Parker, Williams, & Gibson, 2015).

Many studies reported that pain may contribute to the emergence of neuropsychological discomfort symptoms (Atay et al., 2012; Miller et al., 2011; Rodgers et al., 2016; Twycross et al., 2015). Fatigue, pain and depression were clustered among children receiving treatment for leukemia in a study by Hockenberry et al. (Hockenberry et al., 2017). The diversity of the symptoms among the symptom clusters may be due to the use of different measurement tools. However, neuropsychological discomfort-related symptoms consistently occurred in the same cluster.

5. Conclusions

In the present study, both inpatients and outpatient's adolescent experienced the most symptoms during treatment. Furthermore, adolescent inpatients experienced more acute treatment-related symptoms than did outpatients. The identification of symptoms and symptom clusters among adolescent inpatients and outpatients can aid symptom management and enhance adolescents' quality of life. However, the results are not enough to understand and explain symptom clusters among adolescents with cancer.

To help prevent the occurrence of symptom clusters among paediatric cancer patients, nurses must be aware of symptoms and the relationship between symptoms. There is insufficient information on symptom clusters among adolescents outside the hospital setting. Nurses should use symptom screening tools to identify symptoms and symptom clusters in such patients.

This study has some limitations. Firstly, and a major limitation in this study is the small sample size and study performed within a single centre. Secondly, all of the paediatric cancer types and all treatment types which may influence different symptom experiences were included in the study. Thirdly, the children's symptoms were evaluated only one time because of the small sample size and hospital setting, maybe future studies may use repeated measurements with appropriate sample size.

Semerci, R., Kostak, A.M., Eren, T., Savran, F. & Avci, G. (2021). Symptoms and symptom clusters in adolescents with cancer. *International Journal of Emerging Trends in Health Sciences. 5*(2),14 -24. https://doi.org/10.18844/ijeths.v5i2.5559

Despite these limitations, the study's results provide important baseline information about symptom assessment and symptom clusters among inpatients and outpatients adolescents with cancer.

6. Recommendations

Paediatric oncology nurses should monitor not only inpatients but also outpatient adolescents at home and evaluate their symptoms. Besides, nurses should be aware of the symptom clusters related to cancer treatment. Nurses must follow guideline and literature about symptoms and symptom clusters to early treat symptoms and improve quality of care. A sustained focus on research and practice is needed to monitor and alleviate symptoms and symptom clusters during the treatment of children and adolescents with cancer. Therefore, paediatric oncology nurses should do significantly more research in this area.

Conflict of interest

The authors have no conflicts of interest to disclose.

REFERENCES

Ameringer, S., Erickson, J. M., Macpherson, C. F., Stegenga, K., & Linder, L. A. (2015). Symptoms and symptom clusters identified by adolescents and young adults with cancer using a symptom heuristics app. Research in Nursing & Health, 38(6), 436-448. https://onlinelibrary.wiley.com/doi/abs/10.1002/nur.21697

Atay, S., Conk, Z., & Bahar, Z. (2012). Identifying symptom clusters in paediatric cancer patients using the Memorial Symptom Assessment Scale. European Journal of Cancer Care, 21(4), 460-468. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2354.2012.01324.x

Atay, S., Conk, Z., Bahar, Z., & Kantar, M. B. B. (2007). Memorial semptom değerlendirme ölçeği'nin (MSDÖ 10-18) Türkçe geçerlik ve güvenirlik çalışması. Ege Pediatri Bülteni, 14(2), 93-99. https://app.trdizin.gov.tr/publication/paper/detail/T0RBeE5EWTI

Baggott, C., Cooper, B. A., Marina, N., Matthay, K. K., & Miaskowski, C. (2012). Symptom cluster analyses based on symptom occurrence and severity ratings among pediatric oncology patients during myelosuppressive chemotherapy. Cancer Nursing, 35(1), 19-28 https://www.ncbi.nlm.nih.gov/pmc/articles/pmc3237960/

Bal Yılmaz, H., Karayağız Muslu, G., Taş, F., Başbakkal, Z., & Kantar, M. (2009). Çocukların kansere bağlı yaşadıkları semptomlar ve yorgunluğa ebeveyn bakışı. Türk Onkoloji Dergisi, 24(3), 122-127. https://www.academia.edu/download/52077759/5000064636-5000082437-1-PB.pdf

Chang, V. T., Hwang, S. S., Feuerman, M., Kasimis, B. S., & Thaler, H. T. (2000). The memorial symptom assessment scale short form (MSAS-SF). Cancer, 89(5), 1162-1171. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/10964347 .

