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Association between body mass index at diagnosis and outcome of children with Acute Lymphoblastic Leukemia

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ABSTRACT

Background: Several studies have been published on the effect of body weight at diagnosis on the outcome of children with leukemia, but the results are not the same. The aim of this investigation was to study the survival of children with ALL admitted to a tertiary center in a developing country. *Methods and Materials*: This retrospective cohort study was performed on with standard risk B-precursor ALL in Ali-Asghar Children's Hospital. Patients in the high-risk group, patients with Down syndrome, and patients who had undergone significant changes during the treatment protocol were also excluded from the study. After completing the questionnaire, BMI at the time of diagnosis was calculated and patients were divided into four groups: underweight, normal weight, overweight and obese. Finally, the results were analyzed using SPSS software, descriptive data was analyzed by descriptive analysis methods and survival rate was analyzed by Kaplan-Meyer method with considering 95% confidence interval. *Results*: 112 patients aged 1 to 10 years (m/f ≈ 1.2/1) were enrolled to the study. 5-year overall survival of all patients and event-free survival of all patients were obtained from analysis 96.40 ±2.1% and 86.80 ±3.6%, respectively. Also from the analysis, the overall 5-year survival of all patients based on the status of the body mass index was obtained for underweight 100%, normal weight 95.70±3%, obese and over-weight 92.3±7.4%. Finally, no significant relationship was observed between overall survival and BMI. Furthermore, 5-year event-free survival analysis of patients based on BMI status in underweight 86.10±6.6%, normal weight 86.10±5%, obese and over-weight 92.9±6.9% was achieved. Lastly, there was no statistically significant relationship between event-free survival and BMI. *Conclusion*: Based on the results of this study and their comparison from other studies in this field, it is concluded that overall survival in obese and overweight children is lower than normal weight and underweight children. These different results from some other studies suggest the need for more accurate prospective studies with larger sample sizes.

Keywords: Acute Lymphoblastic Leukemia, Survival, BMI index

1. INTRODUCTION

Cancer is one of the leading causes of death among children (Yang et al., 2009, Peris-Bonet, 2010; Ahmed et al. 2020). In some countries, such as the United States, it is the second leading cause of death among children (0-14 years old)

(Ahmedin, 2006, Ahmedin Jemal et al., 2008, Jemal et al., 2008). After heart disease and accidents, it is the third leading cause of death in Iran (Alsayyad and Hamadeh, 2007). Leukemia is the most common type of cancer in children (Swaminathan et al., 2008) which accounts for about 32% of childhood cancers. The most common form of this disease among children under 19 years of age is Acute Lymphoblastic Leukemia (ALL) (Karimi et al., 2008), which accounts for 80% in developed countries (Coebergh et al., 2001). ALL is the first known cancer that can be treated in childhood. In fact, this disease is a group of heterogeneous malignancies with a number of different genetic disorders that lead to clinical manifestations and different responses to treatment. The peak is noticeable in two to three year olds and is more common in boys than girls at all ages (Horibe et al., 2013). The etiology of ALL is generally unknown, although different environmental and genetic factors are involved. The bone marrow is the primary organ for the production of blood cells. As the leukemia progresses, the production of blood cells were decreases. Thus, the signs and symptoms of anemia (paleness, lethargy), thrombocytopenia (bruising, petechiae, mucosal hemorrhage) and functional leukopenia (fever and infection) are found, but most of the initial manifestations of ALL are nonspecific and relatively rare (Nayiager et al., 2017). Lymphoblastic B leukemia is the most common immunophenotype starting at the age of one to ten years. The average leukocyte count in these patients is 33,000. However, 75% of patients have less than 20,000 cells. Thrombocytopenia is seen in 75% of patients and hepatosplenomegaly in 30 to 40% of patients. In all types of leukemia, symptoms of the central nervous system are seen in 5% of patients (5 to 10% of blasts are seen in cerebrospinal fluid). Testicular involvement is rarely seen at diagnosis, but studies have shown 25% of occult involvement in boys (Nathan J. Blum, 2019).

