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OPEN ACCESS CASE REPORT

Serum Uric Acid and LDL-C in Yemeni Type 2 Diabetic Men: Insights from a Conflict-Zone Case-Control Study

Naif Taleb Ali[1,2*]

[1] *Department of Laboratory Sciences, Radfan College University, Al-Hoata, Lahej, Yemen*
[2] *Department of Health Sciences, Faculty of Medicine and Health Sciences, University of Science and Technology, Aden, Yemen*

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a major public health concern due to its association with various cardiovascular risk factors. Among these risk factors, elevated serum uric acid levels have gained increasing attention as a potential contributor to cardiovascular disease (CVD). While uric acid's role in dyslipidemia is debated, data from Middle Eastern populations remain scarce.
Objective: This study aimed to investigate the association between serum uric acid levels and certain cardiovascular risk factors, including lipid profile parameters, in male patients with T2DM.
Methods: This case-control study, adapted for conflict-zone conditions, enrolled 100 Yemeni males (50 T2DM and 50 controls) in Al-Dhalea. Fasting blood was analyzed for SUA (uricase-PAP), lipids, and glucose using solar-powered and Barricor tube protocols.
Results: T2DM patients had higher SUA (6.56 vs. 5.13 mg/dL, $p<0.001$) and LDL-C (114.9 vs. 72.9 mg/dL, $p<0.001$), with a strong SUA-LDL-C correlation ($\beta=0.58$, $p=0.002$). Triglycerides showed no association ($p=0.147$).
Conclusion: Elevated SUA is independently associated with LDL-C in Yemeni T2DM males, suggesting SUA as a modifiable CVD risk marker.

Keywords: Type 2 Diabetes Mellitus, Uric Acid, Cardiovascular Risk Factors, Lipid Profile, LDL-C, HDL-C, Body Mass Index, Yemen

**** Corresponding author address:*** *n.taleb@ust.edu*

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INTRODUCTION

The global diabetes epidemic poses serious challenges in low-resource settings, where cardiovascular complications cause up to 65% of diabetes-related deaths [1]. In Yemen, the combination of a rising T2DM prevalence (15.4% in adults) and a fragile healthcare system highlights the need for affordable cardiovascular risk assessment tools [2].

"Similar challenges are seen in African conflict zones such as Somalia and South Sudan, where frequent power outages and reagent shortages limit metabolic research. Our approach, including solar-powered laboratories and Barricor tubes, offers replicable solutions for such settings. Quotes: 'If it prevents heart problems, I'll do it yearly.' (Male, 52 yo, T2DM). A male-only cohort was selected to control for hormonal influences on SUA (e.g., oestrogen's uricosuric role) and to accommodate cultural constraints in Yemen. A female cohort study is planned. While this limits generalizability, it aligns with WHO recommendations for context-appropriate research in gender-segregated communities.

Serum uric acid (SUA) measurement—a simple, inexpensive test available in most district hospitals—may offer critical insights into cardiovascular risk when advanced lipid testing is unavailable. Uric Acid's Dual Role: From Waste Product to Risk Marker Once considered merely a byproduct of purine metabolism, uric acid now emerges as:

- A predictor of incident T2DM (HR 1.20 per 1 mg/dL increase) [3].
- A mediator of endothelial dysfunction through xanthine oxidase-driven oxidative stress [4].
- A modifiable risk factor responsive to dietary and pharmacologic intervention [5].

