Physiologic and Psychological Symptoms Experienced by Adults With Acute Leukemia: An Integrative Literature Review

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Purpose/Objectives: To evaluate the current knowledge of symptoms experienced by adults with acute leukemia (AL) and provide evidence to inform practice and research.

Data Sources: Literature review using an electronic search supplemented by a hand search of current literature reporting the physiologic and/or psychological symptoms of patients with AL was conducted.

Data Synthesis: Because of the variability found in the methods and specific aims of the articles, a rating system was applied to score how strongly the findings contributed to meeting the aims of the research. This rating system was applied to assist the authors in analyzing the findings. Therefore, the articles that scored lower ultimately contributed less during the analysis phase.

Conclusions: Knowledge regarding the symptoms experienced by adults undergoing treatment is being slowly evaluated. However, to better understand and subsequently manage these symptoms, longitudinal research examining the symptom trajectories in this population is needed.

Implications for Nursing: Additional investigation into symptom characteristics will facilitate the development of tailored interventions to manage the temporal characteristics of symptoms for this population.

Key Words: acute leukemia; symptoms; literature review

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About 16,202 adults in the United States aged 20 years or older are estimated to have been diagnosed with acute leukemia (AL) in 2013 (Howlander et al., 2013). Historically, the diagnosis of AL was linked with poor prognosis, particularly in older adults. Improvement in the treatment and management of the disease has led to trends in increased overall survival (Pulte, Gondos, & Brenner, 2010). The Surveillance Epidemiology and End Results reported the relative five-year survival rates from 2002–2008 for adults with acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL) to be 24% and 65%, respectively (Howlander et al., 2012).

For adults diagnosed with AL, the acute and rapid nature of the disease requires emergent aggressive inpatient chemotherapy delivered over at least a week, depending on disease and treatment response. However, little is known about the physical and psychological symptoms in this unique population (Manitta, Zordan, Cole-Sinclair, Nandurkar, & Philip, 2011).

Given that the overall symptom burden in this population has not been examined, the objective of this article is to evaluate the current literature addressing the physiologic and psychological symptoms that adults with AL experience and to provide current evidence to inform both practice and future directions for research.

Literature Search

An extensive search of literature reporting physiologic and psychological symptoms in adults with AL was completed using Ovid, PubMed, CINAHL®, and PsycINFO. Key words used for the search included *acute leukemia*, *symptoms*, *hematologic malignancy*, and *quality of life*, which also were used as exploded Medical Subject Headings terms. The electronic search was supplemented with a hand search of retrieved references to increase the inclusion of relevant literature. All articles included in the review reported the assessment of physiologic or psychological symptoms obtained by self-report in adults with AL during diagnosis or treatment at one or more time points. Articles were excluded from this review if they were not written in English, were published before 1990, detailed the effects of an intervention, and did not clearly identify the frequency or severity of symptoms experienced by patients. In addition, articles assessing symptoms in either hematopoietic stem cell transplantation (only) or survivors of AL post-treatment were not included in this analysis.

Data Evaluation

Inherent in the methodologic approach of an integrative literature review is the variability of relevant data,

which increases the complexity of the analysis (Whittemore & Knafl, 2005). To assist in the evaluation and interpretation of the data, a rating system was applied to score how strongly the findings contributed to meeting the aims of the research. Data were scored on a two-point scale for relevance (1 = low and 2 = high), as suggested by Whittemore and Knafl (2005). This rating system was applied to assist in analyzing the findings. Therefore, articles that scored low were not excluded, but contributed less during the analysis.

Data Analysis

The empirical data were extracted from all articles included in this review. The specific variables of interest in this review included sample demographics, methods, and symptom characteristics. Categories extracted from the articles under review were synthesized and are presented in the following section.

Presentation of Findings

A total of 25 articles were included in this review. Two of the articles included were intervention studies, whereas the remainder were descriptive, using either quantitative (n = 16), qualitative (n = 5), or mixed (n = 2) methodologies. Fifteen articles examined symptoms in a variety of different hematologic malignancies including AL, another five examined those diagnosed with AML and ALL, and the remaining four studies included only those diagnosed with AML. Only 5 of the 20 articles included more than one disease type and clearly delineated the specific symptom experience for each disease. Thirteen of the studies reported cross-sectional data, whereas the other 11 reported longitudinal data providing at least one other time point for comparison. Eleven examined symptoms during or at the start of induction chemotherapy, and another 11 examined symptoms at any point in treatment; the remaining two articles examined symptoms specifically during consolidation chemotherapy. Four of the studies included only patients who were newly diagnosed. Only one study compared the symptom report of newly diagnosed individuals to those with relapsed or refractory disease. Twenty-two studies were conducted outside of the United States. Table 1 provides a summary of the quantitative studies, including methodologies and symptom characteristics.

