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# The Prognostic Value of C-Reactive Protein and Albumin in Newly Diagnosed Patients with AML

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**ABSTRACT**

**Background**: Acute-phase reactant proteins, particularly C-reactive protein (CRP), play a critical role in the initiation, progression, and recurrence of cancers such as acute myeloid leukemia.

**Materials and Methods:** We retrospectively analyzed 127 newly diagnosed non-M3 acute myeloblastic leukemia (non-M3 AML) patients. We investigated pre-treatment levels of C-reactive protein (CRP), Albumin, and C-reactive protein to albumin ratio (CAR) with cytogenetics, response to induction therapy, recurrence, and overall survival.

**Results:** We did not find any relationship between levels of CRP, Albumin, and C-reactive protein to albumin ratio (CAR) with complete remission rate, recurrence, and risk categorization of patients ($P > 0.05$).
3-and 5- year overall survival was 40.8% (with a standard error of 4.7%) and 30.1% (standard error: 5.3%), respectively. In addition, 3-year and 5-year event-free survival was 31.3% (standard error = 4.4%) and 25.8% (standard error = 4.8%), respectively. The only prognostic factor was allogenic stem cell transplantation (SCT).

**Conclusion:** Although CRP, Albumin, and CAR serve as convenient prognostic markers, they were not predictive of overall survival (OS) and event-free survival (EFS) in AML patients. Further studies are needed in the future to confirm or refute our results.

**Keywords:** Non-M3 AML; Prognostic value; CAR

## INTRODUCTION

Acute phase reaction is a catch-all term referring to upsurging levels of multiple proteins and inflammatory markers secondary to various conditions such as infection, inflammation, and injuries and despite its name, it might also soar in chronic situations like cancers, and chronic inflammatory and infectious diseases [1]. It is blatantly obvious that tumor tissues have a microenvironment in which inflammatory cells are responsible for releasing inflammatory markers leading to epigenetic changes and genomic vulnerability. In acute myeloid leukemia (AML) levels of inflammatory markers such as interlukin- 6 (IL-6) and interlukin- 8 (IL-8) rise in acute myeloid leukemia depict poor prognosis; however, it is worth mentioning that the concurrent elevated level of anti-inflammatory markers like IL-10 would bear a favorite prognosis showing the significance of sustainable balance between inflammatory and non-inflammatory markers[2, 3]. C-reactive protein is one of the acute phase reactant components generated by liver in response to various inflammatory markers particularly IL-6 which are produced secondary to tumor necrosis, tissue injury, and inflammation in different malignancies [4].

On the other hand, albumin is made in liver and generally is assumed to be a biological marker of nutritional status or systemic inflammation[5]. Albumin is considered to be a negative phase reactant meaning that its level declines in almost every disease; so, there might be a solid connection

between reducing the level of albumin and increasing mortality rate or deteriorating health condition[6]. From what has been discussed, it seems that elevated levels of C-reactive protein accompanied by hypoalbuminemia would represent poor prognosis; Hence, the CRP to albumin ratio (CAR) reveals the effect of systemic inflammation and malnutrition having a prognostic value in the majority of cancers[1,7]. According to different situations, they can be utilized as a single marker or in combination with other markers in pretty well-known scoring systems such as CRP/Alb ratio, and Glasgow score. In this regard, CRP more than 1 mg/dl and albumin level less than 35 g/dl is taken as a score one [8].

