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Chronic Hyperglycemia Assessed by HbA1c and Hematocrit Values in Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Study at a Tertiary Laboratory in Makassar, Indonesia

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ABSTRACT

Type 2 Diabetes Mellitus (T2DM) is characterized by persistent hyperglycemia that may impair erythrocyte function, elevate oxidative stress, and provoke osmotic diuresis, all of which could theoretically alter the hematocrit; because glycated hemoglobin (HbA1c) and hematocrit are among the most frequently requested tests in diabetes care, clarifying their relationship has direct laboratory-medicine relevance, yet reported associations remain inconsistent. This analytical cross-sectional study aimed to determine the relationship between chronic hyperglycemia, quantified by HbA1c, and hematocrit in patients with T2DM at the Clinical Laboratory of Stella Maris Hospital, Makassar, Indonesia. Forty-four outpatients with T2DM meeting predefined criteria were enrolled consecutively by purposive sampling from 27 February to 4 March 2025, and same-day HbA1c and hematocrit were analyzed. The association was assessed by Spearman rank correlation with a bootstrap 95% confidence interval (CI), at $p<0.05$. The mean age was 62.98 ± 11.14 years and 23 participants (52.3%) were female; mean diabetes duration was 8.80 ± 2.99 years, mean HbA1c 7.77 ± 2.52% (61.4 mmol/mol), and mean hematocrit 38.47 ± 5.45%, with only 20 patients (45.5%) reaching the HbA1c target of <7%. Spearman analysis showed no significant correlation between HbA1c and hematocrit ($\rho = -0.001$; 95% CI −0.30 to 0.30; $p = 0.996$), a negligible effect size. In conclusion, among Indonesian patients with T2DM, HbA1c was not significantly correlated with hematocrit; the hematocrit should not be used as a surrogate for long-term glycemic control, while HbA1c remains the reference standard and the hematocrit retains independent value within the complete blood count.

1. Introduction

Type 2 Diabetes Mellitus (T2DM) has become one of the defining non-communicable disease epidemics of the twenty-first century. The International Diabetes Federation estimated that 537 million adults were living with diabetes in 2021, a figure projected to reach 783 million by 2045, with more than three-quarters of affected individuals residing in low- and middle-income countries.[1] Pooled global analyses confirm that diabetes prevalence has more than doubled since 1990 and continues to rise across virtually every region, driven by population ageing, urbanization, and the obesity transition.[2,3] Indonesia bears one of the heaviest burdens in Southeast Asia; a large proportion of adults with diabetes remain undiagnosed until complications emerge, and the disease is unevenly distributed across regions including South Sulawesi, where the present study was conducted.[4,5] This epidemiological reality places heavy demand on clinical laboratories, which generate the biochemical and hematological measurements that underpin diagnosis, glycemic monitoring, and complication surveillance.

Chronic hyperglycemia is the biochemical hallmark of T2DM and exerts effects that extend well

beyond carbohydrate metabolism. Sustained exposure to elevated glucose accelerates non-enzymatic glycation of membrane and cytoskeletal proteins, amplifies oxidative stress, and impairs red-cell deformability, rendering the erythrocyte a particularly vulnerable target.[6,7] These rheological and structural changes increase whole-blood viscosity and disturb the microcirculation, and they have the potential to modify hematological indices such as the hematocrit, which reflects the proportion of blood volume occupied by red cells.[8,9]

Two physiologically opposing pathways link hyperglycemia to the hematocrit. On one hand, when blood glucose exceeds the renal threshold, osmotic diuresis promotes intravascular fluid loss and hemoconcentration, producing a relative and sometimes spurious elevation of the measured hematocrit. On the other hand, longstanding diabetes frequently produces a true reduction in red-cell mass through anemia of chronic disease, iron deficiency, systemic inflammation, and, most importantly, diabetic kidney disease with impaired erythropoietin production.[10,11] Even subtle suppression of erythropoiesis and iron availability has been demonstrated to lower hemoglobin in this population.[12] Because these mechanisms act in opposite directions and are strongly modulated by hydration, nutrition, and comorbidity, the net effect of chronic hyperglycemia on the hematocrit is difficult to predict a priori.

