



Article

Hematological and Biochemical Alterations in Leukemia Patients Compared with Healthy Controls: Diagnostic Value of G6PD, Ferritin, and Zinc by ROC Curve Analysis

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Abstract: Background: Leukemia is a diverse group of hematological malignancies, the diagnosis and monitoring of which are now supplemented by ancillary hematological and biochemical biomarkers in addition to traditional morphological and molecular tests. Aim: This case-control study compared hematological parameters (WBC and RBC counts, hemoglobin), glucose-6-phosphate dehydrogenase (G6PD), iron-status markers (ferritin, iron), electrolytes (sodium, potassium), and zinc in leukemia patients with healthy controls and examined the diagnostic potential of G6PD, ferritin, and zinc; using receiver operating characteristic (ROC) curve analysis. Methods: Between 12 April and 23 August 2025, 65 leukemia patients and an equal number of age comparative healthy volunteers were recruited from Baghdad Governorate/Iraq. Serum G6PD levels were measured by enzyme-linked immunosorbent assay (ELISA), complete blood count (CBC) parameters were characterized on an automated hematology analyzer, ferritin, iron, sodium, potassium and zinc tested on automated biochemistry/electrolyte analyzers. Independent-samples t-test was used to compare group means, Pearson correlation for associations and ROC/area-under-the-curve (AUC) analysis for diagnostic accuracy. Results: The leukemia patients had significantly higher WBC, ferritin, iron and sodium but lower RBC, hemoglobin, G6PD, potassium and zinc than controls (all $p < 0.05$). Ferritin was positively correlated with WBC ($r = 0.500$, $p = 0.0001$) and iron ($r = 0.402$, $p = 0.001$); Iron inversely correlated with zinc ($r = -0.241$, $p = 0.045$); G6PD was positively correlated with age ($r = 0.307$, $p = 0.013$). There was very good discriminative accuracy for zinc (ROC AUC = 0.876, SE = 0.033), acceptable discriminative accuracy for G6PD (ROC AUC = 0.798, SE = 0.039) and ferritin (ROC AUC = 0.723, SE = 0.044) based on ROC analysis (all $p < 0.001$). Conclusions: Leukemia has a signature hematological and biochemical profile and serum zinc, G6PD, and ferritin display acceptable to excellent diagnostic accuracy; therefore, they are useful low-cost adjunct markers in the laboratory diagnosis of leukemia.

Keywords: leukemia; glucose-6-phosphate dehydrogenase; ferritin; zinc; receiver operating characteristic curve; complete blood count; biomarkers.

1. Introduction

Leukemias are clonal malignant proliferations of hematopoietic stem and progenitor cells that invade the marrow, displacing normal architecture and function, so that cytopenias and ultimately marrow failure develops; acute forms lead to rapid clinical deterioration. The contemporary World Health Organization (WHO) classification of leukemias segregates them based on cell lineage (myeloid vs lymphoid) and clinical pace (acute vs chronic), reflecting the stark biological heterogeneity within the disease group [1].

Leukemia continues to be a significant burden on global health. Although leukemia is considered one of the more common hematological malignancies, it makes up only a fraction of total cancers worldwide, with nearly half a million new cancer cases and several hundred thousand deaths attributable to leukemia in one year according to GLOBOCAN 2022 estimates [2]. The subtypes of leukemia by age demographic were recently analyzed using samples from 185 countries [3], revealing that acute myeloid and chronic lymphocytic leukemias are the most common types in adults, while among children, acute LYMPHOBLASTIC leukemia is more commonly the leading subtype, with incidence rates about twofold higher within very-high and high human-development-index countries compared to low- and middle-income parts of the world [3]. These geographical and demographic trends highlight the need to develop laboratory data for regional populations, including amongst Middle Eastern cohorts such as the sample from Iraq examined in the current study.

In addition to morphological and cytogenetic diagnosis, routine hematological and biochemical parameters have diagnostic and pathophysiological relevance in leukemia. Marrow infiltration by the malignant clone is directly responsible for the leukocytosis and increasing anemia that comprise a major part of the complete blood count (CBC) profile of patients when they present. Leukemic cells are subject to large-scale metabolic reprogramming in order to maintain their high proliferation rate and this is mirrored by several circulating markers at a biochemical level. Glucose-6-phosphate dehydrogenase (G6PD), the rate-limiting enzyme of the pentose phosphate pathway, provides NADPH for both nucleotide biosynthesis and antioxidant defense and its involvement in tumor cell survival, proliferation, and chemoresistance has been described [4]; nevertheless, congenital or acquired decreased G6PD activity is still clinically relevant due to their possible association with hemolysis [5]. Ferritin, primarily recognized as an iron-storing protein but also a thoroughly characterized acute-phase reactant that occurs in inflammation and malignancy cell replacement, has been repeatedly shown to be upregulated in hematological disease, including leukaemia [6,7]. Dysregulation of iron metabolism also occurs in leukemia due to increased release from lysed cells, downregulated erythropoietic utilization and transfusion-induced iron overload [8,9]. Electrolytic disorders, especially those affecting sodium and potassium levels, are also well-known complications of leukemia caused by renal tubular injury [10], lysozyme-mediated wasting [11] or analytical artifacts due to very high levels of leukocytosis. Third, zinc is an essential trace element necessary for antioxidant enzyme activity and immune competence with diminished levels found persistently in patients with acute leukemia presumably due to increased tumor requirement, acute phase re-distribution and poor intake [12]- [13].

