RESEARCH ARTICLE

Evaluation of P53 Level and Its Relation to Iron Status in Acute Myeloid Leukemia

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Ann Coll Med Mosul 2026; 48 (1):78-89.
Received: 18th Jan. 2026, Revised 28th March 2026, Accepted: 31th May 2026.

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DOI: 10.33899/acmm.v48.i1.60326

ABSTRACT

Background: Mutations in the Tumor suppressor protein53 gene are among the most common genetic alterations observed in human cancers. Iron metabolism may regulate protein53 activity, while protein53 can also influence iron homeostasis.

Aims: To evaluate the level of protein53 in acute myeloid leukemia patients and find the relation between protein53 level and iron status in controls and patients and its relation to disease outcome.

Methods: This case-control study was conducted in Nineveh governorate at Al-Hadbaa Specialized Hospital and Ibn-Sina Teaching Hospital from January to August 2025. It included 44 newly diagnosed acute myeloid leukemia patients and 44 healthy controls. Hematological and biochemical investigations included: complete blood picture, bone marrow aspirate and flowcytometry, serum protein53 and iron studies.

Results: The mean age was (32.95±23.966) years for patients and controls, with a male predominance. There was a statistically significant inverse correlation between protein53 levels and age. Protein 53 levels were higher in patients (141.65±109.546 ng/dl) than controls (95.69±66.428 ng/dl). Serum iron (23.45±11.42 µmol/L) and total iron binding capacity (108.32±47.02 µmol/L) were significantly high in patients. Lower protein53 levels were associated with incomplete remission. Significant correlations were observed between protein53 and serum iron in incomplete remission patients and with total iron-binding capacity in deceased patients.

Conclusion: Serum protein53 levels were increased in patients and associated with poor outcomes, suggesting a supportive diagnostic and prognostic role when combined with other markers.

Keywords: Leukemia, p53, Serum Iron, TIBC, transferrin saturation.

INTRODUCTION

Acute myeloid leukemia (AML) is a malignant clonal hematological disorder characterized by the proliferation and accumulation of non-functional myeloid precursors within the hematopoietic system [1]. Malignant transformation typically takes place at the level of pluripotent stem cells, which possess a limited capacity for self-renewal [2]. Consequently, the normal hematopoiesis is suppressed, resulting in bone marrow failure and may infiltrate various organs and tissues [1]. In the majority of AML cases (classified as de-novo AML) there is no documented exposure to risk factors, and the disease onset is attributed to a series of acquired genetic aberrations. However, in other cases of AML (known as secondary AML) a number of risk factors have been identified including other hematological disorders such as myelodysplastic syndrome and myeloproliferative neoplasms, chemical exposures, ionizing radiation, and congenital diseases [3].

Acute myeloid leukemia form about (1%) of all cancers, with incidence (3.43/100,000) per year, but has increased with age. AML is primarily disease of older adults accounts for about (80%) of all cases [4]. The incidence of AML varies considerably across geographic regions. Higher incidence rates have been reported in high-income regions such as North America, Western Europe, and Australasia, whereas lower rates are generally observed in parts of Asia and Latin America. These geographic differences may reflect variations in genetic susceptibility, environmental exposures, population demographics, and healthcare systems [5]. In Iraq, a comprehensive 2022 study included 412 newly diagnosed AML patients from various governorates. The highest distribution was in age groups (≥70) years (18.52%) and (60–69) years (16.26%) [6].

Recent advances in the management of AML have improved cure rates, reaching approximately 15% in patients older than 60-years and 40% in those younger than 60-years of age [5]. All induction regimens of AML

have the potential to be toxic to the bone marrow and can cause renal failure and cytopenias, especially when tumor lysis syndrome (TLS) occurs after chemotherapy, despite advancements in therapeutic regimens, the prognosis remains very poor in the elderly population [7]. The outcome of AML depends on several factors, including patient age, karyotype, mutations, and comorbid status [8].

Since the Tumor suppressor protein 53 (TP53) gene was first discovered in 1979, it has been regarded as a cornerstone in molecular biology and cancer research[9]. TP53 is a 20-kilobase-pair gene located on chromosome (17p13.1) [10]. P53, the end product of the TP53 gene, exerts its tumor suppressive activity by promoting apoptosis, cell cycle arrest, DNA repair, and several other cellular processes, including senescence, autophagy, and ferroptosis [11]. TP53 mutations are found in about 5–10% of newly diagnosed AML cases. In contrast, their frequency increases to 30–35% in therapy- related AML and AML with myelodysplasia-related changes. Notably, in complex- karyotype AML, TP53 mutations occur in approximately 70% of cases, primarily as a result of selective pressure from acquired resistance to DNA damage induced by chemotherapy and radiotherapy [12].

In AML, TP53 is frequently inactivated through the upregulation of negative regulators such as MDM2, MDM4/MDMX, and E6-associated ubiquitin ligases [13], which promote p53 degradation and suppress its tumor-suppressive activity. Dysregulation of these pathways can contribute to p53 inactivation and leukemogenesis [10].