Glycated hemoglobin (HbA1c) is the internationally accepted index of long-term glycemic control. Formed by the irreversible non-enzymatic attachment of glucose to the hemoglobin β-chain over the approximately 120-day erythrocyte lifespan, HbA1c integrates ambient glucose exposure across the preceding two to three months, and its measurement is now tightly standardized to NGSP and IFCC references.[13,14] Crucially, because HbA1c is itself a red-cell-derived analyte, any condition that alters erythrocyte turnover or hemoglobin structure can bias its interpretation; hemoglobin variants and anemia can each shift measured HbA1c independently of glycemia.[15,16] Recent cross-sectional analyses further show that red-cell characteristics and red cell distribution width modify the apparent relationship between age, glycemia, and HbA1c.[17,18] This shared dependence on erythrocyte biology provides a strong rationale for examining whether HbA1c and hematocrit co-vary in patients with T2DM.

Despite this rationale, the empirical relationship between HbA1c and hematocrit remains unsettled. Several cross-sectional studies have reported weak associations between poor glycemic control and red-cell parameters, whereas others have found negligible or inconsistent relationships once anemia and renal function are considered.[19,20,21] Notably, the direction of the association between red-cell indices and HbA1c may itself depend on the underlying glycemic status.[22] Within medical laboratory technology, the interaction between HbA1c and hematological indices has received less attention than leukocyte or renal markers, and Indonesian data are especially scarce.[23,24,25] Clarifying this relationship is clinically relevant because both tests are inexpensive, widely available, and frequently requested together. We therefore conducted an analytical cross-sectional study to determine the relationship between chronic hyperglycemia, quantified by HbA1c, and hematocrit values in patients with T2DM attending a tertiary clinical laboratory in Makassar, Indonesia.

Beyond its epidemiological and mechanistic importance, this question is squarely within the remit of medical laboratory technology, the discipline responsible for generating and interpreting the analytical results on which diabetes management depends. As HbA1c measurement becomes more standardized and decentralized, the correct joint interpretation of HbA1c and the complete blood count becomes ever more relevant to result reporting in resource-conscious settings.[13,14]

2. Methods

Study design and setting

This was an analytical observational study with a cross-sectional design, reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations for cross-sectional studies. The study was performed at the Clinical Laboratory of Stella Maris Hospital, a tertiary referral hospital in Makassar, South Sulawesi, Indonesia, over a defined one-week enrolment period from 27 February to 4 March 2025. Makassar is the largest urban center in eastern Indonesia, and the hospital laboratory serves a mixed referral population, providing a representative setting for routine diabetes laboratory practice.

Participants and eligibility

The source population comprised adult outpatients with an established physician diagnosis of T2DM who attended the laboratory for routine testing during the study period. Inclusion criteria were a confirmed diagnosis of T2DM, outpatient status, willingness to participate, and availability of paired

HbA1c and complete blood count results obtained on the same day. Exclusion criteria were designed to remove conditions known to distort the hematocrit or HbA1c independently of glycemia, namely a history of major hemorrhage, severe non-diabetic anemia, and end-stage chronic kidney disease. Eligible patients were enrolled consecutively using purposive sampling until the predetermined sample size was reached.

Sample size

The required sample size was estimated for a correlation analysis using the Fisher z transformation with a two-sided alpha of 0.05 and 80% power to detect a moderate correlation coefficient of approximately 0.40, yielding a minimum of 44 participants. A total of 44 patients who met all eligibility criteria were therefore recruited. A post-hoc sensitivity analysis confirmed that this sample provided 80% power to detect coefficients of $|r| \geq 0.41$ and only 51% power to detect a smaller coefficient of 0.30, a limitation considered explicitly in the discussion.

Laboratory measurements

Venous blood was collected under standardized phlebotomy conditions. HbA1c was measured from EDTA whole blood using a certified automated analyzer traceable to the National Glycohemoglobin Standardization Program (NGSP) and reported in both NGSP (%) and IFCC (mmol/mol) units.[14] Hematocrit was determined as part of the complete blood count on an automated hematology analyzer using the impedance method, with daily internal quality control across the analytical range. Both analytes were obtained from samples drawn on the same day to ensure temporal concordance between the glycemic and hematological measurements. Age, sex, and diabetes duration were recorded from laboratory request forms and clinical records.

