Clinical Outcome of Pediatric Acute Myeloid Leukemia Treated at South Egypt Cancer Institute, Assiut University, Egypt

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Abstract

Background: Acute myeloid leukemia [AML] represents 15–20% of pediatric acute leukemia. Although AML is a serious disease, it is treatable and usually curable with chemotherapy with or without a bone marrow /stem cell transplant. Several clinical features can predict complete remission and survival rate in patients with AML. There is a paucity of studies reporting treatment outcome of AML in developing countries. Here we are shedding light on treatment results and factors affecting survival of AML patients in South Egypt Cancer Institute, a tertiary care center in developing country.

Patients and Methods: Medical records of 64 newly diagnosed AML children who admitted in Pediatric Oncology Department, South Egypt Cancer Institute [SECI], Assiut University from January 2009 to December 2018 were retrospectively reviewed for demographic characteristics, clinical features and laboratory studies at presentation, treatment and outcome.

Results: Sixty Four patients were eligible for the study. Forty two patients [65.6%] were males and 22 [34.4%] were females. Mean age was 10.85 ± 4.30 years [range 2-18 years]. The most common subtypes were M4 [18.8%], M1 [14.1%] and M3 [12.5%]. Thirty one patients [48.4%] achieved continuous complete remission [CCR] and on regular follow up. Twelve patients [23.5%] had relapse. Death reported in 33 patients [51.5%]. Three-year overall survival [OS] was [47.8±3.5%] and three-year disease free survival [DFS] was [42.8±5.5%].

Conclusion: Nearly half of patients with AML at our center died from the disease and treatment related toxicity so Improving supportive cares facilities and Intensification of treatment should be done to reduce mortality rates and improving outcome.

Keyword: Acute myeloid leukemia, Children, immunophenotyping, chemotherapy, outcome.

Introduction:

Acute myeloid leukemia [AML] represents 15–20% of pediatric acute leukemia. Majority of AML cases appear de novo, however a minority of cases can present as a secondary malignancy [1].

Acute myeloid leukemia is a highly heterogeneous disease and its diagnosis involves a combination of diagnostic analyses including morphology, immunophenotyping, cytochemistry, and leukemic blasts derived from peripheral blood or bone marrow demonstrating cytogentic and molecular characteristics [2].

Acute myeloid leukemia patients can be risk-classified into a clinically relevant subgroup. The previously used morphology-based French-American British (FAB] classification is nowadays replaced by the World Health Organization [WHO] classification based on immunophenotypic and cytogenetic studies, [3].

Children with AML should be treated within controlled clinical trials, as treatment of childhood AML requires an intensive chemotherapy [CTH], Anthracycline and Cytarabine-based therapy using at least 4 or 5 courses with or without hematopoietic stem cell transplant [HSCT] [4].

Approximately 5% of children with AML have refractory disease [resistant to treatment or cure] and 30% experience relapse [recurrence]. Bone Marrow is the most common site of relapse, with the central nervous system [CNS] being involved in up to 10% of cases including combined relapse, approximately 50% of patients have an early relapse, defined as within one year of initial diagnoses [5].

Although AML accounts for about one fourth of the acute leukemia in children, it is responsible for more than half of the leukemic deaths [6].

The high frequency of treatment related deaths [5-10%], both in treatment protocols for newly diagnosed as well as for relapsed disease and the occurrence of long term side effects such as Anthracycline induced cardiomyopathy illustrate that further intensification of chemotherapy seems no longer feasible. [7].

In this study, we aimed to assess the treatment results of pediatric patients with AML, correlate the response with different prognostic factors and study the common causes of treatment related morbidity and mortality in our institute.

Patients and Methods:

This study was conducted retrospectively on de novo AML patients up to 18 years who admitted in Pediatric Oncology Department, SECI during the period from January, 2009 to December, 2018 with follow up to December 2019. We reviewed the records of all AML patients and collected data included demographic characteristics of the patients and clinical manifestation at presentation [medullary and extra medullary]. Laboratory studies including complete blood count [CBC], leukocytosis a, Bone marrow aspirate [BMA] immunophenotyping [IPT] and cytogenetic studies and cerebro-spinal fluid [CSF] cytology at presentation and follow up. The classification was based on WHO classification upon immunophenotypic and cytogenetic studies. Table [1] [8].