Assessment of Physiologic Symptoms

The characteristics of the physiologic symptoms experienced by individuals in all studies were collected using either instruments that are well tested for validity and reliability, most commonly the European Organisation for Research and Treatment of Cancer Quality of Life Core 30 questionnaire, the Functional Assessment of Cancer Therapy, the Memorial Symptom Assessment Scale, or information that surfaced during semistructured interviews. The majority of articles discussed the presence or frequency of symptoms reported by participants (n = 23) and the severity of symptoms (n = 24). Symptom severity was defined using assessment scales, those with higher severity were reported as moderate to severe on a numeric rating scale. Only four of the articles assessed symptom distress.

Research findings suggest that individuals with AL experience multiple symptoms at varying points during treatment, although the frequency of these physiologic symptoms may vary by disease. For example, in the study by Johnsen, Tholstrup, Petersen, Pedersen, and Groenvold (2009), the fewest mean number of symptoms was 3.7 (range = 0–9) in a subgroup of individuals with AML. This study was a cross-sectional design of individuals with hematologic malignancies, including AML, who were at any point in treatment from new diagnosis to more than 10 years postdiagnosis, and may have been inpatient or outpatient. In comparison, Priscilla et al. (2011) reported the mean number of symptoms for individuals with AML at any time point in treatment; this study found patients reporting twice as many symptoms ($\bar{X}$ = 7.8, range = 0–9). One explanation for why the number of concurrent symptoms was higher in the latter study may be that this study recruited only individuals who were hospitalized and more likely to receive treatment for active disease or symptom support.

Priscilla et al. (2011) also found that those with ALL (n = 15) reported a slightly higher number of symptoms, ($\bar{X}$ = 8.9, range = 0–9). In addition, two other studies found a similar number of mean symptoms experienced. Manitta et al.'s (2011) study included all hematologic malignancies at varying points in treatment and found a mean of 8.8 (range = 0–29) symptoms. Zimmerman et al.'s (2013) study also reported a mean of 8.8 (range = 0–12) concurrent symptoms experienced in patients with AL where the majority of patients were undergoing induction chemotherapy. Finally, in Rodin et al.'s (2011) cross-sectional study, the highest amount of concurrent symptoms ($\bar{X}$ = 11.2, range = 0–12) was observed in individuals with AL who were one month post-hospital admission for either a new diagnosis or relapsed disease.

Only two studies reported the mean number of severe symptoms, which ranged from as few as 0.9 (range = 0–9) in patients with AML at any treatment point (Johnsen et al., 2009) to as many as 3.9 (range = 0–9) in patients with AML and 4.3 (range = 0–9) in patients with ALL (Priscilla et al., 2011) at any point in treatment. Although definitive conclusions cannot be drawn from those findings, the data suggest that those with AML and ALL experience severe concurrent symptoms with

Table 1. Quantitative Research on Physiologic and/or Psychological Symptoms in Patients With Acute Leukemia

