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Metabolic Syndrome As A Predictor Of Incident Type 2 Diabetes And Cardiovascular Events In The Kirkuk Population: A Prospective Cohort Study

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ABSTRACT

Background: Metabolic Syndrome (MetS) is a significant public health concern, but its predictive power and the utility of including hyperuricemia in its definition are not fully characterized in all populations. This study aimed to assess MetS as a predictor for incident Type 2 Diabetes (T2DM) and Cardiovascular Events (CVEs) in an Iraqi cohort and to determine if adding serum uric acid (SUA) to the diagnostic criteria improves risk prediction.

Methods: This prospective cohort study was conducted at the Baba GurGur Diabetic Center in Kirkuk, Iraq. An initial cohort of 379 North Oil Company employees, including administrators, craftsmen, and their families, visiting Kiwan Hospital in northern Kirkuk. Three hundred seventy-nine participants were enrolled in 2015 and followed for 5 years, with 375 participants (98.9% retention) included in the final analysis. MetS was defined using the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria.

AIM: The primary outcomes were incident T2DM and a composite of major non-fatal CVEs. Cox proportional hazards regression was used to calculate hazard ratios (HRs).

Results: The mean age of the cohort was 47.2 ± 9.8 years, and 59.7% were male. The baseline prevalence of standard MetS was 38.4%. Over 1,875 person-years of follow-up, 118 new cases of T2DM, and 32 incident CVEs occurred. The risk for both outcomes increased in a dose-response manner with the number of MetS components. After full adjustment, standard MetS was a significant predictor for both T2DM (HR: 3.95, 95% CI: 2.63–5.93) and CVEs (HR: 2.33, 95% CI: 1.15–4.71). A modified definition including hyperuricemia (MetS-UA) showed a stronger predictive association for both T2DM (HR: 4.31, 95% CI: 2.91–6.38) and CVEs (HR: 2.78, 95% CI: 1.41–5.48). Adding uric acid to the model significantly improved risk discrimination for both T2DM (ΔC-statistic: 0.024, p=0.025) and CVEs (ΔC-statistic: 0.029, p=0.042).

Conclusion: In this Iraqi cohort, MetS is a potent predictor of incident T2DM and CVEs, with risk escalating with the accumulation of metabolic abnormalities. The inclusion of Serum uric acid in the diagnostic criteria significantly enhances the predictive power of MetS for both cardiometabolic outcomes. These findings support aggressive screening for MetS and its components, including uric acid, for primordial prevention.

Keywords
Metabolic syndrome; type 2 diabetes mellitus; cardiovascular events; uric acid; risk prediction; cohort study; iraq.

Abbreviations
MetS: Metabolic Syndrome; T2DM: Type 2 Diabetes Mellitus; CVEs: Cardiovascular Events; SUA: Serum Uric Acid; HDL‐C: High‐Density Lipoprotein Cholesterol; TG: Triglycerides; IDF: International Diabetes Federation; NCEP ATP III: National Cholesterol Education Program Adult Treatment Panel III; IDI: Integrated Discrimination Improvement; NRI: Net Reclassification Improvement.

1. INTRODUCTION

Metabolic syndrome is an accumulation of several disorders that raise the risk of atherosclerotic cardiovascular disease, including myocardial infarction, cerebrovascular accidents, peripheral vascular diseases, insulin resistance, and type II diabetes mellitus. The cluster of metabolic disorders that define metabolic syndrome includes central obesity, insulin resistance, hypertension, and atherogenic dyslipidemia [1,3]. Standard diagnostic frameworks such as NCEP ATP III and the joint IDF/AHA/NHLBI harmonized criteria capture these abnormalities. However, there is ongoing debate about whether additional biomarkers can improve risk stratification. [2,3] Serum uric acid (SUA) is thought to be a meaningful biological marker because of its connection to insulin resistance, endothelial dysfunction, and hypertension. [4,5] Hyperuricemia is strongly linked to increased cardiovascular risk, including hypertension, coronary artery disease, arrythmia, and heart failure. While uric acid, the ultimate product of purine metabolism, is vital for cellular processes, elevated serum levels have been implicated in promoting inflammation and oxidative stress. (6) Within Kirkuk, the burden of MetS among patients with T2DM at the Baba GurGur Diabetic Center has already been documented, underscoring the local relevance of rigorous risk assessment. [7]. [According to a partially nationally representative survey conducted in China in 2009, the prevalence of metabolic syndrome (MetS) was 21.3%, with higher rates observed among individuals residing in urban areas compared to those in rural areas. Furthermore, evidence from another nationally representative cross-sectional study in China demonstrated that the prevalence of MetS increased progressively with age and was consistently higher in females than in males. {8] In Iraq, approximately 1.4 million individuals are living with diabetes, with the reported prevalence of type 2 diabetes mellitus (T2DM) ranging between 8.5% and 13.9%. The constellation of metabolic abnormalities that predispose to T2DM is now widely recognized as metabolic syndrome (MetS). Insulin resistance (IR) plays a central role in the pathophysiology of MetS and has been proposed as its primary underlying mechanism. A study conducted among young, apparently healthy university students in Iraq investigated the association between IR and MetS, demonstrating that greater severity of IR was positively correlated with an increased clustering of MetS risk factors.{9} Cardiovascular disease (CVD) represents a major global health burden and has attracted considerable attention due to its high morbidity and mortality. It is estimated to account for 46.2% of all deaths attributed to non-communicable diseases, highlighting its critical role as a leading cause of premature mortality worldwide. Patients with metabolic syndrome (MetS) are at greater risk of developing cardiovascular disease (CVD) within 5–10 years, and their long-term risk is even higher {10},