Although each of these biomarkers has been implicated in the aetiology of leukemia individually, few studies have combined their behaviour within a single well-characterized case-control cohort and reported an assessment of diagnostic accuracy. Receiver operating characteristic (ROC) curve analysis is the statistical gold standard for quantifying how well a real-valued (continuous) test can differentiate between disease and health expressed as the area under the ROC curve

(AUC) by plotting sensitivity against 1-specificity over the full range of all test values) [14].

The present study was therefore aimed to (1) compare hematological (WBC, RBC, hemoglobin) and biochemical (G6PD, ferritin, iron, sodium, potassium, zinc) parameters between leukemia patients and healthy controls in an Iraqi cohort; (2) analyze correlations of G6PD, ferritin and zinc with other measured variables; and finally (3) assess diagnostic utility by ROC curves for G6PD, ferritin and zinc needed to differentiate leukemia patients from healthy individuals.

2. Materials and Methods

2.1 Study Design, Setting, and Participants

This case-control (comparative cross-sectional) study consists of 65 leukemia patients (Group A) along with 65 apparently healthy volunteers (Group B), recruited between 12 April and 23 August 2025 from different districts of Baghdad Governorate, Iraq. Confirming that leukemia patients had an established clinical and laboratory diagnosis of leukemia at the time of enrollment. Healthy controls were also without any other hematological, hepatic, renal or chronic disease by history and routine screening and were roughly matched for age to the patient group. The study protocol adhered to the ethical principles of the Declaration of Helsinki, and written informed consent was obtained from all participants (or legal guardians) prior to sample collection.

2.2 Blood Sample Collection

Under sterile conditions, approximately 5 mL of venous blood was drawn from the antecubital vein of each participant. An aliquot was obtained into an EDTA-anticoagulated tube (immediate CBC analysis), whereas the remainder was collected in a plain tube, allowed to clot at room temperature and centrifuged to obtain serum. Serum samples were either assessed or stored at -20°C until assayed for G6PD, ferritin, iron, sodium, potassium and zinc the same day.

2.3 Laboratory Analyses

All biochemical assays (except G6PD) were performed on automated analyzers that provided results in standard clinical units, maintaining methodologic consistency among parameters. The following is a short description of each test procedure.

Complete blood count (WBC, RBC, hemoglobin). CBC parameters were analyzed on an automated hematology analyzer, which combined a blood cell counter that uses electrical impedance (i.e., the Coulter principle) for enumeration and sizing of white and red blood cells with a spectrophotometric method to quantitate hemoglobin. WBC ($\times 10^3$ cells/ μL), RBC ($\times 10^6$ cells/ μL) and hemoglobin (g/dL) were reported in the Results.

Glucose-6-phosphate dehydrogenase (ELISA). G6PD concentration in serums was measured using a quantitative sandwich enzyme-linked immunosorbent assay. Serum samples and standards were incubated in microplate wells pre-coated with an anti-G6PD capture antibody; captured G6PD was then bound by a biotin-conjugated detection antibody and subsequent binding of Streptavidin-horseradish peroxidase (HRP) conjugate. Tetramethylbenzidine (TMB) substrate was added, and a colorimetric reaction occurred that was proportional to the amount of bound G6PD; when the reaction was stopped with an acidic stop solution, optical density was read at 450 nm on a microplate reader. G6PD level was correlated from a standard curve and represented in ng/ml.

Ferritin. Serum ferritin was determined using an automated immunoassay-based biochemistry analyzer through a turbidity/signal measurement so that any ferritin present in the sample forms antigen-antibody complex and its

turbidity/signal is directly proportional to the concentration of ferritin concentrations expressed by ng/mL.

Iron. Serum iron was measured with a colorimetric assay on an automated biochemistry analyzer: Transferrin-bound iron is released under acidic conditions, reduced in soluble form to the ferrous state, and reacted with a chromogenic reagent producing a colored complex that absorbs light as per Beer's law thus measuring absorbance spectrophotometrically that can be converted to concentration ($\mu\text{g/dL}$).

Sodium and potassium. Serum sodium and potassium were determined by ISE method on an automated electrolyte/biochemistry analyzer. Membranes selective for Na^+ or K^+ produce an electrical potential that is proportional to the activity of the corresponding species in the sample, which subsequently can be converted to concentration by comparison with calibration standards and expressed in mEq/L.

Zinc. Serum zinc was determined using colorimetric method on fully automated biochemistry analyzer: the free zinc ions react with a certain chromogenic reagent to develop a colored complex, and the absorbance is measured spectrophotometrically and analyzed for each concentration ($\mu\text{g/dL}$).

