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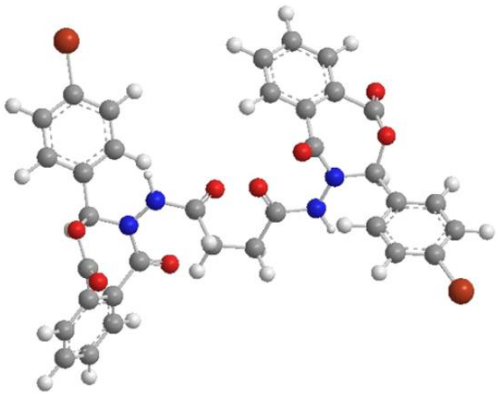

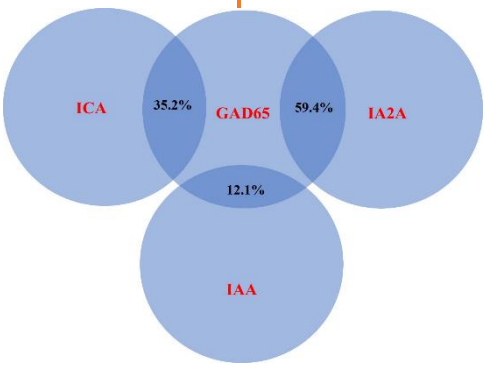

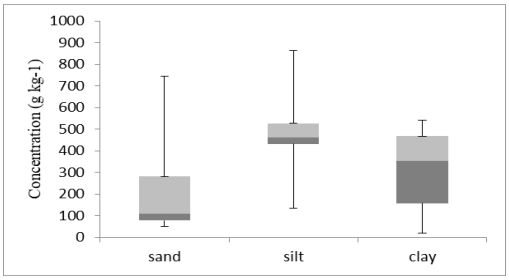

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Leukemia Morbidity and Mortality among Children Admitted to Hiwa Hospital from January 2015 to January 2022: A Retrospective Study

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Abstract

In 2016, 1 out of 3 cancer patients aged less than 20 years old were diagnosed with leukemia. Globally, leukemia is the most common malignancy in children and teenagers. This study aimed to determine leukemia cases' morbidity and mortality rates and their distribution in different areas of Sulaimani, Iraq, for seven years. This retrospective study is based on the Hospital Information System children's leukemia data from January 2015 to January 2022 at the Hematology Department, Hiwa Oncology/Hematology Hospital, Sulaimani, Iraq, using a Cox regression model (Cox, 1972). In 616 recorded children leukemia cases during seven years, 549(89.1%) of them were alive, and only 67(10.9%) died. The majority were male, aged between 5-10 years. Nearly 222(36%) of the patients had A+ blood group, followed by 210(34.1%) O+ blood group, while the minority was AB- group. The study result shows that age, and blood group, were risk factors for increasing leukemia chances by Exp (-0.074) =0.929. Leukemia morbidity rises significantly with age, and leukemia's morbidity rate increases gradually with time. While mortality was decreased. Depends on the forecasting for the next 10 years. Both ALL and AML were common malignancies among diagnosed children.

Introduction

The most popular life-threatening cancer in children is leukemia which represents nearly 1/3 of pediatric malignancies caused by an abnormal propagation of immature blasts and leukocytes **[1]**. This cancer can be either acute which occurs abruptly or chronic which takes an extended period **[2]**. In pediatric leukemias, age is considered the most significant prognostic factor. Almost 30% of children with leukemias are diagnosed under 15 years old, although it is more fatal in children aged one week - 14 years **[3]**. Generally, the prevalence of leukemia increases with age, and 1 in 70 patients might develop leukemia during their lifetime, especially in children <10 years **[4]**.

About 3800 children are diagnosed with acute lymphocytic leukemia (ALL) and rare cases with acute myelocytic leukemia (AML). ALL can occur at any age, but it is more common in children aged 2-5 years, while AML is more common in teenage (15-19 years) **[5]**. In addition, ALL more commonly affects males, especially in Caucasians and Hispanics with poor prognosis, than females **[6]**. About 85% of pediatric ALL is of B-precursor origin, and 15% is T-cell derived **[7]**.