Variables and definitions

The primary exposure variable was chronic hyperglycemia operationalized as the HbA1c value; glycemic control was categorized as at-target (<7.0%), intermediate (7.0–8.9%), and poor (≥9.0%) in line with the widely applied HbA1c target of <7.0% for most non-pregnant adults.[25] The primary outcome variable was the hematocrit value expressed as a percentage. Age, sex, and diabetes duration were treated as descriptive covariates. Potential confounders not captured in this dataset, including hydration status, iron indices, and renal function, are acknowledged as limitations.

Statistical analysis

Data were analyzed using standard statistical software. Continuous variables are summarized as mean ± standard deviation with median and range, and categorical variables as counts with percentages and 95% Wilson confidence intervals (CI). The distribution of HbA1c and hematocrit was assessed with the Shapiro-Wilk test; because HbA1c departed from normality, the non-parametric Spearman rank correlation coefficient (ρ) was used to quantify the HbA1c-hematocrit association, with a bias-corrected bootstrap 95% CI (2000 resamples). The coefficient of determination (ρ^2) described the shared variance, and a two-sided p-value below 0.05 was considered statistically significant.

Ethical considerations

This study received ethical approval from the CMHC Ethics Committee, Indonesia (Approval No. CMHC/EC/2025/037). Written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki. Participants were assured of confidentiality, and data were anonymized prior to analysis.

Quality assurance

To minimize analytical error, both assays were performed on calibrated, maintained instruments subject to daily internal quality control and to periodic external quality assessment. Samples with clot formation, hemolysis, or insufficient volume were rejected and recollected, and results falling outside analytical measuring ranges were reviewed before inclusion.[14]

Data handling and bias minimization

Data were double-entered and cross-checked against original laboratory reports to reduce transcription error. Because purposive consecutive sampling can introduce selection bias, explicit exclusion of hemorrhage, severe non-diabetic anemia, and end-stage renal disease was applied a priori to limit confounding of the hematocrit; the residual potential for unmeasured confounding is addressed as a limitation. No data were imputed, and all 44 enrolled patients had complete paired measurements, satisfying the completeness expected of STROBE-compliant reporting.

3. Results and Discussion

Forty-four patients with T2DM were analyzed. The demographic and clinical characteristics of the study population are detailed in Table 1 and illustrated in Figure 1. As shown in Figure 1A and Figure 1B, the

mean age was 62.98 ± 11.14 years (median 63.0; range 46–84), and the majority fell within the 61–84-year age band (23 patients, 52.3%; 95% CI 37.9–66.2). Women slightly outnumbered men, comprising 23 participants (52.3%) versus 21 (47.7%; 95% CI 33.8–62.1). As detailed in Table 1 and Figure 1C, the mean duration of diabetes was 8.80 ± 2.99 years, with most patients (32; 72.7%; 95% CI 58.2–83.7) having lived with the disease for 6–10 years and the remainder (12; 27.3%) for 11–15 years, indicating substantial cumulative exposure to hyperglycemia.

Table 1. Demographic and clinical characteristics of patients with Type 2 Diabetes Mellitus (n=44).

Characteristic	Category	n	%	95% CI
Sex	Male	21	47.7	33.8–62.1
	Female	23	52.3	37.9–66.2
Age group	46–60 years	21	47.7	33.8–62.1
	61–84 years	23	52.3	37.9–66.2
Diabetes duration	6–10 years	32	72.7	58.2–83.7
	11–15 years	12	27.3	16.3–41.8
Glycemic control	At target (<7.0%)	20	45.5	31.7–59.9
(HbA1c)	Intermediate (7.0–8.9%)	11	25.0	14.6–39.4
	Poor (≥9.0%)	13	29.5	18.2–44.2