In this study, we prospectively evaluated MetS—using NCEP ATP III—and tested whether adding hyperuricemia (MetS‐UA) improves the prediction of incident T2DM and major non‐fatal cardiovascular events (CVEs) over five years.

2. MATERIALS AND METHODS

2.1 Study Framework and Cohort Establishment

2.1.1 Study Design and Setting

This investigation was designed and conducted as a prospective, population-based cohort study at the Baba GurGur Diabetic Center (K1 Hospital/Northern Oil Company), K Baba GurGur.
Diabetic Center, which is located in the K1 Hospital/Northern Oil Company, Kirkuk city. It is receive patients from all parts of Kirkuk governorate and plays an important role in teaching, research, and health services, providing for attending patients with baseline data collection in 2015 and a 5-year reassessment in 2020.

2.1.2 Participant Recruitment and Enrollment

This prospective cohort study was conducted at K/1 General Hospital in Kirkuk, Iraq, a major tertiary care center serving a diverse urban and rural population.
The cohort involved patients from all socioeconomic and ethnic groups, representative of the Kirkuk Governorate.

2.1.3 Inclusion and Exclusion Criteria

Inclusion: age ≥30 years, permanent Kirkuk residency, capacity to consent. Exclusion: excluded individuals who we were unable to contact, prior T1DM/T2DM, prior CVEs, CKD stage ≥3, severe inflammatory disease, pregnancy.

2.1.4 Cohort Follow-up and Retention

Participants were re‑contacted in 2020, with 375 completing follow‑up (98.9% retention). Protocols mirrored baseline to ensure comparability.

2.1.5 Ethical Conduct and Consent

The protocol received ethical approval from the Medical Authority of the North Oil Company. Written informed consent was obtained in line with the Declaration of Helsinki.

2.2 Data Collection and Definitions

2.2.1 Data Collection Protocols

Standardized questionnaires captured collect pertinent information such as age, sex, alcohol consumption patterns (i.e., frequency of drinking of more than two days per week), and current smoking behavior (i.e., active smoker or nonsmoker). Dem, socioeconomic status, lifestyle, and medical/family history. Furthermore, medical records were reviewed to obtain
information on prevalent diseases such as MetS, hypertension (HTN), diabetes mellitus(DM), and dyslipidemia.

2.2.2 Clinical and Anthropometric Measurements

Blood pressure was measured after 5 minutes of rest using a mercury sphygmomanometer. Anthropometry followed standardized procedures; Anthropometric measures were collected according to the WHO's WHOsteps manual. A-Weight was measured in kilograms (kg) using the WHO weighing scale at a precision of 0.1 kg.
B-Height was measured using a standiometer while weight was recorded after measuring the patient bare-footed and with light clothes using a weight balance. On the other hand, the height measurement is recorded to the nearest 0.1 cm.

C-Waist circumference (WC) in centimeters was measured at the midpoint between the lowermost rib and the iliac crest.

D-Body mass index (BMI), which was calculated by dividing weight BMI and WHR were calculated.

2.2.3 Biochemical Analyses

Fasting blood (5 mL) was analyzed for FPG, TG, HDL-C, SUA (BioSystems A25), and HbA1c by HPLC (Bio-Rad). These values was measured at follow-up.

2.2.4 Exposure and Outcomes

MetS was defined by harmonized NCEP ATP III (≥3 of 5 components). A modified definition (MetS‑UA) incorporated hyperuricemia (>7.0 mg/dL men, >6.0 mg/dL womenas) as a sixth component. Primary outcomes were incident T2DM and incident CVEs over 5 years..) {8,11}

2.3 Statistical Analysis

Cox proportional hazards models estimated HRs for outcomes by MetS status with nested adjustments. Discrimination and reclassification were compared using the ΔC‑statistic, IDI, and category‑free NRI. Two‑tailed $p<0.05$ was considered statistically significant.

3. RESULTS

3.1 Cohort Characteristics and Event Rates

Of the 379 participants enrolled at baseline in 2015, complete follow-up data were available for 375 individuals (98.9% retention) in 2020. Four participants were excluded due to loss to follow-up. The total follow-up period corresponded to 1,875 person-years.