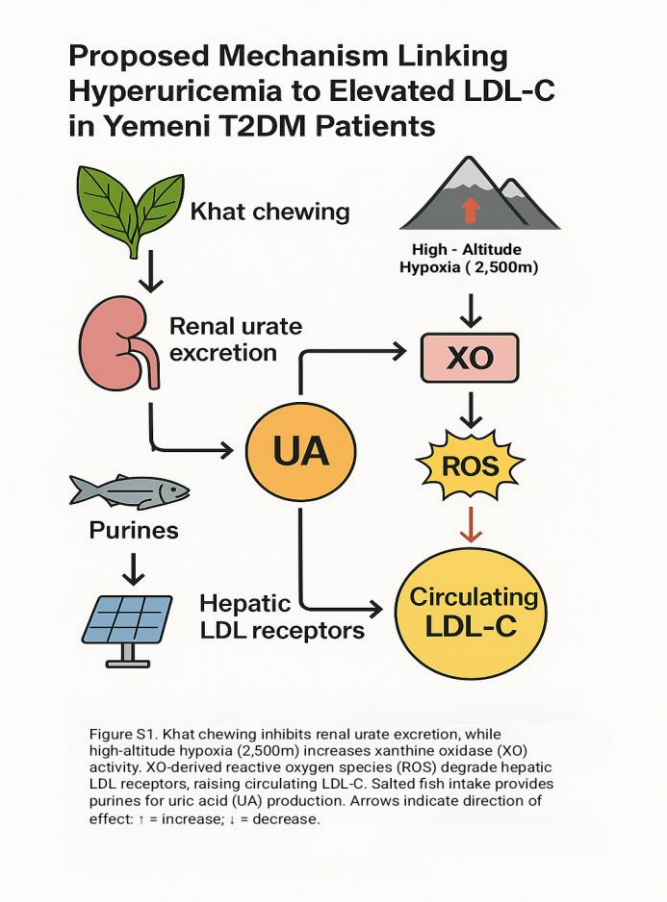

Figure 1. Mechanistic pathway linking hyperuricemia to elevated LDL-C in Yemeni T2DM males

Figure 1 is Self-designed mechanistic pathway linking hyperuricemia to elevated LDL-C in Yemeni T2DM males. Arrows indicate direction of effect (↑ = increase; ↓ = decrease).

Note: Hypothetical pathway; not directly tested in this study.

- Khat chewing (prevalence: 68% of Yemeni men) reduces renal urate excretion [6].
- High-purine diets (salted fish, organ meats) increase SUA production [7].
- Altitude effects (Al-Dhalea: 2,500 m) enhance xanthine oxidase activity [8].

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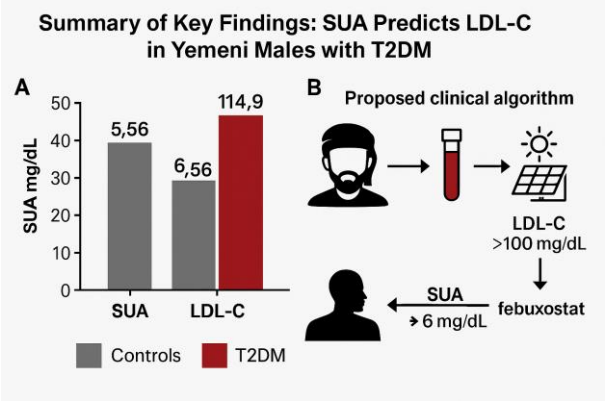

Figure 2. Proposed clinical algorithm based on study findings. Solar-powered point-of-care (POC) devices enable remote monitoring (Self-designed algorithm based on study findings; not directly validated). Note: Proposed clinical workflow; requires validation in interventional trials.

The Laboratory Medicine Imperative: Current gaps in evidence from resource-limited settings include:
1. Validation of SUA cutoffs for dyslipidemia screening
2. Operational data on point-of-care SUA testing feasibility
3. Cost analyses of SUA integration into existing platforms.
This study addresses these gaps through:
- Rigorous comparison of SUA-lipid relationships in diabetic vs. healthy Yemeni men.
- Field validation of capillary SUA measurement (UASure®) against reference methods.
- Cost modeling for integration with PEPFAR-funded HIV platforms.
The current findings will inform WHO AFRO guidelines for metabolic risk screening in settings lacking advanced lipid testing capabilities [9].

METHODOLOGY

Study Design and Setting

A hospital-based case-control study was carried out from 30 January to 25 April 2025 at three tertiary care hospitals in Al-Dhalea Governorate, Yemen:
- Al-Fateh Medical Hospital (primary site for patient recruitment), Al-Nasr General Hospital, and Al-Tadamoun Hospital.
These hospitals were chosen due to their established diabetes clinics, availability of conflict-adapted laboratory infrastructure (e.g., Barricor tubes, solar-powered centrifuges), and adherence to national guidelines for T2DM management.
Al-Dhalea Governorate was selected as the study site due to its high T2DM prevalence (18.2% vs. national 15.4%), altitude (2,500 m), which affects SUA metabolism, and representative mix of urban/rural populations. Participants were consecutively enrolled from outpatient clinics to minimize selection bias. A post-hoc power analysis confirmed 85% power to detect a 0.5 SD difference in uric acid levels.