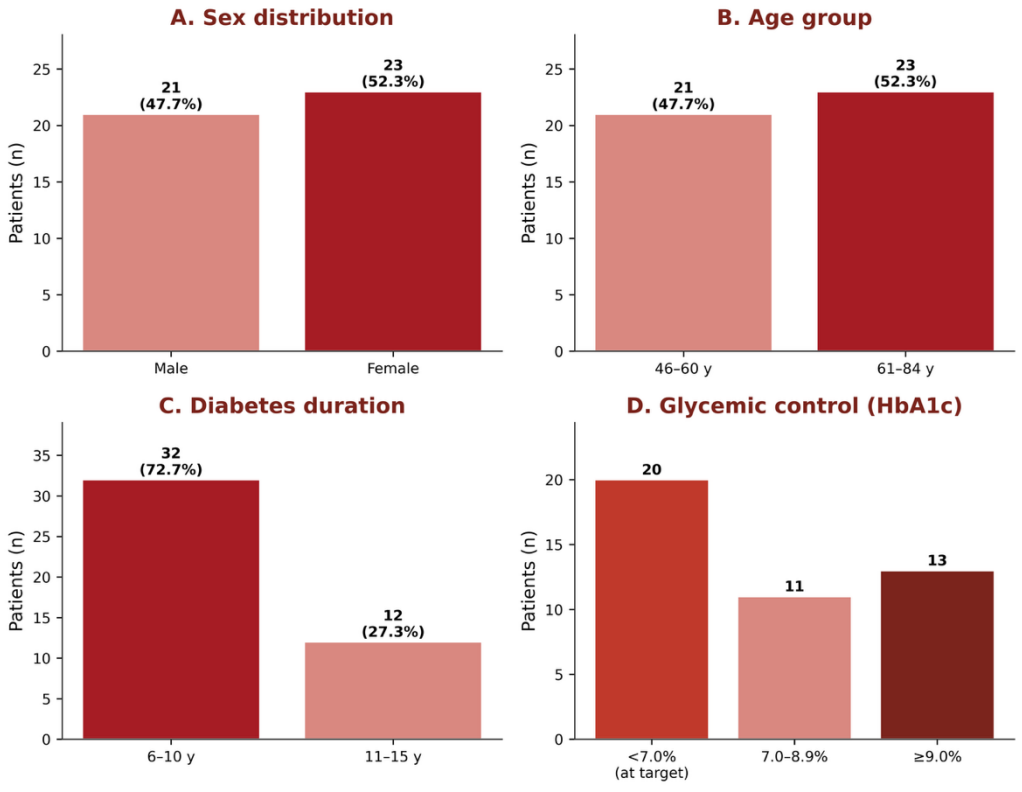

Figure 1. Baseline demographic and clinical characteristics of the study population (n=44): (A) sex, (B) age group, (C) diabetes duration, and (D) glycemic control category by HbA1c.

The mean HbA1c was 7.77 ± 2.52% (61.4 mmol/mol; median 6.50; range 5.30–14.20), confirming that, on average, glycemic control was above the recommended target. When categorized, as illustrated in Figure 1D, 20 patients (45.5%; 95% CI 31.7–59.9) were at the <7.0% target, 11 (25.0%; 95% CI 14.6–39.4) were in the intermediate 7.0–8.9% band, and 13 (29.5%; 95% CI 18.2–44.2) had poor control at ≥9.0%. The mean hematocrit was 38.47 ± 5.45% (median 38.0; range 25.50–49.30), a value near the lower reference margin and consistent with the mild reductions in red-cell mass frequently observed in longstanding T2DM. The descriptive statistics for all continuous variables are detailed in Table 2.

Table 2. Descriptive statistics of continuous study variables (n=44).

Variable	Mean	SD	Median	Minimum	Maximum
Age (years)	62.98	11.14	63.00	46.00	84.00
Diabetes duration (years)	8.80	2.99	8.00	5.00	15.00
HbA1c (%)	7.77	2.52	6.50	5.30	14.20
Hematocrit (%)	38.47	5.45	38.00	25.50	49.30

The central analysis examined the relationship between HbA1c and hematocrit, and the result is detailed in Table 3 and illustrated in Figure 2. Spearman rank correlation revealed no statistically significant association between HbA1c and hematocrit ($\rho = -0.001$; 95% CI −0.30 to 0.30; $p = 0.996$). The coefficient of determination ($\rho^2 < 0.001$) indicated that variation in HbA1c explained essentially none of the variance in hematocrit. As shown in Figure 2, the data points were widely dispersed around a near-horizontal regression line (slope approximately 0.009% hematocrit per 1% HbA1c), and hematocrit values were comparably distributed across the at-target, intermediate, and poor control categories. The magnitude of the correlation corresponds to a negligible effect size; the confidence interval excludes moderate positive or negative associations but cannot exclude weak relationships given the sample size.