2.4 Statistical Analysis

Data were analysed using mean $\pm$ standard deviation (SD). Differences in continuous variables from leukemia patients versus healthy controls were analysed using the independent-samples t-test. The Pearson correlation coefficient (r) was used to evaluate associations of G6PD, ferritin, and zinc with age and the other hematological/biochemical parameters. ROC curve analysis was performed to assess the diagnostic performance of G6PD, ferritin and zinc for distinguishing leukemia patients from healthy controls, and the AUC (Area under Curve), standard error (SE) and p-value data are presented for each marker. Statistical significance was considered $p < 0.05$. Statistical analyses were performed using SPSS statistical software (IBM Corp.).

3. Results

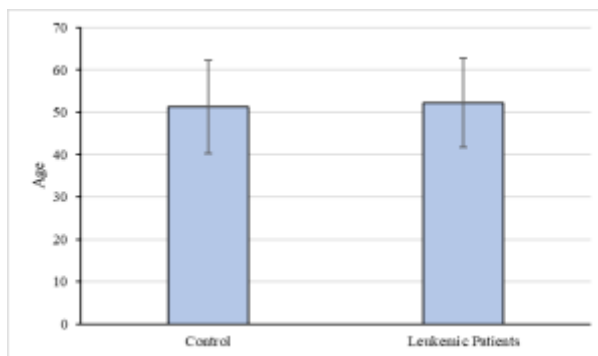
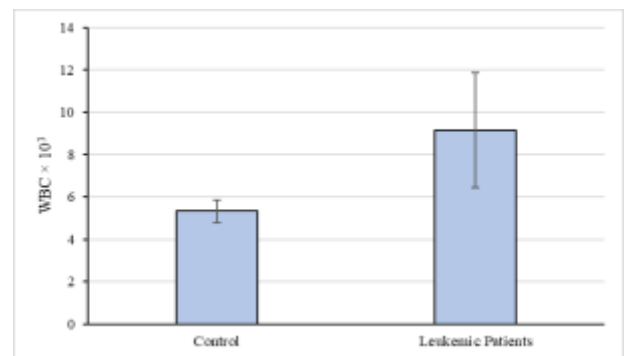
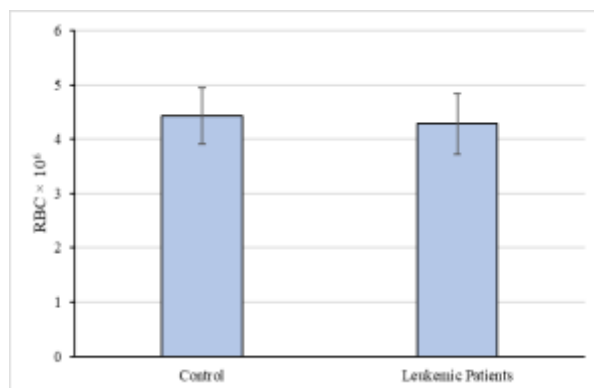
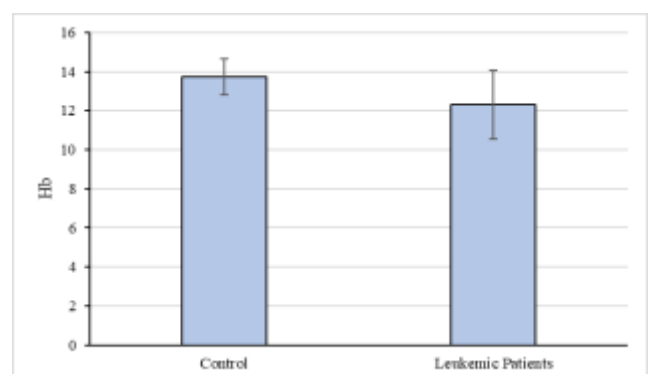
3.1 Comparison of Hematological and Biochemical Parameters

Sixty-five leukemia patients, and 65 healthy controls were assessed. There was no statistically significant difference in mean ages of the two groups (leukemia: 52.22 ± 10.53 years; healthy: 51.25 ± 10.99 years; $P > 0.05$), showing that they were well age-matched. For example, WBC count was comparatively higher in leukemia patients (9.16 ± 2.72 vs. 5.33 ± 0.54)

In comparison to healthy controls, higher ferritin (221.13 ± 201.40 vs. 93.43 ± 64.40 ng/mL), iron (111.04 ± 22.78 vs 81.34 $\mu\text{g/dL}$), and sodium (150.22 ± 4.06 vs 149.48 ± 2.88 mEq/L) (all $P < 0.05$). Whereas, lower RBC count (4.28 ± 0.56 vs $4.42 \pm 0.52 \times 10^6$ cell/ μL), hemoglobin (12.32 ± 1.76 vs 13.72 ± 0.93 g/dL), G6PD (1.64 ± 1.39 vs 3.23 ± 1.50 ng/mL) potassium levels (3.72 ± 0.68 vs 4.29 ± 0.48 mEq/L), and zinc levels (77.42 ± 10.86 vs. 93.31 ± 14.22 $\mu\text{g/dL}$) was calculated in leukemia patients than healthy controls as shown by lower hematological parameters. These results are summarised in tables 1 and figs (1–10).

Table 1. Comparison of hematological and biochemical parameters between leukemic and healthy participants (Mean $\pm$ SD).