The diagnosis of childhood leukemia includes cytochemistry, immunophenotyping, karyotyping, FISH, and molecular genetics in the bone marrow tissues. However, a specific diagnosis can be made on blood samples when the patient's state avoids a bone marrow aspiration **[7]**. Unfortunately, childhood leukemia is well underdiagnosed in some countries, especially in south Asia and sub-Saharan Africa **[8]**.

Currently, leukemia treatment choices are chemotherapy, chimeric antigen receptor (CAR) therapy, and hematopoietic stem cell transplantation (HSCT). In addition, minimal residual disease (MRD) is also recommended to measure therapeutic effectiveness and the possibility of relapse. Consequently, children with ALL have >80% chance of complete cures **[9]**.

Regarding the growth rate of pediatric leukemia in Iraq the incidence was found to be 31.1% or 3.56 per 100000 children in Basrah **[10]** and another study in Sulaimani revealed a greater occurrence of leukemia in males (4.1%) than females (3.6%), especially in teenagers aged <15 years with elevated annual incidence rate (3.4%). The latter group also found that ALL is the most common type of leukemia, with 44% in all cases, followed by chronic myeloid leukemia (CML) (20% of all leukemia incidences), chronic lymphoblastic leukemia (CLL: 18%), and then AML (17%) **[11]**. It was documented in Erbil and Duhok that hematological malignancies were the predominant form of cancer in children and adolescents, exhibiting a higher occurrence among male children compared to females **[12].**

The association between epidemiological factors such as age, gender, race, geographic position, and numerous childhood hematological cancers are well addressed. However, the relationship between blood groups and blood cancers is unknown. Therefore, if the risk factors of hematological cancers are identified for various blood groups, it could aid as a main selection help to determine high-risk communities **[13]**. Thus, this study aims to assess leukemia cases' morbidity and mortality rates and their distribution in different areas of Sulaimani depending on seven years of reported leukemia data at Hiwa hospital.

Materials and Methods

Patients and study design

In this retrospective study, a total of 616 recorded leukemia cases aged 1 week to 19 years during 7 years who visited the Hematology Department at Hiwa Oncology/Hematology Hospital, Sulaimani, Iraq was studied. The data regarding age, gender, residency, blood group, stage of disease, and the most common types of leukemia.

Ethical approval

The study protocol was revised by Scientific Committee and approved by the Ethical Committee at the Department of Nursing, Sulaimani Polytechnique University/Sulaimani, Iraq. Permission was secured from the Sulaimani Cancer Control Division, a central hub for cancer-related information and evidence under the Directorate of Health (DoH). This clearance allowed for the retrieval of data from electronic records, specifically the Hospital Information System (HIS), followed by subsequent statistical analysis.

Statistical analysis

The Cox regression model is commonly used in medical research. The Cox-PH model is a well-recognized statistical technique for exploring the relationship between a patient's survival and several explanatory variables, as it offers an estimation of the effect of treatment on survival after modification for other explanatory variables. If the new model has a significant baseline decrease, it indicates that the new model explains more variance in the outcome and is an improvement. Changing the chi-square from the previous step is the difference between the –2 log-likelihood of the model being scored in the last step and the current step. H_0: explanatory variables are incorporated in the model and H_1: explanatory variables are not contained in the model.

Results

Of 616 admitted children with leukemia cases to Hiwa hospital from January 2015 to January 2021, 549(89.1%) of them were alive, and 67(10.9%) died. About 38(56.7%) of the leukemic patients were alive after their first admission for 1-6 months, and the minority were alive for only >30 months. Approximately

296 (48.1%) patients were aged 5-10 years, 252(40.9%) were aged >10 years, and only 68(11%) were 1-4 years. Male patients were 380(61.7%), and females were 236(38.3%). Nearly 222(36%) of the patients had an A+ blood group, 213(34.6%) had O+, and only 3(0.5%) had an AB- group. Around 530(86%) patients had outpatient treatment, and only 86(14%) had inpatient treatment (Table 1).