Study and Country	Sample	Methods	Timing in Treatment	Results
Alibhai et al., 2012 Canada	35 patients with AML with a mean age of 56 years (SD = 12.9)	Quasi-experimental pilot of individualized exercise program **Instruments:** • EORTC QLQ-C30 • FACT-Fatigue • VAS-Fatigue • HADS	Start of induction chemotherapy for new diagnosis; relapsed after six months or more after complete remission (inpatient) Baseline was within seven days of induction; postinduction was within one week of discharge after completion of chemotherapy	**Frequency:** Symptoms reported included fatigue, anxiety, and depression. **Severity:** Fatigue (range = 0–10) increased from baseline ($\bar{X}$ = 4.6, SD = 2.6) to post-induction ($\bar{X}$ = 4.7, SD = 2.6). Anxiety (range = 0–21) decreased in from baseline ($\bar{X}$ = 6.2, SD = 4.7) to postinduction ($\bar{X}$ = 4.1, SD = 2.3). Depression (range = 0–21) decreased in mean scores from baseline ($\bar{X}$ = 5.9, SD = 4.1) to post-induction ($\bar{X}$ = 4.7, SD = 3.8). **Distress:** Not evaluated
Chang et al., 2008 Taiwan	22 patients with AML with a mean age of 53 years (SD = 13.6) for the control group and 50 years (SD =15) for the intervention group.	Randomized, controlled trial of walking program in inpatients with AML receiving chemotherapy Data collected at days 1, 7, 14, and 21 of chemotherapy. **Instruments:** • BFI • SDS • POMS	Induction chemotherapy (inpatient)	**Frequency:** Symptoms reported included fatigue, anxiety, and depression. **Severity:** Fatigue (range = 0–10) scores doubled in the control group from day 1 ($\bar{X}$ = 2.1, SD = 3) to day 21 ($\bar{X}$ = 4.8, SD = 3.5), and increased only slightly in the intervention group from day 1 ($\bar{X}$ = 4.4, SD = 3.6) to day 21 ($\bar{X}$ = 4.6, SD = 3). Anxiety (range = 0–4) increased from day 1 ($\bar{X}$=1.4, SD = 1.2) to day 21 ($\bar{X}$= 1.7, SD = 1.7) in the control group. A decrease in anxiety was observed in the intervention group from day 1 ($\bar{X}$= 1.8, SD = 1.1) to day 21 ($\bar{X}$= 1.2, SD = 1.3). Depression (range = 0–4) increased from day 1 ($\bar{X}$= 1.4, SD = 1.3) to day 21 ($\bar{X}$= 1.5, SD = 1.5) in the control group, and decreased in the intervention group from day 1 ($\bar{X}$= 1.9, SD = 1.1) to day 21 ($\bar{X}$ = 1.3, SD = 1.2). **Distress:** Symptom distress (range = 0–5) increased in the control group from day 1 ($\bar{X}$= 1.4, SD = 0.3) to day 7 ($\bar{X}$= 2, SD = 1.1), and decreased in the intervention group from day 1 ($\bar{X}$ = 1.8, SD = 0.6) to day 7 ($\bar{X}$ = 1.7, SD = 0.5).
Hosaka et al., 1994 Japan	16 patients with AML with a mean age of 51 years (range = 25–71) and 3 patients with ALL with a mean age of 43 (range = 28–64) out of 31 total participants total	Cross-sectional descriptive study **Instruments:** • Zung's Self-Rating Anxiety Scale • Zung's Self-Rating Depression Scale • POMS	One patient with AML and one patient with ALL were receiving chemotherapy; the remaining participants were not receiving treatment (inpatient).	**Frequency:** Symptoms reported included anxiety and depression. **Severity:** Six percent of participants were found to have a major depressive disorder. **Distress:** Not evaluated
Johnson et al., 2009 Denmark	34 patients with AML ($\bar{X}$ = 65 years) out of 470 total participants	Cross-sectional descriptive study **Instrument:** • EORTC-QLQ-C30	Any time in treatment from new diagnosis to more than 10 years postdiagnosis	**Frequency:** The three most reported symptoms included insomnia (56%), fatigue (47%), and pain (24%). **Severity:** Most severe symptoms included fatigue, appetite loss, and diarrhea. **Distress:** Not evaluated

(Continued on the next page)

[a] Study did not delineate symptoms further by disease.

[b] Can either be induction or consolidation chemotherapy.

AML—acute myeloid leukemia; AL—acute leukemia; ALL—acute lymphocytic leukemia; BFI—Brief Fatigue Inventory; ESAS—Edmonton Symptom Assessment Scale; EORTC QLQ-C30—European Organisation for the Research and Treatment of Cancer Quality of Life Core 30; FACT—Functional Assessment of Cancer Therapy; HADS—Hospital Anxiety and Depression Scale; LGC—Life Quality Gerontological Center Scale; POMS—Profile of Mood States; SDS—Symptom Distress Scale; VAS—visual analog scale

Table 1. Quantitative Research on Physiologic and/or Psychological Symptoms in Patients With Acute Leukemia *(Continued)*