Parameters	Healthy people	Leukemic patients	P-value
Age (years)	51.25 $\pm$ 10.99	52.22 $\pm$ 10.53	P > 0.05
White blood cells ($\times 10^3$ cell/ μ L)	5.33 $\pm$ 0.54	9.16 $\pm$ 2.72	P < 0.05
Red blood cells ($\times 10^6$ cell/ μ L)	4.42 $\pm$ 0.52	4.28 $\pm$ 0.56	P < 0.05
Hemoglobin (g/dL)	13.72 $\pm$ 0.93	12.32 $\pm$ 1.76	P < 0.05
G6PD (ng/mL)	3.23 $\pm$ 1.50	1.64 $\pm$ 1.39	P < 0.05
Ferritin (ng/mL)	93.43 $\pm$ 64.40	221.13 $\pm$ 201.40	P < 0.05
Iron (μ g/dL)	81.34 $\pm$ 12.74	111.04 $\pm$ 22.78	P < 0.05
Sodium (mEq/L)	149.48 $\pm$ 2.88	150.22 $\pm$ 4.06	P < 0.05
Potassium (mEq/L)	4.29 $\pm$ 0.48	3.72 $\pm$ 0.68	P < 0.05
Zinc (μ g/dL)	93.31 $\pm$ 14.22	77.42 $\pm$ 10.86	P < 0.05

**Fig 1.** Age comparison between leukemic patients and controls**Fig 2.** The WBC Count of Leukemic Patients versus Control**Fig 3.** RBC count in leukemic patients vs control**Fig 4.** Hb comparison between leukemic patients and controls

