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Depression in Pediatric Acute Lymphoblastic Leukemia

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Abstract

Objective: This study aims to know the degree of depression in pediatric ALL patients. Patients with ALL, especially children and adolescents, are faced with many psychological and social problems. One of these psychological problems is depression. Children can experience changes in emotional-behavioral function due to the influence of chemotherapy drugs, painful procedures and frequent hospital visits that interfere with their activities and development at their age. **Method:** Descriptive research on ALL children aged 7-18 years at Dr Soetomo General Academic Hospital, Surabaya, East Java, Indonesia. Depression screening using the Indonesian version of the Patient Health Questionnaire-9 (PHQ-9). The data is presented descriptively. **Results:** there were 40 children who were included in this study. Most of the samples experienced mild depression, major depression was found in the age group 7-12 years. Many male and female child experiences mild depression. Most of the patients' mothers were 35 years old and had low economic status. None had a family history of depression. Inpatient care has more severe depression. **Conclusion:** Most of pediatric ALL have mild depression, whose features vary according to sociodemographic and clinical conditions

Keyword: Depression, ALL depression, Child's ALL, Child's ALL depression

I. Introduction

Since the treatment of leukemia patients has shown success in recent years, a psychosocial oncology care approach has been developed. When pediatric ALL patients are diagnosed with leukemia and undergo a long and intensive treatment, the patient and their parents will begin to face the risk of a very high level of psychosocial difficulties^[1]. One of the most studied psychosocial aspects is depression.

Several studies have evaluated depression in pediatric ALL patients with results that vary widely due to differences in the factors evaluated, the characteristics of the sample and the screening instrument used. The study of Khalifa et al comparing ALL patients and their parents with healthy control groups showed that 58% of ALL patients had psychiatric disorders compared to controls. Measurement of depression using the General Health Questionnaire and Hamilton Checklist of Symptoms of Depression Illness showed that patients and their parents with ALL had significant levels of depression compared to controls^[1]. The study of Kunin-Batson et al on ALL Standard Risk patients aged 1-9.9 years by assessing depression using the Behavioral Assessment System for Children, Second Edition: Parent Report Scale (BASC-2) showed that 28.7% of patients ALL experienced an increase in depression at 3 months after chemotherapy^[2]. A study in Uganda on children aged 7-17 years with malignancy stated that most patients (64.8%) had mild depression as measured by the Child Depression Inventory (CDI) and evaluated by the Mini Neuropsychiatric Interview for children and adolescents (MINI-KID)^[3]. Research on pediatric patients with ALL survival shows that genetic factors play a role in the occurrence of depression^[4].

The Regional General Academic Hospital (RSUD) Dr. Soetomo is a type A hospital, as the main reference for most cases of ALL children in East Java, Indonesia, no research has been done regarding depression in children with ALL.

II. METHOD

The study was a descriptive observational with a cross-sectional design in September 2020-March 2021. Samples were taken from children with a clinical diagnosis of ALL at Dr. Soetomo General Hospital Surabaya who met the inclusion and exclusion criteria. Inclusion criteria were children aged 7-18 years, parents signed the informed consent form. Exclusion criteria were patients with incomplete medical record data and hospitalized patients with unstable vital signs (shock, shortness of breath, bleeding, decreased consciousness). The variables studied were age, gender, nutritional status, treatment phase, ALL classification, risk stratification, comorbidities, inpatient care, length of illness, relapse condition, maternal age, and maternal education level, parents' economic status and family history of depression. Enforcement of depression using the Indonesian version of the PHQ-9 screening questionnaire^[5-6]. The questionnaire is filled out by the patient or asked by the researcher. The questionnaire is filled out by the patient or asked by the researcher. Data is processed by descriptive analysis. The ethical clearance was approved by the Ethics Committee of Dr. Soetomo General Academic Hospital (no 0055/KEPK/IX/2020).

III. RESULT

The results of the PHQ-9 questionnaire showed that most of the samples (34 patients, 85%) have mild depression (total PHQ score 0-9). There were 2 subjects classified as severe depression (total PHQ score 20-27) (Table 1).