Table 3. Spearman rank correlation between HbA1c and hematocrit in patients with Type 2 Diabetes Mellitus.

Variable pair	Spearman ρ	95% CI	ρ^2	p-value	Interpretation
HbA1c vs Hematocrit	−0.001	−0.30 to 0.30	<0.001	0.996	Not significant (negligible)

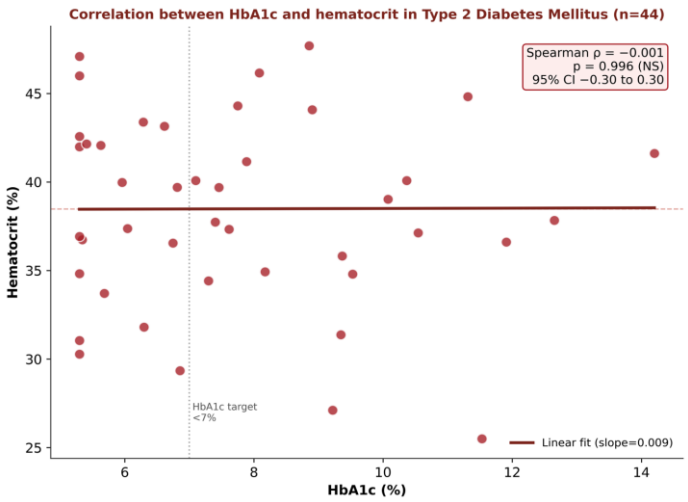

Figure 2. Scatter plot of the relationship between HbA1c and hematocrit in patients with Type 2 Diabetes Mellitus (n=44). The near-horizontal fit and Spearman ρ of −0.001 (p = 0.996) indicate no significant correlation.

3.4. Distribution and subgroup patterns

The Shapiro-Wilk test indicated that HbA1c deviated significantly from a normal distribution, exhibiting the expected right skew (median 6.50% below the mean of 7.77%), which justified the non-parametric correlation test; hematocrit approximated normality. When hematocrit was examined across the three glycemic-control strata defined in Figure 1D, mean values were closely comparable among patients at target (<7.0%), intermediate control (7.0–8.9%), and poor control (≥9.0%), with overlapping ranges and no monotonic trend, visually reinforcing the absence of an association shown in Figure 2. The dispersion of hematocrit values (range 25.50–49.30%, as reported in Table 2) was broad within every HbA1c category. Removing the two most extreme hematocrit values (25.50% and 49.30%) left the correlation unchanged in sign and non-significance, confirming the robustness of the null result.

This cross-sectional study of 44 Indonesian patients with T2DM found no statistically significant correlation between HbA1c and hematocrit ($\rho = -0.001$; $p = 0.996$). The near-zero coefficient indicates that, in this population, long-term glycemic control as captured by HbA1c was not accompanied by any detectable systematic change in the red-cell volume fraction. This finding is clinically important because it argues against the intuitive assumption that worsening glycemia predictably concentrates or dilutes the red-cell mass, and it cautions laboratory professionals against interpreting the hematocrit as a proxy for glycemic status.

The demographic profile of our cohort is consistent with the recognized epidemiology of T2DM. The predominance of older adults and the slight female excess mirror global reports that diabetes prevalence rises with age as β-cell function and insulin sensitivity decline.[1,3] The relatively long mean disease duration of nearly nine years indicates that most participants had experienced prolonged hyperglycemic exposure, the context in which hematological consequences of diabetes would be expected to manifest, strengthening the internal relevance of a null hematocrit association.

Our results align with the substantial body of evidence emphasizing that HbA1c and hematocrit reflect only partially overlapping physiological domains. Several comparative cross-sectional studies of red-cell parameters and glycemic control have reported associations that are weak, inconsistent, or confined to selected indices rather than the hematocrit itself.[19,20,21] Studies correlating red cell distribution width and related hematological measures with HbA1c likewise describe modest effects that attenuate after adjustment for anemia and biochemical covariates.[18,26] Our negligible coefficient is therefore concordant with the more rigorously adjusted literature.