Cheng, K. K., Wong, E. M., Ling, W. M., Chan, C. W., & Thompson, D. R. (2009). Measuring the symptom experience of Chinese cancer patients: a validation of the Chinese version of the memorial symptom assessment scale. Journal of Pain and Symptom Management, 37(1), 44-57. DOI: https://doi.org/10.1016/j.jpainsymman.2007.12.019

Collins, J. J., Byrnes, M. E., Dunkel, I. J., Lapin, J., Nadel, T., Thaler, H. T., . . . Portenoy, R. K. (2000). The measurement of symptoms in children with cancer. Journal of Pain and Symptom Management,19(5),363-377. DOI: https://doi.org/10.1016/S0885-3924(00)00127-5

Semerci, R., Kostak, A.M., Eren, T., Savran, F. & Avci, G. (2021). Symptoms and symptom clusters in adolescents with cancer. *International Journal of Emerging Trends in Health Sciences. 5*(2),14 -24. https://doi.org/10.18844/ijeths.v5i2.5559

Collins, J. J., Devine, T. D., Dick, G. S., Johnson, E. A., Kilham, H. A., Pinkerton, C. R., . . . Portenoy, R. K. (2002). 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 and Symptom Management, 23(1), 10-16. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/11779663 .

Erdem, E. (2016). Lösemisi olan çocuklarda semptom kümelemesi ve ebeveynlerin bakım yükü arasındaki İlişki. (Master's Thesis), Gazi Üniversitesi Sağlık Bilimleri Enstitüsü Ankara. Retrieved from https://tez.yok.gov.tr/UlusalTezMerkezi/tezSorguSonucYeni.jsp

Erickson, J. M., MacPherson, C. F., Ameringer, S., Baggott, C., Linder, L., & Stegenga, K. (2013). Symptoms and symptom clusters in adolescents receiving cancer treatment: a review of the literature. International Journal of Nursing Studies, 50(6), 847-869. https://doi.org/10.1016/j.ijnurstu.2012.10.011

Given, B., Given, C. W., Sikorskii, A., Jeon, S., Sherwood, P., & Rahbar, M. (2006). The impact of providing symptom management assistance on caregiver reaction: results of a randomized trial. Journal of Pain and Symptom Management, 32(5), 433-443. DOI: https://doi.org/10.1016/j.jpainsymman.2006.05.019

Gonzalez-Mercado, V. J., Williams, P. D., Williams, A. R., Pedro, E., & Colon, G. (2017). The symptom experiences of Puerto Rican children undergoing cancer treatments and alleviation practices as reported by their mothers. International Journal of Nursing Practice, 23(1), e12500. https://onlinelibrary.wiley.com/doi/abs/10.1111/ijn.12500

Hockenberry, M. J., Hooke, M. C., Rodgers, C., Taylor, O., Koerner, K. M., Mitby, P., . . . Pan, W. (2017). Symptom trajectories in children receiving treatment for leukemia: a latent class growth analysis with multitrajectory modeling. Journal of Pain and Symptom Management, 54(1), 1-8. DOI: https://doi.org/10.1016/j.jpainsymman.2017.03.002

Hongo, T., Watanabe, C., Okada, S., Inoue, N., Yajima, S., Fujii, Y., & Ohzeki, T. (2003). Analysis of the circumstances at the end of life in children with cancer: symptoms, suffering and acceptance. Pediatrics International, 45(1), 60-64. https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1442-200X.2003.01668.x

Kim, H.-J., McGuire, D. B., Tulman, L., & Barsevick, A. M. (2005). Symptom clusters: concept analysis and clinical implications for cancer nursing. Cancer Nursing, 28(4), 270-282. https://journals.lww.com/cancernursingonline/Fulltext/2005/07000/Symptom_Clusters__Concept_Analysis_and_Clinical.5.aspx

Kurt Sadırlı, S. (2008). Kanserli hastalarda semptom kontrolünün değerlendirilmesi. (Master's Thesis), Trakya Üniversitesi, Edirne. Retrieved from https://tez.yok.gov.tr/UlusalTezMerkezi/tezSorguSonucYeni.jsp

Linder, L. A., Al-Qaaydeh, S., & Donaldson, G. (2018). Symptom characteristics among hospitalized children and adolescents with cancer. *Cancer Nursing, 41*(1), 23-32. https://journals.lww.com/cancernursingonline/Fulltext/2018/01000/Symptom_Characteristics_Among_Hospitalized.4.aspx