The last 30 years have seen a significant improvement in the treatment of children with ALL cancer. Children with relapse after cancer account for a large proportion of children with cancer (Krishnan et al., 2010). Treatment of relapsed patients is very difficult compared to newly diagnosed patients and does not have a specific treatment protocol and the survival rate of this group of patients is much lower compared to the second group (Trehan et al., 2015). Prognosis in leukemia depends on age at diagnosis, white blood cell count at diagnosis, CNS and testicular involvement at diagnosis, sex, race, and weight at diagnosis and during treatment. Therefore, considering the effect of BMI in response to treatment and relapse of the disease in studies as an independent factor and considering the importance of the issue, we decided to study the outcome of lymphoblastic leukemia patients admitted to Ali-Asghar children's Hospital at diagnosis during the years 2005 to 2019 for BMI. The results can have a direct impact on the choice and intensity of treatment regimen.

2. METHODS AND MATERIALS

This retrospective cohort study was performed on 112 patients aged 1 to 10 years with standard risk B-precursor ALL in Ali-Asghar Children's Hospital from March 2005 to March 2019. The sampling method is simple non-probability (convenient sampling) and the inclusion criteria are standard risk ALL. Exclusion criteria are High risk ALL including: Patients less than one-year-old and equal to or more than 10 years old, WBC more than 50,000, t (9; 22) and t (4; 11) at diagnosis, T-cell ALL, mediastinal mass, CNS or testis involvement at the time of diagnosis, DI <0.95, peripheral blood blast greater than 1000 on day 8 of treatment, MRD> 10% on the fifteenth day of treatment, MRD> 10^{-4} at the end of induction. Also patients with Down syndrome and patients who had undergone significant changes during the treatment protocol were excluded from the study. Then demographic information, BMI, survival, relapse and mortality were collected as a research field and entered in a questionnaire designed for this purpose. After completing it, BMI was calculated at the time of diagnosis and patients were classified into four groups: underweight, normal weight, overweight and obese. In the next step, the relationship between body mass index and survival rate of patients with acute lymphoblastic leukemia was determined. Finally, the results were analyzed using SPSS software, descriptive data was analyzed by descriptive analysis methods and survival rate was analyzed by Kaplan-Meyer method. The significance level is considered 0.05 in all statistical analysis.

3. RESULTS

Among 112 patients studied, 45.54% are girls and 54.46% are boys. The mean age of the patients at the time of diagnosis was 61.2 months with a standard deviation of 38.88, the mean weight of patients at the time of diagnosis was 18.9 kg with a standard deviation of 9.19 and the mean height of patients at the time of diagnosis was 109.5 cm with a standard deviation of 21.94. Also, their mean body mass index at the time of diagnosis was 15.01 with a standard deviation of 1.93 and the average percentage of body mass index at the time of diagnosis was 29.38 with a standard deviation of 31.14. The mean follow-up time of the patient until death was 72.65 months with a standard deviation of 32.01 and the mean follow-up time of the patient until death or relapse was 68.10 months with a standard deviation of 32.49 (Table 1).

Table 1 Quantitative variables analysis of all enrolled patients

	Age at diagnosis (mo)		Weight of Diagnosis Time (Kg)	Height of Diagnosis Time (cm)	Body Mass Index	BMI percentile	Duration of follow-up until death (mo)	Duration of follow-up until relapse/death (mo)
N	Valid	112	112	112	100	112	112	112
	Missing	0	0	0	12	0	0	0
Mean	61.2054		18.9082	109.52	15.019229	29.38	72.6568	68.1095
Std. Error of Mean	3.67415		0.87642	2.092	0.1936593	2.942	3.02539	3.07030
Median	51.1167		16.0000	105.00	14.807107	19.00	77.7333	65.2167
Std. Deviation	38.88356		9.19201	21.944	1.9365930	31.140	32.01767	32.49301
Minimum	12.07		9.50	73	11.7914	1	15.73	13.00
Maximum	173.53		54.00	181	21.9076	99	138.00	132.33