Iron is a vital element for all living organisms, playing an important role in many cellular functions, including oxygen transport and cell proliferation [14]. Furthermore, it serves as an essential cofactor in key metabolic processes such as DNA synthesis[15]. Iron metabolism has a regulatory role in modulating p53 activity, and conversely, p53 can influence iron homeostasis. Studies have shown that iron overload results in reduced p53 expression [16], while iron depletion leads to the accumulation of p53 [17].

The study aims

To evaluate the level of p53 in AML patients and its relation to clinical and laboratory parameters, including age, gender, complete blood count (CBC), blast percentage and to find the relation between the p53 level and iron status in normal controls and patients, and its relation to disease outcome.

PATIENTS AND METHODS

This case-control study was conducted in Nineveh governorate at AL-Hadbaa Specialized Hospital and Ibn-Sina Teaching Hospital between January 2025 and August 2025. It included 44 cases of newly diagnosed AML. Diagnosis was confirmed by CBC, blood film, bone marrow study, and flow cytometry. A total of 44 healthy individuals were included in the control group, and they were age- and sex-matched to the patients.

The inclusion criteria

Patients newly diagnosed with AML of all age groups, who were not receiving any chemotherapy before blood collection.

The exclusion criteria

Patients with AML already receiving chemotherapy, and those with a recent blood transfusion.

Blood sampling and sample handling

Five milliliters (mls) of peripheral venous blood were collected by venipuncture from each patient prior to induction of chemotherapy and samples were collected from the control group as well. Two milliliters of blood were placed in the K3EDTA tube, immediately inverted several times, and then placed on a blood rotator at room temperature to ensure complete mixing with the anticoagulant and used within one hour for CBC analysis. Another three milliliters were placed in a gel clot activator tube and allowed to clot at room temperature. Then it was centrifuged at 2000 rpm for 15 minutes to separate the serum, which was used for p53 analysis and iron studies. Blood samples from 44 healthy volunteers were used as controls for CBC, p53, and iron studies.

Investigations

Complete Blood Count (CBC)

Complete blood count, an automated hematological analyzer (Sysmex/ XN-350) is used to perform a CBC, including WBC, RBC, Hb and platelet indices, on all patients and controls samples.

Peripheral Blood and Bone Marrow Examination

Peripheral blood and bone marrow aspirates were prepared using the standard hematological techniques previously described in published studies [18]. The peripheral blood and bone marrow smears were examined to establish the diagnosis and to assess remission on days (21–28) following the initiation of remission induction treatment.

Serum p53 Assay

P53 assay, done by a sandwich enzyme immunoassay performed using a 40-microliter serum sample, using the immunoassay Analyzer and the p53 ELISA kit by Biont, No: YLA0366HU. The test was performed according to the kit instructions using a semiautomated device, Chromate.

Iron Profile Assessment

Iron studies, including serum iron and total iron binding capacity (TIBC), were tested using a fully automated Abbott c4000 bioch. instrument. Transferrin Saturation was calculated according to the following equation:

$$TS\ (\%)\ =\ (Serum\ Iron\ /\ TIBC)\ \times\ 100$$

Statistical analysis

All statistical analysis was performed using SPSS (Statistical Package for the Social Sciences) software. Chi-square and One-way ANOVA test were used to compare categorical variables. Pearson's correlation analysis was performed to evaluate the relationship between p53 levels and various hematological parameters. A p-value of (< 0.05) was considered statistically significant. Data analysis was carried out using Microsoft Excel 2016 and SPSS version 23.

RESULTS

The distribution and comparing of the studied groups according to mean age and age groups was demonstrated in Table 1. This table elicited that there was no significant statistical difference concerning the mean age and age groups and the most frequent age group was (>55 years).

Comparing the sex among the studied groups was illustrated in Table 2 which showed that the males were more frequent than the females in both studied groups and the difference was statistically not significant.

A comparison of the studied hematological parameters and p53 level between controls (n=44) and patients with AML (n=44) is shown in Fig. 1. A significant reduction has been observed in HB (Fig. 1a) and platelet count (Fig. 1b). Comparing WBC indices showed a notable non-significant elevation of WBC count in patients with AML (Fig. 1c) in addition to significant reduction in both Neutrophils (Fig. 1d) and lymphocytes (Fig. 1e) and elevation of monocytes (Fig. 1f) though this elevation did not achieve statistical significance.

Expression of p53 was higher in patients with AML compared to controls. However, this increased expression did not reach statistical significance (Fig. 1g)

Table 2
Comparing the sex among the studied groups.

Characteristic	Cases	Controls	p-value
Male, No. (%)	25 (56.8)	24 (54.5)	0.830
Female, No. (%)	19 (43.2)	20 (45.5)	
Male: Female (ratio)	1:0.76	1:0.83	

Table 1
Comparing the mean age and age groups among the studied groups.

