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Preliminary effect of Anthracycline Type and Dose on Remission Induction Outcomes in Adult Acute Myeloid Leukemia

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Abstract:
Introduction: Acute myeloid leukemia (AML) is a highly aggressive hematologic malignancy that necessitates timely remission-induction therapy. The standard 3+7 regimen of cytarabine and anthracycline use endures to this day, but anthracycline type and dose impact treatment outcomes in real-world conditions is clinically relevant today.
Aim: In adults with de novo AML on standard 3+7 protocol, remission induction response and survival outcomes were evaluated and the influences of anthracycline type and dose on complete remission rates were evaluated.
Subject and Methods: We performed a prospective observational cohort study with 53 newly diagnosed de novo AML adult patients from one tertiary institution on time, from December 2023 to December 2024. Induction therapy was provided to patients with cytarabine for 7 days and either daunorubicin (45–90 mg/m²) or doxorubicin (30 mg/m²) for 3 days. The diagnosis and classification were based on cytomorphology and flow cytometry using FAB criteria. Bone marrow examination measured treatment response using the treatment remission standard definitions. Analysis of logistic regression and Kaplan–Meier survival was conducted.
Results: The mean age was 35.0 ± 14.3 years, male-to-female ratio was 1.25:1. FAB-M2 was the most common subtype (43.4%). Complete remission (CR) occurred in 62.3%, partial remission 11.3%, no response in 22.6% and induction mortality 3.8%. Although not statistically significant, CR rates were higher with daunorubicin than with doxorubicin (69.2% versus 42.9%). CR rates were significantly higher for daunorubicin 90 mg/m² than 45 mg/m² (OR 8.5, p=0.014). It was a 37.9% 1-year overall survival, median 8 months survival. Survival by anthracycline type and dose were not statistically different.
Conclusion: Adult AML patients showed remission rates at standard 3+7 induction therapy, however acceptable. Higher doses (90 mg/m²) of daunorubicin were associated with better remission outcomes than lower doses. Fit older adults had comparable remission rates with younger patients. Daunorubicin may elicit an induction response increase without significant safety reduction with dose-optimized daunorubicin therapy.

Keywords: *Acute Myeloid Leukemia, AML, 3+7 protocol, Induction therapy, Daunorubicin, Doxorubicin, Complete remission, Anthracycline dose, Treatment outcomes*

1. Introduction

Acute myeloid leukemia (AML) is a heterogeneous group of hematologic malignancies that arise from the clonal proliferation of abnormal myeloid precursor cells in the bone marrow. These malignant cells demonstrate impaired differentiation and uncontrolled growth, leading to suppression of normal hematopoiesis and replacement of healthy marrow elements. Consequently, patients develop varying degrees of anemia, neutropenia, and thrombocytopenia, which are responsible for the major clinical manifestations including fatigue, recurrent infections, and bleeding tendencies.

AML is typically an aggressive disease and is rapidly fatal if left untreated; therefore, early diagnosis and prompt therapeutic intervention are essential. Current diagnostic and classification approaches rely on a combination of morphologic, immunophenotypic, cytogenetic, and molecular features as adopted by the World Health Organization (WHO) classification system. [1–3]

The recognition of leukemia as a distinct disease entity date back to the nineteenth century, when Virchow first described abnormal white blood cell predominance and introduced the term leukemia. Subsequent advances identified acute and chronic forms and established the bone marrow as the primary site of origin. Over time,

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improvements in staining techniques and microscopy enabled more accurate morphologic classification. The French–American–British (FAB) classification later standardized AML subtypes based on cytomorphology and cytochemistry. However, this system had limitations, including inter-observer variability and limited prognostic value because it did not incorporate cytogenetic and molecular abnormalities. These limitations led to the development of the WHO classification, which integrates genetic and clinical features and distinguishes biologically and prognostically relevant AML entities, including de novo AML, myelodysplasia-related AML, and therapy-related AML. [4]

AML is the most common acute leukemia in adults, accounting for approximately 80 percent of acute leukemia cases in this age group, while it represents a much smaller proportion in children. The reported incidence in the United States and Europe ranges from 3 to 5 cases per 100,000 population annually. The disease shows a strong age association, with incidence increasing markedly in older individuals and a median age at diagnosis of approximately 65 years. A slight male predominance has been observed, and incidence appears broadly similar across racial groups with minor variations. Several environmental and genetic risk factors have been implicated in AML development, including exposure to chemicals, ionizing radiation, tobacco, prior chemotherapy, and inherited genetic syndromes such as trisomy 21 and bone marrow failure syndromes. In some patients, AML evolves from preexisting clonal hematologic disorders such as myelodysplastic syndromes and myeloproliferative neoplasms. [5–12]