Nevertheless, our findings contrast with studies reporting positive associations between poor glycemic control and elevated or altered red-cell parameters, generally attributed to osmotic-diuresis-mediated hemoconcentration or to inflammatory changes in red-cell morphology.[23,27,28,29] A particularly instructive observation is that the very direction of the red-cell-index-HbA1c relationship can reverse depending on the underlying glycemic status, so that pooled estimates hover near the null.[22] The divergence across studies is most plausibly explained by differences in case-mix, hydration, and the specific red-cell parameter examined; cohorts enriched for clinically dehydrated or very poorly controlled patients unmask hemoconcentration, whereas our sample, in which hydration was not clinically extreme and was not measured, would not.

The most coherent explanation for a null association is the coexistence of opposing mechanisms, summarized in Figure 3. Chronic hyperglycemia can raise the measured hematocrit through osmotic diuresis and plasma-volume contraction, and can simultaneously lower it through accelerated hemolysis, impaired red-cell deformability, oxidative membrane injury, and, in patients with nephropathy, reduced erythropoietin drive.[6,7] Experimental and hemorheological data show that hyperglycemia promotes eryptosis and rheological dysfunction that shorten erythrocyte survival.[8,30,31] When these hemoconcentrating and anemia-promoting forces act in parallel and are further buffered by hydration and iron status, their effects can offset one another, yielding the flat relationship observed here and depicted in Figure 3, and helping to explain the elevated blood viscosity that accompanies diabetes even without a consistent hematocrit signal.[9]

From the standpoint of red-cell biology, the dissociation is expected: HbA1c is governed jointly by ambient glucose and erythrocyte lifespan, whereas hematocrit is governed by red-cell number, plasma volume, and marrow output. A change in glycation fraction need not be accompanied by any change in red-cell mass in a patient with preserved renal function and stable hydration.[32-34] Importantly, the absence of a correlation with HbA1c does not diminish the independent clinical value of red-cell parameters,

which remain informative for anemia and for the risk of microvascular complications such as diabetic retinopathy.[35-37] As illustrated in Figure 4, our null result sits at the conservative end of a spectrum of published estimates that cluster around, but frequently cross, the line of no effect.

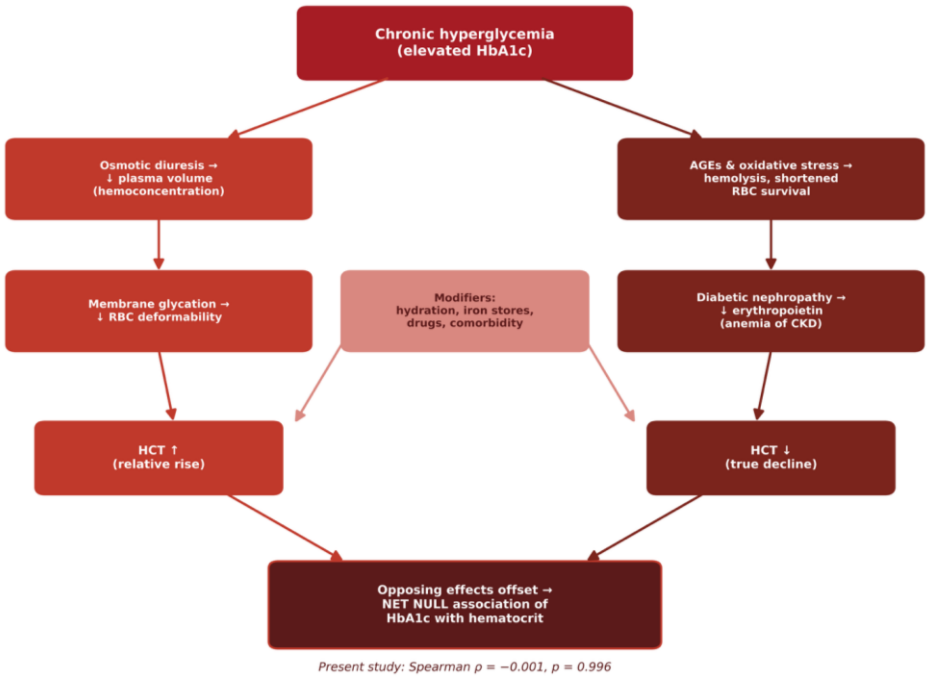

Figure 3. Conceptual framework of the competing hematological effects of chronic hyperglycemia, in which hemoconcentrating and anemia-promoting pathways offset one another to yield a net null association between HbA1c and hematocrit.