Variable	Cases	Controls	p-value
Mean age (years)	32.95 ± 23.966	32.17 ± 20.006	0.868
Age groups (years)	No. (%)	No. (%)	p-value
≤5	4 (9.1)	3 (6.8)	
6–10	6 (13.6)	6 (13.6)	
11–15	3 (6.8)	3 (6.8)	
16–20	5 (11.4)	4 (9.1)	
21–25	4 (9.1)	4 (9.1)	
26–30	3 (6.8)	3 (6.8)	0.670
31–35	1 (2.3)	2 (4.5)	
36–40	1 (2.3)	2 (4.5)	
41–45	2 (4.5)	2 (4.5)	
46–50	2 (4.5)	3 (6.8)	
51–55	3 (6.8)	3 (6.8)	
>55	10 (22.7)	9 (20.5)	

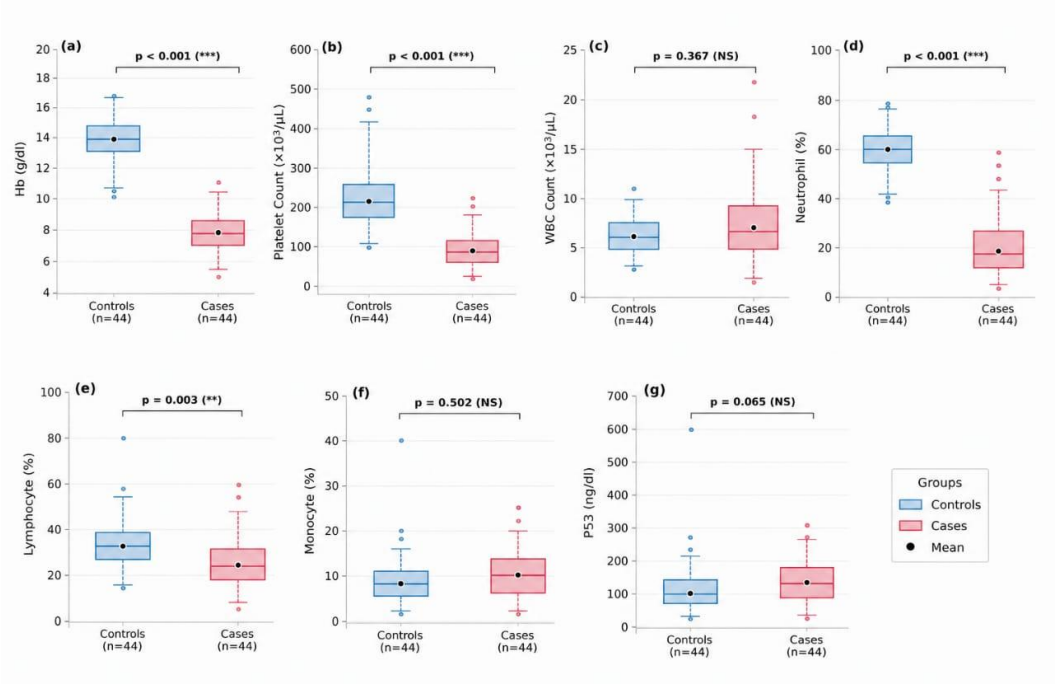

Fig. 1. Comparisons between cases and controls for the studied parameters. (a) HB, (b) platelet count, (c) WBC count, (d) Neutrophil %, (e) Lymphocyte %, (f) Monocyte %, (g) P53.

A statistically significant mild inverse correlation was observed between age and p53 concentration (r = -0.311, p = 0.040, n = 44), indicating that p53 levels tend to decline modestly as patient age increases (Fig. 2).

Fig. 3 (a–h) displayed the pearson correlation coefficients between p53 levels and eight hematological parameters including, hemoglobin, WBC count, neutrophil, lymphocyte, and monocyte percentages, platelet count, peripheral blood blasts, and bone marrow blasts among AML patients. All observed correlations were weak, ranging from a complete absence of correlation with bone marrow blasts (r = 0.000, p = 1.000) to the highest observed value with monocyte percentage (r = 0.160, p = 0.305), and none reached statistical significance (all p > 0.05).

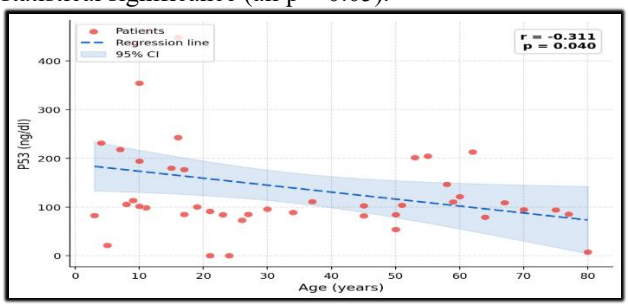

Fig. 2. Correlation between p53 and age among AML patients. The dashed regression line confirmed the negative trend, while the shaded 95% confidence interval reflected the degree of uncertainty around the estimated.

The distribution of iron profile parameters among the studied groups was shown in Fig. 4. A significant elevation has been noted for serum iron, TIBC and transferrin saturation % among cases of AML compared to control (Fig. 4 a, b and c) collectively suggesting dysregulation of iron metabolism in AML patients.

A weak negative correlation was observed between p53 and serum iron levels indicating a possible but inconclusive inverse relationship between iron accumulation and p53 expression in AML (Fig. 5).