Table [1]: WHO Classification of Myeloid Neoplasms and Acute Leukemia [8]

1. **Acute myeloid leukemia with recurrent genetic abnormalities:**
   a. AML with t (8; 21) (q22; q22); RUNX1-RUNX1T1.
   b. AML with inv (16) (p13.1q22) or t (16; 16) (p13.1; q22); CBFB-MYH11.
   c. APL with t (15; 17) (q22; q12); PML-RARA.
   d. AML with t (9; 11) (p22; q23); MLLT3-MLL.
   e. AML with t (6; 9) (p23; q34); DEK-NUP214.
   f. AML with inv (3) (q21q26.2) or t (3; 3) (q21; q26.2); RPN1-EVI1.
   g. AML (megakaryoblastic) with t (1; 22) (p13; q13); RBM15-MKL1.
   h. Provisional entity: AML with mutated NPM1.
   i. Provisional entity: AML with mutated CEBPa.
2. **Acute myeloid leukemia with myelodysplasia-related changes**
3. **Therapy-related myeloid neoplasms**
4. **Acute myeloid leukemia, not otherwise specified**:
   a. AML with minimal differentiation.
   b. AML without maturation.
   c. AML with maturation.
   d. Acute myelomonocytic leukemia.
   e. Acute monoblastic/monocytic leukemia.
   f. Acute erythroid leukemia.
      I. Pure erythroid leukemia.
      II. Erythroleukemia, erythroid/myeloid.
   g. Acute megakaryoblastic leukemia.
   h. Acute basophilic leukemia.
   i. Acute panmyelosis with myelofibrosis.
5. **Myeloid sarcoma**
6. **Myeloid proliferations related to Down syndrome**
   a. Transient abnormal myelopoiesis.
   b. Myeloid leukemia associated with Down syndrome.
7. **Blastic plasmacytoid dendritic cell neoplasm**

Routine imaging studies done at diagnosis and during treatment including: Abdominopelvic sonar, Magnatic resonance imaging [MRI] brain and Multislice computed tomography [MSCT] chest and paranasal for fungal screening during attacks of fever neutropenia. . The cytogenetic studies were performed only in AML-M3 patients at diagnosis that was confirmed by t[15;17] and follow up during treatment cycles.

Treatment protocol received:

During the period from 2009 to 2012, patients were treated with modified AML-BFM trials [3&7 protocol] includes 2 cycles of Induction CTH [Cytarabine 100mg/m ^{2} for 7 days and Doxorubicin 25mg/m^{2}for 3 days] and 12 cycles of maintenance alternating CTH every 3 months for one year and assessment of response was done after 2 courses of induction, and every 3 cycles of maintenance *[9]*. During the period from 2013 up till now, the treatment protocol is modified Medical Research Council [MRC] AML protocol includes 2 cycles of Induction CTH [Cytarabine 100mg/m ^{2} for 10 days ,Daunorubicin 50mg/m^{2}for 3 days , Etoposide 100mg/m^2 for 5 days and intrathecal Cytarabine age adjusted dosing on day1] and 3 cycles of consolidation CTH [Mitoxantrone 10mg/m^2 for5 days, Cytarabine 1.0 gm/m^2/12h for 3 days and intrathecal Cytarabine age adjusted dosing on day1] and assessment of response was done after each course of induction and consolidation CTH *[10]*. Acute promyelocytic leukemia [APL] received All Trance Retinoic Acid [ATRA] based protocol of Creutzig et al.[9] includes Induction phase[ATRA 25mg/m^2 for 60 days and Idarubicin 12mg/m2 for 3 days], 3 cycles of consolidation every 14 days and maintenance phase for 2 years[ATRA 25mg/m^2 for 14 days/3months ,6-mercaptopurine 50mg/m^2/day and Methotrexate 25mg/m^2/day weekly] .Assessment of treatment response after each cycle of induction and after consolidation includes [complete remission [CR] b, induction failure c ,continuous complete remission and death]. We evaluated survival outcomes, as regards disease-free survival [DFS] and overall survival [OS], in correlation with different characteristics.

a Leukocytosis: total leucocyte count [TLC]>50x10^3 /mL which considered high risk.

b Complete remission: absence of leukemic blasts in peripheral blood and CSF , < 5% blasts on BMA [M1] and no evidence of extramedullary disease after induction phase.

c Induction failure: Failure to achieve complete remission after induction phase .