Clinically, AML usually presents with symptoms related to bone marrow failure. Most patients experience generalized fatigue and weakness due to anemia, increased susceptibility to infections due to neutropenia, and bleeding manifestations such as petechiae, ecchymoses, epistaxis, or gingival bleeding due to thrombocytopenia. Fever is frequently present and is most often infection-related, requiring urgent evaluation and empiric antimicrobial therapy, particularly in neutropenic patients. Additional findings may include bone discomfort, leukemic skin infiltration, gingival hypertrophy, and, less commonly, central nervous system involvement or extramedullary tumor masses known as myeloid sarcoma. Because early symptoms are often nonspecific, the onset of disease may be difficult to determine precisely, and some patients show prior subtle hematologic abnormalities before diagnosis. [13–29]

Diagnosis of AML depends on peripheral blood and bone marrow evaluation demonstrating increased myeloblasts, supported by cytochemical staining, flow cytometry, cytogenetic analysis, and molecular testing. Most patients show circulating blasts on peripheral smear, variable leukocyte counts, anemia, and thrombocytopenia. Immunophenotypic profiling typically demonstrates expression of myeloid markers such as CD13, CD33, CD34, CD117, and HLA-DR, although patterns vary among subtypes. Cytogenetic and molecular abnormalities are of major prognostic importance and form a central component of modern AML classification and risk stratification systems. [4, 30-53]

Treatment of AML is broadly divided into remission induction and post-remission therapy. Induction therapy commonly consists of intensive combination chemotherapy, often based on cytarabine and an anthracycline, with the aim of achieving complete remission by eliminating leukemic blasts and restoring normal marrow function. Post-remission strategies, including consolidation chemotherapy and hematopoietic cell transplantation in selected patients, are required to reduce relapse risk and improve long-term survival. Prognosis varies widely depending on age, performance status, cytogenetic and molecular risk factors, and whether the leukemia is de novo or secondary. Therefore, accurate biologic classification and risk assessment are essential for optimal therapeutic planning. [4, 54–75] The aim of the study to evaluate the overall response rate of AML patients in response to remission induction with single standard treatment protocol of 3 days daunorubicin (60 – 90 mg/m^2/day), or doxorubicin (30 mg/m^2/day) with 7 days cytarabine (continuous infusion 100 mg/m^2/day)

2. SUBJECTS AND METHODS:

Study setting:

An observational prospective cohort study, that included 53 adult patients diagnosed with *de novo* AML, the study performed for 1 year started from December-2023 till December-2024, in a single center (Baghdad Teaching hospital, Medical city complex, Baghdad, Iraq).

The committee concerned with human rights for research purposes has reviewed our administrative research and give us approval on order no. 97/4/2

Study subjects:

Eligible patients were included in the study after receiving either first or second induction protocol, older patients were included if they have good performance status (assessed using ECOG performance status) [76]

Knowing that all the financial resources was done by researcher themselves and there is no other source like hospitals or national centers offer a financials aids.

Inclusion criteria:

- Adults (>14 years)
- Newly diagnosed AML

Exclusion criteria:

- Acute promyelocytic leukemia (FAB M3)
- Patients with severe comorbidities (unable to receive 3 + 7 protocol).
- Ejection fraction below 45%
- high-risk myelodysplastic syndrome (MDS) (>10% marrow blasts)
- poor performance status (≥3 using ECOG performance status)

- patients offered low dose SC cytarabine

Data collection:

Clinical data and therapeutic outcomes were gathered by researchers and centralized enrollement was used to collect data then each researcher record clinically al steps and pateints participated in this study, the rules everyone follows to make sure the work is consistent.

Laboratory assessment of AML:

Wright Giemsa stain, Sudan Black and Peroidic Acid Schiff cytochemical staining were used for the cyto-morphological evaluation, with Flow-cytometry as confirmation of the diagnosis and determine the AML subtypes based on FAB classification. [52]

During the period of neutropenia post induction patients have offered supportive measures using blood products and antibiotics (if infection were conformed or suspected).

Bone marrow evaluation was done on day 14 post induction upon complete recovery of peripheral blood counts using blast cells percentage count, **2.7**

Distributions of patients on dose and type of anthracyclines:

The patients were classified in to four groups:

Group 1: take daunorubicin 45 mg/m^2

Group 2: take daunorubicin 60 mg/m^2

Group 3: take daunorubicin 90 mg/m^2

Group 4: take doxorubicin 30 mg/m^2

The distribution of patients on groups was done by senior physician and was randomly distributed on these groups.