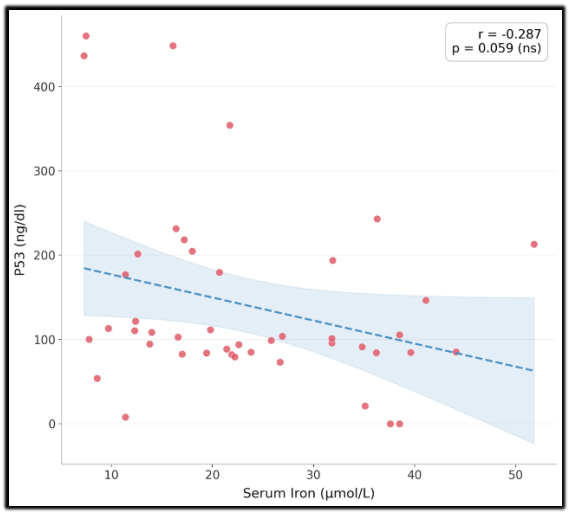

Fig. 5. Correlation of p53 with serum iron among AML cases

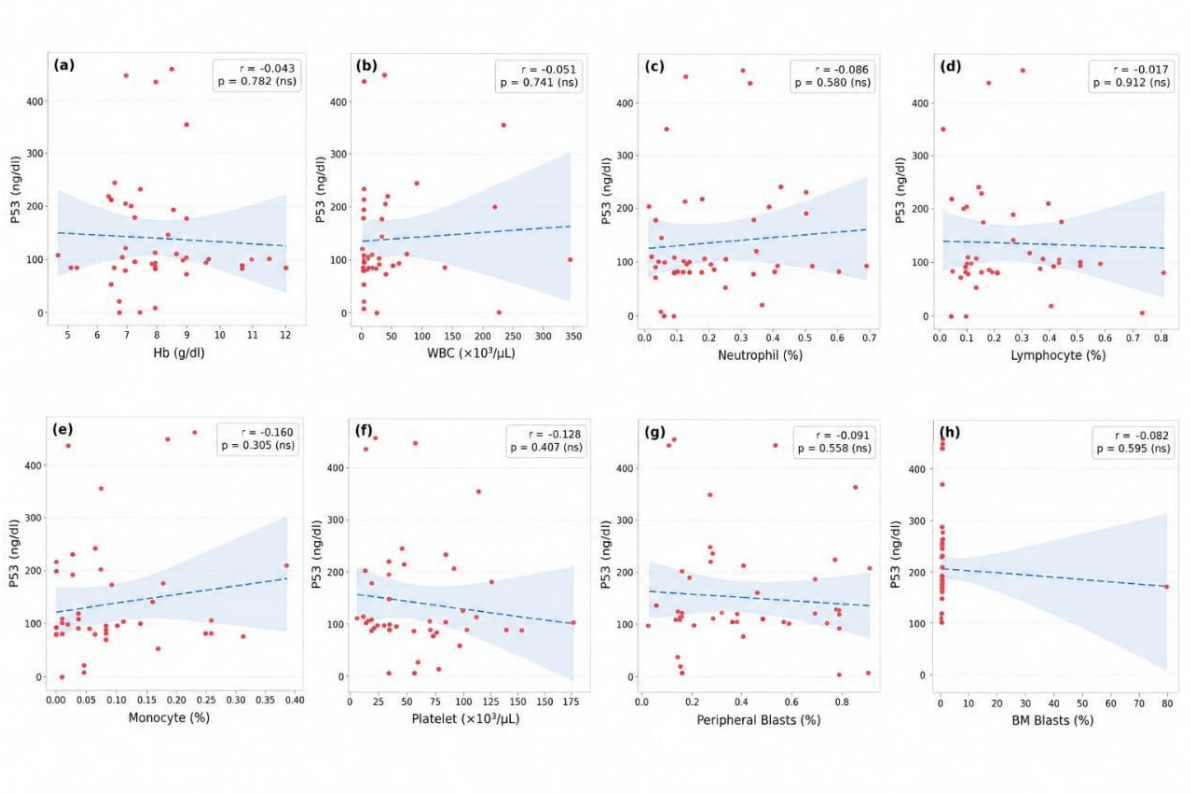

Fig. 3. Correlation of p53 with hematological parameters.
(a) HB, (b) WBC count, (c) Neutrophil %, (d) Lymphocyte %, (e) Monocyte %, (f) platelet count, (g) Peripheral blasts %, (h) Bone marrow blasts %.