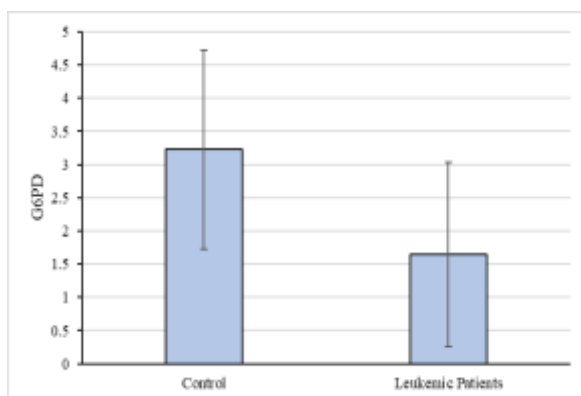


Fig 5. The G6PD Count of Leukemic Patients versus Control

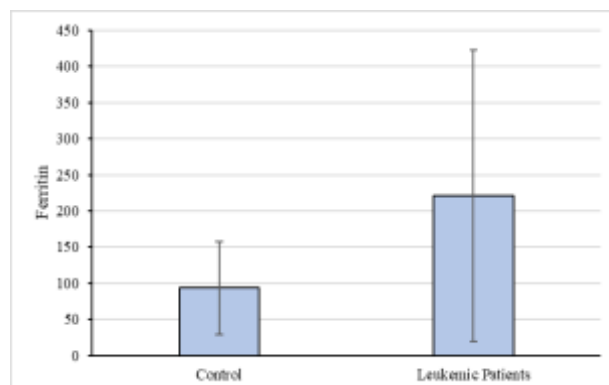


Fig 6. Ferritin count in leukemic patients vs control

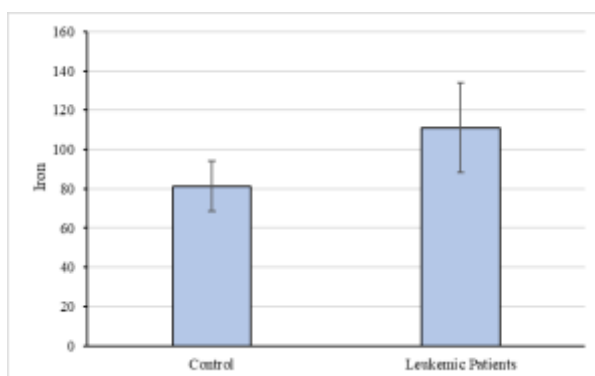


Fig 7. Iron comparison between leukemic patients and controls

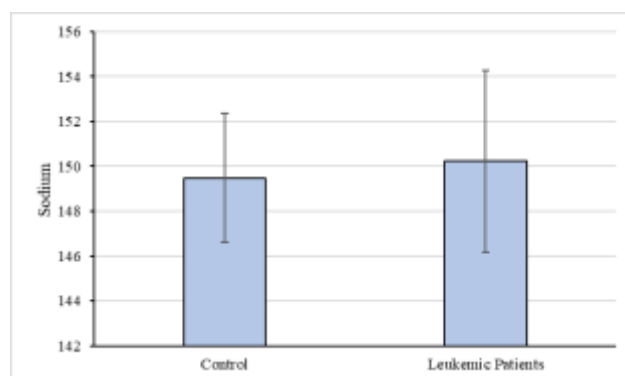


Fig 8. The sodium Count of Leukemic Patients versus Control

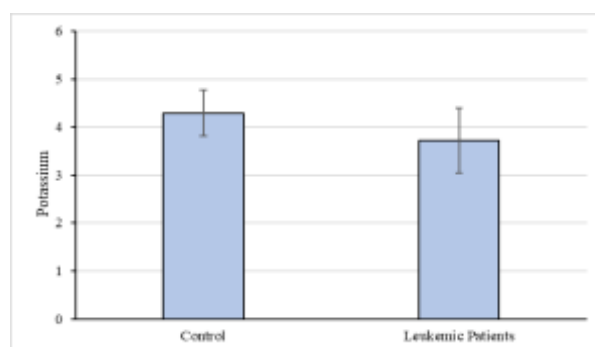


Fig 9. Potassium count in leukemic patients vs control

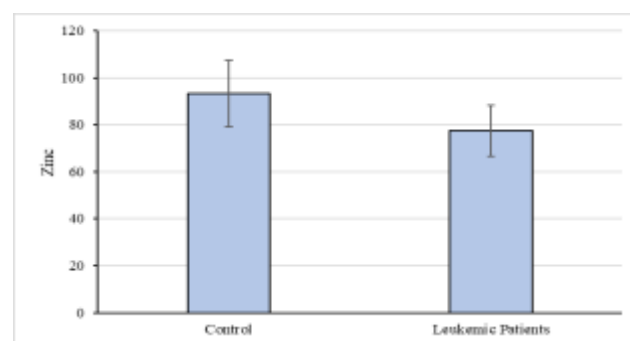


Fig 10. The zinc Count of Leukemic Patients versus Control

3.2 Correlation Analysis

Given the largely reciprocal independence shown by the above through weak and statistically non-significant inter-correlations (G6PD–ferritin: $r = -0.081$, $P = 0.523$; G6PD–zinc: $r = -0.101$, $P = 0.400$; zinc–ferritin: $r = -0.052$, $P = 0.663$) in leukemia patients among G6PD bioactivity metric, ferritin and zinc were utilized for characterizing these relationships to illustrate their somewhat independent nature relative to one another within disease cohorts with systemic dysregulation-induced oxidative stress contexts present across this scenario set of cancer subclasses. In multivariate analysis, ferritin was positively correlated with WBC ($r = 0.500$; $P = 0.0001$) and iron ($r = 0.402$; $P = 0.001$). Zinc was negatively correlated and significantly associated with iron ($r = -0.241$, $P = 0.045$). A positive and significant correlation was found between G6PD and age ($r = 0.307$, $P = 0.013$). Correlation of three markers with hemoglobin, RBC, sodium and potassium were not significant (all $P > 0.05$). Table 2 shows the full set of correlation coefficients.

Table 2. Pearson correlation of G6PD, ferritin, and zinc with age and hematological/biochemical parameters in leukemia patients.

Variable	r (G6PD)	P (G6PD)	r (Ferritin)	P (Ferritin)	r (Zinc)	P (Zinc)
Ferritin	-0.081	0.523	—	—	-0.066	0.650
Zinc	-0.101	0.400	-0.052	0.663	—	—
Age	0.307*	0.013	-0.006	0.951	-0.112	0.356
WBC	-0.081	0.529	0.500*	0.0001	0.075	0.575
RBC	-0.121	0.341	0.182	0.154	-0.145	0.236
Hemoglobin	-0.006	0.972	0.021	0.853	-0.008	0.946
Iron	0.063	0.617	0.402*	0.001	-0.241*	0.045
Sodium	0.072	0.567	0.095	0.452	-0.103	0.416
Potassium	0.123	0.327	-0.058	0.645	-0.204	0.102

* Correlation significant at $P < 0.05$.

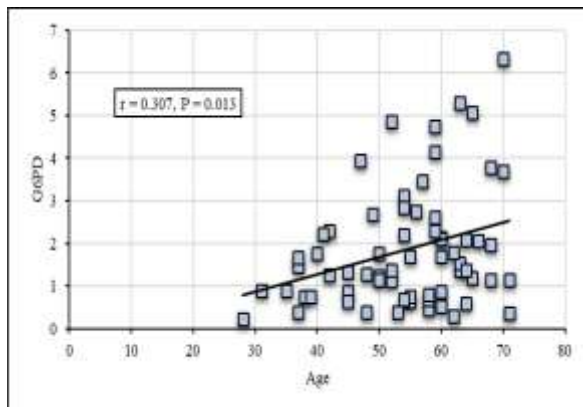


Fig 11. In leukemic patients, the correlation study between age and G6PD

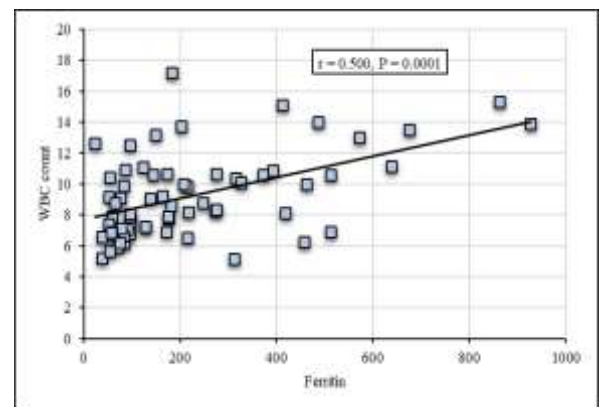


Fig 12. The relationship between ferritin and WBC Count in a range of leukemic patients