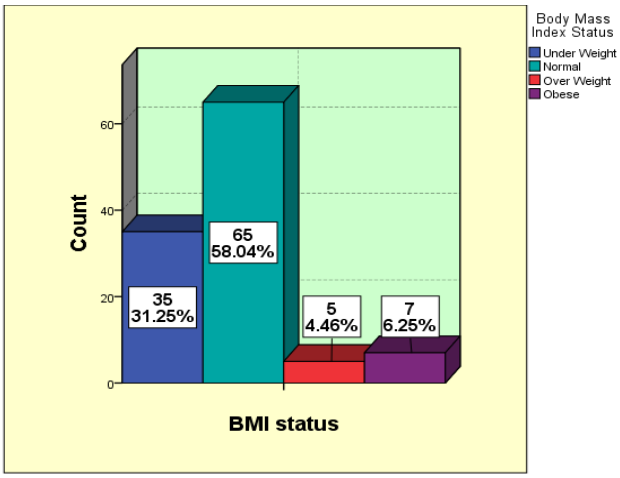
The comparison of the mean of the quantitative variables between the two BMI subgroups including "underweight and normal weight" and "overweight and obese" was performed and the results are as follows: The mean age of patients at the time of diagnosis was 61.52 in under and normal weight and 58.57 in over and obese weight and standard deviation was 39.74 and 32.14, respectively. Also, no significant relationship was observed between age at diagnosis and BMI.

The mean weight of patients at the time of diagnosis in underweight and normal weight was 18.30 and in over weight and obese was 23.84 and the standard deviation was 8.76 and 11.41, respectively. Finally, a significant relationship was observed between weight at the time of diagnosis and BMI. The mean height of patients at the time of diagnosis was 109.47 in underweight and normal weight and 109.88 in over and obese weight and the standard deviation was 22.12 and 21.36, respectively. Then no significant relationship was observed between height and BMI (Table 2).

Table 2 Comparison the mean of quantitative variables between two groups for BMI status

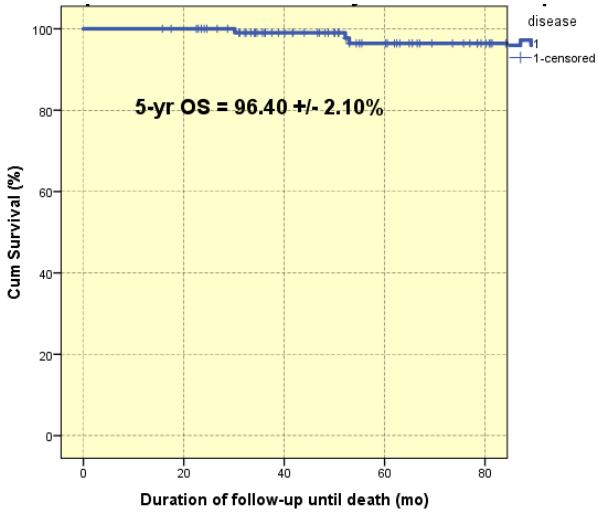
	BMI status 2	N	Mean	Std. Deviation	Std. Error Mean	P value
age at diagnosis (mo.)	Under and normal weight	100	61.5210	39.74247	3.97425	0.805
	Over and Obese weight	12	58.5750	32.14233	9.27869	
Weight of Diagnosis Time (Kg)	Under and normal weight	100	18.3041	8.76320	0.88522	
	Over and Obese weight	12	23.8417	11.41343	3.29477	0.048
Height of Diagnosis Time (cm)	Under and normal weight	100	109.47	22.121	2.235	
	Over and Obese weight	12	109.88	21.369	6.169	0.953
BMI percentile	Under and normal weight	100	21.59	22.669	2.267	
	Over and Obese weight	12	94.25	4.224	1.219	0.0001
Body Mass Index	Under and normal weight	90	14.591521	1.4485378	0.1526893	
	Over and Obese weight	10	18.868601	1.4870865	0.4702580	0.0001

Among the 112 patients, BMI in 35 patients were underweight (31.25%), 65 patients were normal weight (58.04%), 5 patients were overweight (4.46%) and 7 patients were obese (6.25%) (Graph 1).