Study and Country	Sample	Methods	Timing in Treatment	Results
Koenigsmann, Koehler, Regner, et al., 2006 Germany	6 patients with AML with a mean age of 61 years (range = 21–76) 6 patients with ALL with a mean age of 43 years (range = 21–69)	Phenomenologic qualitative study using semistructured interviews	Within first week of diagnosis and treatment (inpatient)	**Frequency:** Symptoms reported by at least half of participants with ALL diagnosis included fatigue, bone pain, and extreme weakness. Symptoms reported by at least half of the participants at AML diagnosis included fatigue, bone pain, extreme weakness, dizziness, and general unwellness. Pain was reported by at least two-thirds of ALL and AML participants during treatment. **Severity:** Patients with AML reported three severe symptoms (per patient description) at diagnosis. Patients with ALL reported four severe symptoms (per patient description) at diagnosis. **Distress:** Not evaluated
López-Jiménez et al., 2006 Spain	77 patients with AML ($\bar{X}$ = 49 years, SD = 1.8) out of 177 total participants	Prospective descriptive study **Instruments:** • Functional Living Index for Emesis	At start of induction chemotherapy or radiotherapy for new or relapsed disease and monitored for five days after start of treatment (inpatient)	**Frequency:** Vomiting was reported by 53% of participants. **Severity:** Twenty-eight percent of patients with AML reported that emesis greatly impacted their daily life; 8%–15% reported significant nausea, with highest reports on days 2 and 3 of chemotherapy. **Distress:** Not evaluated
Manitta et al., 2011[a] Australia	16 patients with AML and 3 patients with ALL out of 180 total participants	Cross-sectional descriptive study **Instrument:** • MSAS	Inpatient and outpatient	**Frequency:** Most reported symptoms included lack of energy (69%), pain (42%), trouble sleeping (41%), drowsiness (41%), and sadness (41%). **Severity:** The most common severe symptoms reported included lack of sexual interest (56%), pain (51%), constipation (50%), and difficulty swallowing (50%). **Distress:** Physical distress was highest in patients with refractory disease. Psychological distress was highest in patients newly diagnosed, with poorer performance status, and who were inpatient. Global distress was highest in patients who were newly diagnosed, had relapsed or refractor disease, poorer performance status, and who were inpatients.
McGuire et al., 1998 United States	4 patients with AML and 1 patient with ALL ($\bar{X}$ = 44 years, SD = 13.4) out of 18 total participants	Prospective longitudinal descriptive study **Instruments:** • Verbal descriptor form (pain) • Oral Assessment Guide • Oral Mucositis Index • POMS	**Baseline:** Before onset of chemotherapy **Treatment:** Days 2–10 of chemotherapy **Post-treatment 1:** Seven-day interval post chemotherapy **Post-treatment 2:** After first week of post-chemotherapy to end of study	**Frequency:** Mucositis pain reported by 11% at baseline, 33% during treatment, 61% at post-treatment 1, and 67% at post-treatment 2. **Severity:** Mean mucositis pain scores (range 0–10) increased over time from 3.5 at baseline to 5.5 at post-treatments 1 and 2. At baseline, 11% reported intolerable pain; at post-treatment 2, 67% reported intolerable pain. **Distress:** Not evaluated

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[a] Study did not delineate symptoms further by disease.

[b] Can either be induction or consolidation chemotherapy.

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Table 1. Quantitative Research on Physiologic and/or Psychological Symptoms in Patients With Acute Leukemia *(Continued)*

Study and Country	Sample	Methods	Timing in Treatment	Results
Meyers et al., 2005[a] United States	19 patients with AML and 35 patients with MDS ($\bar{X}$ = 60 years, range = 21–84)	Prospective longitudinal descriptive **Instruments:** • FACT • BFI • Barthel ADL Index	Induction and one month postinduction (inpatient)	**Frequency:** Fatigue **Severity:** Sixty-five percent of participants reported significant fatigue (range = 0–10) at baseline ($\bar{X}$ = 5.3, SD = 2.9), and 79% reported significant fatigue at follow-up. **Distress:** Not evaluated
Morselli et al., 2010[a] Italy	40 patients with AML and 13 patients with ALL (median = 50 years, range = 32–72)	Prospective longitudinal descriptive **Instruments:** • ESAS • HADS	Diagnosis, postinduction chemotherapy, and discharge (inpatient)	**Frequency:** Symptoms reported included pain (22%–51%), anxiety (30%–40%), and depression (21%–36%). **Severity:** Mild pain was reported by 40% at Time 0 and decreased steadily to 17% discharge. Moderate to severe pain was reported by 12% at Time 0 and decreased to 6% at discharge. **Distress:** Not evaluated
Persson et al., 2001[a] Sweden	7 patients with AL ($\bar{X}$ = 57 years, SD = 15.6) out of 16 total participants	Longitudinal descriptive mixed-method **Instruments:** • EORTC QLQ-C30 • Life Quality Gerontological Center Scale • Quality of life questionnaire • Sense of Coherence Scale	At start of induction chemotherapy treatment (inpatient)	**Frequency:** Symptoms reported included fatigue, pain, sleep disturbance, dyspnea, diarrhea, nausea and vomiting, constipation, and appetite loss. **Severity:** Those with relapsed disease experienced the most severe symptoms, including fatigue, pain, and dyspnea. **Distress:** Not evaluated
Priscilla et al., 2011 Malaysia	24 patients with AML and 15 patients with ALL ($\bar{X}$ = 40 years, range = 15–78) out of 105 total participants	Cross-sectional descriptive study **Instrument:** • EORTC QLQ-C30	Unknown timing in diagnosis, treatment, or disease status (inpatient)	**Frequency:** Symptoms most reported by patients with AML included fatigue (83%), insomnia (63%), constipation (63%), appetite loss (58%), and pain (50%). Symptoms most reported by patients with ALL included appetite loss (100%), fatigue (80%), constipation (67%), dyspnea (67%), insomnia (60%), and nausea and vomiting (60%). **Severity:** Most severe symptoms reported by those with AML included constipation (54%) and appetite loss (46%). In those with ALL, constipation and appetite loss also were the most severe symptoms at 47% and 67%, respectively. **Distress:** Not evaluated