Assessment of response to remission induction:

The following criteria were used to classify the response in AML patients: [77]

1. **Complete remission (CR):** Bone marrow blasts <5 percent; absence of blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count >1.0 x 10^9/L (1000/µL); platelet count >100 x 10^9/L (100,000/µL); independence of red cell transfusions. All criteria need to be fulfilled; marrow evaluation should be based on a count of 200 nucleated cells in an aspirate with spicules; if ambiguous, the exam is repeated after 5 to 7 days; flow cytometric evaluation may help to distinguish between persistent leukemia and regenerating normal marrow; a marrow biopsy should be performed in cases of dry tap, or if no spicules are obtained; no minimum duration of response required.
2. **Partial remission (PR):** all hematologic criteria of CR; decrease of bone marrow blast percentage to 5 to 25 percent; and decrease of pretreatment bone marrow blast percentage by at least 50 percent.
3. **Relapse:** Bone marrow blasts ≥5 percent; or reappearance of blasts in the blood; or development of extramedullary disease.

Statistical analysis:

Binary logistic regression analysis used to calculate the odd ratio (OR) and their 95% confidence intervals, when the outcome can be categorized into 2 binary levels.

Kaplan–Meier analysis used to estimate median time of the cumulative percentage of survival (or any surrogate end points), the Logrank test used to calculate the p value and compare the significant between each groups.

Overall survival (OS) was measured from date of diagnosis to death from any cause. Progression free survival (PFS) measured from date of diagnosis to death any cause or relapse.

SPSS 20.0.0, GraphPad Prism 7.0 software package used to make the statistical analysis, p value considered when appropriate to be significant if less than 0.05

3. RESULTS:

Demographic data:

Fifty-three patients with AML were included in this study, mean age of AML patients was 35.0 ± 14.3 years ranging from 17 – 64 years, with male to female ratio of 1.25:1 and 15.1% of the total patients above or equal to 60 years, as illustrate in table 3.1.

Table 3.1: demographic data of all the patients (n = 53)

Variables	Value
Age (years), mean ± SD (range)	35.0 ± 14.3 (17 – 64)
<30 years	25 (47.2%)
30 – 39 years	12 (22.6%)
40 – 49 years	6 (11.3%)
50 – 59 years	2 (3.8%)
≥60 years	8 (15.1%)
Gender	
Female	23 (43.4%)
Male	30 (56.6%)

Number of patients (n) = 53

FAB classification of AML patients:

About 43.4% of the AML patients had M_2 disease, followed by M_4, M_1, M_5, M_6 and M_0, as illustrate in table 3.2 and figure 3.1.

Table 3.2: distribution of AML patients according to FAB classification

FAB classification	Number (%)
M_0	2 (3.8%)
M_1	7 (13.2%)
M_2	23 (43.4%)
M_4	11 (20.8%)
M_5	5 (9.4%)
M_6	5 (9.4%)