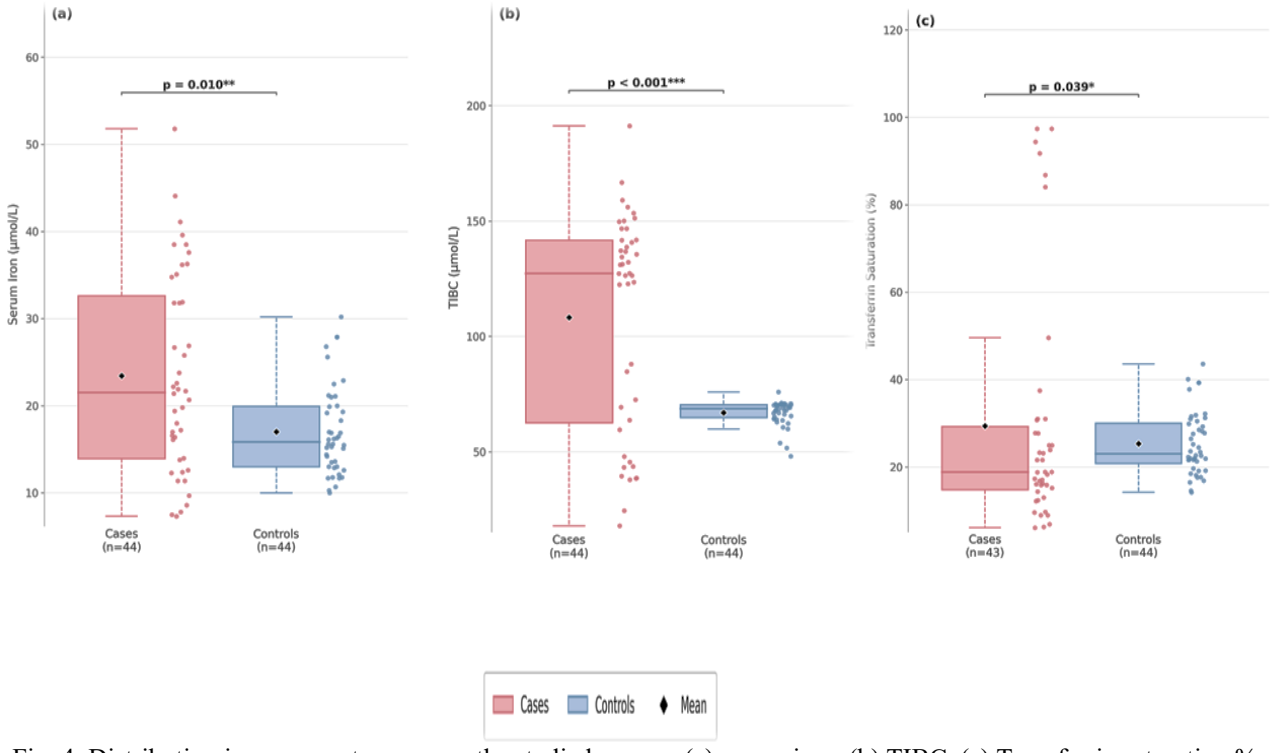

Fig. 4. Distribution iron parameters among the studied groups. (a) serum iron, (b) TIBC, (c) Transferrin saturation %.

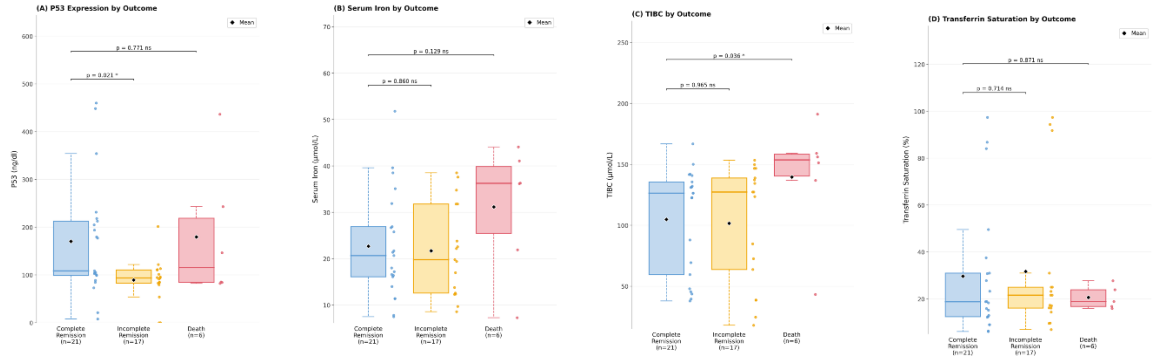

Fig. 6. Comparison of p53 expression and iron parameters according to patient outcomes. (a) P53, (b) serum iron, (c) TIBC, (d) Transferrin saturation %

In the current study, the majority of patients achieved complete remission, accounting for 21 out of 44 cases (47.8%), while 17 patients (38.6%) had incomplete remission. The remaining 6 patients (13.6%) died during the follow-up period.

Comparing p53 expression and iron parameters across the three patient outcome groups showed that the highest and the lowest mean p53 levels were recorded among deceased patients and in patients with incomplete remission respectively. However, the difference was not statistically significant (Fig. 6a).

With respect to iron parameters, deceased patients showed the highest mean serum iron, and TIBC (Fig. 6b and Fig. 6c). While transferrin saturation was highest among the incomplete remission group (Fig. 6d). Despite the observed differences, none of them reached statistical significance.

Fig. 7 showed the Receiver Operating Characteristic (ROC) curve for p53 expression. The area under the curve (AUC) was 0.614 (95% CI: 0.489–0.732). At the optimal cut-off value of (98.77 ng/dl), p53 yielded a sensitivity of (56.8%) and a specificity of (70.5%).