Acute myeloid leukemia is a heterogeneous malignancy arising from changes in the bone marrow environment and can be divided into three risk categories according to the European Leukemia Net (ELN) guideline risk assessment, including favorable, intermediate, and adverse risk groups [9]. In AML such as other cancers, it has been proposed that some autoimmune, inflammatory, and infectious diseases play a pivotal role in the pathogenesis and progression of the disorder by inducing genetic and epigenetic variation; so, it means that inflammatory and anti-inflammatory markers might contribute to the change of tumor micro-environments. Some documented inflammation-related index systems such as systemic immune-inflammation index (SII), prognostic nutritional index (PNI), and C- reactive protein/ albumin ratio (CAR) have been used as beneficial markers for the prediction of survival in malignancies[10-12] even though in AML, limited numbers of biomarkers can predict the mortality rate and complication of the disease, multiple studies have revealed that the same as other solid malignancies, serum albumin level greater than 35 g/dl is significantly associated with superior overall survival[13, 14.] To cap it all, due to the huge role of inflammatory markers in the initiation, progression, and relapse of AML, it seems obvious that CAR would be the most convenient and affordable parameter to follow patients with acute myeloid leukemia after receiving chemotherapy or bone marrow transplant. In this article, we aim to investigate the prognostic value of CAR, CRP, and albumin in newly diagnosed patients with non-M3 AML, as to the best of our knowledge, there have not been a lot of studies related to the prognostic value of CAR in AML patients.

## MATERIALS AND METHODS

This study was a cross-sectional study in which patients with AML-non M3 who were younger than 70 years old received a standard regimen of 7+3 and then, underwent two various pathways according to cytogenetic risk stratification: low-risk patients received an intermediate dose of Cytarabine (IDAC) and others opted for allogenic bone marrow transplantation even though we did not perform any autologous bone marrow transplantation in our centers. The study was conducted in Namazi and Amir hospitals from January 2019 to January 2021 participated. Out of 464 patients referred to the hospitals with the primary diagnosis of Acute leukemia, 77 patients were excluded because of other diagnoses such as chronic myelogenous leukemia (CML), myelodysplastic syndrome (MDS), and so forth. In addition, 36 cases were AML-M3, 49 patients were off-age limits, and 45 patients were AML patients experiencing relapse. In addition, 60 patients with AML did not receive the standard 7+3 regimen, and 197 patients were new cases of AML; however, 70 patients who had incomplete records were excluded from the study. Eventually, 127 patients were analyzed even though out of them 15 patients had not any cytogenetic and karyotype study. Data such as CRP, Alb, lactate dehydrogenase (LDH), white blood cell (WBC), bone marrow (BM) biopsy and aspiration reports, cytogenetic study, and karyotype were gathered. On the other side, we did not have a facility for checking CEBPA and MPL1; therefore, we had to categorize our patients according to other cytogenetic markers. It is worth mentioning that all laboratory markers such as albumin and C-reactive protein were measured on the first day of patients' admission. Albumin was reported with g/ dl and CRP with mg/dl. Including criteria were being younger than 70 years old, newly diagnosed non-M3 AML receiving a standard regimen of 7+3; while patients with other diagnoses, having relapse or receiving treatments other than 7+3 regimen were excluded from the study.

**Statistical analysis**

Data were analyzed by IBM SPSS software version 23. The Kolmogorov-Smirnov test was used to check the normality of the data. Descriptive data were presented as median, range, and frequency. Comparison of quantitative variables was done by the Mann-Whitney test between the two groups and the Kruskal-Wallis test among more than two groups. Kaplan Meier analysis was conducted to illustrate the survival curve for overall survival and EFS. Log-rank test was used to compare OS and EFS among different groups. Cox regression analysis was performed to determine independent variables influencing on overall survival and event-free survival of the patients. A P-value < 0.05 was considered to be statistically significant. Risk categorization of patients was done according to ELN 2022.

**RESULT**

Of those 127 patients included in our study, 65 (51.2%) were men and the rest of them were women 62 (48.8%) with a median age of 47 years (range: 19-69 years). As shown in Table 1, 33.1% of patients underwent allogenic bone marrow transplantation and 40.2% received salvage therapy. Approximately, 34.6% of all patients experienced recurrence, as well as 60.6% of patients died because of AML. Complete remission occurred in 67.7% of patients receiving a standard 7+3 regimen as an induction therapy.

As mentioned previously, we assumed to investigate the possible links between albumin, C-reactive protein, and CRP/Alb and risk categorization of AML-non M3. Our statistical analysis has shown that albumin, CRP, and CRP/Alb ratio did not have any statistically meaningful correlation with different risk groups (P- values of 0.345, 0.605, and 0.546, respectively) (Table 2).