Ethical consideration

The research proposal was approved from ethical committee of South Egypt Cancer Institute, Assuit University. All other rules advised by the ethical committee were applied and written consent was taken from patient's relatives.

Statistical analysis:

Statistical analysis was performed using the Statistical Package for Social Sciences [SPSS] version

23 [SPSS Inc., Chicago, IL] for Windows. Data was presented as numbers and percentages or mean ± standard deviation. The Kaplan Meier method was used for survival analysis. P value was considered significant if < 0.05 and highly significant if < 0.01. DFS was calculated from the date of bone marrow examination documenting remission till date of relapse. OS was calculated from the date of presentation at our center till last date of follow up. Early mortality rate was defined as death within 30 days of initiation of induction chemotherapy. The cutoff point of our study was December 2019.

Results:

In this study, sixty four eligible patients were recorded with exclusion of 15 files due to incomplete data or early death within first week of admission. AML patients account for 8.8 % out of 900 patients with hematological malignancy during study period.

Forty two patients [65.6%] were males and 22 [34.4%] were females. Mean age at time of diagnosis was 10.85 ± 4.30 years [range 2-18 years], 19 patients [29.7%] in the age group <10 yrs. versus 45[70.3%] in the age group ≥10 yrs.

Regarding clinical presentation, fever reported in 14 patients [23.4%], 6 patients [10.2%] had pallor, 15 patients [25.3%] had external bleeding and 18 patients [29.7%] had organomegally. Eleven patients [17.2%] were presented by neurological manifestations [6 had increased increase intracranial pressure [ICP], 3 had convulsion and 2 had cranial nerve palsies]. Three patients [4.7%] presented by bilateral orbital swelling [myeloid sarcoma]. Few number of patients had bone pain, fatigue, and general weakness [9%].. Concerning hematological data at presentation, Mean TLC was 38.60 ± 31.78 10^9/L and majority [81.2%] of patients had a favorable TLC [<50 x 10^9/L.]. The most common subtype was M4 in 12 patients [18.8%] followed by M1 in 9[14.1%] patients and M3 in 8[12.5%] patients. Table [2] shows clinicolaboratory characteristics data of 64 eligible patients

Cerebro-spinal fluid cytology was done at presentation in 20 patients only due to severe thrombocytopenia and was negative for malignant cells

. MRI brain was done for 11 patients with neurological manifestations revealed presence of leukemic infiltrates in 6 patients only [10.2%].

Treatment Results

Complete response [M1] with therapy occurred in 43[8APL and 35 other subtypes][67.2%] patients [M1] following different regimens of therapy and failure to achieve complete remission [M2&M3][induction failure]was in 9 patients [14%],all patients with APL achieve CR with no induction failure Table [3].

Table [3] shows treatment analysis of each subtypes of studied AML patients and their outcome.

Treatment related morbidity:

Bone marrow suppression grade II-III [severe neutropenia] reported in 29 patients (45.3%) [16 patients were survived, 13 patients were complicated and died] and bleeding tendency [severe thrombocytopenia] in 24[37.5%]. Gastrointestinal toxicity reported in 54 % of patients in the form of mucositis in 12 patients [18.8%], typhlitis in 13 patients [19.4%] diagnosed clinically and by imaging studies, and hepatotoxicity [grade II-III] in 10 patients [15.6%].

Outcome of eligible patients:

In this study, twelve patients were relapsed. 8/12 patients [66.6%] had early relapse and 4/12 [33.3%] had late relapse, 10 patients [83.8%] had medullary type while 2 patients had CNS relapse and there was no combined detected cases of relapse. There were 33 patients died [51.5%] distributed as following; twelve patients/64 [18.7%] died during induction phase; [8 due to sepsis and 4 due to bleeding tendency], nine patients/52 [17.3%] died in remission due to severe bone marrow suppression and infection and all relapsed patients died; [8 due to disease progression and 4 due to severe infection and sepsis], Thirty one patients [48.4%] include 8 patients with APL and 23 patients with other subtypes achieved continuous complete remission [CCR] and on regular follow up.