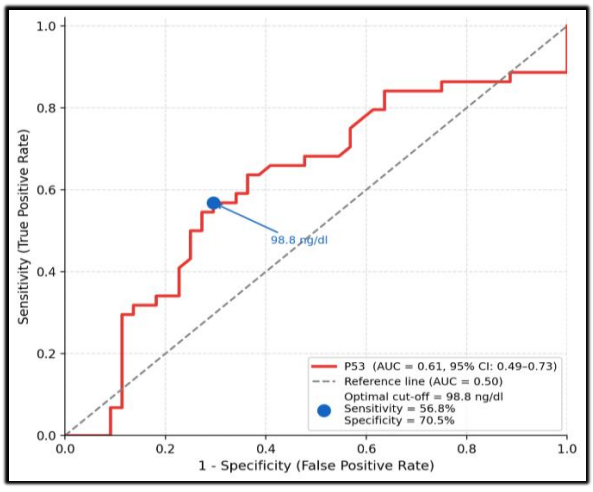

Fig. 7. ROC curve and AUC for p53 expression in AML

DISCUSSION

Acute myeloid leukemia is a highly aggressive hematologic cancer in which disruption of normal myeloid differentiation results in accumulation of blast cells and deterioration of bone marrow function [3]. Although therapeutic strategies have improved over time, overall long-term survival remains limited particularly among elderly patients, reflecting the continued need to identify dependable biomarkers for diagnostic and prognostic application [7]. The tumor suppressor protein 53, encoded by the TP53 gene, is one of the most studied molecules in cancer biology [10].

In AML, TP53 dysfunction whether through direct mutation, MDM2/MDMX-mediated degradation, or loss of ARF impairs apoptosis and cell cycle control, contributing to leukemogenesis and chemotherapy resistance [19]. Recent studies suggest a bidirectional relationship between p53 and iron metabolism [16]. Therefore, this study evaluated serum p53 levels in newly diagnosed AML patients and investigated their association with hematological and iron parameters, and treatment outcomes. According to hematological parameters, AML patients in the present study demonstrated the typical manifestations of bone marrow dysfunction, including significantly lower hemoglobin levels, platelet counts, neutrophil percentages, and lymphocyte percentages compared with healthy controls, together with a higher monocyte percentage [20]. These results are consistent with previous studies involving AML patients [7]. These abnormalities are mainly attributed to the replacement of normal hematopoietic tissue by proliferating leukemic cells. Since malignant myeloid precursors may arise from different stages of hematopoietic differentiation, including pluripotent stem cells, myeloid progenitors, or monocytic lineages, variability in white blood cell distribution is commonly observed among AML cases [8]. Although total white cell counts were elevated in patients relative to controls, the difference was not statistically significant, possibly due to the marked heterogeneity of leukocyte counts among AML

subtypes, which may vary from marked leukocytosis to aleukemic forms [21].

The present study revealed significant elevation of serum p53 levels in newly diagnosed AML patients compared to healthy controls. This observation is consistent with previous reports that also demonstrated elevated circulating p53 levels among AML patients when compared with normal individuals [22]. The elevation of p53 can be explained by two potential mechanisms. The first involves the accumulation of mutant p53. In contrast to wild-type p53 which is tightly regulated through MDM2-mediated ubiquitination and rapid proteasomal degradation [23], mutant p53 exhibits impaired interaction with MDM2, resulting in intracellular protein accumulation and consequently higher circulating concentrations [24]. The second mechanism, relates to the temporary stabilization of wild-type p53 in response to the intense genomic instability and replicative stress intrinsic to leukemic proliferation, activation of DNA damage response pathways may transiently increase wild-type p53 stability, even in the absence of TP53 mutations [25]. Since serum ELISA cannot differentiate between these two mechanisms, future studies should incorporate molecular assessment of TP53 mutational status to provide a more accurate interpretation of circulating p53 levels [26].

Other researchers have reported contrasting findings, with significantly lower serum p53 levels in AML patients compared to controls [19]. This difference may result from the biological heterogeneity of AML. Cohorts in which TP53 pathway inactivation occurs predominantly through non-mutational mechanisms such as MDM2 overexpression, loss of ARF, or promoter methylation, would be expected to exhibit lower or near-normal circulating p53 levels, since wild-type protein continues to be actively degraded [27]. By contrast, cohorts with higher TP53 mutation rates, particularly those enriched with therapy-related AML or complex-karyotype disease would be expected to show elevated serum p53 due to mutant protein accumulation [28]. Variations in patient characteristics, AML subtypes, cytogenetic risk profiles, and ELISA methods used among different studies may also contribute to discrepancies in reported findings [26]. These observations emphasize an important limitation of measuring serum p53 alone, as the functional nature of the detected protein cannot be determined without parallel molecular analysis [25].