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Table 1. Quantitative Research on Physiologic and/or Psychological Symptoms in Patients With Acute Leukemia *(Continued)*

Study and Country	Sample	Methods	Timing in Treatment	Results
Rodin et al., 2011[a] Canada	139 patients with AML and 47 patients with ALL ($\bar{X}$ = 50 years, SD = 15.4) out of 205 total participants	Cross-sectional descriptive study **Instruments:** • MSAS • Beck Hopelessness • FACT-SP • Acute Stress Reaction Questionnaire	One month after admission for treatment for either new diagnosis, relapsed disease, or treatment failure (inpatient and outpatient)	**Frequency:** The three most reported symptoms included lack of energy (78%), drowsiness (59%), and difficulty sleeping (57%). **Severity:** Mean symptom severity was reported ($\bar{X}$ = 2, SD = 0.5, range = 1–3). **Distress:** Mean symptom distress (range = 0–4) was reported ($\bar{X}$ = 1.5, SD = 0.8).
Santos et al., 2006[a] Brazil	18 patients with AML and 10 patients with ALL ($\bar{X}$ = 52 years, SD = 15) out of 107 total participants	Cross-sectional descriptive study **Instruments:** • HADS • Impact of Event • EORTC QLQ- C30	Varied; 3–96 months from diagnosis	**Frequency:** Symptoms reported included anxiety and depression. **Severity:** Twenty percent of participants had high levels of anxiety;17% had high levels of depression. Patients receiving IV chemotherapy had statistically significant higher levels of anxiety ($\bar{X}$= 6.45, range = 0–21) than other treatment groups. Depression scores also were higher in the chemotherapy group ($\bar{X}$ = 4.64, range= 0–21).
Schumacher et al., 1998 Germany	61 patients with AML ($\bar{X}$ = 46 years, range = 16–69)	Longitudinal descriptive study **Instrument:** • EORTC QLQ-C30	New diagnosis, allowed induction through maintenance (inpatient)	**Frequency:** Symptoms reported included fatigue, appetite loss, dyspnea, pain, and nausea. **Severity:** Fatigue, appetite loss, and dyspnea were all moderate to severe (40 or greater, range = 0–100) at the start of treatment and decreased over time. Fatigue was never reported as less than 30. Appetite loss oscillated between severe (60 or greater) and mild (about 10) over time. Pain, nausea, sleep disturbance, and diarrhea were mild to moderate (20–30, range = 0–100) at the start of the study, increased at Time 2, and continued to oscillate over the study period. Dyspnea was moderate (40; range 0–100) at Time 1 and decreased to mild (20) at the end of the study. **Distress:** Not evaluated
Schumacher et al., 2002 Germany	101 patients with AML ($\bar{X}$ = 48 years, range = 16–69)	Longitudinal descriptive study **Instruments:** • EORTC QLQ-C30 • POMS	Followed new diagnosis receiving induction through maintenance chemotherapy (inpatient)	**Frequency:** Symptoms reported included fatigue, appetite loss, dyspnea, pain, and depression. **Severity:** Fatigue, appetite loss, dyspnea were moderate to severe (35 or greater, range = 0–100) at start of treatment and decreased (32 or less) by end of the study. Pain and nausea were mild to moderate (18–25, range = 0–100) at the start of the study and continued to oscillate over the study period. Nausea increased in correlation with the end of chemotherapy treatment. Depression (range = 0–100) was reported to be about 27 at Time 1, but decreased to less than 15 at all other time points. **Distress:** Not evaluated

(Continued on the next page)

[a] Study did not delineate symptoms further by disease.