Number of patients (n) = 53

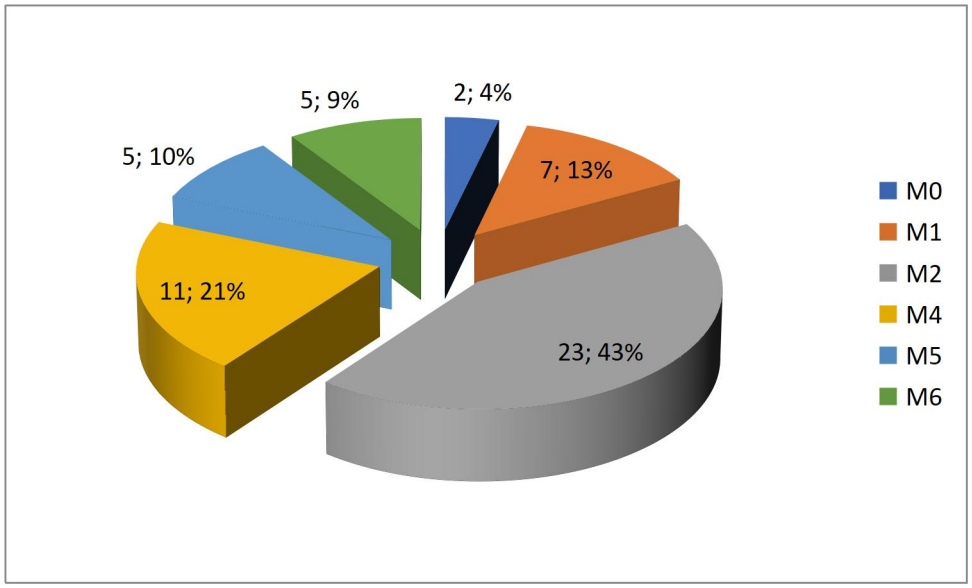

Figure 3.1: pie-chart of AML subtypes distribution according to FAB classification (data presented as number and percentage [percentage were rounded to the nearest natural number])

The most commonly used anthracycline for induction was daunorubicin (73.6%), with different doses used include 45 mg/m^2 equal to 9.4%, 60 mg/m^2 equal to 26.4% and 90 mg/m^2 equal to 37.7% as illustrated in table 3.3

Table 3.3: descriptive data about type of anthracycline used and its doses

Anthracycline	Number (%)
Daunorubicin	39 (73.6%)
45 mg/m^2	5 (9.4%)
60 mg/m^2	14 (26.4%)
90 mg/m^2	20 (37.7%)
Doxorubicin (30 mg/m^2)	14 (26.4%)

Number of patients (n) = 53 , daunorubicin (n) = 39, doxorubicin (n) =14

Clinical outcome of induction:

Complete remission was achieved by 62.3% of the patients, while 22.6% achieved no response, 11.3% partial remission and 3.8% died, as illustrate in table 3.4

Table 3.4: clinical outcome after remission induction

Outcome	Number (%)
Complete remission (CR)	33 (62.3%)
Partial remission (PR)	6 (11.3%)
No response (R)	12 (22.6%)
Death	2 (3.8%)

Number of patients (n) = 53

Age (using 60 years as cut point) did not predict complete remission; gender also did not predict complete remission, while daunorubicin used had modest effect to predict better complete remission compared to doxorubicin (statistically was not significant), as illustrated in table 3.5.

Table 3.5: association between different predictors and complete remission

Variables		Not CR	CR	RR (95%CI)	P value
Age	<60 years	18 (40.0%)	27 (60.0%)	0.8 (0.548 – 1.516)	0.426
	≥60 years	2 (25.0%)	6 (75.0%)		
Gender	Female	8 (34.8%)	15 (65.2%)	0.870 (0.420 – 1.725)	0.779
	Male	12 (40.0%)	18 (60.0%)		
Anthracycline	Daunorubicin	12 (30.8%)	27 (69.2%)	0.539 (0.288 – 1.083)	0.087
	Doxorubicin	8 (57.1%)	6 (42.9%)		

RR: relative risk, CI: confidence interval

Number of patients (n) = 53

Daunorubicin in a dose of 90 mg/m^2 predict complete remission significantly with 8.5 folds increased in the rate of CR compared to daunorubicin in dose of 45 mg/m^2, while 60 mg/m^2 predict weakly 2 folds increased CR compared to 45 mg/m^2, as illustrated in table 3.6

Table 3.6: association between different doses of daunorubicin with complete remission

Doses	Not CR	CR	OR (95%CI)	P value
60 mg/m^2	6 (42.9%)	8 (57.1%)	2.000 (0.250 – 15.991)	0.394
90 mg/m^2	3 (15.0%)	17 (85.0%)	8.500 (1.001 – 74.424)	0.014
45 mg/m^2	3 (60.0%)	2 (40.0%)	Reference	

OR: odd ratio, CI: confidence interval
Bootstrapping was performed and based on 994 samples

Number of patients (n) = 39

Patients with M_1, M_2, M_4 had the highest CR rates, the rest of the data are illustrated in table 3.7.

Table 3.7: complete remission according to FAB classification

FAB	Not CR	CR
M_0	2 (100.0%)	0 (0.0%)
M_1	2 (28.6%)	5 (71.4%)
M_2	6 (26.1%)	17 (73.9%)
M_4	4 (36.4%)	7 (63.6%)
M_5	3 (60.0%)	2 (40.0%)
M_6	3 (60.0%)	2 (40.0%)

Number of patients (n) = 53

Side effect and adverse events:

The most side effect were anemia 69.8% and neutropenic fever 64.2%, 35.8% had weight loss and 15.1% had cannula site infection, as illustrated in table 3.8