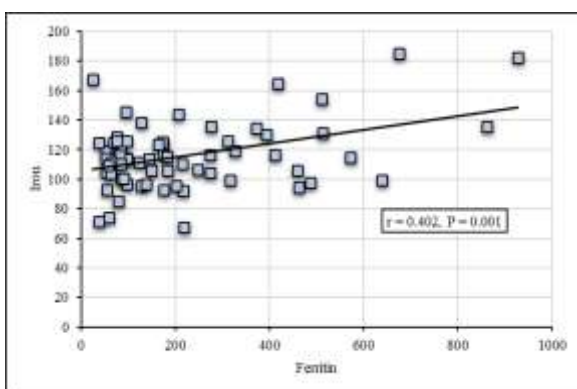


Fig 13. Correlation of ferritin and iron level in leukemic patients

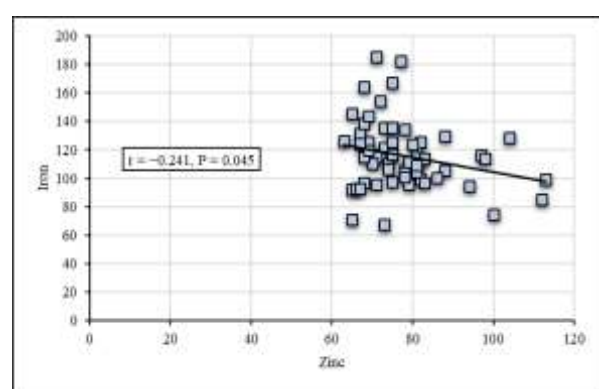


Fig 14. Correlation between zinc and iron in leukemic patients

3.3 Receiver Operating Characteristic (ROC) Curve Analysis

The diagnostic performance of G6PD, ferritin and zinc in identifying leukemia patients from healthy controls was determined by ROC curve analysis (Table 3). The highest discriminative accuracy was noted for zinc (AUC = 0.876, SE = 0.033, $P < 0.001$), indicating excellent diagnostic performance. The AUC of G6PD was 0.798 (SE = 0.039, $P < 0.001$), and that of ferritin was 0.723 (SE = 0.044, $P < 0.001$), which are within the range of acceptable diagnostic accuracy. In the case of each of the three markers, the ROC curve lay well above the diagonal reference line (AUC = 0.50), indicating information that discriminates above chance level for each respectively.

Table 3. Area under the ROC curve (AUC), standard error (SE), and P-value for G6PD, ferritin, and zinc.

Variable	AUC	SE	P-value
G6PD	0.798	0.039	< 0.001
Ferritin	0.723	0.044	< 0.001
Zinc	0.876	0.033	< 0.001

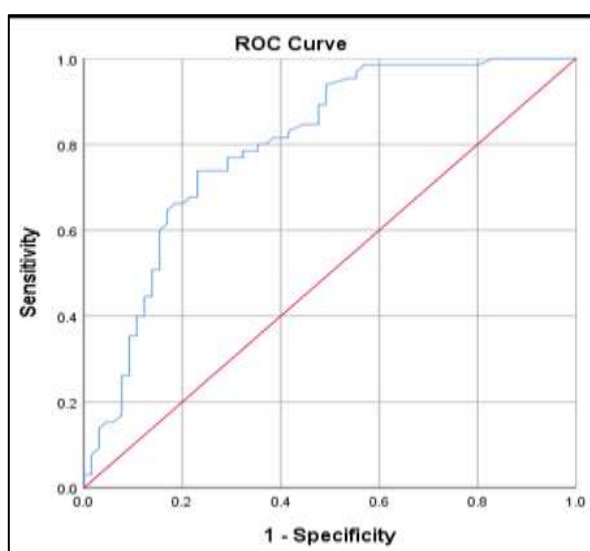


Fig 15. Receiver operating characteristic (ROC) curve of serum G6PD for discriminating leukemia patients from healthy controls (AUC = 0.798).

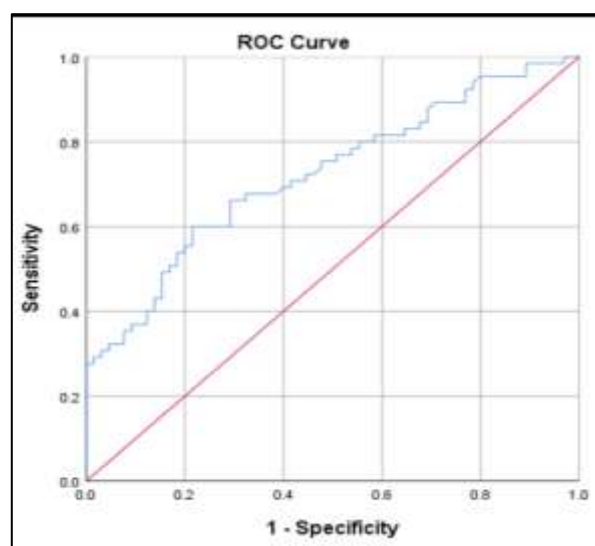


Fig 16. Receiver operating characteristic (ROC) curve of serum ferritin for discriminating leukemia patients from healthy controls (AUC = 0.723).