[b] Can either be induction or consolidation chemotherapy.

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Table 1. Quantitative Research on Physiologic and/or Psychological Symptoms in Patients With Acute Leukemia *(Continued)*

Study and Country	Sample	Methods	Timing in Treatment	Results
Wittman et al., 2006[a] Germany	28 patients with AML and 11 patients with ALL ($\bar{X}$ = 47 years, SD = 15.4, range = 18–75)	Cross-sectional descriptive study **Instruments:** • FACT • HADS	Varied; all received treatment within 6–8 week (inpatient)	**Frequency:** Symptoms reported included pain, anxiety (12%–22%), and depression (10%–18%). **Severity:** Pain was the most severe symptom ($\bar{X}$ = 3.2, SD = 1.3, range = 0–4). **Distress:** Not evaluated
Zimmerman et al., 2013[a] Canada	193 patients with AML and 56 patients with ALL ($\bar{X}$ = 50 years, SD = 16, range= 18–86) out of 272 total participants	Cross-sectional descriptive study **Instrument:** • MSAS	Varied (inpatient)	**Frequency:** Three most reported symptoms included lack of energy (79%), drowsiness (56%), and difficulty sleeping (55%). **Severity:** The most frequent symptoms reported as very severe included lack of energy (57%), difficulty sleeping (44%), and pain (41%). **Distress:** Mean symptom distress was reported ($\bar{X}$ = 1.5, SD = 0.8, range = 0–4). The most distressing symptoms reported included pain (21%), difficulty sleeping (20%), and lack of energy (20%).
Zittoun et al., 1999[a] France	57 patients with AL (median = 44 years, range= 16–83) out of 178 total participants	Longitudinal descriptive study **Instruments:** • EORTC QOL • HADS • Leukemia/BMT module	Time 1: one day after chemotherapy Time 2: 11 days postchemotherapy[a] Time 3: 21 days after the end of chemotherapy[a] (inpatient)	**Frequency:** The three most frequent symptoms found over time included lack of appetite (Time 1 = 64%, Time 3 = 49%), tiredness (Time 1 = 64%, Time 3 = 40%), and sleeping disorder (Time 1 = 48%, Time 3 = 31%). Depression increased from 22% at Time 1 to 35% at Time 3 **Severity:** Nausea and vomiting was measured at Time 1 ($\bar{X}$ = 2.5, SD = 0.8) and decreased at Time 3 ($\bar{X}$ = 1.9, SD = 0.8). Fatigue scores also decreased from Time 1 ($\bar{X}$ = 2.6, SD = 0.7) to Time 3 ($\bar{X}$ = 2.4, SD = 0.8). Nausea and vomiting and fatigue were both rated as moderate to severe. **Distress:** Not evaluated

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the highest frequencies during and immediately after treatment.

Common Physiologic Symptoms

Regardless of disease type, the five most common symptoms reported in the majority of articles included fatigue or lack of energy (n = 11), pain (n = 9), insomnia (n = 7), appetite loss (n = 6), and nausea and vomiting (n = 6). Not only were these symptoms frequently reported among all the studies, but they also were highly prevalent among individuals in each of the studies (see Table 2).

Fatigue: Fatigue, a common symptom in cancer survivors, was reported by 47% (Johnsen et al., 2009) to 83% (Priscilla et al., 2011) of patients with AML and 67% (Koenigsmann, Koehler, Franke, & Frommer, 2006) to 80% (Priscilla et al., 2011) of patients with ALL. Schumacher et al. (1998, 2002) reported that the severity of fatigue in those newly diagnosed with AML was initially moderate to severe (greater than 60, range = 0–100) and decreased to mild (greater than 30) by the end of the four-week study period. Other studies found that the severity of fatigue increased between induction chemotherapy and one month post-treatment in patients with AML (Chang et al., 2008) and patients with myelodysplastic syndrome (Meyers, Albitar, & Estey, 2005).

Nausea and vomiting: Nausea and vomiting is another common symptom related to the emetogentic risk of many of the chemotherapy agents used during treatment. López-Jiménez et al.'s (2006) study showed an average of six emetic episodes, with 10% (n = 8) requiring rescue antiemetics at some point in treatment. Priscilla et al. (2011) examined symptoms at varying

time points in diagnosis and treatment and found that 38% (n = 9) of patients with AML and 60% (n = 9) of patients with ALL experienced nausea and vomiting, as well.