3.8: Common side effect

Variables	Daunorubicin	Doxorubicin	Total	p-value
	39	14		
Anemia	27 (69.2%)	10 (71.4%)	37 (69.8%)	0.878
Neutropenic fever	26 (66.7%)	8 (57.1%)	34 (64.2%)	0.524
Weight loss	15 (44.1%)	4 (28.6%)	19 (35.8%)	0.317
Cannula site infection	6 (15.4%)	2 (4.3%)	8 (15.1%)	0.922

Number of patients (n) = 53, Daunorubicin =39, Doxorubicin =14

Overall response:

One year overall survival was 37.9% for all patients; type of anthracycline did not show statistical difference between daunorubicin and doxorubicin however daunorubicin show higher 1 – year OS 41.4% vs. 28.6%for doxorubicin, 90 mg/m^2 daunorubicin had the highest 1 year OS (46.9%) compare to 45 mg/m^2 (40%) and 60 mg/m^2 (33.5%); however it was not statistically significant, as illustrated in table 3.9 and figures 3.2 to 3.4.

Regarding the median survival time per months in table below we can see that the higher group is daunorubicin 60 mg/m^2 in with median equal to 10 months followed by 90 mg/m^2 with 9.3 months and then 45 mg/m^2 with median survival months equal to 7.5 months these differences between overall survival and median survival below to that

the median survival is study middle point of data set when the number are arranged in order which focus only on the center of the distribution.

Table 3.9: overall survival of the AML patients and its relation to anthracycline

Variables	1 – year OS (Percentage)	Median (95%CI) (Months)	P value
All patients	37.9%	8.0 (5.9 – 10.1)	
Type of anthracycline			0.285
Daunorubicin	41.4%	9.3 (5.7 – 12.8)	
Doxorubicin	28.6%	6.5 (4.1 – 8.9)	
Effect of daunorubicin doses			0.974
60 mg/m^2	33.5%	10.0 (6.1 – 13.9)	
90 mg/m^2	46.9%	9.3 (3.0 – 15.5)	
45 mg/m^2	40.0%	7.5 (1.1 – 13.9)	