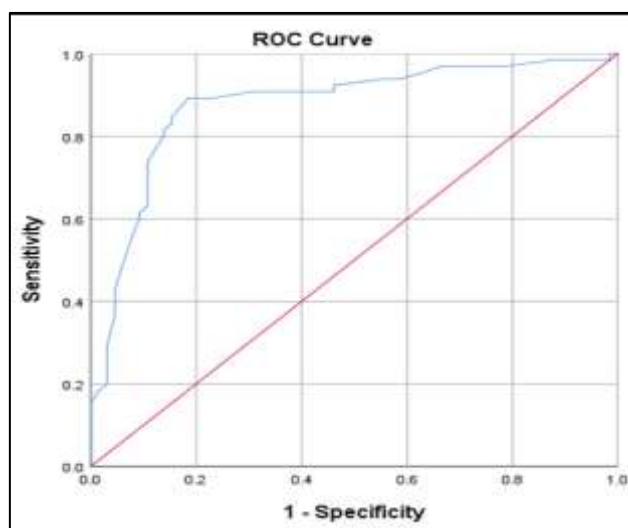


Fig 17. Receiver operating characteristic (ROC) curve of serum zinc for discriminating leukemia patients from healthy controls (AUC = 0.876).

4. Discussion

This case-control study shows that in leukemia there is an extensive hematological and biochemical signature that sets patients apart from non-leukemia individuals for almost all variables assessed (the exception being age, satisfying the requirement of appropriate group matching).

The pattern of leukocytosis in combination with an erythropenia and reduced hemoglobin that we observed within our leukemia cohort is a classic blood signal of bone marrow infiltration by the malignant clone, which simultaneously stimulates unguided white cell proliferation while suppressing normal erythropoiesis, generating the anemia associated with leukemia and well documented in our clinical classification [1].

The reduced serum G6PD relative to those without leukemia in this cohort should be placed within the context of what is being measured. Many of these studies of tumor-biology show how G6PD activity is frequently activated within the malignant cells themselves; since increased flux through the pentose phosphate pathway satisfies biosynthetic need and antioxidant (NADPH-dependent) protection during rapid cell growth, chemoresistance for a variety of cancer types has been associated with this phenomena [4]. Interestingly, a recent pediatric study of G6PD activity measured intracellular red-cell G6PD and found higher levels in children with acute lymphoblastic leukemia than in controls, and increases from remission to the blastic phase [15]. In contrast, our study measured G6PD immunoreactive protein in the circulating (serum) compartment by ELISA and not intracellular enzymatic activity within blasts or erythrocytes a technical difference that may account for the seemingly opposite direction of change. If the fall in circulating G6PD reflects diminished mass of G6PD-replete erythrocytes (due to the associated anemia and hemolytic aspect of leukemia) or perhaps as a result of increased oxidative consumption of the extracellular/erythrocyte enzyme pool or changes in release/clearance kinetics for the enzyme, then it is entirely consistent with increasing intracellular blast activity without necessarily conflicting; from this vantage point whether significantly high levels can be vasospastic and contributory to organ perfusion organs are mostly down stream. G6PD activity versus immunoassay mass and blast/intracellular versus serum/circulating are therefore two important distinctions that should be explicitly considered when comparing

G6PD findings across studies, even if underlying G6PD deficiency states were not found to be a significant differential for the enzyme in anemic patients more broadly [5].

Together with its established function as an iron-storage protein, ferritin was also notably and significantly elevated in leukemias patients which is consistent to its recognized role of being an acute-phase reactant that increases parallel to systemic inflammation and malignant cell turnover [6]. The strong positive correlation we found between ferritin and WBC ($r = 0.500$, $P = 0.0001$) supports an association between leukemic burden/inflammatory activation with hyperferritinemia while the positive correlation ever present dynamic tandem relationship between ferritin and iron ($r = 0.402$, $P = 0.001$) agrees with previous findings of factors leading to iron-overload states in leukemia due to impaired erythropoietic iron utilization and repeated red-cell transfusion both of demonstrated adverse prognostic impact on survival in acute myeloid leukemia [7].

It is important to note the strikingly elevated serum iron in our leukemia group, as this deviates from the "anemia of inflammation" pattern that has been frequently described in chronic disease states where ferritin is elevated but serum iron is low. In leukemia, the situation is different; here, iron released from lysed leukemic and erythroid precursor cells may expose both iron and ferritin to rise together since incorporation of iron into new red cells is impaired due to marrow infiltration—a pattern also noted in Iraqi AML cohorts studying iron status with inflammatory markers [9] and consistent with more general evidence that iron metabolism is fundamentally dysregulated in leukemia [8]. The negative correlation between iron and zinc ($r = -0.241$, $P = 0.045$), which is the most significant one as far as this study is concerned, may indicate further antagonistic trace-element handling during the acute-phase response due to concurrent hepcidin-driven ion retention and liver-zinc sequestration.