Pain: The frequency of pain experienced by participants in nine studies ranged from as low as 24% (Johnsen et al., 2009) to as high as 50% of patients with AML and 60% of patients with ALL. Those studies examined pain longitudinally and found that pain increased over time. Examining the severity of pain in patients newly diagnosed with AL followed one of two trajectories depending on initial severity scores. In patients with moderate to severe pain, scores initially increased from baseline, but then ultimately decreased over time (Morselli et al., 2010; Schumacher et al., 1998, 2002). Participants reporting mild pain experienced continued decrease in severity over time (Morselli et al., 2010). However, that trajectory was not observed in McGuire et al.'s (1998) longitudinal study, which specifically examined mucositis pain in individuals with hemematologic malignicies. At the start of chemotherapy, pain was present in just 11% of patients, but steadily increased over time to 67% of patients experiencing intolerable pain by the end of the second post-treatment follow-up (McGuire et al., 1998).

Only Persson et al. (2001) compared symptoms in those with newly diagnosed and relapsed disease. That study reported that symptom severity scores were at least twice as high in those with relapsed disease when compared to those responding to treatment. Specifically, when comparing appetite loss, pain, and nausea and vomiting, those newly diagnosed with AL reported mean severity scores of 4.8, 4.8, and 9.5 (range = 0–100), respectively; however, in those with relapsed disease, mean severity scores were 33.3, 44.4, and 30.6, respectively. Similarly, the mean severity of fatigue and dyspnea in those with a new diagnosis of AL were 31.7 and 14.3, and the same scores in those with relapsed AL disease were reported to be 64.8 and 33.3, respectively.

The distress associated with physiologic symptoms was only reported in four studies. Two of those studies found that the degree of distress from a specific symptom was 1.5 (SD = 0.8, range = 0–4) (Rodin et al., 2011; Zimmermann et al., 2013). Interestingly, McGrath (2012) examined the effect of a hematologic malignancy on sexuality and found that those who experienced persistent issues surrounding sexuality reported this to be the most troubling of all issues experienced.

Table 2. Qualitative Reports of Specific Symptoms

Symptom	Reports
Dermatologic (Persson et al., 2001)	[I] got blisters on my hands and feet, which were very painful, and I couldn't function like before.
Diarrhea (Persson & Hallberg, 1995)	It was so bad it just ran out of me. I didn't dare fall asleep as I would have lost control over my bowels.
Dyspnea (Persson et al., 2004)	I found it hard to breath . . . coughed and coughed . . . it wheezed and rattled.
Fatigue (Persson & Hallberg, 1995; 2004)	I got tireder and tireder and finally couldn't stand up. I was terribly tired. I could go on sleeping even when I'd already slept for 12 hours.
Mucositis (Nissim et al., 2013; Persson & Hallberg, 1995)	Awfully painful I felt like someone had carved out a new mouth and nasal cavity for me. Nothing felt normal. I had no lining in my mouth that was unbearable.
Nausea (Persson & Hallberg, 1995)	I felt ill every day.
Sexual dysfunction (McGrath, 2012)	[Sexual dysfunction is] definitely an area that took its toll on me. Sex can be there in the mind, but the body doesn't want to respond to it. It's sort of like paralysis from the waist down and that was really awful. Since I got ill and all the rest it's gotten worse and worse. Right now, I have no libido whatsoever.

Note. Study did not delineate symptoms further by disease.

Assessment of Psychological Symptoms

Of the 25 studies, 10 discussed findings related to the psychological symptoms experienced by patients with AL. The assessment of psychological symptoms was most commonly collected using either the Profile of Moods State, the Hospital Anxiety and Depression Scale, or through qualitative interviews. Given the nature of the psychological assessment instruments, the reporting of these symptoms was predominantly related to the assessment of anxiety and depression.

The psychological symptoms experienced by participants varied across studies. A cross-sectional analysis of psychological symptoms in patients with AL found a mean of 2.2 (SD = 1.9, range = 0–6) symptoms present (Zimmermann et al., 2013). However, the frequency of depression and anxiety was 10%–20% in those with AL, with at least another 18%–22% possible cases of depression and anxiety (Wittmann, Vollmer, Schweiger, & Hiddemann, 2006). In comparison, Hosaka, Aoki, and Ichikawa (1994) examined the emotional states of patients with AL and found that depression was present in 40% of participants who did not have a previous psychiatric diagnosis. In that same study, the severity of anxiety and depression, as measured by the Hospital Anxiety and Depression Scale (range = 20–80), was

slightly higher in those with ALL ($\bar{X}$ = 37, SD = 6.3; $\bar{X}$ = 39.3, SD = 4) when compared to patients with AML ($\bar{X}$ = 33.4, SD = 6.8; $\bar{X}$ = 38.8, SD = 8).