OS: overall survival, CI: confidence interval
Kaplan Meir analysis was performed

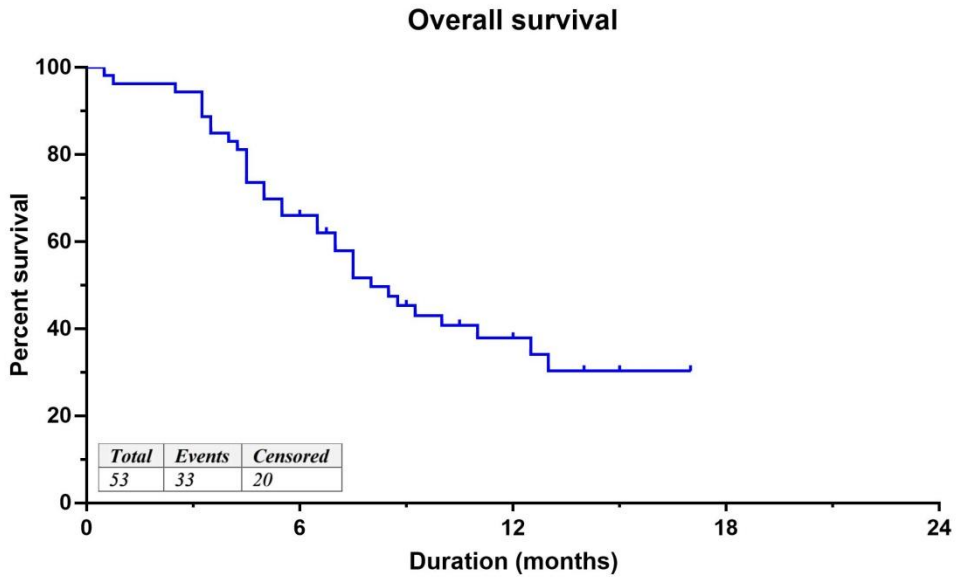

Figure 3.2: overall survival

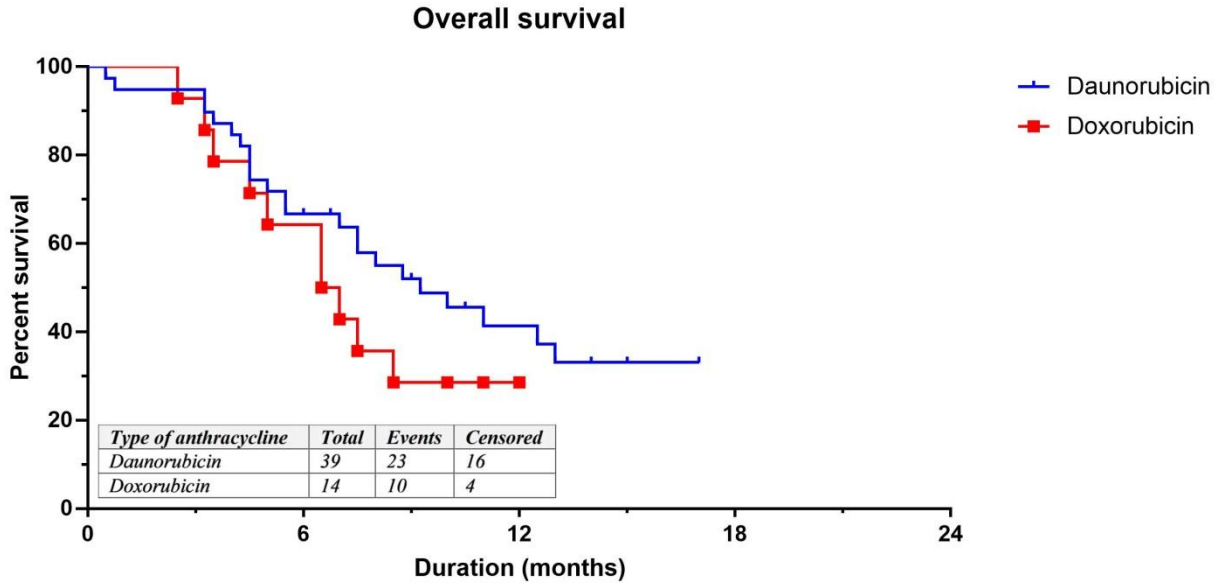

Figure 3.3: effect of anthracycline on OS

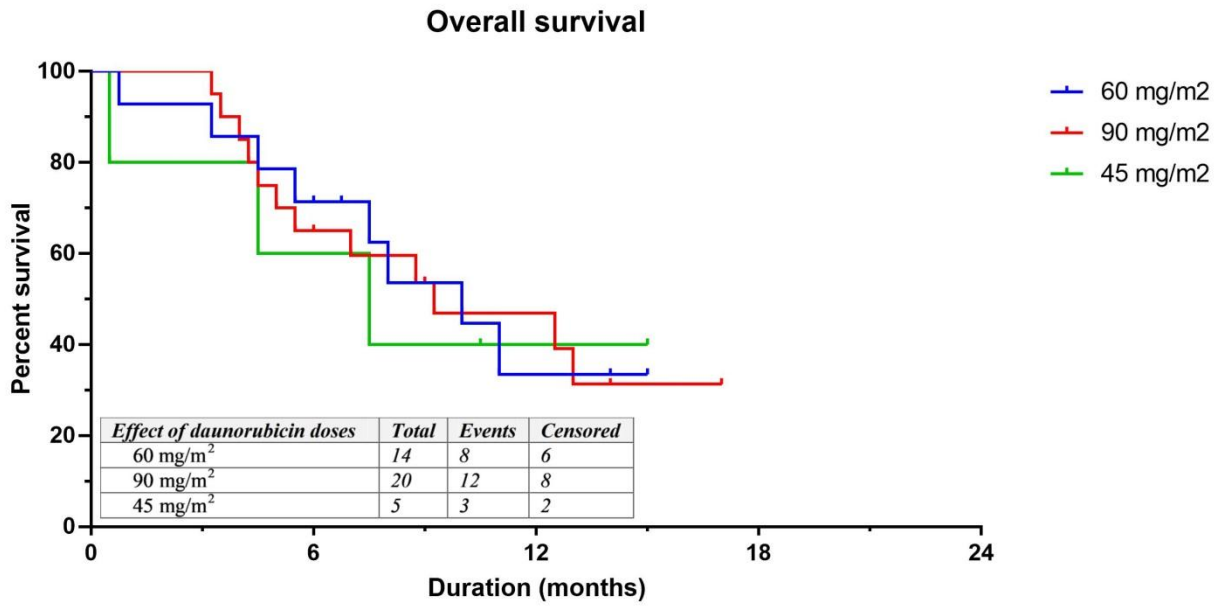

Figure 3.4: effect of doses of daunorubicin on OS

4. DISCUSSION:

The Iraqi protocol for management of AML induction use the Daunorubicin as the standard dose for treatment, in this study we try to compare that standard therapy with other anthracyclines present in our country and regarded as second line therapy (Doxorubicin).