The current study demonstrated a statistically significant mild negative correlation between serum p53 levels and patient age, indicating that younger patients tend to have higher p53 levels. This finding differs from reports by other investigators who observed no significant association between serum p53 levels and age in AML patients [29]. One possible explanation is the variation in disease biology between different age groups. In younger patients, de novo AML is more frequently associated with acute genetic alterations and pronounced replicative stress, factors that may promote greater stabilization and accumulation of p53 [26]. In older patients, AML frequently evolves from antecedent clonal hematopoiesis or myelodysplastic states, where prolonged selective pressure may favor the emergence of leukemic clones that have already inactivated p53 pathway through non-mutational mechanisms, leading to lower detectable protein levels [30]. The modest sample size of this study and the wide age range introduce additional variability that may have influenced this association, and the finding should therefore be interpreted with caution. No statistically significant correlations were identified between serum p53 levels and any of the hematological parameters measured at diagnosis, including hemoglobin, total WBC count, neutrophil, lymphocyte, and monocyte percentages, platelet count, or peripheral blood and bone marrow blast percentages. This finding is in agreement with the results of some investigators who similarly found no significant associations between p53 and peripheral hematological indices in AML [22], and supports the concept that p53 dysregulation operates primarily at the molecular and cellular level rather than being directly reflected in peripheral blood counts [31]. By contrast, other studies have reported significant correlations between p53 expression and blast percentages, hemoglobin, and other hematological parameters [29]. The variation may reflect differences in the proportion of TP53-mutated cases, which present with more aggressive morphology and higher blast burdens [32], or differences in the timing of sample collection related to the stage of disease evolution [25].

Regarding iron metabolism, the current study demonstrated a significant elevation in serum iron, TIBC, and transferrin saturation in AML patients compared to controls, indicating disruption of systemic iron homeostasis in the leukemic state[33]. The elevation of serum iron in AML has been reported by other investigators [34]. In AML, the progressive replacement of erythroid precursors by leukemic blasts reduces the demand for iron in erythropoiesis, resulting in iron redistribution from the marrow into the circulation [35]. Additionally, leukemic cells themselves express high levels of transferrin receptors, strongly competing for circulating iron to meet their accelerated proliferative demands [36]. The elevated TIBC observed in this cohort is an interesting finding; TIBC is primarily a measure of circulating transferrin, and its elevation may reflect nutritional differences, the relatively younger age profile of this study, or disease-specific alterations in transferrin synthesis [37]. Other researchers have reported inconsistent iron profiles in AML patients, with some demonstrating markedly elevated serum iron levels and near-complete transferrin saturation, whereas others described only mild alterations [34], such variability may be attributed to differences in patient characteristics,

nutritional condition, and disease severity at the time of evaluation [33].

Correlation analysis in the current study showed a mild inverse association between serum p53 and serum iron levels in AML patients, although this relationship did not achieve statistical significance. In contrast, a significant inverse correlation with transferrin saturation was observed among healthy controls. These findings are in agreement with prior experimental studies indicating that iron overload may suppress p53 expression via direct heme-p53 interaction and alterations in p53 subcellular distribution and stability [17], while iron depletion through chelation has the opposite effect, promoting p53 accumulation and downstream target activation [38]. The absence of statistical significance in the AML patients may be explained by the influence of multiple interacting biological factors, including the extent of TP53 mutational burden [26], disease stage, and the varying effects of iron-independent p53 stabilizing signals, such as oncogene activation and replicative stress [39].

According to treatment outcomes, nearly half of patients achieved complete remission after induction therapy, whereas the remaining patients displayed incomplete remission or died during the follow-up period. These outcomes are generally consistent with those reported by other studies evaluating AML patients treated with standard induction regimens [40], however, outcome rates may vary considerably according to factors such as patient age, cytogenetic risk profile, and the quality of supportive care available at different treatment centers [41]. The complete remission rate observed in the present study falls within the range reported by Iraqi and regional researchers [42], and is consistent with the expected outcomes for a mixed-age cohort receiving conventional induction chemotherapy [7]. The most important finding in relation to outcomes was the p53 levels across the three outcome groups. Patients who achieved complete remission and those who died both exhibited significantly higher mean p53 levels compared to patients with incomplete remission, whereas the complete remission and death groups were not statistically different from each other. The coexistence of elevated p53 with both improved and adverse outcomes that reflects the biological role of p53 in AML [25]. In complete remission patients, elevated p53 likely represents functional, wild-type protein activity. When chemotherapy induces DNA damage and replicative stress, wild-type p53 is stabilized leading to activation of downstream pathways involved in apoptosis and cell-cycle regulation, through induction of pro-apoptotic mediators such as BAX, NOXA, and PUMA, as well as regulatory proteins such as p21/CDKN1A, collectively driving leukemic cell death and enabling marrow recovery [31,43]. In this context, elevated p53 is a marker of a competent tumor-suppressive response rather than disease aggressiveness [44].