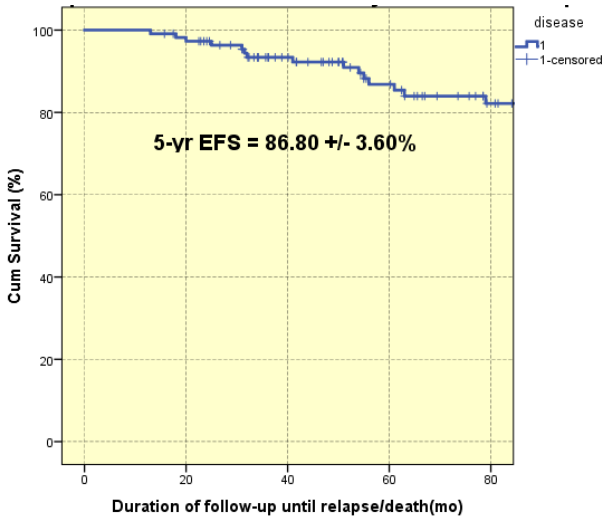


Graph 1 Distribution of all enrolled patients for BMI status

The distribution percentage of patients' body mass index was from about 3% to 50%. 5-year overall survival of all patients was 96.40±2.1% (Graph 2), and event-free survival of all patients was 86.80±3.60% (Graph 3). Also, from the 5-year overall survival analysis of all patients based on body mass index status in underweight: 100%, Normal-weight: 3.0% 95.70% and in over-weight and in obese: 92.30±7.40% were obtained. Finally, no significant relationship was observed between overall survival and BMI.