Survival analysis:

Median follow up time of patients with all subtypes of AML except APL was [32 months], range [8-58 months]. 3-year OS ± SE was [36.4±5.5%] for these patients Fig. [1]. Median DFS of patients with all subtypes of AML except APL was 28.97 month, range [10-52.4 months]. 3-year DFS ± SE was [35.6±3.5%] for these patients Fig. [2].

Univariate analysis of the effect of different prognostic factors on survival: Age, sex and TLC, IPT and treatment protocols had no statistical significance upon survival of all AML types except APL. Table [5].

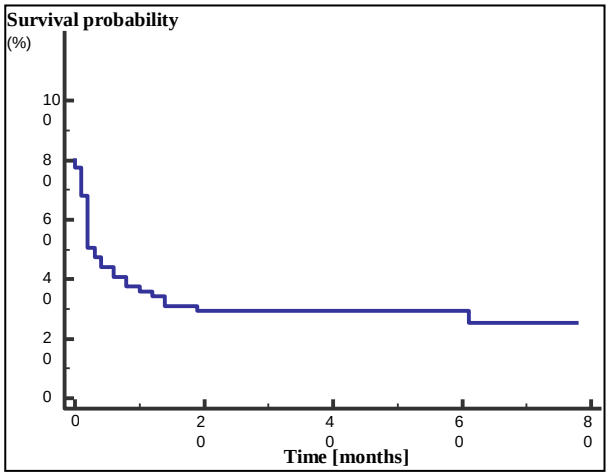

Fig. [1]: 3-year Overall survival curve of 56 AML patients of all subtypes except APL

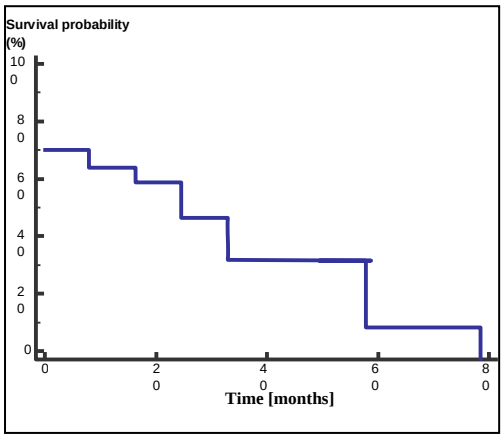

Fig. [2]: 3-year DFS curve of 56 AML patient of all subtypes except APL

Table [2]: Clinico-laboratory characteristics data of the 64 eligible

Variable	No [%]
Age :	
• Mean (range)	10.85 ± 4.30 (2-18 years)
• < 10 years	19 [29.7%]
• ≥ 10 years	45 [70.3%]
Sex :	
• male	42 [65.6%]
• female	22 [34.4%]
• Male : female ratio	2:1
Clinical presentation	
• Medullary disease	37 [57.8%]
• Extra medullary disease	33[51.5]
Hemoglobin cons.	
• Mean Hemoglobin [g/dl]	7.62 ± 2.09
• < 6 g/dl	19 [29.7%]
• 6-10 g/dl	32 [50%]
• > 10 g/dl	13 [20.3%]
TLC number	
• Mean TLC [$x10^9$/l]	38.60±31.78
• < 50 [$x10^9$/l]	52 [81.2%]
• > 50 [$x10^9$/l]	12 [18.8%]
Platelets number	
• Mean platelets number [$x10^9$/l]	43 ± 39.91
• < 50 [$x10^9$/l]	45 [70.3%]
• 50-100 [$x10^9$/l]	6 [9.4%]
• > 100 [$x10^9$/l]	13 [20.3%]
IPT classification	
• M0	8 [12.5%]
• M1	9 [14.1%]
• M2	8 [12.5%]
• M3	8 [12.5%]
• M4	12 [18.8%]
• M5	6 [9.4%]
• M6	5 [7.8%]
• M7	8 [12.5%]
Chemotherapy protocol	
• AML-BFM protocol	35[54%]
• 3&7 protocol	21[32.8%]
• APL protocol	8 [12.5%]

Data expressed as frequency [percentage], mean [SD]. [APL] Acute promyelocytic leukemia, [TLC] total leucocyte count, [AML] Acute myeloid leukemia, [BFM] Berlin Frankfurt Muenster.