Table 1. PHQ-9 assessment score

PHQ-9 score	Depression classification	N	%
0-4	<i>None-minimal</i>	23	57,5
5-9	<i>Mild</i>	11	27,5
10-14	<i>Moderate</i>	4	10
15-19	<i>Moderately severe</i>	0	0
20-27	<i>Severe</i>	2	5

The sample age group is more at the age of 7-12 years, severe depression only occurs in this age group. Both sexes experience mild depression (Table 2).

Table 2. PHQ-9 assessment score based on patients' sociodemographic

Characteristics	(n)	(%)	PHQ-9 score				
			0-4	5-9	10-14	15-19	20-27
Age							
7-12 years old	31	77,5	19	7	3	0	2
13-18 years old	9	22,5	4	4	1	0	0
Sex							
Male	25	62,5	14	6	4	0	1
Female	15	37,5	9	5	0	0	1

Most of the mothers were 35 years old and mild depression was common in both groups. Most sample have low economic status. Severe depression is experienced by mothers with low levels of education. All sample parents were married and there was no family history of depression (Table 3).

Table 3. PHQ-9 measurement result based on family sociodemographic characteristics

Characteristics	(n)	(%)	PHQ-9 score				
			0-4	5-9	10-14	15-19	20-27
Maternal age							
< 35 years old	17	42,5	11	4	1	0	1
≥ 35 years old	23	57,5	12	7	3	0	1
Economic status							
Low	22	55	13	5	3	0	1
High	18	45	10	6	1	0	1
Maternal education level							
Low	19	47,5	12	4	1	0	2
High	21	52,5	11	7	3	0	0
Marital status							
Married	40	100%	23	11	4	0	2
Divorced/not married	0	-	0	0	0	0	0
Family history of depression							
Present	0	-	0	0	0	0	0
None	40	100%	23	11	4	0	2

Severe depression occurs in both normal and malnutrition nutritional status. Severe depression occurs in both the induction and maintenance phases. None of the samples with ALL types L2 and L3. The high-risk stratification had more moderate-severe depression. Hospitalization is more likely to cause severe depression. The percentage of samples with comorbidities had more moderate to severe depression. Severe depression is more common in the duration of illness more than 2 months. The absence of relapse actually more experienced moderate to severe depression (Table 4)

Table 4. PHQ-9 measurement results based on patient clinical characteristics

Characteristics	(n)	(%)	PHQ-9 score				
			0-4	5-9	10-14	15-19	20-27
Nutritional status							
Malnutrition			18	6	3	0	1
Wasting	1	2,5					
Stunting	7	17,5					
Overweight	5	12,5					
Obesity	15	37,5					
Normal nutritional status	12	30	6	4	1	0	1
Treatment phase							
Induction	10	25	2	5	2	0	1
Consolidation	4	10	1	2	1	0	0
Maintenance	25	62,5	19	4	1	0	1
Reintensification	1	2,5	1	0	0	0	0
ALL classification							
ALL L1	37	92,5	23	7	4	0	2
ALL L2	3	7,5	1	2	0	0	0
ALL L3	0	0	0	0	0	0	0
Risk stratification							
High	28	70	14	10	2	0	1
Standard	12	30	9	1	2	0	0
Inpatient care							
Inpatient	29	72,5	16	7	4	0	2
Outpatient	11	27,5	7	4	0	0	0
Comorbidities							
Present	4	10	1	0	2	0	1
None	36	90	22	11	2	0	1
Length of illness							
≤ 2 months	5	12,5	2	2	1	0	0
> 2 months	35	87,5	21	9	3	0	2
Relapse condition							
Relaps	12	30	9	3	0	0	0
None	28	70	14	7	4	0	2

IV. DISCUSSION

The occurrence of psychological disorders including depression is a very complex interaction between the effects of the disease itself, the hospital atmosphere and the influence of chemotherapy. Studies in adults have found an association between chemotherapy such as vincristine, interferon, procarbazine, and asparaginase with depression. If the patient receives radiation treatment, it can cause irreversible neurocognitive disorders. In addition, feeling lethargic, pain, nausea, vomiting due to chemotherapy will make the child not interested in doing any activity so that conditions like this will lower the depression threshold [7].