Table 1: Descriptive variables of the study samples.

Variable	Item	Frequency	Percent
Patient	Alive (0)	549	89.1
	Death (1)	67	10.9
Time (Month)	1-6	38	56.72
	7-12	12	17.91
	18-24	7.0	10.45
	25-30	5.0	7.46
	>30	5.0	7.46
	Total	67	100
Age (Year)	1-4	68	11.0
	5-10	296	48.1
	>10	252	40.9
	Mean±SD	9.897 ~10 ± 4.32	
Gender	Male (1)	380	61.7
	Female (2)	236	38.3
Blood group	A+ (1)	222	36.0
	A- (2)	10	1.6
	B+ (3)	102	16.6
	B- (4)	15	2.4
	O+ (5)	213	34.6
	O- (6)	18	2.9
	AB+ (7)	33	5.4
	AB- (8)	3.0	0.5
Location of treatment	Inpatient (1)	86	14.0
	Outpatient (2)	530	86.0
	Total	616	100.0

Table 2 on omnibus tests of model coefficients demonstrates a significant result obtained by the chi-square test, which means that the explanatory variables are inserted in the model. Furthermore, the -2 Log likelihood decreased by 21.645 before adding the explanatory variables, while in this study, the -2 Log likelihood was increased to 416.089 after adding the explanatory variables. The significance value of less than 0.05 indicates that the current model output performs the null model. As mentioned, models which the data fit well will have higher likelihoods than models which the data do not fit well.

Table 2: Omnibus tests of cox model coefficients

Omnibus Tests of Model Coefficients									
-2 Log Likelihood	**Overall (score)**			**Change from Previous Step**			**Change from Previous Block**		
	Chi-square	**Df**	**P-value**	**Chi-square**	**Df**	**P-value**	**Chi-square**	**Df**	**P-value**
416.089	21.645	5.0	0.001	20.212	5.0	0.001	20.212	5.0	0.001

Table 3 assess whether explanatory variables such as (age, gender, blood group and place of treatment) have a significant or non-significant impact on morbidity and mortality of leukemia. Additionally, a positive coefficient signifies a poorer prognosis, while a negative coefficient suggests a protective effect associated with the respective variable. The value of explanatory age, gender, blood group and location of treatment were (-0.074, -0.019, -0.147 and 0.736) then there was a statistically significant negative effect (age, and Blood group) on the morbidity and mortality of leukemia because the results of the p-value was less than alpha 0.05, and also there was no statistically significant effect (gender) on the morbidity and mortality of leukemia ($p<0.05$).

Table 3: Variables in the equation for cox regression

Predictor	B	SE	Wald	Df	P-value	Exp(B)	95% CI for Exp(B)	
							Lower	Upper
Age	-0.074	0.033	4.985	1	0.026*	0.929	0.871	0.991
Gender	-0.019	0.253	0.006	1	0.940	0.981	0.598	1.611
Blood group	-0.147	0.072	4.089	1	0.043*	0.864	0.749	0.996
Location of treatment	0.736	0.306	5.775	1	0.016*	2.089	1.145	3.808

*: Significant difference

Table 4 indicates that the probability of survival times of patients constantly changed until the duration of survival reached 180 days, where the probability of survival for them is 0.25, and the probability of survival in 360 days is 0.15, while this probability in 540 days is 0.07. The probability of survival is 0.07 for 720 days. Also, we found that the survival rates have increased in the earlier stage of the disease (Figure 1).

Table 4: Life table analysis.