Table [3]: Assessment of treatment response after induction and after consolidation

BMA response	AML-BFM protocol [N=35]	3&7 protocol (N=21)
AFTER INDUCTION		
• **M1**	23/35 [65.7%]	12/21 [57%]
• **M2**	4/35 [11.4%]	3/21 [14.3%]
• **M3**	0	2/21 [9%]
Induction deaths	8/35 [22.8%]	4/21 [19%]
CR	23/35 [65.7%]	12/21 [57%]
AFTER CONSOLIDATION	27/35 [77%]	17/21 [80.7%]
Deaths in CR	7/27 [26%]	2/17 [11.7%]
Relapse (all died)	6/27 [22%]	6/17 [35.3%]
CCR =23/56	14/27 [51.8%]	9/17 [52.9%]

[AML] Acute myeloid leukemia, [BFM] Berlin Frankfurt Muenster, [CR] complete remission,[CCR] continuous complete remission.

Table [4]: Treatment protocol for each subtype of AML of the studied patients

IPT classification	3&7 protocol [N=21]	AML-BFM protocol [N= 35]	*M3 protocol [N=8)*	*deaths of each subtype [N= 33]*
M0	5 [23%]	3 [8.5%]	8[100%]	3 [9%]
M1	2 [9.5%]	7[20%]		3 [9%]
M2	1 [4.7%]	7 [20%]		6 [18%]
M3	0	0		0
M4	7 [33.7%]	5 [14.3%]		10 [30%]
M5	2 [9.5%]	4 [11.4%]		2 [6%]
M6	1 [4.7%]	4 [11.4%]		3 [9%]
M7	3 [14.3%]	5 [14.3%]		6 [18%]

[IPT] immunophenotyping , [AML] Acute myeloid leukemia, [BFM] Berlin Frankfurt Muenster

Table [5]: Overall and disease-free survival of all types of AML patients except APL and its relation to different factors

variable	Overall survival at 3 year. ± SE%	Disease free survival at 3 year± SE%
Age groups		
<10 years	37 months	35.3 months
>10 years	31 months	24.2 months
p. value	0.42	0.36
Sex		
Male	41 [95%CI= 29-52]	37.7 [95%CI= 26-50]
Female	35 [95%CI= 20-49]	41 [95%CI= 25-48.2]
p. value	0.33	0.47
TLC		
<50 [x10^9/l]	39 months	37 months
>50 [x10^9/l]	33 months	31.8 months
p. value	0.32	0.45
IPT		
M0	50.8 months	9.5 months
M1	52.3 months	8.3 months
M2	38 months	8.2 months
M4	42 months	7.7 months
M5	46.2 months	9.1 months
M6	42.3 months	8.1 months
M7	41.8 months	7.8 months
p. value	0.36	0.41
Treatment protocol		
3&7 protocol	34 [95%CI= 22-49]	35 [95%CI= 21.5-42.5]
AML-BFM	31 [95%CI= 22-41]	36.8 [95%CI= 23.4-43.4]
p. value	0.39	0.48

The Kaplan Meier method was used for survival analysis .Level of confidence was kept at 95% and hence, P value was considered

Discussion:

Treatment of AML in resource poor settings is challenging because of lack of supportive care facilities, high cost of treatment and poor access to stem cell transplantation. Our aim in the current study is to assess the treatment results of pediatric patients with AML, correlate the response with different prognostic factors and study the common causes of treatment related morbidity and mortality in our locality.

In this study the mean age at time of diagnosis was 10.8 ± 4.3 years [range 2-18 years] and the majority 45[70.3%] are above 10 years which is more than what was reported by *Nashwa et al.* [11] where the mean age of 8.6±5.3 years [range 8 months -15.8 years].

Regarding the gender forty two patients [65.6%] were males and 22 [34.4%] were females with male to female ratio 1.8:1 which match with what reported by Egyptian study where 58.1% males and 41.9% females with male to female ratio [1.39:1] [11].

Children with AML often present with signs and symptoms that reflect bone marrow infiltration with leukemic blasts and the extent of extramedullary disease spread. [12].