Alternatively, in patients who died, elevated p53 most likely reflects the accumulation of dysfunctional mutant protein. Mutant p53 may acquire gain-of-function oncogenic properties, involving promotion of cell survival, enhancement of chemoresistance, and suppression of other p53 family members [45,46]. In this setting, high serum p53 is a marker of pathway failure rather than activation [44]. Patients with incomplete remission displayed the lowest p53 levels of the three groups, which may indicate inadequate p53 pathway engagement leading to a state of partial therapeutic response [13]. This interpretation is supported by the molecular classification framework provided by the 2022 European LeukemiaNet (ELN) recommendations, which identify TP53-mutated AML as a distinct adverse-risk entity characterized by dismal outcomes regardless of treatment intensity [28]. The co-occurrence of high p53 levels and poor survival in the deceased groups in the present study is consistent with this adverse-risk biology [47]. Furthermore, the observation that complete remission patients had relatively lower serum iron levels compared to deceased patients, despite comparably high p53 levels, supports the hypothesis that the functional status of p53 is the key determinant of outcome, and that iron overload may amplify leukemic aggressiveness in the context of dysfunctional p53 [48]. Iron excess promotes the generation of reactive oxygen species via Fenton chemistry, causing oxidative DNA damage and genomic instability [49]. When p53 is functional, such damage activates apoptosis; when p53 is mutant, the same damage may drive further mutagenesis without repair, creating a vicious cycle of genomic deterioration and treatment failure [50].

The significant inverse correlation between p53 and serum iron in the incomplete remission group, and between p53 and TIBC in the deceased group, provides further mechanistic insight. These correlations suggest that as iron burden increases, p53 expression is progressively suppressed consistent with experimental findings showing that iron overload inhibits p53 signaling [51] and that this suppression is most pronounced in outcome groups characterized by inadequate therapeutic response. In the incomplete remission group, moderate iron-mediated p53 suppression may contribute to insufficient apoptotic signaling in response to chemotherapy [42]. In deceased patients, where TIBC showed the strongest inverse correlation with p53, the relationship between high iron redistribution and low effective p53 activity may represent an iron-p53 feedback circuit in which iron-driven oxidative stress perpetuates p53 pathway inactivation, further impairing the cellular response to genotoxic therapy [49].

The receiver operating characteristic (ROC) analysis demonstrated that serum p53 had moderate diagnostic discriminatory ability for AML, with an area under the curve of (0.614) and a sensitivity of (56.8%) and specificity of (70.5%) at the optimal cutoff. These

values indicate that while serum p53 is elevated in AML relative to healthy controls, its standalone diagnostic performance is insufficient for clinical use as a sole diagnostic test. This is in contrast to higher discriminatory values reported by some other investigators, where p53 ELISA showed considerably stronger sensitivity and specificity [52,53]. These variations likely reflect the differences in study populations, the frequency of TP53-mutated cases, the assay methods and commercial kits used, in addition to differences in cutoff determination methodology [25]. The moderate diagnostic performance observed in the present study suggests that serum p53 is better considered a complementary biomarker rather than an independent diagnostic tool, providing additional information when interpreted together with hematological, morphological, cytogenetic, and molecular data [54].

The results of this study indicate that measuring serum p53 levels may reveal clinical and biological information, particularly when interpreted together with iron metabolism parameters and treatment response. The observed relationship between p53 and iron metabolism, along with the differing prognostic implications of elevated p53 according to its functional status, indicates a complex interaction between these pathways in the biology of AML [50]. Future studies that include simultaneous TP53 mutation testing together with broader cytogenetic and molecular characterization may help clarify the clinical relevance of serum p53 levels and improve their interpretation in AML patients [28]. In addition, therapeutic approaches designed to restore p53 activity, including MDM2 inhibitors or small molecule p53 reactivators, as well as strategies aimed at reducing iron overload through chelation therapy, may represent promising options that deserve further prospective investigation in molecularly stratified AML populations [55].

CONCLUSIONS

Serum p53 levels were elevated in AML patients compared with healthy controls. The dual roles of p53 in AML may explain why increased p53 levels were associated with both favorable and unfavorable outcomes. This paradox likely reflects the complex biological behavior of p53. It can act as a tumor suppressor under normal conditions but may promote therapy resistance and disease progression when mutated. P53 expression may be associated with prognosis, especially in relation to iron status, supporting a potential interaction between iron metabolism and leukemogenic pathways. Although serum iron levels were not significantly associated with outcomes, their elevation among non-survivors may indicate a role of iron overload in adverse disease biology. P53 alone appears insufficient as a standalone biomarker. Combining p53 assessment with iron parameters and molecular profiling may improve prognostic assessment and guide targeted therapeutic strategies.

Acknowledgment

we would like to thank all the patients who participated in this study, as well as the medical and laboratory staff at Al-Hadbaa Specialized Hospital and Ibn-Sina Teaching Hospital for their support and cooperation throughout the study period.

Funding Declaration

None.

Conflict of Interest

The authors declare that there are no conflicts of interest.

Ethical consideration

Ethical approval for this study was obtained from the Iraqi Board for Medical Specializations, Scientific Council of Pathology (Path 77, 31 October 2024), and from the Ministry of Health / Nineveh Health Department (No. 2025004, 8 January 2025). Written informed consent was obtained from all participants prior to their enrollment in the study.

Author Contributions

Duaa Saad Mahmood: Conceptualization, data collection, laboratory and statistical analysis, and writing the original draft of the manuscript.

Dr. Sadeel Osama Al-Shabkhoon: Supervision, study design, critical revision of the manuscript, and final approval of the submitted version.

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