Acute myeloid leukemia is a hematological emergency that require prompt and effective treatment as soon as a confirmed diagnosis is established, since early treatment will provide better clinical outcome by increasing complete remission rate (CR) and overall survival (OS). [78]

In the current study mean age of patients was 35.0 ± 14.3 years with 8 (15.1%) of the patients were more than or equal to 60 years, our finding was in agreement with previous Iraqi study in which Naji in 2014 [78] found in his study mean age is 36.7 ± 14.8 years, also it was similar to another Iraqi study Al-Khalissi [79] in 2008 reported the median age is 41 years with 19% with age above 60 years. [78,79] It was slightly lower than older international study in 1994 in which it was reported to 50 years (mean age), with 32% older than 60 years, however they mentioned that the age in their study was slightly older than reported in literature. [80] Ohtake *et al* in 2011 reported the median age to be 47 years and this study designed to assess the response in patients younger than 65 years, [81] which is consistence with Kern *et al* study with median age of 53 years, [82] indicating mean age of de novo AML Iraqi patients present at younger age. In the current study the male to female ratio was 1.25:1, which was in agreement with Naji study with 1.5:1 male to female ratio, [78] and with Al-Khalissi study with 1.07:1 male to female ratio, [79] the gender distribution was similar to international study like Kern *et al* with 227/222 (1.02:1) M:F ratio, [82] this similarity of AML gender distribution indicate that AML is not relate to specific gender.

In the current study FAB classification was adopted to classify the patients since molecular study was not available for the majorities of the patient, the pattern of AML subtype of AML was: M_2 represent 43.4% of the patients, followed by M_4 with 20.8% that M_1 13.2%, while in Naji study M_2 had the highest frequency with 49%, followed by M_1 13% and M_5 11%, [78] while in Al-Khalissi study M_2 present 6%, M_4 present 27.5% and M_1 19%, [79] while in Kern *et al* it was M_2 with 33.6%, M_1 with 21.2% and M_4 with 21%, [82] with similar findings in Ohtake *et al* study, [81] indicating the current study patients sub-classification was similar to previous published studies.

In the current study complete remission was obtained by 62.3% of the patients (according to various types of induction protocols), with patients with M_2 showing the highest proportion for CR with 73.9%, followed by M_1 with 71.4% and M_4 with 63.6% while the two patients with M_0 did not achieved CR, in Naji study the CR in AML patients was 58% (47 patients treated with 3 days 30 mg/m^2 doxorubicin + 7 days continuous infusion of 100 mg/m^2 cytarabine), which was in agreement with the current study, [78] also our findings was in agreement with Al-Khalissi study in which CR was achieved in 55.5% and PR in 10.5%, [79] historically CR achieved in 50% - 58% as shown in Yates *et al* study in 1982, in which they used 3 + 7 protocol

(patients received 7 days continues infusion of 100mg/m^2 cytarabine + either one the three anthracycline 45 or 30 mg/m^2 daunorubicin or 30 mg/m^2 doxorubicin), [83]

Mayer *et al* in 1994 reported CR after remission of 64% for AML patients which is closely to our findings, [80] in more recent years the post-remission CR is improving as shown in Ohtake *et al* study in 2011; it reach 77.5%. Niparuck *et al* in 2009 reported post-remission 81.2% with 5 years OS 22.2% and 5 years DFS of 41%, [84] Miyawaki *et al* in 2005 show post-remission CR 78.7%, with patient having M_2 (82.7%), M_4 (80.5%), while patients with M_0, M_6 and M_7 had the poorest CR, with 5 years OS 52.4% and 5 years DFS 58.4%, [85] Büchner *et al* in 2012 reported post-remission CR 62%. The results of current study were in agreement with these previous Iraqi and International studies showing a similarity in outcome in terms of overall post-remission CR.