In our study, 18 patients [29.7%] had organomegaly, fever in 14 patients [23.4%], 6 patients [10.2%] had pallor, and 15 patients [25.3%] had external bleeding, few number of patients had bone pain, fatigue, and general weakness [9%] was matched with studies conducted in developing countries [13], [14] *and* [11] and not comparable with Turkish study as bleeding [76.5%], fever [58.8%], and fatigue [47%] were the presentation [15].

As regarding features of extramedullary infiltration, 17.2% of our patients presented by neurological manifestation and 4.7% presented by myeloid sarcoma and bilateral orbital swelling which is approaching the Brazilian results of *Burnett et al., 2007* [16] who reported neurological manifestation in 19% of their patients and was higher than the results of *Testi et al., 2005* [17] which reported neurological manifestation in 9.6% of patients of this study. This lower incidence of myeloid sarcoma in developed countries may be due to larger sample size and early diagnosis.

Concerning hematological data at presentation, mean TLC was 38 x 10^9/L and majority [81.2%] of patients had a favorable TLC [<50 x 10^9/L.] which more than the study conducted by *Tae et al., 2018* [18] as the median WBC count at diagnosis was 13,900/µL, and 10.8% of the patients had a WBC count of at least 100,000/µL and Indian study where the median WBC was 16,700/ µL[19]

In our study there were many limitation in diagnosis including cytogenetic studies, and molecular characteristics which used in risk stratification of treatment and detection of residual disease.

The incidence of APL among the AML cases in children vary from 2% in Switzerland to >50% in Nicaragua [20]. However, APL incidence among eastern Mediterranean countries is not well documented. A multicenter study from Lebanon reported 25% APL cases among AML patients [21]. In Turkey, a study disclosed an incidence of APL as 17 patients [20.5%] among 83 AML patients at childhood [15].In this study, APL was reported in 8 [12.5%] of the studied patients.

Response to induction therapy has been a major prognostic factor since the beginning of risk stratification. The amount of blasts remaining in the bone marrow after the first course of induction therapy divide patients into three groups: complete remission with blasts less than 5 % [M1], in partial remission patients have blasts between 5 and 15 % [M2], and with resistant disease they have more than 15 % blasts in the bone marrow [M3]. [4].

In the current study complete response [CR]after induction therapy was 67.2% for all studied patients

43/64 patients following different regimens of therapy with significantly lower than what internationally reported studies in developed countries [USA] [22] that showed CR rate >90%, this was due to high supportive care to decrease treatment related mortality and morbidity.

Induction failure was recorded in 9/ 52[18%] of our patients [M2 and M3 patients], which was consistent with National Cancer Institute [NCI] - Egypt and higher than what reported in developed countries [7.2%] [22] , this relatively higher incidence of induction failure in our study and in NCI may be due to modifications done to the original protocol.

Relapse remains the major cause of treatment failure in pediatric AML. Relapse occurred in 12/ 52[23.5%] of patients, this was nearly similar to Indian study [23] in which relapse constituted [23%] of patients, and lower than Egyptian study in which relapse was [35.4%] (11).

Deaths represented 51.5%] in our study, which was greatly higher than reported deaths in India as a developing country [39%] and Europe as a developed country [25%] [24] and [25], However it is lower than deaths in NCI -Egypt which accounted for [61.8%] [11].

All relapsed patients 12/52[24.5%] died which were mostly due to disease progression and bone marrow suppression. This is unlike to *Faulk et al* [22] who found deaths in relapse in [10%] which due to differences in management and supportive care facilities.

Thirty one out of 64 patients [48.4%] still alive and in continuous complete remission, this is lower than results of *Chen et al., 2014* [25] [61%] in developed countries and to some extent better than Iranian study by *Eivazi-Ziaei et al., 2005* [26] and *Nashwa et al., 2018* [11] where CCR was 28.4% and 38.2% respectively.

Infectious complications were reported to occur at 76% which was higher than *Inaba et al., 2008* [27] which reported infectious complications in 42 % and these relatively high results reflects our strong need to follow more restrict infection control measures and improve our health care facilities.