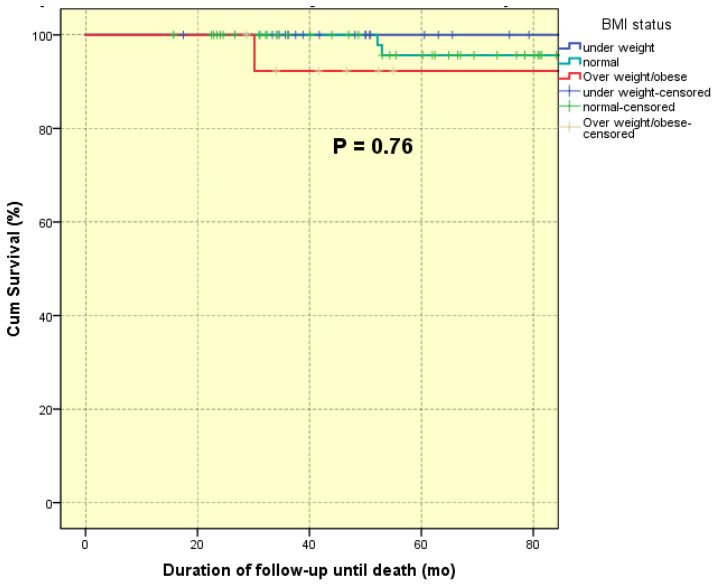


Graph 2 Overall survival analysis of all enrolled patients



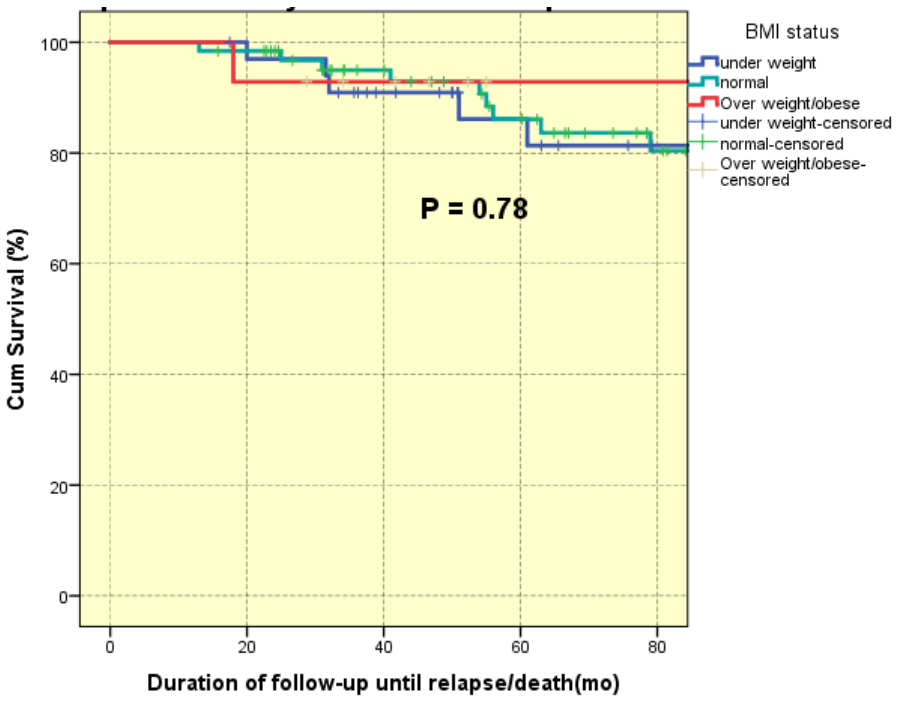
Graph 3 Event-free survival analysis of all enrolled patients

5-year event-free survival analysis of patients based on BMI status was presented in underweight: 86.10±6.60%, in normal-weight: 86.10±5%, in over-weight and in obese: 92.90±6.9%. Consequently, no significant relationship was found between event-free survival and BMI (Graph 4).



Graph 4 Overall survival analysis of all enrolled patients for BMI status

5-year overall survival of all patients was 96.40±2.1%, event-free survival of all patients was 86.80±3.60%. Also, from the 5-year overall survival analysis of all patients based on body mass index status in underweight: 100%, normal-weight: 95.70±3% and in over-weight, obese: 92.30±7.40% were obtained. Then, no significant relationship was observed between overall survival and BMI. 5-year event-free survival analysis of patients based on BMI status in underweight: 86.10±6.6%, in normal weight: 86.10±5% and in overweight and obese: 92.9±6.90%. Finally no significant relationship was found between event-free survival and BMI (Graph 5).



Graph 5 EFS analysis of all enrolled patients for BMI status

4. DISCUSSION

As mentioned, leukemia is one of the most common childhood cancers. Its prognosis also depends on the age and number of white blood cells, involvement of the CNS and tests at the time of diagnosis, sex, race, and weight at the time of diagnosis and during treatment. Considering the effect of BMI on response to treatment and disease relapse in studies as an independent factor, we decided to study the outcome of lymphoblastic leukemia patients admitted to Ali-Asghar Hospital at diagnosis during the years 2005 to 2015 for BMI. The results can have a direct impact on the choice and intensity of treatment regimen. Butturini et al. (2007) retrospectively examined obesity and its outcomes in 4,260 children with ALL in the United States in 2007. 5-year event-free survival was lower in obese patients and the risk of relapse was higher in obese patients. In our study, event-free survival was higher in obese patients and their overall survival was lower. In a cohort study, Gelelete et al. examined overweight as a prognostic factor in children with ALL in 2011(Gelelete et al., 2011). The aim of their study was to evaluate the prognostic effect of obesity and being overweight on five-year EFS in children with ALL. Their studies showed that obesity and overweight are independent predictors of relapse risk in high-risk and moderate-risk children. Also in our study, overall survival was lower in obese and overweight children.