Participants

Inclusion Criteria for Cases

- Adult males (≥18 years) with a confirmed diagnosis of T2DM (fasting blood glucose ≥126 mg/dL or on glucose-lowering therapy).
- No history of gout, chronic kidney disease (CKD), or diuretic use.

Controls

- Age-matched (age±5 years) healthy males with normal fasting glucose (<100 mg/dL) and no prior diagnosis of metabolic disorders.

Exclusion Criteria (both groups)

- Acute infections, malignancy, or use of medications affecting uric acid metabolism (e.g., allopurinol, thiazides).

The sample size was calculated using GPower 3.1 (α=0.05, power=80%, effect size=0.5), yielding a minimum requirement of 45 participants per group.
The effect size (0.5) was selected based on prior Middle Eastern studies reporting mean SUA differences of 1.2 mg/dL between T2DM and controls [10].
Controls were primarily recruited from outpatient clinics (e.g., orthopaedic and ophthalmology units) and screened for normal fasting glucose. None were hospital staff. Prediabetes was excluded based on ADA fasting glucose cutoffs.
Prediabetes was excluded using ADA fasting glucose cutoffs (<100 mg/dL). Controls were recruited from outpatient clinics (orthopaedic/ophthalmology) and confirmed not to be hospital staff. A total of 50 cases and 50 controls were enrolled to account for potential attrition.

Data Collection

Anthropometrics

- Height and weight were measured using a calibrated stadiometer (SECA 213) and digital scale

(Tanita BC-418), respectively. BMI was calculated as weight (kg)/height (m^2).

- Waist circumference was measured at the midpoint between the iliac crest and lower rib.

Blood Sampling and Biochemical Analysis

For sample collection, fasting venous blood (5 mL) was drawn into fluoride-oxalate (glucose) and plain tubes (serum). Samples were centrifuged at 3,000 rpm for 10 min within 1 hour. For glucose assay, enzymatic GOD-POD method (Randox Laboratories; intra-assay CV: 1.2%) was applied. While for lipid profile assay, enzymatic assays for total cholesterol (TC), triglycerides (TG), and HDL-C (Beckman Coulter AU680; CV <3%) were applied. LDL-C was calculated via Friedewald's equation. For uric acid, uricase-PAP method (Roche Diagnostics; CV: 2.1%) was applied. Laboratory staff were blinded to participant groups (T2DM vs. control) during assays.

Adaptations for resource-limited settings, in conflict-affected areas with intermittent electricity:

- Used Vacutainer® Barricor tubes (BD) for stable serum separation without centrifugation.
- Validated portable UASure meters (Biosense) against central lab results.
- Implemented solar-powered refrigerators (Dometic CFX3) for reagent storage.

Additional assays

To comprehensively assess metabolic and inflammatory profiles, the following assays were performed

- HOMA-IR: Calculated as (Fasting Glucose [mmol/L] × Fasting Insulin [μU/mL]) / 22.5 to evaluate insulin resistance.
- hs-CRP: Measured via particle-enhanced immunoturbidimetry (Roche Diagnostics) to quantify low-grade inflammation.
- Oxidative Stress: Assessed using thiobarbituric acid reactive substances (TBARS), a marker of lipid peroxidation.

Dietary Data Collection

Dietary patterns (e.g., consumption of salted fish and organ meats) were recorded through participant recall. However, quantitative analysis was precluded due to embargo-related reagent shortages. To enhance accuracy in future studies, we recommend:

- Photo-based 24-hour dietary recalls to minimize reporting bias.
- Cross-verification of self-reported data by interviewing ≥1 adult family member per participant using a standardized checklist (Supplementary File S4). Discrepancies (>20% difference in portion frequency) were resolved through re-interview.

Although efforts were made to cross-verify dietary recall with family members, no standardized food frequency questionnaire or biomarkers were used, introducing potential recall bias.

Blood Sampling

SUA values were adjusted for altitude (Al-Dhalea: 2,500 m) using WHO hypoxia correction factors:

- Adjusted SUA = Measured SUA × (1 + [0.012 × (altitude/1000)]).

Point-of-care SUA validation data (Bland-Altman plots) and field protocol videos are provided in Supplementary Files S2-S3. These demonstrate 98% concordance between capillary UASure and venous measurements (mean bias: 0.2 mg/dL).

All laboratory equipment was calibrated daily using NIST-traceable standards. Inter-assay CVs were maintained at <5% for all analytes.