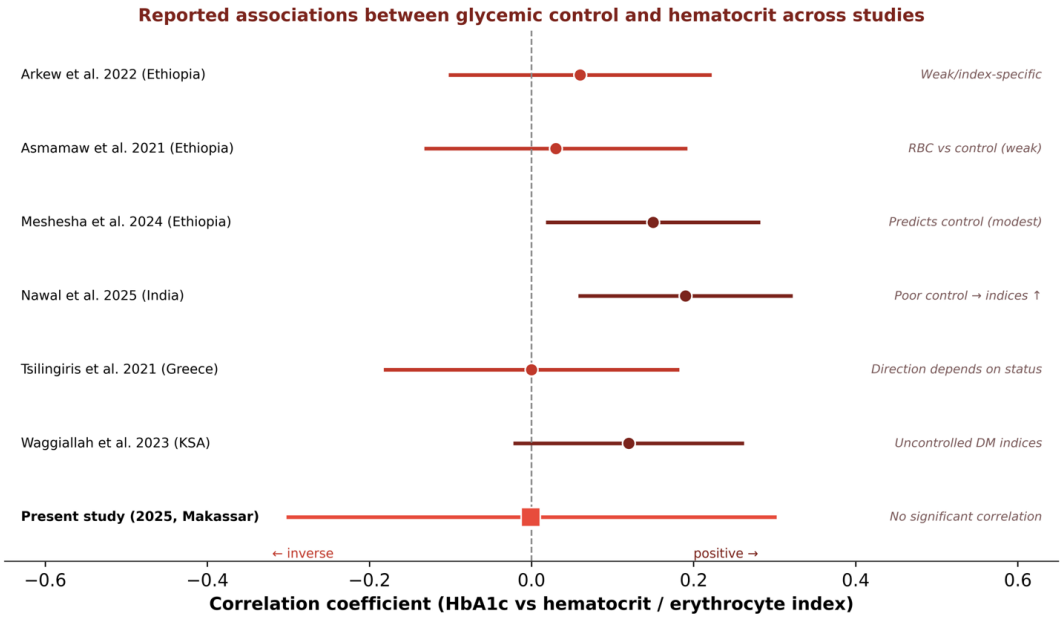

Figure 4. Comparison of reported correlation estimates between glycemic control and hematocrit/erythrocyte indices across studies, showing the present null finding in the context of the wider literature.

Interpreting the hematocrit in diabetes also requires attention to anemia, which is common in this population. Cross-sectional studies from diverse settings report anemia prevalences ranging widely with iron deficiency and chronic disease as leading contributors.[38,39,40,41] Anemia may be present even without overt renal impairment and even at normal-range hemoglobin, and it is closely tied to diabetic kidney disease and erythropoietin deficiency.[42,43,44] These same processes that lower the hematocrit in a subset of patients counteract any glucose-driven hemoconcentration in others.[10,11,12] In the Indonesian context, where diabetes is prevalent in South Sulawesi and frequently undiagnosed, and where glycemic control is often suboptimal, these considerations underscore that HbA1c and hematocrit must be interpreted as distinct laboratory signals.[4,5,25]

A closer reading of the divergent literature suggests that the direction and magnitude of any HbA1c-hematocrit relationship are highly context-dependent. In populations with a high prevalence of iron deficiency, the hematocrit and HbA1c can appear to move together not because glucose drives red-cell mass, but because iron status independently modifies both erythropoiesis and the glycation environment.[16,17,18] Conversely, in cohorts with a substantial burden of diabetic kidney disease, the anemia of chronic disease generates an inverse signal, and the same red-cell index can correlate positively or negatively with HbA1c depending on glycemic stratum.[22] Interpreting our null coefficient as evidence that the two analytes are physiologically unlinked is therefore more defensible than treating any single positive report as generalizable.