Linder, L. A., Ameringer, S., Baggott, C., Erickson, J., Macpherson, C. F., Rodgers, C., & Stegenga, K. (2015, August). Measures and methods for symptom and symptom cluster assessment in adolescents and young adults with cancer. *Seminars in Oncology Nursing* , 31 (3), 206-215. http://dx.doi.org/10.1016/j.soncn.2015.05.002

Lopes-Júnior, L. C., Bomfim, E. d. O., Nascimento, L. C., Pereira-da-Silva, G., & Lima, R. A. G. d. (2015). Theory of unpleasant symptoms: support for the management of symptoms in children and adolescents with cancer. *Revista Gaucha de Enfermagem, 36*(3), 109-112. http://dx.doi.org/10.1590/1983-1447.2015.03.51465

Semerci, R., Kostak, A.M., Eren, T., Savran, F. & Avci, G. (2021). Symptoms and symptom clusters in adolescents with cancer. *International Journal of Emerging Trends in Health Sciences. 5*(2),14 -24. https://doi.org/10.18844/ijeths.v5i2.5559

Macpherson, C. F., Linder, L. A., Ameringer, S., Erickson, J., Stegenga, K., & Woods, N. F. (2014). Feasibility and acceptability of an iPad application to explore symptom clusters in adolescents and young adults with cancer. *Pediatric Blood & Cancer, 61*(11), 1996-2003. https://onlinelibrary.wiley.com/doi/abs/10.1002/pbc.25152

Miller, E., Jacob, E., & Hockenberry, M. J. (2011). Nausea, pain, fatigue, and multiple symptoms in hospitalized children with cancer. Oncology Nursing Forum, 38(5), pE382-E393. https://onf.ons.org/sites/default/files/X04063486U603578_first.pdf

Rodgers, C., Hooke, M. C., Ward, J., & Linder, L. A. (2016). Symptom clusters in children and adolescents with cancer. Seminars in Oncology Nursing. 32(4), 394-404. https://doi.org/10.1016/j.soncn.2016.08.005

Rodgers, C., Hooke, M. C., Taylor, O., Koerner, K. M., Mitby, P., Moore, I., ... & Pan, W. (2019, March). Childhood cancer symptom cluster: Leukemia and health-related quality of life. Oncology Nursing Forum. 46(2), 228–237. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8106538/

Twycross, A., Parker, R., Williams, A., & Gibson, F. (2015). Cancer-related pain and pain management: sources, prevalence, and the experiences of children and parents. Journal of Pediatric Oncology Nursing, 32(6), 369-384. https://journals.sagepub.com/doi/abs/10.1177/1043454214563751

Tranmer, J. E., Heyland, D., Dudgeon, D., Groll, D., Squires-Graham, M., & Coulson, K. (2003). Measuring the symptom experience of seriously ill cancer and noncancer hospitalized patients near the end of life with the memorial symptom assessment scale. Journal of Pain and Symptom Management, 25(5), 420-429. DOI: https://doi.org/10.1016/S0885-3924(03)00074-5

Twycross, A., Parker, R., Williams, A., & Gibson, F. (2015). Cancer-related pain and pain management: sources, prevalence, and the experiences of children and parents. Journal of Pediatric Oncology Nursing, 32(6), 369-384. https://journals.sagepub.com/doi/abs/10.1177/1043454214563751

Wang, J., Jacobs, S., Dewalt, D. A., Stern, E., Gross, H., & Hinds, P. S. (2018). A longitudinal study of PROMIS pediatric symptom clusters in children undergoing chemotherapy. Journal of Pain and Symptom Management, 55(2), 359-367. https://doi.org/10.1016/j.jpainsymman.2017.08.021

Williams, P. D., Williams, A. R., Kelly, K. P., Dobos, C., Gieseking, A., Connor, R., . . . Del Favero, D. (2012). A symptom checklist for children with cancer: the Therapy-Related Symptom Checklist-Children. Cancer Nursing, 35(2), 89-98. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/21760487

Wolfe, J., Orellana, L., Ullrich, C., Cook, E. F., Kang, T. I., Rosenberg, A., . . . Dussel, V. (2015). Symptoms and distress in children with advanced cancer: prospective patient-reported outcomes from the PediQUEST study. Journal of Clinical Oncology, 33(17), 1928. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4451175/

Yeh, C. H., Wang, C. H., Chiang, Y. C., Lin, L., & Chien, L. C. (2009). Assessment of symptoms reported by 10- to 18-year-old cancer patients in Taiwan. Journal of Pain and Symptom Management, 38(5), 738-746. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/19748760 .