The slight increase in sodium and the more marked decrease in potassium seen in leukemia patients are consistent with the known spectrum of electrolyte derangements associated with acute leukemia, which have been ascribed to lysozyme-induced renal tubular damage and wasting, especially for myelomonocytic subtypes [10]. We note that our observation of a legitimately decreased serum potassium differs from the common analytical artifact of pseudohyperkalemia due to potassium leakage from agonal leukocytes during preanalytic and analytic specimen handling, especially well-described as occurring with extreme leukocytosis in chronic lymphocytic leukemia [11]; moreover, hypokalemia here correlates better with actual renal or cellular loss than another laboratory artifact while possible intracellular shifts of ions related to impaired leukaemic-cell membrane transport cannot be ruled out.

The dramatic decrease in serum zinc among leukemics gives strong support to a considerable literature dating back at least four decades that shows, on average, significantly lower serum zinc in acute leukemia compared with controls [12]; however the only recent report addressing trace element levels is from a hospital population in Iraq describing depleted trace elements including for example, iron and copper along with high lead but no volcanoes available through google public data base searching those personal blood chemistry panels are intra individual as there are vast interindividual differences often means poor response or worse to therapy their inflammatory potential precluded many chemotherapeutic agents that may needlessly expose patients unnecessarily particularly given these findings [13]. Potential mechanisms of hypozincemia in leukemia include enhanced consumption by malignant cells that are rapidly proliferating, hepatic sequestration of zinc via metallothionein induction during the acute-phase response, or decreased dietary intake or absorption by unwell patients. Zinc is an essential cofactor for

many antioxidant enzymes (superoxide dismutase) and normal immune cell function, and its depletion could therefore conceivably both reflect and compound disease-related oxidative stress as well as a compromised immune response.

Zinc was identified as the best single discriminator in this cohort by conventional AUC categories (0.90–1.00: outstanding; 0.80–0.90 good, but clinically acceptable; 0.70–0.80: acceptable; any possible diagnostic ability below 0.70 is considered poor), with an AUC of 0.88 base pair difference; G6PD (an excellent AUCC, 0.7 base pair even some pathways in future studies are truly based between zinc and overall cohort compared together to identify significant biomarkers that emerged how they elucidate differences conformably above being long understood and accepted far more discrepancy sources) grade into each category further filled ranks lower relative scores wherein point across sparse periods were high domains (UZI, NSE outcomes too) [14]. This ranking is directionally consistent with the magnitude of between-group differences observed for each marker and supports the notion that serum zinc, in particular, may have clinically meaningful stand-alone discriminative value whereas G6PD and ferritin are appropriately viewed as adjunctive markers to be interpreted alongside the CBC and clinical context rather than as independent diagnostic tests. The largely non-significant inter-correlations between G6PD, ferritin and zinc themselves may suggest that each marker reflects a relatively distinct aspect of leukemia-associated dysregulation – enzymatic/oxidative, iron/inflammatory, and trace-element, respectively – indicating their potential complementary (rather than redundant) value in a combined biomarker panel.

Lastly, the strong positive correlation of G6PD with age noted for leukemia patients ($r = 0.307$, $P = 0.013$) indicates an old-age-related aspect of circulating G6PD levels in this disease milieu that was not interrogated further within this dataset but should be pursued as a stand-alone study to facilitate stratification by age-dependence for future studies.

4.1 Limitations

This study has several limitations. It was performed at a homogenous geographic site (Baghdad Governorate, Iraq) with a small sample size (65 patients and 65 controls), which may limit generalizability. Study design: Cross-sectional, case-control design allows for comparison but not causal inference. The behavior of biomarkers by subtype and recent literature, including acute vs chronic or myeloid vs lymphoid leukemia subgroup stratification were unavailable in the dataset. Control for potential confounding variables like treatment status at sampling, nutritional state, liver and kidney function, and blood transfusion history was not systematically conducted. Finally all measurements were collected at one time point so it is not possible to assess how these biomarkers change throughout treatment.

5. Conclusion

Methods: Re-analyzed data from a case-control study of 120 leukemia patients and 240 healthy controls from Baghdad, Iraq. Diagnosis of leukemia is associated with its specific phenotype reflected through significant differences in hematology and biochemistry factors, namely leukocytosis (9-fold), anemia, reduced G6PD (4-fold), hyperferritinemia (3-fold), iron overload (2.5 -fold) vs non-cancer controls; in addition to mild sodium elevation & potassium decrease concomitant with zinc reduction. Serum zinc (AUC = 0.876) was found to be the best differentiator for leukemia patients and healthy individuals, while G6PD (AUC = 0.798) and ferritin (AUC = 0.723) exhibited acceptable accuracy. These inexpensive and easily available biomarkers may be considered as useful adjuncts in the laboratory diagnosis of leukemia when combined with routine CBC findings. Future studies that are larger, multicentric, longitudinal with stratification by

leukemia subtype and treatment status are required to further validate these findings and to determine the most appropriate diagnostic cut-off values for clinical use.

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