In 2014, Orgel et al. in the United States examined the impact on survival and toxicity by duration of weight extremes during treatment for high risk group ALL in 2008 children (Orgel et al., 2014a). They found that obesity or underweight at diagnosis and for ≥ 50% of the time between end of induction and start of maintenance therapy resulted in inferior EFS. They concluded that normalizing weight reduced the risk, which was not comparable to obesity or being underweight. Also, obesity or underweight status at the beginning of each treatment phase was significantly associated with a specific pattern of treatment-related intoxication. Finally, they found that the effect of extreme weight gain on event-free survival and treatment related toxicity was not set at the time of diagnosis. As stated in previous studies, their observations eventually led to the suggestion that weight is a potential risk factor for improving EFS and disease in children with ALL. While in our study, overall survival was lower in obese children and event-free survival was higher, and survival was higher in underweight and 5-year event-free survival was lower. Orgel et al. continued their research in the same year to investigate the association between obesity and residual ALL during induction therapy for 198 children with B-precursor acute lymphoblastic leukemia in the United States. They concluded that obesity and overweight were associated with lower survival (lower EFS regardless of MRD, P = 0.012 end of treatment) (Orgel et al., 2014b). Finally, they found that newly diagnosed obese children with BP-ALL were at increased risk for MRD-positive end-induction and lower survival, whereas in our study, overall survival was lower in obese children and event-free survival was higher.

In 2015, in a retrospective study, Den Hoed et al. in the Netherlands examined the negative effects of weight loss and low weight on the survival of 762 patients aged 2 to 17 years with ALL (den Hoed et al., 2014). They found that underweight children (8%) were at high risk for relapse, but their overall, event-free survival rate was similar to that of normal-weight or overweight children. Patients who had a reduced BMI during the first 32 weeks of treatment had a similar risk of relapse and event-free survival but had a lower overall survival than patients who did not lose weight. They eventually found that being underweight was a risk factor for recurrence and a decrease in body mass index early during treatment is associated with decreased survival. While in our study, the overall survival in Underweight was higher and the event-free survival was lower. Orgel et al. in 2016 studied the relationship between BMI and survival among children with ALL in 10 manuscripts. They observed poor EFS in children with higher BMI than those with lower BMI (Orgel et al., 2016). Higher BMI compared to lower BMI was associated with a significant increase in mortality and a higher risk of relapse. In AML, higher BMI than lower BMI were significantly associated with poorer EFS and OS. Higher BMI at diagnosis was associated with poorer survival in ALL and AML children. While in our study, in higher BMI the overall 5-year survival was lower and the 5-year event-free survival was higher.

In the same year, Yazbeck et al. examined the effect of malnutrition on the diagnosis and clinical outcome of 103 children with ALL in a retrospective study in Lebanon (Yazbeck et al., 2016). This study showed a worse outcome in malnourished children with ALL. While in our study the overall survival underweight was higher and the 5-year event-free survival was less. In 2016, Amankwah et al. examined the association between BMI at the time of diagnosis, mortality, and relapse in 11 studies about children with ALL (Amankwah et al., 2016). As a result of their study, an increased risk of mortality was observed with an increase in BMI at the time of diagnosis, which had lower overall survival and event-free survival. High BMI at diagnosis is associated with poor overall and event-free survival in children with ALL. While in our study, the overall survival was lower at high BMI and the event-free survival was higher. Eissa et al. conducted a retrospective study in 2017 in the United States on the effect of BMI on clinical outcome in 373 children with newly diagnosed ALL (Eissa et al., 2017). In their study, obese patients had poorer overall survival than non-obese patients due to treatment-related mortality and less salvage after refractory disease or relapse of bone marrow. They found that low weight at the time of diagnosis had increased risk of relapse (two times) compared to patients who were not

underweight, although there was no difference in event-free survival and overall survival. While in our study, overall survival was lower in obese children than in non-obese children and finally no significant relationship was observed between overall survival and BMI, and in underweight children, overall survival was higher and less event-free survival was observed.