The dramatic improvement of outcomes in pediatric AML over the last 3 decades has been achieved with intensification of chemotherapy, improvements in supportive care, wider application of various hematopoietic stem cell transplantations [HSCT], recent advances in stratification into risk groups based on cytogenetics and more recently on molecular genetics, and early response evaluation by minimal residual disease. Currently, the overall survival [OS] in pediatric AML patients ranges from 60 – 70% [28] , [29] and [18].

In this study, 3-years OS was [36.4.8±5.5%], which less than Egyptian study [45.1%] [11] and also less than results reported in developed countries as Japan [75%] [28], Europe [69%] [30] and the United States [64%] [29] may be due to difference in number of included patients and management, but nearly similar to that of developing countries in Asia, such as China [33%] [13] Thailand [35%] [14] and India [36%] [19].

The 3-years -DFS was [35.6± 3.5%], which matched to what reported in NCI- Egypt study [11], which were [39±11.2%].

Univariate analysis of the effect of different prognostic factors on survival; age, sex, TLC and treatment protocols had no statistical significance effect on OS and DFS, which was consistent with *Faulk et al* [22].

At the end of our retrospective study which one of limitation also, the pattern at diagnosis and survival quite similar in developing countries.

Better diagnosis, risk stratification, supportive care with economic growth, refinement of HSCT techniques including a better selection of patients based on prognostic groups, and stem cell donor selection will needed to increase survival of our patients.

List of Abbreviations:

AML: acute myeloid leukemia
APL: acute promyelocytic leukemia
ATRA: all-trans retinoic acid
BMA: bone marrow aspirate
CBC: complete blood count
CNS: central nervous system
CSF: cerebrospinal fliud
CTH: chemotherapy
DFS: disease free survival
OS: over free survival
FAB: French-American British
ICP: intracranial pressure
IPT: immunophenotyping
MRI: magnetic resonance imaging
MSCT: multi slice computed tomograghy
TLC: total leukocytic count
WHO: world health organization

Conclusion:

Nearly half of patients with AML at our center died from the disease and treatment related toxicity so Improving supportive cares facilities and Intensification of treatment should be done to reduce mortality rates and improving outcome.

References:

1- Döhner H, Weisdorf DJ, Bloomfield CD. Acute Myeloid Leukemia. N Engl J Med. 2015 Sep 17;373(12):1136-52.
2- Trachtenberg BH, Landy DC, Franco VI, et al. Anthracycline-associated cardiotoxicity in survivors of childhood cancer. Pediatr Cardiol. 2011 Mar;32(3):342-53.
3- Webb DK, Wheatley K, Harrison G, et al. Outcome for children with relapsed acute myeloid leukaemia following initial therapy in the Medical Research Council (MRC) AML 10 trial. MRC Childhood Leukaemia Working Party. Leukemia. 1999 Jan;13(1):25-31.
4- Arlene R, Rachel K. Acute Myeloid Leukemia in Lanzkowsky's manual of pediatric hematology and oncology, sixth edition, 2016, pp 413- 453.
5- Seiter NJ, Raetz EA, Ritter J, et al. Acute Lymphoblastic Leukemia. In: Cancer in Children

and Adolescents. Jones and Bartlett Publishers International [London], 2011, pp 161-183.