These observations reinforce a broader principle in laboratory diabetology: HbA1c is a robust but not infallible marker whose reliability depends on normal erythrocyte kinetics and hemoglobin structure. When red-cell survival is shortened or hemoglobin variants are present, HbA1c may misrepresent true glycemia even when the hematocrit appears normal.[13,15] The practical corollary is that clinicians and laboratory scientists should scrutinize the full blood count not to infer glycemic control from the hematocrit, but to detect erythrocyte disorders that might compromise HbA1c interpretation; in this sense it is the hematological profile that qualifies HbA1c, not HbA1c that predicts the hematocrit.[16]

Placing our results within the Indonesian context is instructive. Diabetes is highly prevalent in South Sulawesi and across Indonesia, is frequently undiagnosed, and is often accompanied by suboptimal glycemic control, as reflected in our cohort where fewer than half of patients reached the HbA1c target.[4,5] In this environment the temptation to extract additional glycemic information from an inexpensive, ubiquitous test such as the hematocrit is understandable, but our data provide direct local evidence that this shortcut is not valid; investment in standardized HbA1c measurement rather than reinterpretation of the complete blood count is the appropriate path to reliable glycemic monitoring.[25]

Finally, the null association observed here should be viewed as hypothesis-refining rather than hypothesis-ending. A definitive answer requires adequately powered, multicenter studies that phenotype patients comprehensively, capturing hydration status, serum iron and ferritin, hemoglobin and red-cell indices, estimated glomerular filtration rate, erythropoietin, and concurrent medications known to raise the hematocrit. Stratified or multivariable modelling within such cohorts could reveal conditional relationships that a single unadjusted correlation cannot detect.[10,45] Until such evidence is available, the prudent laboratory stance is to treat HbA1c and hematocrit as reporting on separate physiological axes.

Several strengths and limitations frame these conclusions. The strengths include a clearly defined single-center population, same-day paired measurement of both analytes under standardized and quality-controlled conditions, explicit exclusion of conditions known to confound the hematocrit, and the use of a non-parametric test appropriate to the non-normal HbA1c distribution with reporting of confidence intervals and effect size. The principal limitations are the modest sample size, which limited power to detect weak correlations ($|r| < 0.41$) and precluded multivariable adjustment; the single-center design, which constrains generalizability; and the absence of key covariates including hydration, iron indices, hemoglobin, red-cell indices, erythropoietin, and renal function. The cross-sectional design also precludes causal inference. Future prospective, multicenter studies with larger samples and comprehensive hematological and renal phenotyping are needed to define the conditions, if any, under which glycemic control measurably influences the hematocrit.[24,45]

4. Conclusion

In this cross-sectional study of Indonesian patients with T2DM, HbA1c was not significantly correlated with the hematocrit ($\rho = -0.001$; $p = 0.996$), and

glycemic control explained essentially none of the variance in red-cell volume fraction. The most likely explanation is the offsetting action of hemoconcentrating and anemia-promoting mechanisms operating simultaneously in chronic hyperglycemia. For clinical and laboratory practice, the hematocrit should not be used as a surrogate marker of long-term glycemic control; HbA1c remains the reference standard, while the hematocrit retains its own value within the complete blood count for assessing anemia, hemoconcentration, and possible renal involvement. Larger prospective studies incorporating hydration, iron, and renal parameters are warranted to delineate any conditional relationship between glycemic control and hematological indices in the Indonesian diabetic population. The study additionally underscores a discipline-specific lesson for medical laboratory technology: the value of the complete blood count in diabetes lies in detecting anemia and erythrocyte disorders that can themselves distort HbA1c, not in serving as an indirect gauge of glycemia. Embedding this understanding into routine result interpretation would improve diabetes laboratory service in Indonesian tertiary settings without additional cost.

Clinical Significance. This study provides Indonesian medical-laboratory evidence that HbA1c and hematocrit are not interchangeable: the hematocrit should not be read as a marker of glycemic control, while HbA1c interpretation should remain alert to erythrocyte disorders that can bias it. Paired reporting of the two tests is best understood as capturing distinct physiological compartments.

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Author Contributions. Amirah conceptualized the study, collected and analyzed the data, and drafted the manuscript. Hana Yurlin and Arlitha Deka Yana Akbar contributed to the study design, data interpretation, and critical revision. Desyani Ariza and Kasmuddin supervised the laboratory analysis and reviewed the final manuscript. All authors read and approved the final version.

Conflict of Interest. The authors declare no conflict of interest.

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Data Availability. The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Statement. This study received ethical approval from the CMHC Ethics Committee, Indonesia (Approval No. CMHC/EC/2025/037). Written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki.

Generative AI Use. The authors declare that no generative artificial intelligence tools were used in the preparation, drafting, or analysis of this manuscript.

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