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Original Article

Pediatric Acute Lymphoblastic Leukemia in Rawalpindi

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Abstract

Objective: To identify the incidences of ALL, it's Diagnostic, clinical and its prognostic aspect from CMH Rawalpindi hospital Pakistan

Methods: Diagnosis and screening for ALL was done at CMH Rawalpindi from 2010-2021. During this time, 981 individuals under the age of 19 who had recently been diagnosed with acute lymphoblastic leukemia. Cytological, immunophenotypic, and cytogenetic criteria were employed to diagnose. Chi-square and Fisher's exact tests assessed prognostic factor associations.

Results: The collected data from 2010-2021, showed that Males predominated the incidence rate 626 (63.8%), average diagnostic age was 6.3-0.5 years. Results showed that 207(21.10%) were children less than 3 years old, 587(59.80%) were between 3-10 years old. While 187(19%) were above age of 10. After statistical analysis, patients at standard risk were found to be (496)50.5% while 485(49.5%) were at high risk. The collected data reported prevalence of ALL in (850)86.6% patients while 131(13.3%) patients were diagnosed with Albl. The survival rate of patients having disease and that of survival rate with disease free conditions was found in 655(66.7%) and 326(33.3%) patients respectively. Patients with normal nutritional status 726(74%), with moderate eating 165(16.80%) and eating severely 90(9.2%) was reported and analyzed.

Conclusion: ALL is found to be one of threat in young children and adolescence. There is a threat of relapse even after recovery from ALL when treated specifically in adolescence. Early prognosis and diagnosis of ALL is necessary to mitigate its effects and to avoid its recurrence. Health authorities in this regard should provide the required facilities to overcome this menace.

Keywords: Acute Lymphoblastic Leukemia, Malignancy, T-ALL, Standard risk, High risk.

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Introduction

In children the commonly occur blood malignancy is Acute Lymphoblastic Leukemia (ALL). Approximately ALL represents a total of 75-80% of the leukemias in the age of childhood. Whilst the incidence rate in children below the age of 15 years is 3-4 cases per 100,000. Moreover, besides affecting children of all ages, the incidence predominates from age 2 to 5 years, and predominantly affect boys.[1] Being a heterogeneous disease, ALL subtypes vary in a variety of ways, including aspects like biology, cellularity, and molecular structure. The subtypes can also vary in terms of treatment response and recurrence risk and are linked to various outcomes.[2]

Especially in groups with the greatest prognosis, the present advancements in oncology medicine have led to a decent improvement of 90% in pediatric survivability.[3] This transformation is principally attributable to the adoption of risk-adjusted therapy, modified supportive care, and medication modifications focusing on patients' unique pharmacodynamics and pharmacogenomics.[2,4] Clinical, biological, and genetic variables, such as gender and age, Leukocyte counts at diagnosis, immunophenotypic analysis, cytological and cytogenetic characteristics, and timely bone marrow response to the initiated therapy, are used to classify individuals into various risk groups.[5] To assess their early response to

treatment, patients with ALL are currently encouraged to evaluate their MRD at the conclusion of induction.[6] Prognostic variables, risk categorization, survival analysis, and therapy evaluation have improved local and national understanding of pediatric malignancies. CMH Rawalpindi Pakistan researched and diagnosed ALL in children and adolescents. The incidence and prognosis for ALL and AlBl was done and its effects on patients.

Methods

The study was done from 2010-2021 at CMH Rawalpindi Pakistan. Patients were screened and diagnosis for ALL was done. Data was collected from different patients with age of up to 19 years. The patients were grouped as children with ages 3-9 years old and ages 10 or above. After diagnosis and screening patients were analyzed for hemoglobin level, WBC level, their nutritional patterns and other variables like platelets level. Statistical analysis was done and patients were grouped in to risk groups standard and high-risk groups on the basis of the obtained statistical data.

SPSS 25 was used for statistical analysis. Patients were described by descriptive statistics. The chi square test examined variables, prognostic factors, and response. The 0.05, or 5 percent, p-value cutoff was set as the threshold for statistical significance.

Results

Data were collected from a total of 981 (ALL) Patients from 2010 to 2021 from the pediatric hemato-oncology of (ALL) patient CMH Rawalpindi Hospital. Patient data including age group, Sex, Laboratory Reports, Diagnosis, Survival Status, Nutritional status, Risk group etc. A total of 981 (ALL) Patients presented to the Rawalpindi hospital. The study period of 10 years. Of these 981 patients, 626(63.8%) were males while 355(36.2%) were Females Figure 1.