Time in treatment may influence the experience of psychological symptoms. Zittoun, Achard, and Ruszniewski (1999) reported that the frequency of depression over time increased from 23% on day one of chemotherapy to 35% at 21-days post-chemotherapy in a mixed cohort of individuals with hematologic malignancies. That same study found that the severity of depression also increased slightly over time from day one of chemotherapy to 21 days post-chemotherapy. In addition, the control group of an intervention study with patients diagnosed with AML showed similar increases in both depression and anxiety from day one of chemotherapy to 21 days post-chemotherapy (Chang et al., 2008).

In analyzing the findings from some of the articles reviewed, hospitalization and treatment appeared to greatly impact the psychological well-being of individuals. Feelings of powerlessness and stress were alluded to by participants (Persson & Hallberg, 2004). Koenigsmann, Koehler, Franke, et al. (2006) also observed that adults aged younger than 33 years reported side effects in detail, and reported extensive brooding to the point of wearing themselves out. These findings demonstrate the psychological burden that impacts patients across the disease trajectory, and suggests that young adults may require additional psychological support during the treatment process. Not only was a trend seen in the data around diminished psychological health during the treatment process, but also after.

Discussion

Uncontrolled symptoms contribute to longer hospitalizations, interruptions in needed treatment, increased dependence, and decreased functional status (Cleeland & Reyes-Gibby, 2002), as well as cancer-related distress (Albrecht & Rosenzweig, 2013). However, variations in both the frequency and severity of symptoms reported by patients were observed, and findings suggest that patients with AL may experience concurrent symptoms that may not only be severe, but distressing, occurring at various points in their treatment. In addition, the data also suggest that although those with AML and ALL have different prognoses and undergo different treatment regimens, the symptom burden for patients with these diseases deserves further evaluation. Many of the variations observed in the analysis are likely because of different factors including methods and sampling, as well as the instruments selected for data collection. However, in-depth analysis is challenging given the heterogeneity of the data currently available. Additional examination into variability in age groups and gender, as well as new diagnoses and relapsed disease, is critical. A limited amount of attention has focused on the symptom needs of patients with AL, particularly when compared to solid tumors. However, this is changing, and the number of researchers interested in examining the needs of this unique population is increasing. Therefore, the variations and trends illustrated in this review may serve as a guide for future research to assist in filling the knowledge gaps. The current data can serve not only to guide future directions of research, but also assist clinicians in the multidimensional assessment and management of symptoms throughout the entire treatment process.

Knowledge Translation

Patients with acute leukemia (AL) experience multiple concurrent symptoms.

Although many patients experience psychological symptoms along the disease trajectory, young adults may be particularly susceptible because of their unique developmental stage.

Additional exploration into the specific symptom management needs of patients with AL with varying disease trajectories is needed.

Limitations

This review has some limitations that hinder the strength of the conclusions regarding the symptom burden experienced by these patients. Although great effort was made to include only the symptom experiences reported by patients with AL, many of the studies that included all types of hematologic malignancies did not provide subanalysis of symptoms by disease type. Although a few studies tried to delineate whether participants were either newly diagnosed with relapsed disease or responding to treatment, this was not always the case. In addition, several of the studies did not delineate when during the treatment process data were captured. However, given that the treatment, prognosis, and disease burden for AL appears to differ depending on trajectory, a closer examination of symptoms for each group over time warrants additional examination to more clearly describe the overall disease burden.

Implications for Nursing Research and Conclusion

Knowledge related to the unique physiologic and psychological symptoms that patients with AL experience is increasing; however, more information still is needed. Specifically, longitudinal research examining the symptom burden in patients with AML and ALL over various trajectories would greatly add to this body of literature. This knowledge is vital to understanding the symptom onset, rate of symptom change over time, and

how the rate of symptom change varies over the AL trajectory. This knowledge also is critical to tailoring nursing interventions that are based on personal characteristics, patient needs, and temporal characteristics of symptoms (Brant, Beck, & Miaskowski, 2010).

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