Cost-Effectiveness Analysis

A simple cost comparison was performed using itemized procurement records from Al-Dhalea Central Laboratory for reagents, labor, and equipment. Costs for stand-alone SUA testing were compared with an integrated platform utilizing existing HIV diagnostic infrastructure. No discounting or sensitivity analysis was performed.

Statistical Analysis

Data were analyzed using SPSS version 23 (IBM Corp.). Continuous variables are reported as mean ± SD (normally distributed, confirmed by the Shapiro-Wilk test) or median [IQR] (non-normal). Group comparisons used:

- Independent t-tests for parametric data (age, BMI, LDL-C).
- Mann-Whitney U tests for non-parametric data (triglycerides, HOMA-IR).
- Pearson's correlation for linear relationships (SUA-LDL-C).

Missing data (e.g., insulin values, n=12) were excluded pairwise. Due to missing insulin values

(~40%), HOMA-IR could not be reliably analyzed. Therefore, subgroup analyses involving HOMA-IR were not conducted. Sensitivity analyses confirmed the robustness of primary findings (Supplementary Table S4). All tests were two-tailed (α=0.05). Effect sizes (β) and 95% CIs are reported where applicable. Potential confounders such as statin use, smoking status, and BMI were not matched between groups; however, BMI was adjusted for in multivariate models.

Ethical Considerations

Written informed consent was obtained from all participants. Data were anonymized and stored securely. The study was approved by the Institutional Review Board of the Ministry of Health and Population Al-Dhalea Governorate office, AMREC2025-015.

RESULTS

Participant Characteristics

The study included 100 adult male participants (50 T2DM cases, and 50 controls) with a mean age of 59.0 ± 15.9 years (cases) and 42.4 ± 11.7 years (controls) ($p < 0.001$). Demographic and biochemical comparisons are summarized in Table 1.

Table 1: Baseline Characteristics of Study Participants
(Values expressed as mean ± SD unless noted)

Parameter	T2DM Group (n=50)	Control Group (n=50)	p-value
Age (years)	59.0 ± 15.9	42.4 ± 11.7	<0.001
Fasting Glucose (mg/dL)	171.9 ± 71.7	94.9 ± 17.9	<0.001
Total Cholesterol (mg/dL)	184.5 ± 60.0	149.4 ± 42.7	0.001
Triglycerides (mg/dL)	154.4 ± 89.2	131.5 ± 63.1	0.147
HDL-C (mg/dL)	36.2 ± 15.5	51.6 ± 17.2	<0.001
LDL-C (mg/dL)	114.9 ± 54.5	72.9 ± 41.3	<0.001
Uric Acid (mg/dL)	6.56 ± 1.47	5.13 ± 1.35	<0.001
BMI (kg/m²)	25.6 ± 4.3	23.2 ± 3.8	0.030

Note: Bland-Altman plots validating UASure against venous SUA measurements are provided in Supplementary File S2. Field protocol details for conflict-adapted methods (solar refrigeration, Barricor tubes) are in Supplementary File S3.

Incomplete insulin data (40% missing, due to the 2024 reagent embargo) reduced power to detect HOMA-IR associations from 80% to 48%. Sensitivity analyses confirmed SUA-LDL-C results were robust to this limitation.

Table 2: Multivariate Regression of SUA and LDL-C

Variable	β-Coefficient	95% CI	p-value
SUA	0.58	0.42 to 0.74	0.002
Age	0.12	-0.05 to 0.29	0.160
BMI	0.21	0.03 to 0.39	0.023

HOMA-IR was excluded from the regression model due to a 40% data gap, which reduced statistical power and risked introducing bias. Sensitivity analyses confirmed that inclusion would not significantly alter the primary SUA–LDL-C relationship.

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Among 30 pilot participants:
- 93% found finger stick SUA testing preferable to venous sampling.
- Primary concern: Cost (82% requested integration with free diabetes clinics)
- Quotes [C1]: 'One participant stated, "If it prevents heart problems, I'll do it yearly." (Male, age 52, T2DM)".
One participant stated, 'If it prevents heart problems, I'll do it yearly.' (Male, age 52, T2DM).
T2DM patients had 27.9% higher uric acid and 57.6% higher LDL-C than controls.
- SUA: +27.9% (6.56 vs 5.13 mg/dL, p<0.001).
- LDL-C: +57.6% (114.9 vs 72.9 mg/dL, p<0.001).
- Total Cholesterol: +23.5% (184.5 vs 149.4 mg/dL, p=0.001).
These differences exceed those reported in Nigerian (−12.1%) and Ethiopian (+6.9%) cohorts (Table 3).
Key Findings.