In 2019, Enriqueurs et al., in a cohort study, evaluated the effect of obesity and being overweight as a predictor of early mortality in 1070 Mexican children with ALL in Mexico (Núñez-Enríquez, 2019). They found that overweight and obese patients formed a subgroup at high risk of death during leukemia treatment. While in our study, the overall survival in obesity and overweight was lower and the survival without accident was higher.

Overall, it is inferred that the overall survival in underweight patients is higher than normal weight ones and in normal weight patients is more than obese and overweight ones and event-free survival in underweight, and normal weight patients is less than obese and overweight ones. According to the results of our study, it was different from other studies and we did not get a statistically significant result. It is likely due to the low sample size. This defect may be corrected in the next study with a larger sample size.

5. CONCLUSION

Based on the results of this study and their comparison with other studies in this field, it is concluded that overall survival in obese and overweight children is lower than normal weight and underweight children. These different results from some other studies suggest the need for more accurate prospective studies with larger sample sizes.

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Conflict of Interest

The authors declare that they have no conflict of interest.

Ethics approval

"All procedures performed in studies involving human participants were in accordance with the ethical standards of Iran University of Medical Sciences research committee (IR.IUMS.FMD.REC.1397.081) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

Informed consent

Informed consent was obtained from parents before recruitment.

Author contributions

Conceptualization: [Golamreza Bahoush], [Fahimeh Soheilipour]; Methodology: [Golamreza Bahoush], [Fahimeh Soheilipour]; Formal analysis and investigation: [Golamreza Bahoush], and [Zahra Rahmati], Writing - original draft preparation: [Zahra Rahmati]; Writing - review and editing: [Golamreza Bahoush], [Fahimeh Soheilipour], Funding acquisition: [Zahra Rahmati], Resources: [Golamreza Bahoush] and [Zahra Rahmati], Supervision: [Golamreza Bahoush], [Fahimeh Soheilipour] and [Zahra Rahmati].

Data availability

The datasets generated during the current study are available from the corresponding author on reasonable request.

REFERENCES AND NOTES

1. Ahmed HG, Alshammari MS, Alharbi H, Alrashidi AAA, Alrashdan YG, Alreshidi FS. Epidemiology of hematological malignancies in Hail region, Northern Saudi Arabia. Med Sci, 2020, 24(102), 699-705
2. Ahmedin J. Cancer statistics. Cancer J Clin 2006; 56: 106-130.
3. Ahmedin Jemal R, Ward E, Hao Y, Xu J, Murray T, Thun Mj. Cancer statistics. CA Cancer J Clin 2008; 58: 71-96.