A stratification of the patients is important to choose the optimal therapeutic plan, in the current study elderly patient represent 15.1% of the patients (their age between 60 - 64 years) so they offered the standard 3 + 7 protocol but with lower doses of daunorubicin 45mg/m^2 (or 30 mg/mg^2 in case of doxorubicin), there was difference in the rate of CR between patients age more than or equal 60 or less than 60 (RR = 0.8, p = 0.426) but it did not reach the statistical significance, in many studies age appear to important predictor of outcome, Mayer *et al* show post-remission CR is 75% in patients age less than 40 years, 68% in patients age 40 – 60 years, and 47% in patients above 60 years, [80] however in this study (like others) patients age was up to 86 years (which is excluded in the current study) since extreme elderly cannot offered stranded 3+7 induction protocol instead modified protocol like low dose SC Ara-C in offered which provide less survival benefit. Miyawaki *et al* support this explanation since the post-remission CR was similar across the age groups; in which 15 – 24 years (CR = 77.2%), 25 – 34 years (CR = 76.9%), 35 – 44 years (CR = 81.8%), 45 – 54 years (CR = 80.3%), 55 – 64 years (CR = 76.5%). [85]

In the current study the type of anthracycline and the dose of daunorubicin is a significant predictor of post-remission CR, in which daunorubicin had modest effect by improving the CR compared to doxorubicin 69.2% vs. 42.9% (RR = 0.539, p = 0.087), while 90 mg/m^2 (85.0% post-remission CR) appear to predict 8.5 folds increase rate of post-remission CR compared to 45mg/m^2, which is 6 folds better that 60mg/m^2 (57.1% post-remission CR). Our findings was in agreement with phase III study in which 657 patients were randomized to receive either 45 mg/m^2 or 90 mg/m^2 with 100mg/m^2 seven days of continuous IV infusion cytarabine, post-remission CR was 71% vs. 47% in 90 and 45 mg/m^2 respectively, with median OS 24 vs. 16 months, with similar rate of grade III/IV/V adverse events between both arms, [86,87] in another study using cytarabine at dose of 200 mg/m^2 with similar randomization to the previous phase III study show 83% vs. 72% post-remission CR in 90 vs. 45 mg/m^2 daunorubicin dose, with 5 years OS (47% vs. 35%). [88]

In the current study the overall survival was 37.9% (1 years estimate), with median survival of 8 months, our finding was lower than reported by Burnett *et al* study (AML17 trial) they reported 2 – years survival was 59% for daunorubicin and 60% for daunorubicin; however this study based on patients receiving two induction regimens making patients in this trial receiving more intensive induction than the current study; the 1st is with either 60 or 90 mg/m^{2}daunirubicin for three days with continues infusion of cytarabine, followed by 50 mg/m^2 daunorubicin for 3 days, [89] in Alwan *et al* study in Iraq the median OS at 2 years was 7 months, which was similar to findings, [90] in Al-Khalissi study 5 years OS was 30% (with 40% OS in 1 year) which is also similar to our findings, [79] these two Iraqi study done in 2009 and 2013 show similarity to the finding of the current study.

Regarding the median survival time per months in table 3.9 we can see that the higher group is daunorubicin 60 mg/m^2 in with median equal to 10 months followed by 90 mg/m^2 with 9.3 months and then 45 mg/m^2 with median survival months equal to 7.5 months these differences between overall survival and median survival below to that the median survival is study middle point of data set when the number are arranged in order which focus only on the center of the distribution.

In clinical research and statistics median is vital because medical data is rarely perfectly symmetrical.

On future we should focused on increase sample size more than in this study and if we can do across sectional study between groups and also on future studies should study the effect of dose selection on white blood cell count with regarding to the age of patients this will add to study more explanation for effect of dose on remission phase of disease.

5. CONCLUSION:

- Complete remission was achieved in 62.3% of AML patients, with M_2, M_4 showing the best CR rate compared to the rest of AML types
- Patients age between 60 – 64 years have similar CR rate to young adults
- Daunorubicin appear to offer better CR than doxorubicin
- Daunorubicin at dose of 90 mg/m^2 appear to be better in term of CR than 45 mg/m^2 and 60 mg/m^2

RECOMMENDATIONS:

- Use of daunorubicin in a dose of 90 mg/m^2 instead of other doses because it offer better survival outcome and had similar side effect profile, elderly patients with good performance status can be treated effectively with standard 3+7 protocol with comparable CR rate.
- Increase the sample size in future study will confirmed on stabilization of data and results more than in our study.
- Use of common terminology criteria of adverse events (CTCAE) for classification of adverse drug reactions focusing on severe and life threatening consequences adverse drug reactions.

LIMITATION OF STUDY:

- The number of sampled patients is small especially in subdivided group and this small number in sample size may lead to some of bias in data so we recommend to increase the number of patients in future studies that confect on construction of results.
- On future study should focus on other adverse drug reactions especially white blood cells counts, cardiac-toxicities, cardiac-eco study, liver functions and renal indices, focus on anthracyclines cardiac toxicities for each dose and their differences as the main adverse drug reactions.

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