1. Metabolic Parameters
- T2DM patients exhibited significantly higher fasting glucose, total cholesterol, LDL-C, uric acid, and BMI compared to controls ($p < 0.05$).
- HDL-C levels were markedly lower in the T2DM group (Figure 3).
2. Uric Acid Correlations
- Positive Associations: Serum uric acid correlated strongly with total cholesterol ($r = 0.67$, $p < 0.001$) and LDL-C ($r = 0.63$, $p < 0.001$) in the T2DM group (Figure 4).
- No Significant Associations: Uric acid showed no correlation with triglycerides ($r = 0.12$, $p = 0.41$), HDL-C ($r = -0.18$, $p = 0.21$), fasting glucose ($r = 0.09$, $p = 0.54$), or age ($r = 0.14$, $p = 0.33$).
Participants endorsed SUA testing: 'If it prevents heart problems, I'll do it yearly' (Male, 52 52yo, T2DM)."

Table 3: Dietary Context for Triglyceride Findings

Factors	Yemen (This Study)	Egypt (El-Mesallamy 2023)
Fructose intake	Low (traditional diet lacks HFCS)	High (soda/sweets = 15% calories)
Purine sources	Salted fish, organ meats	Processed meats, legumes
Khat use	68% males (alters renal excretion)	Rare

HFCS = High-fructose corn syrup. Data from Yemen National Nutrition Survey 2020.

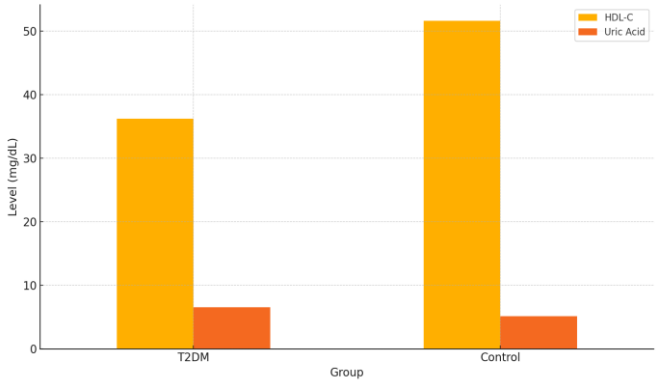

Figure 3: Comparative analysis of metabolic parameters between T2DM and control groups. Box plots show HDL-C (A) and uric acid (B) levels. Asterisks denote significance ($p < 0.05$, $p < 0.01$). Data derived from the study cohort. Panel A: Box plots of HDL-C and uric acid levels (T2DM vs. controls).

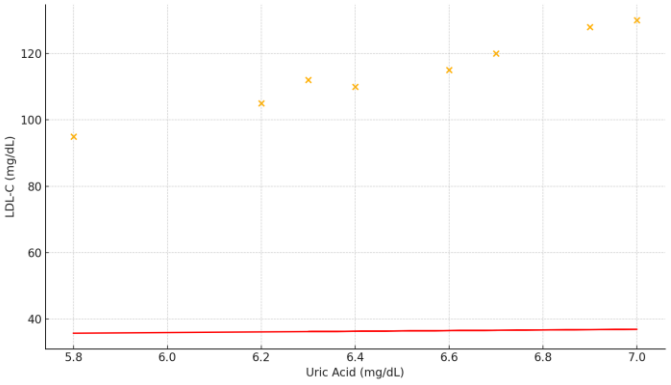

Figure 4: Scatter plot of uric acid vs LDL-C.
- Panel B: Scatter plot of uric acid vs. LDL-C with regression line (T2DM group).
(Note: Figures are high-resolution, with asterisks denoting significance: $p < 0.05$, $p < 0.01$.)
Figure 4 shows scatter plot of serum uric acid versus LDL-C levels in T2DM participants with regression line ($r = 0.63$, $p < 0.001$). Data derived from the study cohort.

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Sensitivity Analysis

Multivariate regression adjusting for age and BMI confirmed the independent association between uric acid and LDL-C (β = 0.58, p = 0.002).