Interval Start Time (day)	Number Entering Interval	Cumulative Proportion Surviving at End of Interval	SE of Cumulative Proportion Surviving at End of Interval
0.0	67	0.43	0.06
180	29	0.25	0.05
360	17	0.15	0.04
540	10	0.07	0.03
720	5	0.07	0.03
900	5	0.06	0.03
1080	4	0.00	0.00

Table 5 indicated that in 2015, there were 68 cases of leukemia; the majority of them were alive (89.71%), and only 10.29% were dead. There was increased morbidity throughout the timeline, while mortality was decreased. Regarding the forecasting for the next 10 years' future output, time morbidity will be higher compared to the last seven years; however, mortality will decrease (Table 5, Figure 2).

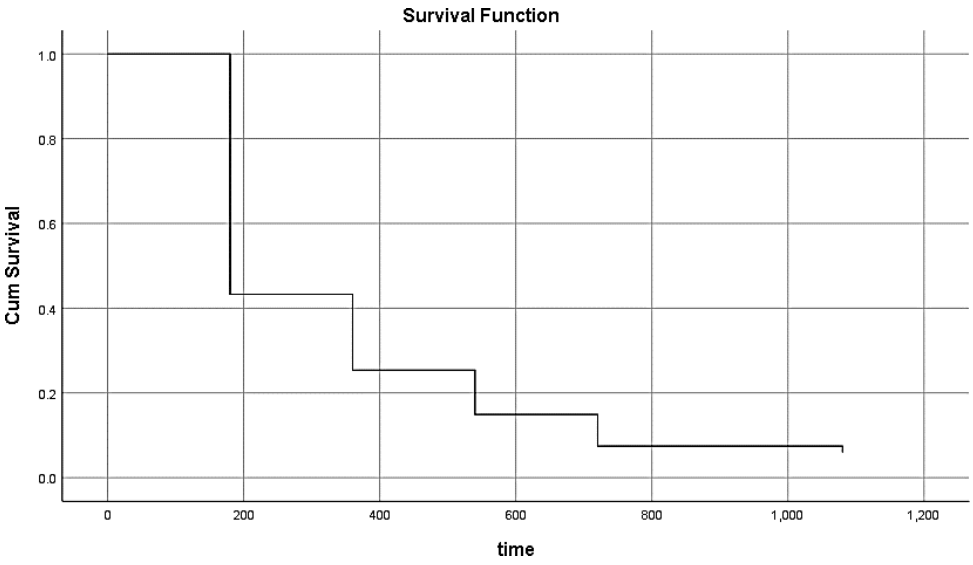

Figure 1: The survival rate of leukemia patients that increased in the earlier time of the disease.

Table 5.: Forecasting test for morbidity and mortality of leukemia in 17 years' time from 2015-2032.

Year	Died		Alive		Total
	No.	%	No.	%	
2015	7	10.29	61	89.71	68
2016	12	15.58	65	84.42	77
2017	11	13.92	68	86.08	79
2018	9	11.54	69	88.46	78
2019	12	11.11	96	88.89	108
2020	7	9.46	67	90.54	74
2021	9	6.82	123	93.18	132
Total	67	10.88	549	89.12	616
2022	8	6.10	120	93.90	128
2023	7	5.12	135	94.88	142
2024	7	4.28	152	95.72	159
2025	6	3.58	171	96.42	177
2026	6	2.99	192	97.01	198
2027	6	2.49	216	97.51	222
2028	5	2.07	243	97.93	248
2029	5	1.73	273	98.27	278
2030	4	1.44	308	98.56	312
2031	4	1.19	346	98.81	350
2032	4	0.99	389	99.01	393
Total	62	2.38	2545	97.62	2607