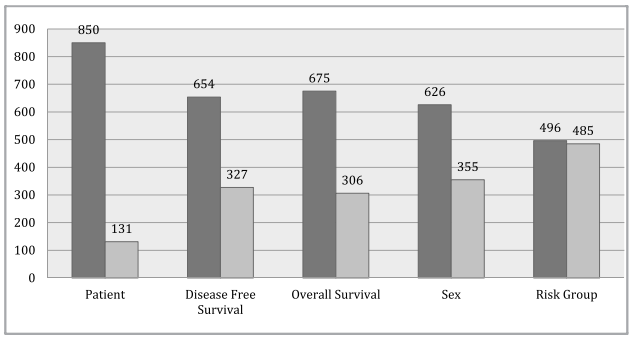

Figure 1: *Shows the socio-demographic Characteristics of patients.*

Distributed according to the age group, 207 (21.10%) of patients were found that they had their age group less than 3 Years, 587(59.80%) patient were found that they had their age group 3-10 years, while the remaining patients i.e. 187(4%) came in the age group of greater than 10. The nutritional status of patients is shown in the above visualization 726 (74%) of patient eat normally, 165 (16.80%) of patients eat moderately while the remaining 90(9.2%) patients eat severely Figure 2.

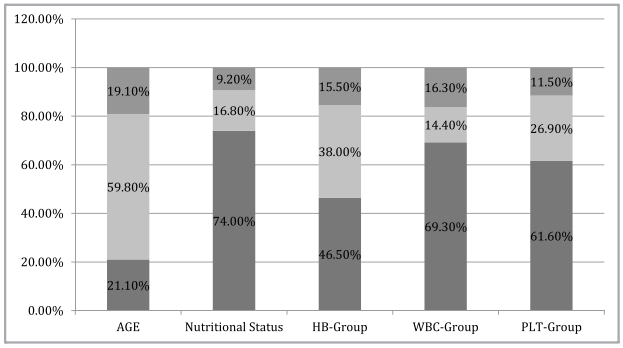

Figure 2: *Shows different parameters associated with ALL*

Out of total, 496(50.5%) number of patients they had standard risk, while the remaining were at the high risk. 850(86.6%) patient Diagnosed that they had ALL type of cancer, while 131(13.3%) number of patients Diagnosed they had (Albl) Table 1.

Table 1: *Shows different parameters associated with ALL*

Variable	Category	Number	Valid Percentage
Patient	T-ALL	850	86.6%
	LBL	131	13.4%
Disease Free Survival	Disease	654	66.7%
	Relapse	327	33.3%
Overall Survival	Alive	675	68.8%
	Death	306	31.2%
Hemoglobin Group	Hb <7	456	46.5%
	Hb 7 to 10	373	38.0%
	Hb > 10	152	15.5%
WBC-Group	WBC < 50	680	69.3%
	WBC 50 to100	141	14.4%
	WBC >100	160	16.3%
Platelets group	PLT< 50	604	61.6%
	PLT 50-150	264	26.9%
	PLT >150	113	11.5%
Diagnosis	Pre B ALL	801	81.7%
	T ALL	108	11.0%
	ALL	44	4.5%
	LBL	28	2.9%

Table 2: *Shows the socio Demographic Characteristics of patients.*

Variable	category	Number	Valid Percentage
Sex	Male	626	63.8%
	Female	355	36.2%
Age group	<3Years	207	21.1%
	3-10years	587	59.8%
	>10	187	19.1%
Nutritional Status	Normally	726	74.0%
	Moderately	165	16.8%
	Severely	90	9.2%
Category	Entitle	626	64.0%
	CNE	265	26.8%
Risk Group	Standard Risk	496	50.6%
	High Risk	485	49.4%
Death	Yes	293	29.9%
	No	671	68.4%

In this study 655 (66.7%) number of patient they are surviving but they have disease, while 326(33.3%) of patient were surviving disease free means that they relapse from the disease shows in the above Table 2.

The above table 3 Chi square test is applied to check the association between a demographic factor and hematological with (total ALL) patients. The significant p-value (p=0.000) is less than our specified alpha value 0.05 so, so there is an association between age group and hemoglobin group and platelet group, while the p value is greater than alpha value so, there is no association between age group and white blood cell. No association fount between gender and hematological results. The significant p-value is less than our specified alpha value 0.05 so, there is association between Risk group and hemoglobin group, white blood cell and platelet group.

Discussion

There is little study on the epidemiology of acute lymphoblastic leukemia in children in KPK, Pakistan. The current investigation focuses on Pakistan's prevalence of ALL as well as its diagnostic, clinical, and prognostic characteristics. The participants' ages have a positive impact on the prognosis. Little children and infants (until the age of 9) have a bad prognosis as a result.[7] Numerous reasons contribute to the poor prognosis: hepatosplenomegaly, high leukocyte counts, lack of CD10 markers, Pro-B immunophenotype, and poor response to induced therapy.[8] The data from the current study comprised 59.80% of children who were above nine years old. Teenagers had a low survival percentage and very high re-occurrence rates, according to earlier research. The catastrophic results in this population may be caused by an increasing number of biologically high-risk leukemias, such as mixed-lineage leukemia (MLL) and [BCR-ABL1] Breakpoint Cluster Region protein-Abelson murine leukemia viral oncogene homolog 1 rearrangements, in addition to risk factors like elevated total leukocyte count.[9] 46.5 percent of patients, or roughly 14.4 percent of cases, had severe anemia (Hb 50.0 109 cells/L) in worldwide studies that reported WBC counts >50.0 109 cells/L. T-ALL was found in 86.6 percent of the population.[10] Significant features are more common in T-ALL patients in this study, especially if they are male and/or older than 9 years old. The findings presented by Goldberg et al. are significantly impacted by the outcomes that are discussed below. T-cell immunophenotype has long been considered a poor clinical predictive factor in pediatric ALL, even if its effects have been mitigated by contemporary risk-adapted therapy