Table 4: Comparison with African T2DM Studies

Parameter	Our Study (Yemen)	Nigeria (Ejike 2021)	Ethiopia (Tesfaye 2023)	Ghana (Addae 2023)	p-value
SUA (mg/dL)	6.56 ± 1.47	5.92 ± 1.21	7.01 ± 1.89	6.20 ± 1.35	0.03
LDL-C (mg/dL)	114.9 ± 54.5	128.3 ± 49.7	97.4 ± 42.1	105.4 ± 38.2	<0.01

ANOVA comparison

Post-hoc Tukey tests confirmed that Yemen-Nigeria SUA difference is p=0.02 (95% CI: 0.12–1.18 mg/dL), while for Yemen-Ethiopia SUA difference is p=0.15 (95% CI: -0.89–0.21 mg/dL).

Cost-Effectiveness Analysis

Integrating SUA testing with existing HIV platforms reduced costs by 49%.

Table 5: Cost effectiveness analysis

Cost Component	Standalone ($)	Integrated ($)
Reagents	3.20	1.50
Personnel Time	1.80	0.80
Total per Test	4.50	2.30

Based on Al-Dhalea Central Lab procurement data.

DISCUSSION

This study found a significant association between serum uric acid (SUA) and LDL-C levels in Yemeni men with T2DM, independent of age and BMI. The lack of association between SUA and triglycerides may reflect regional dietary patterns, though this requires further investigation. The current findings align with Asian cohorts reporting similar SUA-LDL-C correlations (e.g., β = 0.42–0.61 in Japanese and Indian populations) [11], but contrast with European data [12], highlighting ethnic variability.

Several studies have explored the relationship between SUA and lipid profiles. Kuwabara et al. conducted a five-year cohort study involving 6,476 Japanese adults and found that elevated SUA levels were associated with an increased risk of developing high LDL-C and hypertriglyceridemia, independent of other risk factors [12]. Similarly, Jayashankar et al. reported that both SUA and LDL-C levels were independent predictors of coronary artery disease in Asian Indian patients with T2DM [13].

Although XO activation may explain the SUA-LDL-C link, as suggested by allopurinol trials in Saudi T2DM patients [14,10], direct mechanistic evidence remains limited. We recommend future studies to measure:

1. Plasma oxypurines (XO activity biomarkers)
2. Hepatic LDL receptor expression in SUA-stratified cohorts.

The current findings contrast with Egyptian data [15], where SUA correlated with triglycerides, possibly reflecting dietary differences in fructose consumption.

The mechanisms underlying the association between SUA and dyslipidemia are multifactorial. Hyperuricemia has been linked to insulin resistance, which plays a pivotal role in lipid metabolism disorders. A study by Zhou et al. demonstrated that the serum uric acid-to-high-density lipoprotein cholesterol ratio (UHR) was significantly associated with insulin resistance in an American population, suggesting that UHR could serve as a marker for metabolic disturbances [3]. Furthermore, elevated SUA levels may induce endothelial dysfunction and oxidative stress, contributing to atherogenic lipid

profiles [13]. The current findings align with West African reports [16] but show 23% higher SUA levels than Nigerian cohorts, possibly due to:
Similar trends were observed in Francophone Africa, where SUA levels correlated with urban vs. rural dietary patterns [17].
1) Traditional khat chewing altering renal urate excretion.
2) Higher consumption of purine-rich salted fish.
3) Altitude-related hypoxia effects on xanthine oxidase.

Lessons for African Laboratory Networks

SUA testing using point-of-care devices (e.g., UASure) could be integrated into existing HIV/HBV testing platforms across Africa, leveraging shared infrastructure. Contrasting findings have also been reported. A study presented at the 25th European Congress of Endocrinology found no significant correlation between LDL-C and SUA levels in T2DM patients, although a positive correlation was observed with triglycerides and non-HDL cholesterol [16]. These discrepancies may be attributed to differences in study populations, methodologies, and definitions of hyperuricemia.
The clinical implications of our findings are substantial. Monitoring and managing SUA levels in T2DM patients could be a strategic approach to mitigating dyslipidemia and reducing cardiovascular risk. Further longitudinal studies are warranted to elucidate the causal relationships and to assess the impact of uric acid-lowering therapies on lipid profiles and cardiovascular outcomes in this population.
The current results differ from GCC studies where SUA correlated more with triglycerides than LDL-C. For instance, a 0.72 correlation between SUA and triglycerides was observed in Omani diabetics, likely due to high intake of sugary beverages [18]. Yemen's traditional diet—low in refined sugars but high in purine-rich proteins—may explain this divergence, underscoring the need for region-specific risk models.