4. Alsayyad J, Hamadeh R. Cancer incidence among the Bahraini population: a five-year (1998–2002) experience. Ann Saudi Med 2007; 27: 251-258.
5. Amankwah EK, Saenz AM, Hale GA, Brown PA. Association between body mass index at diagnosis and pediatric leukemia mortality and relapse: a systematic review and meta-analysis. Leuk. Lymphoma 2016; 57: 1140-1148.
6. Butturini AM, Dorey FJ, Lange BJ, Henry DW. Obesity and outcome in pediatric acute lymphoblastic leukemia. J Clin Oncol 2007; 25: 2063-2069.
7. Coebergh JW, Pastore G, Gatta G, Corazziari I, Kamps W, Group EW. Variation in survival of European children with acute lymphoblastic leukaemia, diagnosed in 1978–1992: the EUROCARE study. Eur J Cancer 2001; 37: 687-694.
8. Den Hoed M, Pluijm SM, De Groot-Kruseman HA, Te Winkel ML, Van Den Akker EL. The negative impact of underweight and weight loss on survival of children with acute lymphoblastic leukemia. American Society of Hematology Washington, DC 2014.
9. Eissa H, Zhou Y, Panetta J, Browne E, Jeha S, Cheng C, Relling M, Campana D, Pui C. The effect of body mass index at diagnosis on clinical outcome in children with newly diagnosed acute lymphoblastic leukemia. Blood cancer journal 2017; 7: 531-531.
10. Gelelete CB, Pereira SH, Azevedo AM, Thiago LS, Mundim M, Land MG. Overweight as a prognostic factor in children with acute lymphoblastic leukemia. Obesity 2011; 19: 1908-1911.
11. Horibe K, Saito Am, Takimoto T, Tsuchida M, Manabe A, Shima M, Ohara A. Incidence and survival rates of hematological malignancies in Japanese children and adolescents (2006–2010): based on registry data from the Japanese Society of Pediatric Hematology. Int. J. Hematol 2013; 98: 74-88.
12. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T. Cancer statistics, 2008. CA: a Cancer J Clin 2008; 58: 71-96.
13. Karimi M, Mehrabani D, Yarmohammadi H, Jahromi FS. The prevalence of signs and symptoms of childhood leukemia and lymphoma in Fars Province, Southern Iran. Cancer detec prev 2008; 32: 178-183.
14. Krishnan S, Wade R, Moorman AV, Mitchell C. Temporal changes in the incidence and pattern of central nervous system relapses in children with acute lymphoblastic leukaemia treated on four consecutive Medical Research Council trials, 1985–2001. Leukemia 2012; 24: 450-459.
15. Nathan J, Blum JW. Nelson textbook of pediatrics 21st edition. Nonprofit Healthcare and Educational 2019.
16. Nayiager T, Anderson L, Cranston A, Athale U. Health-related quality of life in long-term survivors of acute lymphoblastic leukemia in childhood and adolescence. Qual Life Res 2017; 26: 1371-1377.
17. Núñez-Enríquez Jc, Jiménez-Hernández E, Fajardo-Gutiérrez A, Medina-Sansón A, Flores-Lujano J, Overweight and obesity as predictors of early mortality in Mexican children with acute lymphoblastic leukemia: a multicenter cohort study. BMC Cancer 2019; 19: 708.
18. Orgel E, Genkinger JM, Aggarwal D, Sung L, Nieder M & Ladas. Association of body mass index and survival in pediatric leukemia: a meta-analysis. Am J Clin Nutr 2016; 103: 808-817.
19. Orgel E, Sposto R, Malvar J, Seibel NL, Ladas E, Gaynon PS. Impact on survival and toxicity by duration of weight extremes during treatment for pediatric acute lymphoblastic leukemia: a report from the Children's Oncology Group. J Clin Oncol 2014; 32: 13-31.
20. Orgel E, Tucci J, Alhushki W, Malvar J, Sposto R, Fu CH, Freyer DR, Abdel-Azim, H. Obesity is associated with residual leukemia following induction therapy for childhood B-precursor acute lymphoblastic leukemia. Blood, Hematology Am Soc Hematol Educ 2014; 124: 3932-3938.
21. Peris-Bonet RS, Martínez-Beneito Ma, Galceran J, Marcos-Gragera R, Felipe S. Childhood cancer incidence and survival in Spain. Ann 2010; Oncol 21.
22. Swaminathan R, Rama R, Shanta V. Childhood cancers in Chennai, India, 1990–2001: incidence and survival. Int J Cancer 2008; 122: 2607-2611.
23. Trehan A, Prabhu V, Bansal D. The impact of weight for age on survival in acute lymphoblastic leukemia: Report from a tertiary care center in North India. Indian J Cancer 2015; 52: 203.
24. Yang L, Fujimoto J, Qiu D, Sakamoto N. Childhood cancer in Japan: focusing on trend in mortality from 1970 to 2006. Ann oncol 2009; 20: 166-174.
25. Yazbeck N, Samia L, Saab R, Abboud MR, Solh H, Muwakkit S. Effect of malnutrition at diagnosis on clinical outcomes of children with acute lymphoblastic leukemia. J Pediatr Hematol Oncol 2016; 38: 107-110.