When it comes to the relationships of albumin, CRP, and CRP/Alb ratio with recurrence of disease, they did not bear any relationship with disease recurrence according to our study (With P-values of 0.819, 0.252, and 0.356, respectively); however, the median CRP/Alb ratio was lower in patients experiencing recurrence than their counterparts who did not experience recurrence. Last but not least, there were no significant correlations between albumin, CRP, and CRP/Alb ratio with complete remission (P-values of 0.196, 0.385, and 0494, respectively) even though apart from Alb level, level of CRP and CRP/Alb ratio were higher in patients who did not reach complete remission than that of those who achieved it (Table 2).

The overall survival curve of patients is demonstrated in Figure 1. The estimated mean Overall survival time for patients with AML-non M3 in our study was 32.3 months (95% CI = 27.5-37.2) although 3 and 5- year overall survival was 40.8% (with standard error of 4.7%) and 30.1% (standard error: 5.3%) respectively. In addition, the estimated mean event-free survival was 27.6(95% CI: 22.8-32.3) months, and 3- year and 5-year event-free survival would be 31.3% (standard error of 4.4%) and 25.8% (standard error = 4.8%), respectively.

The association of risk assessment categories, markers (CRP ≤1 mg/dl and CRP > 1 mg/dL; Alb ≥ 3.5 and Alb < 3.5 g/dL; CRP/Alb ratio ≤ 1.015 and CRP/Alb ratio > 1.015)[8], and allogenic bone marrow transplantation with overall survival (OS) and event-free survival (EFS)were evaluated. Apart from CRP, Alb, and CRP/Alb ratio, other parameters showed significant correlations with overall survival and event-free survival. The significant results are summarized in Table 3. The mean overall survival and event-free survival were remarkably higher in patients undergoing allogeneic hematopoietic stem cell transplantation compared to patients receiving IDAC (P < 0.001 and P = 0.002 respectively). Also, risk assessment revealed a significant correlation with overall and event-free survival of patients; the longest and the shortest survival duration were observed in favorable and adverse groups both for overall survival (P = 0.009) and event-free survival (P = 0.011), respectively.

Variables with a P-value < 0.2 in univariate analysis (allogenic graft, risk assessment, and CRP) were entered into the Cox regression model (Table 4). Receiving therapies other than allogenic graft was recognized as an independent risk factor for both overall survival and event-free survival in AML patients (Hazard ratio, 95% CI, P value: 2.77, 1.55-4.97, 0.001 and 1.71, 1.02-2.84, 0.040, respectively). Also, the risk assessment group was determined as an independent risk factor for both overall survival

(intermediate, adverse, and non- otherwise specified (NOS) groups compared to the favorable group, P < 0.05) and event-free survival (intermediate and adverse groups compared to the favorable group P < 0.05) in AML patients.

**Table 1:** Demographic and clinical characteristics of patients with AML-non-M3

| Parameters | Value |
|---|---|
| Age (year) median, min-max | 47, 19-69 |
| Sex m/f | 65/62 (51.2/48.8) |
| Allogenic graft N (%) | 42 (33.1%) |
| Salvage therapy N (%) | 51 (40.2%) |
| Recurrence N (%) | 44 (34.6%) |
| Death N (%) | 77 (60.6%) |
| Complete remission N (%) | 86 (67.7%) |

**Table 2:** The association of Alb, CRP, and CRP/Alb ratio with risk assessment, recurrence, and complete remission in patients with AML-non M3 undergone induction and consolidation therapy