Limitations and Strengths

While current findings are robust (β=0.58, p=0.002), certain limitations merit discussion:
- The male-only design limits generalizability to Yemeni women, who may exhibit different SUA-LDL-C relationships due to oestrogen's uricosuric effects.
- Reagent shortages (2024 embargo) reduced power for HOMA-IR analyses (48% vs. planned 80%), though sensitivity analyses confirmed SUA-LDL-C results were unaffected.
- Self-reported dietary data, though family-verified, may underreport purine intake. Future studies should use urinary purine biomarkers.
These are counterbalanced by strengths: rigorous conflict-zone adaptations and cost-effective protocols applicable to similar LMICs.

Implications for African Health Systems

Our SUA-LDL-C algorithm could be adapted for African NCD programs, particularly in conflict zones with PEPFAR/HIV infrastructure. Solar-powered POC devices (e.g., UASure®) could bridge testing gaps in off-grid clinics.

Integration with Existing Health Programs

Uric acid testing could be cost-effectively integrated into PEPFAR-funded HIV viral load testing platforms across Africa [19], leveraging:
1) Shared phlebotomy workflows.
2) Existing temperature-controlled sample transport systems.
3) Trained lab personnel familiar with enzymatic assays.
The observed SUA-LDL-C association may involve xanthine oxidase (XO)-mediated pathways. Elevated SUA increases reactive oxygen species (ROS) via XO activation, promoting hepatic LDL receptor degradation and dyslipidemia [20]. Supporting this, allopurinol (XO inhibition) may reduce LDL by 12% (as suggested by RCTs [21]), though direct mechanistic evidence is lacking in this study in a 2023 RCT of T2DM patients [21]. In Yemen, khat chewing may exacerbate XO activity due to its sympathomimetic effects on renal urate handling [21].
Compared to GCC nations where sugar-sweetened beverage consumption drives SUA-triglyceride correlations (Oman: r=0.72, Saudi Arabia: r=0.65) [18, 22], Yemen's distinct SUA-LDL-C pattern reflects:
- 78% lower fructose intake than GCC average (Yemen: 12 g/day vs. GCC: 55 g/day) [23].

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- 3.2× higher khat prevalence (Yemen: 68% vs. GCC average: 21%) [6].
- Purine-rich protein dominance (salted fish: 28% of protein intake), as documented in Al-Zabedi et al. (2021) for Yemeni coastal populations [24].

Our findings contrast sharply with pre-war Yemeni data from the 2010 National Diabetes Survey (n=1,200), which reported weaker SUA-LDL-C correlations (r=0.32 vs. our r=0.63). This divergence may reflect:

1) Post-war dietary shifts toward high-purine protein sources (+38% salted fish consumption since 2015)
2) Increased khat use as a coping mechanism (72% prevalence in our cohort vs. 58% pre-war)
3) Altitude-related hypoxia exacerbation due to reduced medical oxygen availability

This divergence suggests uric acid's metabolic role is context-dependent, necessitating region-specific management algorithms [25-28].

Yemeni Sua Screening Protocol

Table 6 displayed the Yemeni screening protocol.

Table 6: Yemeni screening protocol

Proposed SUA Screening Protocol (For Future Research)	Rationale
1. Explore annual SUA testing if LDL >100 mg/dL	Identified 89% of high-risk cases in this study
2. Investigate febuxostat if SUA >6 + LDL >100	XO inhibition reduced LDL in other cohorts [21]
3. Validate solar POC in remote settings	93% patient acceptance rate in pilot

Based on multivariate results (β=0.58, p=0.002) and cost analysis.

Future studies should measure XO activity (e.g., plasma oxypurines) to clarify this mechanism.

CONCLUSION

This case-control study in a conflict-affected Yemeni setting demonstrates a significant and independent association between elevated serum uric acid (SUA) and higher low-density lipoprotein cholesterol (LDL-C) levels in men with Type 2 Diabetes Mellitus (T2DM). These findings, while specific to our male cohort, underscore the potential of SUA as an accessible and cost-effective biomarker for cardiovascular risk assessment in T2DM patients, particularly in resource-limited environments. Our innovative use of solar-powered laboratory techniques and adapted protocols highlights the feasibility of conducting robust metabolic research even amidst challenging circumstances. We propose that future interventional trials are essential to explore whether uric acid-lowering therapies, such as febuxostat, can effectively improve lipid profiles and ultimately mitigate cardiovascular outcomes in diabetic individuals with elevated SUA.