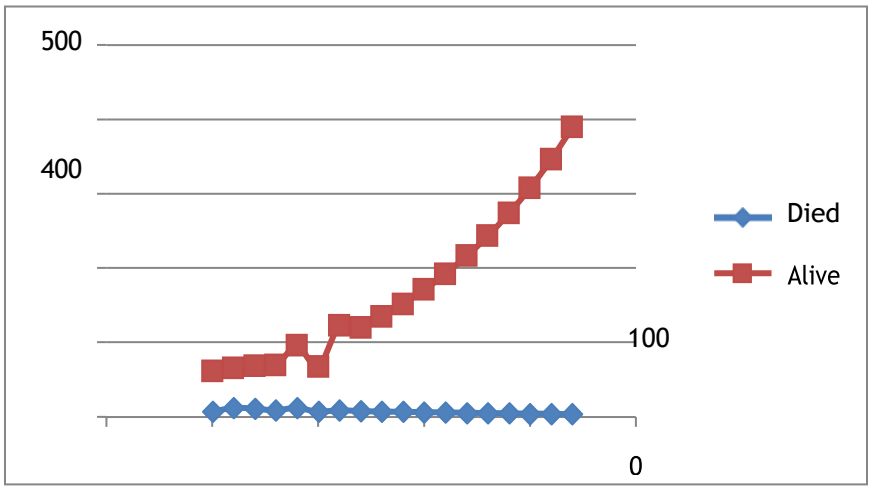

Figure 2: Morbidity and mortality of leukemia from 2015-2032.

Discussion

In recent years, there has been significant progress in educating people about how to protect themselves from hematological malignancies, especially through lifestyle changes. However, in 2015, thousands of people migrated from other cities in Iraq to Sulaimaniyah due to civil war, political issues, and economic disturbances in their respective areas. This migration might be positively linked to the increase in the incidence of pediatric leukemia in this city.

Following the overthrow of the Iraqi regime in 2003, there was a rapid transformation in the way of life for the Kurdish population. This transformation had an impact on cancer patterns and occurrences within Kurdistan. The use of various chemical weapons of mass destruction in three devastating wars in Iraq may have contributed to environmental contamination and an increase in cancer rates, notably a significant rise in hematological malignancies. Unfortunately, there is limited published data available that provides insights into specific cancer types in Kurdistan, despite the Eight Years Cancer Registration in Sulaimaniyah Province-Kurdistan-Iraq **[11]**.

Over the span of seven years, the annual proportion of documented childhood leukemia cases in Sulaimaniyah experienced a modest rise, increasing from 89.7% to 93.18%. Concurrently, the mortality rate showed a decline, dropping from 10.29% to 6.82%. This observation aligns with the results of studies assessing leukemia prevalence in various Iraqi provinces. Specifically, in 2006, the prevalence of leukemia in Sulaymaniyah province was 2.97 per 100,000 inhabitants, and it increased to 3.57 per 100,000 inhabitants in Iraq between 2006 and 2014, signifying a significant rise **[14]**.

Nevertheless, these findings contrast with another study suggesting that the incidence of childhood leukemia has remained oddly stable over the past two decades in Nordic countries like Sweden, Denmark, Norway, Finland, and Iceland **[15, 16]**. Similarly, a study conducted in Costa Rica between 2000 and 2014 indicated that the incidence rate of childhood leukemia has not significantly changed over time [17]. However, these results are in agreement with research conducted in India **[18, 19]** and a study in the USA, which noted a notable increase in ALL incidences among Hispanic White children **[20].**Furthermore, in this study, most patients belong to the age group 5-10 years (close to half of the total), <1/2 patients were aged >10 years, and only 11% belonged to the 1-4 years' age group. These results agreed with the findings of another descriptive study conducted in Iraq **[22]** and in the USA **[17]**, which found that a higher percentage of their samples were aged 1-10 years. Regarding the gender of the patients, males were more affected by leukemia than females, which is in line with other studies conducted in different countries. Instantly, the mechanism behind this

concern is not fully clear but might be because sex-specific hormones such as estrogen protect leukemia cells or might be related to mutations of certain genes located on the X chromosome **[22]**.