| Variables / Groups | Albumin (g/dL) Median (min-max) | P | CRP (mg/dL) Median (min-max) | P | CRP/Alb ratio Median (min-max) | P |
|---|---|---|---|---|---|---|
| Risk assessment* | | 0.345 | | 0.605 | | 0.546 |
| NOS (n = 10) | 3.9 (3.1-4.6) | | 31.5 (1-150) | | 7.6 (0.2-48.3) | |
| Adverse (n = 31) | 3.7 (2.6-4.7) | | 26 (1-150) | | 7.0 (.2-55.5) | |
| Intermediate (n = 53) | 3.9 (2.7-5.1) | | 12 (1-150) | | 3.4 (0.2-55.5) | |
| Favorable (n = 18) | 3.7 (2.6-4.6) | | 37.5 (1-150) | | 9.4 (0.2-57.6) | |
| Recurrence | | 0.819 | | 0.252 | | 0.356 |
| Yes (n = 44) | 3.9 (2.6-4.8) | | 14 (1-150) | | 3.7 (0.2-57.6) | |
| No (n = 83) | 3.8 (2.2-5.1) | | 30 (1-150) | | 7.5 (0.2-68.1) | |
| Complete remission | | 0.196 | | 0.385 | | 0.494 |
| Yes (n = 86) | 3.8 (2.2-5.1) | | 17.5 (1-150) | | 4.8 (0.2-68.1) | |
| No (n = 41) | 3.9 (2.6-5.0) | | 33 (1-150) | | 8.4 (0.2-57.6) | |

*Missing data (n = 15)

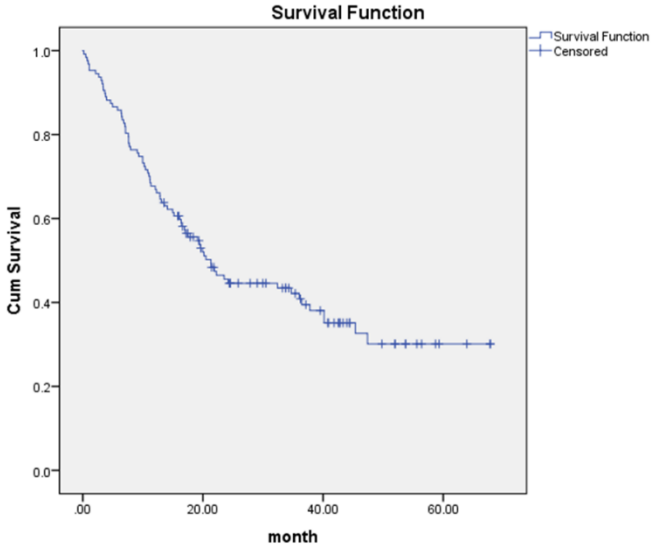


Figure 1. Overall survival of patients with AML- non-M3

**Table 3**: Comparison of OS and EFS amongst different groups of AML patients based on allogenic graft and risk assessment

| Survival / Variables | Overall survival | | Event-free survival | |
|---|---|---|---|---|
| | Estimated mean survival time (month) | 95% Confidence interval | Estimated mean survival time (month) | 95% Confidence interval |
| Allogenic graft | | | | |
| Yes (n = 42) | 47.7 | 39.8-55.7 | 38.1 | 29.6-46.6 |
| No (n = 85) | 23.2 | 18.6-27.8 | 20.7 | 16.2-25.3 |
| P value | <0.001 | | 0.002 | |
| Risk assessment* | | | | |
| Favorable (n=18) | 50.6 | 37.8-63.4 | 40.0 | 28.7-51.3 |
| Intermediate (n=53) | 30.8 | 24.2-37.4 | 25.8 | 19.5-32.2 |
| Adverse (n=31) | 22.1 | 14.3-29.9 | 17.2 | 10.3-24.1 |
| NOS (n=10) | 26.8 | 13.5-40.2 | 26.1 | 12.0-40.1 |
| P | 0.009 | | 0.011 | |

*Missing data (n=15)