6- West AH, Godley LA, Jane E Churpek JE. Familial myelodysplastic syndrome/acute leukemia syndromes: a review and utility for translational investigations. Ann N Y Acad Sci. 2014 Mar;1310(1):111-8..
7- Vardiman JW, Thiele J, Arber DA, et al. The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: rationale and important changes. Blood. 2009 Jul 30;114(5):937-51.
8- Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016 May 19;127(20):2391-405.
9- Creutzig U, van den Heuvel-Eibrink MM, Gibson B, et al. Diagnosis and management of acute myeloid leukemia in children and adolescents: recommendations from an international expert panel. Blood. 2012 Oct 18;120(16):3187-205.
10- Lipshultz SE, Giantris AL, Lipsitz SR, et al. Doxorubicin administration by continuous infusion is not cardioprotective: the Dana-Farber 91-01 Acute Lymphoblastic Leukemia protocol. J Clin Oncol. 2002 Mar 15;20(6):1677-82.
11- Nashwa ME, Alaa ME, Lobna ME, et al. Outcome of Risk Adaptive Therapy in Pediatric Acute Myeloid leukemia at National Cancer Institute, Cairo University, Egypt, MD thesis, 2018..
12- Longo D. Malignancies of Lymphoid Cells. In: Harrison's Principles of Internal Medicine [18th edition], ch. 15, ISBN 978-007-174889-6. McGraw-Hill Professional [New York], 2011.
13- Xu XJ, Tang YM, Song H, et al. Long-term outcome of childhood acute myeloid leukemia in a developing country: experience from a children's hospital in China. Leuk Lymphoma. 2010 Dec;51(12):2262-9.
14- Wiangnon S, Veerakul G, Nuchprayoon I, et al. Childhood cancer incidence and survival 2003-2005, Thailand: study from the Thai Pediatric Oncology Group. Asian Pac J Cancer Prev. 2011;12(9):2215-20.
15- Aksu T, Fettah A, Bozkaya İO, et al. Acute Promyelocytic Leukemia in Children: A Single Centre Experience from Turkey Mediterr J Hematol Infect Dis. 2018 Jul 1;10(1):e2018045.
16- Tedja AT, Wirawan R. Erythroleukemia. Indonesian journal of clinical pathology and medical laboratory 2017; 23(2):197-202.
17- Testi AM, Biondi A, Lo Coco F, et al. GIMEMA-AIEOPAIDA protocol for the treatment of newly diagnosed acute promyelocytic leukemia (APL) in children. Blood. 2005 Jul 15;106(2):447-53.
18- Song TY, Lee SH, Kim G, et al. Improvement of treatment outcome over 2 decades in children with acute myeloid leukemia Blood Res. 2018 Mar;53(1):25-34.
19- Radhakrishnan V, Thampy C, Ganesan P, et al. Acute Myeloid Leukemia in Children: Experience from Tertiary Cancer Centre in India Indian J Hematol Blood Transfus. 2016 Sep;32(3):257-61.
20- Zhang L, Samad A, Pombo-de-Oliveira MS, et al. Global characteristics of childhood acute promyelocytic leukemia. Blood Rev. 2015 Mar;29(2):101-25..
21- Farah RA, Horkos JG, Bustros YD, et al. A Multicenter Experience from Lebanon in Childhood and Adolescent Acute Myeloid Leukemia: High rate of Early Death in Childhood Acute Promyelocytic Leukemia. Mediterr J Hematol Infect Dis. 2015 Jan 1;7(1):e2015012.
22- Faulk K, Gore L, Cooper T. Overview of therapy and strategies for optimizing outcomes in de novo pediatric acute myeloid leukemia. Paediatr Drugs. 2014 Jun;16(3):213-27.
23- Tyagi A, Pramanik R, Chaudhary S, et al. Cytogenetic Profiles of 472 Indian Children with Acute Myeloid Leukemia. Indian Pediatr. 2018 Jun 15;55(6):469-473.
24- Swaminathan R, Rama R, Shanta V. Childhood cancers in Chennai, India, 1990-2001: incidence and survival. Int J Cancer. 2008 Jun 1;122(11):2607-11.
25- Chen KH, Liu HC, Liang DC, et al. Minimally early morbidity in children with acute myeloid leukemia and hyperleukocytosis treated with prompt chemotherapy without leukapheresis J Formos Med Assoc. 2014 Nov;113(11):833-8.
26- Eivazi-Ziaei J. Control of acute myeloid leukemia morbidity in northwest Iran. Asian Pac J Cancer Prev. Oct-Dec 2005;6(4):472-3.
27- Inaba H, Fan Y, Pounds S, et al. Clinical and biologic features and treatment outcome of children with newly diagnosed acute myeloid leukemia and hyperleukocytosis. Cancer. 2008 Aug 1;113(3):522-9.
28- Horibe K, Saito AM, Takimoto T, et al. 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 Jul;98(1):74-88.
29- Dama E, Pastore G, Mosso ML, et al. Time trends and prognostic factors for survival from childhood cancer: a report from the Childhood Cancer Registry of Piedmont (Italy). Eur J Pediatr. 2006 Apr;165(4):240-9.
30- Ward E, DeSantis C, Robbins A, et al. Childhood and adolescent cancer statistics, 2014. CA Cancer J Clin. 2014 Mar-Apr;64(2):83-103.