With the development of chemotherapy in ALL children, the survival of ALL children is increasing. Quality of life (health-related quality of life) which includes physical, cognitive, social and emotional conditions is important in ALL patients. On the other hand, ALL children often experience neurocognitive and psychosocial problems during and after chemotherapy. One of the psychosocial problems experienced by ALL children is depression. The differences in the diagnostic instruments used, the diversity of the samples, and the differences in the age groups that were evaluated gave varying prevalence^[7-8]. In addition, children with malignancy who experience depression often miss a diagnosis of depression because symptoms and signs of depression such as weight loss, sleep disturbances, feelings of sadness are often only associated with the medical condition of the malignancy^[3].

Longitudinal research conducted by Myers on 159 standard risk ALL children aged 2-10 years using the BASC-2 PRS instrument showed that 1 month after the diagnosis was made depression was 21.7%, the percentage of depression 6 months after diagnosis was 28.6% and 12 months after diagnosis. This study did not distinguish the severity of depression^[9].

Research by Rivas-Molina et al., stated that of 46 acute leukemia patients in adolescents and young adults, 43 (94%) experienced depression as measured by the CDI instrument. Among these patients, most of them had severe depression (53%), 26% moderate, and 21% mild^[10].

The study of Kunin-Batson et al., using the BASC-2 instrument found that depression can be experienced in ALL children aged 1-9.9 years at standard risk during therapy up to 3 months after therapy. A total of 28% of the sample experienced depression at 3 months after therapy. Samples who experienced depression at 6 months after diagnosis had a greater risk of depression until 3 months after diagnosis (OR=7.88; 95% CI 2.61-23.81; p=0.0002)^[2]. This is thought to be related to the influence of steroids and parental fears of a possible relapse.

The study of Akimana et al., in children aged 7-17 years with various types of malignancy (leukemia about 26.7% of the total sample) evaluated depression using CDI. The results of this study found 26% among 352 children who had depression, especially mild depression degrees^[3].

The results of the measurement with the PHQ-9 questionnaire in our study showed that most of the samples (34 patients, 85%) were grouped in the mild depression group (total PHQ score 0-9). Among the mild depression group 23 (57.5% of all subjects) of them had a PHQ-9 0-4 score which means no depression and the percentage of mild depression was 27.5%. The percentage of our subjects who had major depression was only 5%. Even though our study uses different instruments, the percentage of mild depression is relatively the same as that of Akimana et al (26.7%)^[3] and Rivas-Molina et al (21%) but in Rivas-Molina et al study the highest percentage is severe depression (53%)^[10], in contrast to our study where the percentage of major depression was the smallest (5%).

Our study found mild depression was slightly more common in the age group 13-18 years compared to 7-12 years (87.5% vs. 84.4%), while major depression was slightly more common in the age group 7-12 years (15.6% vs 12.5%). In terms of age grouping, our study is close to that of Rivas-Molina et al and Akimana et al. It is estimated that this is due to various hormonal changes during adolescence, social expectations and the ability of adolescents to express their emotions better than the age of children. What distinguishes our study from that of Rivas-Molina et al is that the instrument in Rivas-Molina et al uses CDI and the sample is only in the standard risk group.

Research by Myers, shows that more men (85%) who experience depression^[9]. The number of subjects in our study were male but the percentage who experienced mild depression was more female (93.3% vs 80%). Moderate-severe depression was more common in males (20% vs. 6.7%).

The number of mothers aged 35 years experienced more mild depression (88.2% vs. 82.6%), while mothers aged < 35 years experienced more severe depression (17.4% vs 11.8%). Increasing maternal age will improve the quality of life in terms of psychological maturity when facing problems, including readiness when dealing with ill conditions. Mothers feel they have a demand to achieve social responsibility to help children

become qualified so that mothers will try to manage their emotional abilities so that sick children can get through it well by providing psychological support.