**Table 4:** Cox regression analysis of covariates associated with OS and EFS in AML patients

| Survival / Variables | Overall survival | | | Event free survival | | |
|---|---|---|---|---|---|---|
| | Hazard ratio | 95% Confidence interval for the hazard ratio | P | Hazard ratio | 95% Confidence interval for the hazard ratio | P |
| Allogenic graft | | | | | | |
| No. | 2.77 | 1.55-4.97 | 0.001 | 1.71 | 1.02-2.84 | 0.040 |
| Risk assessment | | | | | | |
| Intermediate | 2.79 | 1.09-7.18 | .033 | 2.39 | 1.06-5.37 | 0.035 |
| Adverse | 4.15 | 1.58-10.91 | .004 | 3.54 | 1.52-8.20 | 0.003 |
| NOS | 3.60 | 1.09-11.92 | .036 | 2.39 | 0.791-7.23 | 0.123 |
| CRP | | | | | | |
| CRP > 1 mg/dL | 0.64 | 0.30-1.34 | 0.230 | 0.66 | 0.33-1.34 | 0.253 |

Index category: yes in allogenic graft, favorable in risk assessment, and CRP ≤ 1 mg/dL in CRP

**DISCUSSION**

Acute myeloid leukemia is a heterogeneous disease with complex cytogenetic and molecular abnormalities. After induction therapy, patients go under various post-remission consolidation treatments according to their risks[15]. Although intensive induction chemotherapy might lead to nearly 50% to 70% complete remission, relapse is one of the main culprits of treatment failure[16]. Relapse of AML after hematopoietic stem cell transplantation is about 30%-40% and it bears a poor prognosis, as the 3 and 5-year survival of these patients is 20%-30% and 28% [17].

Patients with acute myeloid leukemia suffer from some constitutional symptoms such as fatigue and fever which are claimed to be attributed to elevated levels of inflammatory markers [18, 19]. In other words, inflammation may affect tumor biology and decrease treatment response; for instance, inflammatory cytokines have been revealed to be associated with clonal evolution and disease progression in AML [20]. One study done by Wahab Ali et al. has shown that CRP did not predict response to chemotherapy; however, it might predict infection and inflammation in patients with AML post-chemotherapy [21].

Meanwhile, albumin synthesis is affected by nutritional status and diseases. A low level of serum albumin represents an adverse prognosis in some solid malignancies and hematologic malignancies such as multiple myeloma. In one study in 2021, serum albumin levels had a significant impact on treatment-related complications, short-term mortality, and overall survival. In this study, patients with normal albumin levels had lower 30-day and 60-day mortality compared with patients who had hypoalbuminemia although, in our study, albumin did not have prognostic value for median overall survival and event-free survival [22, 23]. CRP/ albumin ratio has been proposed to be an independent prognostic factor compared to other inflammatory markers in some solid cancers[24-26]. As a result, in these groups of people increased CRP to albumin ratio might be prognostic; therefore, it can be checked regularly[27]. In other words, high pretreatment CAR is associated with poor overall survival and a high 5-year mortality ratio in some solid cancers[28].

When it comes to AML, Senjo et al. have shown that neither serum CRP level nor albumin did not predicts the prognosis of AML; however, the CAR ratio would be representative of multiple factors in a single patient. Therefore, a high CAR ratio in AML patients might indicate poor prognosis due to active inflammation status secondary to AML rather than coincidence of infection, other malignant tumors, or collagen disease [29]. In our study, CRP/albumin ratio, CRP and albumin did not bear any prognostic value in different risk groups of acute myeloid leukemia; while in a study performed previously, high CAR was linked with unfavorable clinical outcomes and adverse risk stratification. Moreover, this study revealed that high CAR was associated with shorter overall survival (OS) and event-free survival (EFS) in intermediate-risk AML patients younger than 65 years old[30]. On the other hand, we did not find any significant statistical correlation between CAR, CRP, and albumin with the estimated median overall survival and median event-free survival; however, other studies were not in line with our results. In one large meta-analysis about the effect of CFA, a novel score which was comprised of CRP, fibrinogen level, and albumin, depicted that the higher the CFA ratio the shorter progression-free survival, disease-free survival, and overall survival. In addition, patients who had higher CFA had lower complete remission, which was in contrast with our study[31, 32].