The present study demonstrated that the number of reported leukemia between 2015-2021 is affected and correlated to some factors, especially ABO blood grouping. These outcomes are not supported by research conducted in Baghdad, Iraq, which found no significant association between ABO blood grouping and diverse independent variables with childhood AML **[23]**. However, another study in Diyala, Iraq, approved that childhood leukemia rate was directly related to age, gender, and blood group, with most recorded cases recorded in the age group 1-5 years. Additionally, it was indicated that blood group O and RhD positive are risk factors for the incidence of ALL in children, and group AB and RhD negative children seemed to be less susceptible **[24]**. Furthermore, it was found that 36% of the patients had an A+ blood group, followed by O+ (34.6%), and the minority was an AB- (0.5%). These findings are close to the results of the case-control study in Iran, which found that the highest percentage of the sample was O+ blood groups, and the fewest rate was AB+ **[25]**.

The descriptive variables of this study found that around 549(89.12%) of the patients were alive and only 67(10.88%) died during 7 years. These findings agreed with the results of another study, which found the five-year relative survival rate for leukemic children to be 69.8% **[27]**. Similarly, a study in the USA found a survival rate to be 90% **[21]**, and another study in Brazil experienced almost twofold better survival rates for leukemia patients **[26]**. These high rates of survival might be related to an early diagnosis, enhanced conditions for treatment, socioeconomic status, awareness, and stage of the disease **[28. 29]**.

This study also found that ALL is the leading and most common type of leukemia in children, followed by AML, in which 28 cases were diagnosed as leukemia in both genders in 2015, while only 20 cases were diagnosed in 2016. As a percentage, ALL remains on the top of leukemia cases, although the number of cases is decreased. These findings agreed with the outcomes of a study conducted in Erbil, Iraq, which found that 88.9% of childhood leukemia are ALL, followed by AML **[30].**

Additionally, most participants (86%) were treated in outpatient, and only 14% were in inpatient treatment. Following the diagnosis of ALL, each patient undergoes a three-phase chemotherapy regimen: Induction Phase (1 month): During this initial phase, patients are required to stay in the hospital continuously for one month to receive daily treatment as inpatients. Consolidation Phase (1 to 6 months): In this phase, which spans from 1 to 6 months, patients receive treatment as outpatients. There is no need for them to stay in the hospital. They come in weekly and monthly for their treatments. Maintenance Phase (from 6 years to the end of treatment, which varies for girls and boys, typically around 2.2 years for girls and 3.2 years for boys, following the UKALL protocol): Similar to the consolidation phase, patients in the maintenance phase receive treatment in outpatient.

These findings are connected to the assessment of a patient's condition at a later point, aligning with a study conducted in Erbil. This study revealed that most individuals in the sample with ALL were diagnosed during the advanced time of the disease. Consequently, Urgent measures are required to tackle the factors that are leading to the increased occurrence of cancer in these two areas within the Kurdistan Regional Government (KRG) **[30].**

According to the forecasting test for the next 10 years' future output and depending on the previous 7 years of the recorded data, the study expected and projected the trend until 2032. The study found morbidity is going to be higher compared to the last 7 years; however, the mortality rate is going to decrease. For instance, in 2015, there were 68 cases of leukemia; the majority of them were alive (89.71%), and only 10.29% were dead. While in 2032, the morbidity of leukemia among children and teens will rise from 128 newly diagnosed cases to 393 cases, while, fortunately, the mortality rate will significantly drop from 6.1% to 0.99%.

Conclusions

We realized that most patients were males in the middle to late childhood. The study also displays the rate of new leukemia cases and their distribution in Sulaimani. The findings showed that the leukemia rate decreased significantly with age, while its morbidity increased with time. Besides, the study indicates that ALL and AML

are the most common malignancies among children. Therefore, the present study recommends an early detection of disease through the implementation of some routine screening tests. Additionally, this study suggests the improvement of lifestyle and awareness of illness by the family, such as avoiding exposure to unnecessary radiation, smoking, alcohol consumption during pregnancy, and eating a healthy diet. Thus, future interventional studies are needed to enhance the leukemia child's quality of life.

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Conflict of interest

The authors confirm that they are not affiliated with or involved in any organization or entity with financial interests.