Our subjects from the low socioeconomic status group had slightly more prevalence than the high (55% vs 45%). Moderate-severe depression was more common in the low economic status group (18.2% vs 11.1%). This study is in line with that of Myers and Akimana et al. but the two researchers did not share the degree of depression. Low economic status is at risk for psychosocial disorders due to expensive medical costs and they lose productive time to earn income. As for people with low economic status, health insurance can be done by financing the National Health Insurance, but for other purposes such as living expenses and transportation to hospitals, it will cause problems for patients. The cost of treatment for ALL is more expensive than the cost of living and transportation but guaranteed by National Health Insurance. With parents not thinking about expensive medical costs, more attention will be paid to child care and this will support the child's psychological aspect.

Our study showed that mothers with higher education levels had more mild depression (90.5% vs. 78.9%), while mothers with lower education levels had more moderate-severe depression (21.1% vs. 9.5%) Research are in line with Myers' study. The higher the level of education will affect a person's mindset so that it is earlier in recognizing the symptoms of the disease, easier to find information, more anticipatory in dealing with an illness condition. With this mindset, the mother will be able to provide better care for the child so that it will also affect the child's psychology.

Our subjects all had married parents. Our research is different in foreign countries where it is still natural for a woman to have children without getting married. If a mother without a husband faces a child with a malignant condition, it will be a tremendous stress for the mother, and the mother's psychological condition will indirectly greatly affect the child's psychological condition.

Research on non-cancer children shows that genetics has a role in depression and anxiety^[11]. None of our study subjects had a family history of depression based on history taking.

Research by Rivas-Molina et al., showed that the type of ALL showed no significant relationship with the occurrence of depression in children with ALL^[10]. Our study was mostly with L1 LLA, while L2 and L3 ALL as many as 3 people all with mild depression.

In our study, most of the patients were hospitalized, the degree of depression was moderate to severe and all of the outpatients had mild depression severity. Treatment in the hospital with the atmosphere, disturbed sleep, procedures that cause pain are conditions that will increase the risk of psychological disorders including depression^[12].

The condition of children with ALL is included in the immunocompromised group so they are susceptible to comorbid diseases. Infection remains a major cause of morbidity and mortality in pediatric patients with ALL undergoing chemotherapy^[13]. Our study subjects who had co-morbidities had more moderate-to-severe depression than those without comorbidities (75% vs. 8.5%). Our study subjects were all with co-morbidities of pneumonia, and COVID-19. With these comorbidities, they will require longer hospital stays, treatment in isolation rooms, the child's condition will get worse, chemotherapy can be delayed, the pain will increase so that it will affect the child's psychological condition.

Depression in ALL patients can occur from the initial diagnosis, during therapy, and even several years after therapy. When the diagnosis of ALL is made, the emotional response will go through several stages. Initially, there will be rejection or distrust that will cause a sense of despair, followed by a dysphoric phase. The patient will show anxiety and depression, until finally in the final phase, the patient enters the adaptation phase. A review that analyzed depression in children with malignancy, with different sample characteristics related to age group, instrument used and type of malignancy found that 12 studies mostly found no relationship between length of illness and depression^[7]. Our study subjects used a 2-month limit with consideration of the induction phase of about 6 weeks so with 2 months it was assumed that the patient had entered a better adaptation phase. The difference with other studies is related to the difference in instruments to determine depression as well as the time limit used.

Research by Rivas-Molina et al., showed that the incidence of relapse showed no significant relationship with the occurrence of depression in children with acute leukemia or with the severity of depression ($p = 0.810$)^[10]. With a relapse condition, the child's quality of life will be increasingly disturbed due to the treatment received, disruption of daily activities, and worries about the disease^[8].

Our study showed that moderate-to-severe depression was more common in children in the induction treatment phase than in other phases, while mild degrees were more common in the maintenance phase. Our study is in line with the Rivas-Molina study, only that Rivas-Molina does not divide the severity of depression. The induction treatment phase, which is the initial phase of therapy, will create a burden for parents and children, related to the patient's medical condition (pain, hospitalization), the initial psychological phase

where there will generally be rejection or distrust of the diagnosis, as well as various bodily reactions due to chemotherapy.

V. Conclusion

Most of pediatric ALL have mild depression, whose features vary according to sociodemographic and clinical conditions

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Conflict of Interest

The Authors declare that there is no conflict of interest.

Ethical Approval

The ethical clearance was approved by the Ethics Committee of Dr. Soetomo General Academic Hospital (no 0055/KEPK/IX/2020).

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