Last but not least, we noticed that the only factors affecting overall survival, overall and event-free survival, are allogenic bone marrow transplantation and risk groups although CRP, CAR, and albumin did not have any relationship with survival in these patients which was in contrast with a previous study in which albumin and CRP hurt AML patients' survival who underwent bone marrow transplantation[33]. In addition, Shal et al. concluded that albumin less than 35 g/dl had an independent prognostic value for AML patients' survival, which was not aligned with our study[14].

## CONCLUSION

Despite other studies in which albumin, CRP, and CAR had a meaningful relationship with OS and EFS, in our study, we did not find any similar results. In other words, in our study, albumin, CRP, and CAR were not prognostic and predictive in AML- non-M3 patients. As our study was retrospective and we had a small sample size and missing data, future prospective studies with larger and more complete data might be beneficial for consolidation or rejection of our results.

### REFERENCES


1. Bruserud Q, Aarstad HH, Tvedt THA. Combined C-reactive protein and novel inflammatory parameters as a predictor in cancer- What can we learn from the hematological experience. Cancers (Basel). 2020; 12 (7):1966.
2. Wang CS, Sun CF. C- reactive protein and malignancy: clinic- pathological association and therapeutic implication. Chang Gung Med J. 2009; 32(5): 471- 82.
3. Craver BM, Alaoui KE, Scherber RM, et al. The critical role of inflammation in the pathogenesis and progression of myeloid malignancies. Cancers (Basel). 2018; 10(4):104.
4. Cai Y, Zhao Y, Dai Q, et al. Prognostic value of the albumin- globulin ratio and albumin- globulin score in patients with multiple myeloma. J Int Med Res. 2021;49(3): :300060521997736.
5. Levitt DG, Levitt MD. Human serum albumin homeostasis: a new look at the role of synthesis, catabolism, renal and gastrointestinal excretion, and the clinical value of serum albumin measurements. Int J Gen Med. 2016: 9: 229-55.
6. Yang S, Zhao K, Ding X, et al. Prognostic significance of hematological markers for patients with nasopharyngeal carcinoma: a meta-analysis. J Cancer. 2019; 10(11): 2568-2577.
7. Haruki K, Shiba H, Horiuchi T, et al. Impact of the C-reactive protein to albumin ratio on long-term outcomes after hepatic resection for colorectal liver metastasis. Am J Surg. 2017; 214(4): 752- 756.
8. Skar ET, Wendelbo Q, Reikvam H. The prognostic impact of C- reactive protein and albumin in patients diagnosed with acute myeloid leukemia. EJHaem. 2024: 5(6):1223-1235.
9. Döhner H, Wei AH , Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. *Blood.* 2022; 140 (12): 1345–1377.
10. Zhang Y, Xiao G. Prognostic significance of the ratio of fibrinogen and albumin in human malignancies: a meta-analysis. Cancer Manag Res. 2019; 11: 3381- 3393.
11. Li N, Tian GW, Wang Y, et al. Prognostic role of the pretreatment C- reactive protein/ albumin in solid cancers: A meta-analysis. Sci Rep. 2017;7: 41298.
12. Kristinsson SY, Bjorkholm M, Hultcrantz M, et al. Chronic immune stimulation might act as a trigger for the development of acute myeloid leukemia or myelodysplastic syndromes. J Clin Oncol. 2011; 29(21): 2897- 2903.
13. Wang N, Desai A, Ge B, et al. Prognostic value of hypoalbuminemia at diagnosis in de novo non-M3 acute myeloid leukemia. Leuk Lymphoma. 2020; 61(3): 641-649.
14. Shah A, Fox A, Bradshaw D, et al. Serum albumin as a prognostic marker for overall survival in acute myeloid leukemia. Preprints. Org. (www. Preprinting. Org). 2024 Jun 11: 10.20944
15. Stelmach P, Trumpp A. Leukemia stem cells and therapy resistance in acute myeloid leukemia. Haematologica. 2023; 108(2): 353-366.
16. Lachowiez CA, Long N, Saultz J, et al. Comparison and validation of the 2022 European Leukemia Net guidelines in acute myeloid leukemia. Blood Adv. 2023; 7(9): 1899-1909.
17. Leotta S, Condorelli A, Sciortino R, et al. Prevention and treatment of acute myeloid leukemia relapse after hematopoietic stem cell transplantation: The state of the art and future perspectives. J Clin Med. 2022; 11(1): 253.
18. Chan DSM, Bandera EV, Greenwood DC, et al. Circulating C-reactive protein and breast cancer risk-systemic literature review and meta-analysis of prospective cohort study. Cancer Epidemiol Biomarkers Prev. 2015; 24(10): 1439-49.
19. Lacourt TE, Kavelaars A, Galloway- Pena JR, et al. Association of inflammation with symptom burden in patients with acute myeloid leukemia. Psychoneuroendocrinology. 2018; 89: 203- 208.
20. Blinder S, Luciano M, Horejs- Hoeck J. The cytokine network in acute myeloid leukemia (AML): A focus on pro- and anti-inflammatory mediators. Cytokine Growth Factor Rev. 2018;43: 8- 15.
21. Loh KP, Tooze JA, Nicklas BJ, et al. Inflammatory biomarkers, geriatric assessment, and treatment outcomes in acute myeloid leukemia. J Geriatric Oncol. 2020; 11(3): 410-416.
22. Doucette K, Percival ME, Williams L, et al. Hypoalbuminemia as a prognostic biomarker for higher mortality and treatment complications in acute myeloid leukemia. Hematol Oncol. 2021; 39(5):697- 706.
23. Filliatre- Clement L, Broseus J, Muller M, et al. Serum albumin or body mass index: Which prognostic factor for