References

1. Clarke R.T., Van den Bruel A., Bankhead C., Mitchell C.D., Phillips B., Thompson M.J. (2016). Clinical presentation of childhood leukaemia: a systematic review and meta-analysis. *Archives of Disease in Childhood.* 101(10):894-901.

2. Ahmad S.M., Ahmed B.S., Khidhir K.G., Rahman H.S. (2022). Prospective quantitative gene expression analysis of kallikrein-related peptidase KLK10 as a diagnostic biomarker for childhood acute lymphoblastic leukemia. *PeerJ.* 10:e13489.

3. Davis A., Viera A.J., Mead M.D. (2014). Leukemia: an overview for primary care. *American Family Physician.* 89(9):731-738.

4. Cazzola A., Cazzaniga G., Biondi A., Meneveri R., Brunelli S., Azzoni E. (2021). Prenatal origin of pediatric leukemia: lessons from hematopoietic development. *Frontiers in Cell and Developmental Biology.* 8:618164.

5. Terwilliger T., Abdul-Hay M. (2017). Acute lymphoblastic leukemia: a comprehensive review and 2017 update. *Blood Cancer Journal.* 7(6):e577-e577.

6. Legano L., McHuhg M., Palusci V. (2009). Current problems in pediatric and adolescent health care. *Child Abuse and Neglect.* 39(2):31-57.

7.Creutz ig U., van Den Heuvel-Eibrink M.M., Gibson B., Dworzak M.N., Adachi S., de Bont E., Harbott J., Hasle H., Johnston D., Kinoshita A. (2012). Diagnosis and management of acute myeloid leukemia in children and adolescents: recommendations from an international expert panel. *Blood, The Journal of the American Society of Hematology.* 120(16):3187-3205.

8. Ward Z.J., Yeh J.M., Bhakta N., Frazier A.L., Atun R. (2019). Estimating the total incidence of global childhood cancer: a simulation-based analysis. *The Lancet Oncology.* 20(4):483-493.

9. Yonan A., Jacques C., Fletcher T., Suk-In T., Campbell R.B. (2022). An Overview of Conventional Drugs and Nano Therapeutic Options for the Treatment and Management of Pediatric Acute Lymphoblastic Leukemia. *Anti-cancer Agents in Medicinal Chemistry.* 22(18):3050 - 3061.

10. Habib O., JG H., JM A.-D. (2016). Cancer of children in Basrah-Iraq: Person and time characteristics. *The Medical Journal of Basrah University.* 34(2):77-85.

11. Karim Z.A., Khidhir K.G., Ahmed R.A., Hassan H.A., Karim D.O. (2016). Leukemia Study in 11. Sulaymaniyah Province, Kurdistan, Iraq. Chinese Medical Journal. 129(02):244-245.

12. Khoshnaw N, Mohammed HA, Abdullah DA. (2015). Patterns of cancer in Kurdistan - results of eight years cancer registration in Sulaymaniyah Province-Kurdistan-Iraq. Asian Pac J Cancer Prev. 16:8525–31.