Table 3: *Association of Demographic factors and hematological factors with ALL Patients.*

Variable	Categories	WBC-Group				Haemoglobin-Group				Platelets-Group			
		<50	50-100	>100	p-value	<7	7-10	> 10	p-value	< 50	50-150	>50	p-value
Age	<3Years	136	36	35		117	69	21		154	35	18	
	3-10years	419	84	84	**0.071**	283	226	78	**0.00**	357	167	63	**0.00**
	>10	125	21	41		56	78	53		93	62	32	
Gender	Male	431	88	107	**.66**	281	248	97	**.349**	369	176	81	**.52**
	Female	249	53	53		175	125	55		235	88	32	
Nutritional Status	Normally	488	115	123		335	281	110		439	205	82	
	Moderately	125	20	20	**.056**	83	57	25	**.66**	112	35	18	**.33**
	Severely	67	6	17		38	35	17		53	24	13	
Death	Yes	193	74	26	**.096**	178	51	64	**0.001**	146	102	45	**.381**
	No	397	189	85		490	88	93		304	263	104	
Risk Group	Standard Risk	323	125	48	**0.047**	496	0	0	**0.00**	255	189	52	**0.00**
	High Risk	281	139	65		184	141	160		201	184	100	

and the advantage of supportive care.[11] However, because of their immunophenotype, these patients had an extremely high risk of induction failure, isolated CNS recurrence, and early relapse.[12] A favorable conclusion in this study was linked to a DI >1.16. (Table 3). At the conclusion of generalization, every patient with DI >1.16 was still alive, had insufficient cancelation, and had not experienced a first repeat. our findings are consistent with previously reported studies by arico and dastuge et al,[7,13] which showed a strong association between hyperdiploidy and favorable prognostic factors such as age between one and five years, a WBC count of 1000 cells/L at diagnosis, and a WBC count of more than 5.0 109 cells/L. It may be possible to identify patients whose EFS rates were significantly lower and who did not respond effectively to treatment. Patients receiving GBTLI-ALL-99 therapy who did not respond effectively also had lower EFS rates (between 45 and 52 percent).[14] More than 90% of induction therapy patients remained alive after four years, according to Manabe et al., who reported that their peripheral blood did not contain lymphoblasts on the eighth day.[15] According to Vaghela et al., 29 95% of trial participants achieved remission at the end of induction, which confirms the prognostic validity of peripheral lymphoblast counts on the eighth day following induction therapy.[15] This is consistent with data from Brazil and other countries, despite concerns expressed in a few papers regarding the importance of the least residual illness response to remission induction therapy that was done exclusively for morphological analysis (MRD). In the current sample, the OS and EFS at age five were 71.2 percent and 72.2 percent, respectively. Anticipating this, individuals at low risk were more likely to survive (83%) compared to those at high risk (59.1%). (Figure 1A and B). Comparable rates were 74.2 1.7% for the GBTLI-ALL-99 operation and 68.8 1.80% for the GBTLI-ALL-93 therapy, with a substantial difference favoring low-risk patients. Our statistics are somewhat more accurate than those of previous studies by liete et.al (2017) and Pereira (2018), but they are not as good as the information currently provided by collaborative pediatric cancer therapy organizations in the United States and Europe. In 21,23 cases, those with B-ALL had better OS and EFS, despite the difference not being statistically significant. By comparison, six years following GBTLI-ALL-93 treatment, the EFS for T-ALL patients was significantly lower.[16] Despite the higher likelihood of induction failure and recurrence, the Dana Farber team identified no differences in survival between B-ALL T-ALL and, which may help to explain this discrepancy. (78 percent at 4% vs. 86 percent at 1%).

In the current investigation, patients with WBC levels of 50.0 109 cells/L at diagnosis, older than nine years, and high peripheral lymphoblast counts (>1000 cells/L on Day 8) had a considerably higher risk of poor survival. OS was also better in children under nine. Except for CD10 expression, FAB classification, and DI, no additional predictive factors were significant. This trial's clinical and analytical results generally reflect former studies and GBTLI-ALL 93 and 99 protocols. Age, baseline WBC count, and early treatment response were independent predictors in multivariate analysis, whereas gender, FAB classification, CD10 expression, and DI were not.[17] The expected survival rate was lower than in wealthy nations. EFS was lower than the literature after 5 years. However, low-risk folks performed better.

Conclusion

ALL is found to be one of threat in young children and adolescence. There is a threat of relapse even after recovery from ALL when treated specifically in adolescence. Early prognosis and diagnosis of ALL is necessary to mitigate its effects and to avoid its recurrence. Health authorities in this regard should provide the required facilities to overcome this menace.

Conflict of Interest: *None*

Funding Source: *None*

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