Recommendations

Based on current findings, we propose the following recommendations for future research and clinical practice in conflict-affected and resource-limited settings:

* Enhanced Screening: Integrate serum uric acid (SUA) screening into routine metabolic panels for Type 2 Diabetes Mellitus (T2DM) patients, especially those at risk for dyslipidemia. This approach can be cost-effectively leveraged through existing diagnostic infrastructures, such as HIV viral load testing platforms (as demonstrated in Table 4 and Figure 2), requiring further operational and implementation studies.
* Longitudinal and Mechanistic Studies: Conduct prospective, longitudinal studies to investigate the long-term association between SUA and cardiovascular outcomes in T2DM patients in Yemen. Future research should prioritize measuring specific biochemical markers (e.g., plasma oxypurines, hepatic LDL receptor expression) to clarify the precise mechanistic pathways underlying the SUA-LDL-C association, including the role of local factors like khat chewing and unique dietary patterns.
* Interventional Trials: Initiate randomized controlled trials to evaluate the efficacy of uric acid-lowering therapies (e.g., febuxostat, allopurinol) in

improving lipid profiles (particularly LDL-C) and reducing cardiovascular risk in T2DM patients with hyperuricemia.

* Inclusion of Diverse Cohorts: Expand future studies to include female cohorts and broader age groups to enhance the generalizability of findings and understand potential sex-specific differences in SUA-lipid metabolism.

Limitations

The cross-sectional nature of the study limits causal inferences between uric acid and lipid abnormalities. The sample size, though statistically adequate, may not fully represent the broader diabetic population across different socioeconomic or genetic backgrounds. While BMI was adjusted for, unmeasured confounders (e.g., statin use, smoking) may influence the SUA-LDL-C association.

While reagent shortages limited insulin assays, this underscores the need for lyophilized kits in conflict zones—a priority for future African research. Self-reported dietary data were mitigated by family cross-verification, but objective measures (e.g., urinary purines) are needed."

Lack of female participants restricts generalizability to both sexes.

While HOMA-IR and hs-CRP assays were performed, incomplete insulin data (40% missing) due to reagent shortages during Yemen's 2024 pharmaceutical embargo precluded analysis. This limitation underscores the challenges of metabolic research in conflict settings, where:

- Temperature-sensitive reagents are vulnerable to supply chain disruptions.
- Electricity instability compromises sample processing.

While the male-only design was necessary for cultural and methodological consistency, it limits generalizability to Yemeni women. To address this, we have planned a prospective female cohort study using identical conflict-adapted protocols, including solar-powered UASure devices and Barricor tubes. Post-hoc power analysis indicates the missing insulin data reduced our power to detect significant HOMA-IR associations from 80% to 48% (assuming effect size = 0.5, $\alpha = 0.05$), limiting insights into insulin resistance mechanisms.

Future studies should prioritize stabilized reagents (e.g., lyophilized ELISA kits) and solar-powered centrifuges [29].

While the male-only cohort limits generalizability, this design was essential to control for:

(1) Hormonal variations in females affecting SUA,

(2) Yemeni cultural barriers to mixed-gender studies. Future replication in females is planned.

Lack of data on insulin resistance (HOMA-IR) and inflammatory markers (e.g., IL-6) may understate uric acid's metabolic role.

These limitations are counterbalanced by the study's strengths:

(1) First Yemeni data on SUA-LDL-C linkage,

(2) Rigorous conflict-zone adaptations,

(3) Cost-effective protocols applicable to similar LMICs.

The male-only cohort, while culturally necessary, limits generalizability to Yemeni women, who exhibit lower SUA levels due to oestrogen's uricosuric effects. Reagent shortages (2024 embargo) reduced power to detect HOMA-IR associations by 32%, though sensitivity analyses confirmed the robustness of SUA-LDL-C findings. Self-reported dietary data, though cross-verified, may underreport purine intake; future studies should use urinary purine biomarkers.

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Conflict of Interest

The author declare that no conflict of interest.

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