13. Forsythe A., Breland T., Majumdar S., Elkin T.D., Johnson D., Megason G. (2010). Gender differences in incidence rates of childhood B-precursor acute lymphocytic leukemia in Mississippi. *Journal of Pediatric Oncology Nursing.* 27(3):164-167.
14. AL- Hashimi M Y, (2021). Incidence of Childhood Leukemia in Iraq, 2000-2019. Asian Pac J Cancer Prev. 22(11):3663-3670
15. Gupta S., Teachey D.T., Chen Z., Rabin K.R., Dunsmore K.P., Larsen E.C., Maloney K.W., Mattano Jr L.A., Winter S.S., Carroll A.J. (2022). Sex-based disparities in outcome in pediatric acute lymphoblastic leukemia: a Children's Oncology Group report. *Cancer.* 128(9):1863-1870.
16. Steliarova-Foucher E., Colombet M., Ries L.A., Moreno F., Dolya A., Bray F., Hesseling P., Shin H.Y., Stiller C.A., Bouzbid S. (2017). International incidence of childhood cancer, 2001–10: a population-based registry study. *The Lancet Oncology.* 18(6):719-731.
17. Erdmann F., Li T., Luta G., Giddings B.M., Alvarado G.T., Steliarova-Foucher E., Schüz J., Mora A.M. (2018). Incidence of childhood cancer in Costa Rica, 2000–2014: an international perspective. *Cancer Epidemiology.* 56:21-30.
18. Das S., Paul D.K., Anshu K., Bhakta S. (2017). Childhood cancer incidence in India betweem 2012 and 2014: Report of a population-based cancer registry. *Indian Pediatrics.* 54(12):1033-1036.
19. Asthana S., Labani S., Mehrana S., Bakhshi S. Incidence of childhood leukemia and lymphoma in India. *Pediatric Hematology Oncology Journal.* 2018;3(4):115-120.
20. Barrington-Trimis J.L., Cockburn M., Metayer C., Gauderman W.J., Wiemels J., McKean-Cowdin R. (2017). Trends in childhood leukemia incidence over two decades from 1992 to 2013. *International Journal of Cancer.* 140(5):1000-1008.
21. Stjernfelt K.-J., von Stedingk K., Wiebe T., Hjorth L., Kristoffersson U., Stenmark-Askmalm M., Olsson H., Øra I. (2020). Increased cancer risk in families with pediatric cancer is associated with gender, age, diagnosis, and degree of relation to the child. *Cancer Epidemiology, Biomarkers & Prevention.* 29(11):2171-2179.
22. Yaseen O.K. (2015). Relationship between Age, Gender and ABO Blood Groups in Childhoods Cancer. *Diyala Journal of Medicine.* 8(2):65-68.
23. Ghali H.H., Nayeef A.M., Hameed A.H., Fawzi G.M. (2017). Relationship between ABO and Rh Blood Groups withChildhood Acute Lymphoblastic Leukemia. *IOSR Journal of Research & Method in Education.* 7(2):86-89.
24. Abd-Allateef M.H. (2021). *Blood Groups Relationship with Incidence of Malignancy in Children*, University of Diyala;
25. Tavasolian F., Abdollahi E., Vakili M., Amini A. (2014). Relationship between ABO blood group and Acute Lymphoblastic Leukemia. *Iranian Journal of Pediatric Hematology and Oncology.* 4(1):1-4.
26. Lins M.M., Santos M.d.O., de Albuquerque M.d.F.P.M., de Castro C.C.L., Mello M.J.G., de Camargo B. (2017). Incidence and survival of childhood leukemia in Recife, Brazil: A population-based analysis. *Pediatric Blood & Cancer.* 64(8):e26391.
27. Petridou E.T., Dimitrova N., Eser S., Kachanov D., Karakilinc H., Varfolomeeva S., Belechri M., Baka M., Moschovi M., Polychronopoulou S. (2013). Childhood leukemia and lymphoma: time trends and factors affecting survival in five Southern and Eastern European Cancer Registries. *Cancer Causes & Control.* 24(6):1111-1118.
28. Hunger S.P., Mullighan C.G. (2015). Acute lymphoblastic leukemia in children. *New England Journal of Medicine.* 373(16):1541-1552
29. Jaime-Pérez J.C., García-Arellano G., Herrera-Garza J.L., Marfil-Rivera L.J., Gómez-Almaguer D. (2019). Revisiting the complete blood count and clinical findings at diagnosis of childhood acute lymphoblastic leukemia: 10-year experience at a single center. *Hematology, Transfusion and Cell Therapy.* 41:57-61.
30. Amen K.M. Abdullah O.S., . Amin A S, Mohamed Z A. , Bestoon B, et al.,. (2020). Cancer Incidence in the Kurdistan Region of Iraq: Results of a Seven-Year Cancer Registration in Erbil and Duhok Governorates, Asian Pac J Cancer Prev. 23(2): 601–615.