survival in patients with acute myeloid leukemia. Hematol Oncol. 2019; 37(1): 80-84.
24. Liu M, Wang L. Prognostic significance of preoperative serum albumin, albumin-to-globulin ratio, and prognostic nutritional index for patients with glioma: A meta-analysis. Medicine (Baltimore). 2020; 99 (27): e20927.
25. Seebacher V, Grimm C, Reinthaller A, et al. The value of serum albumin as a novel independent marker for prognosis in patients with endothelial cancer. Eur J Obstet Gynecol Reprod Biol. 2013; 171 (1): 101-6.
26. Kharfan-Dabaja MA, Chavez JC, Yu D, et al. Severe hypoalbuminemia at day 90 predicts worse non-relapse mortality and overall survival after allogeneic hematopoietic stem cell transplantation for acute myelogenous leukemia and myelodysplastic syndrome. Biol Blood Marrow Transplant. 2011; 17(3): 384- 93.
27. Yu ST, Zhou Z, Cai Q, et al. Prognostic value of the C-reactive protein/ albumin ratio in patients with laryngeal squamous cell carcinoma. Onco Targets Ther. 2017: 10: 879- 884.
28. Xu HJ, Ma Y, Deng F, et al. The prognostic value of C-reactive protein/ albumin ratio in human malignancies: an updated meta-analysis. Onco Targets Ther. 2017: 10: 3059-3070.
29. Senjo H, Onozawa M, Hidaka D, et al. High CRP-albumin ratio predicts poor prognosis in transplant ineligible elderly patients with newly diagnosed acute myeloid leukemia. Sci Rep. 2022; 12(1):8885.
30. Dou L, Shi M, Song J, et al. The prognostic significance of C- reactive protein to albumin ratio in newly diagnosed acute myeloid leukemia patients. Cancer Manag Res. 2022: 14: 303- 316.
31. Heini AD, Hugo R, Berger MD, et al. Simple acute phase protein score to predict long-term survival in patients with acute myeloid leukemia. Hematol Oncol.2020; 38(1): 74-81.
32. Li B, Deng H, Lei B, et al. The prognostic value of fibrinogen to albumin ratio in malignant tumor patients: a meta-analysis. Front Oncol. 2022; 12: 985377.
33. Artz AS, Logan B, Zhu X, et al. The prognostic value of serum C- reactive protein, ferritin, and albumin prior to allogeneic transplantation for acute myeloid leukemia and myelodysplastic syndromes. Haematologica. 2016; 101 (11): 1426- 1433.