The baseline characteristics of the analytical cohort are presented in Table 1. The cohort had a mean age of 47.2 years, with a majority being male (59.7%). A notable portion of the population reported being current smokers (26.9%), and 168 (44.8%) Physical inactive. The prevalence of metabolic syndrome according to the standard NCEP ATP III criteria was 38.4% (n=144).

Characteristic	Category	Value
Age Group (years)	30–39	90 (24.0%)
	40–49	108 (28.8%)
	50–59	119 (31.7%)
	≥60	58 (15.5%)
Sex	Male	224 (59.7%)
	Female	151 (40.3%)
Educational Status: Not read or write		35 (9.3%)
	Primary School	98 (26.1%)
	Secondary School	134 (35.7%)
	High School	108 (28.8%)
Lifestyle		
Current Smoker	Yes	101 (26.9%)
Physical Activity	Inactive	168 (44.8%)
Family History		
Family History of T2DM	Yes	131 (34.9%)
Family History of HTN	Yes	157 (41.9%)
Family History of IHD	Yes	89 (23.7%)
Anthropometric Indices		**Mean ± SD**
Body Mass Index (kg/m²)		29.4 ± 4.7
Waist Circumference (cm)	Men	97.6 ± 11.3
	Women	91.5 ± 10.8
Clinical & Biochemical		**Mean ± SD**
Systolic Blood Pressure (mmHg)		129.8 ± 16.5
Fasting Plasma Glucose (mg/dL)		106.3 ± 28.1
HDL-Cholesterol (mg/dL)	Men	41.2 ± 8.9

	Women	46.8 ± 9.5
Triglycerides (mg/dL)		179.9 ± 98.5
Serum Uric Acid (mg/dL)	Men	6.8 ± 1.5
	Women	5.7 ± 1.3
Metabolic Syndrome Prevalence		
Standard MetS (NCEP ATP III), n (%)		144 (38.4)
Modified MetS-UA, n (%)		158 (42.1)

Table 1: Baseline Characteristics of the Kirkuk Metabolic Syndrome Cohort (N=375)

3.2 Prevalence of Metabolic Syndrome by Uric Acid Level

As shown in **Table 2**, the prevalence of MetS was significantly higher among individuals with hyperuricemia. In men with high SUA levels (>7.0 mg/dL), the prevalence of MetS was 65.8%, compared to just 29.7% in men with normal SUA. A similar pattern was observed in women, where those with high SUA (>6.0 mg/dL) had a MetS prevalence of 59.6%, versus 19.2% in those with normal levels.

Baseline SUA Category	Total Participants (N)	Participants with MetS (n)	Prevalence of MetS (%)
Men	**224**	**94**	**42.0%**
Normal SUA (≤7.0 mg/dL)		148	44 29.7%
High SUA (>7.0 mg/dL)	76	50	65.8%
Women	**151**	**50**	**33.1%**
Normal SUA (≤6.0 mg/dL)		99	19 19.2%
High SUA (>6.0 mg/dL)	52	31	59.6%

Table 2: Prevalence of Metabolic Syndrome by Baseline Serum Uric Acid (SUA) Level

3.3 Impact of Family History on Disease Incidence

Over the 5-year follow-up period, 118 new cases of T2DM were identified (incidence rate: 63.0 per 1,000 person-years), and 32 incident CVEs occurred (incidence rate: 17.1 per 1,000 person-years). As detailed in **Table 3**, a positive family history was associated with a higher incidence of disease. Individuals with a family history of T2DM had a 44.3% incidence of developing the disease themselves, compared to 24.6% in those without a family history.

Baseline Family History	Total (N)	Incident T2DM, n (%)	Incident CVEs, n (%)
Family Hx of T2DM			
Yes	131	58 (44.3%)	14 (10.7%)
No	244	60 (24.6%)	18 (7.4%)
Family Hx of HTN			
Yes	157	56 (35.7%)	19 (12.1%)
No	218	62 (28.4%)	13 (6.0%)
Family Hx of IHD			
Yes	89	32 (36.0%)	13 (14.6%)
No	286	86 (30.1%)	19 (6.6%)

Table 3: Correlation of Family History with 5-Year Incidence of T2DM and CVEs

3.4 Contribution of Individual MetS Components to Patient Outcomes

Analysis of the baseline MetS components among those who developed complications reveals distinct patterns (Table 4). For individuals who later developed T2DM, elevated fasting glucose was the most common preceding abnormality, present in 84.7% of cases. For those who developed CVEs, elevated blood pressure (78.1%) and hypertriglyceridemia (75.0%) were the most frequent baseline components.

Baseline MetS Component	Event-Free Group (n=225)	Incident T2DM Group (n=118)	Incident CVEs Group (n=32)
	n (%)	n (%)	n (%)
Abdominal Obesity	70 (31.1%)	71 (60.2%)	18 (56.3%)
Elevated Fasting Glucose	59 (26.2%)	100 (84.7%)	20 (62.5%)
Hypertriglyceridemia	64 (28.4%)	68 (57.6%)	24 (75.0%)
Low HDL-Cholesterol	92 (40.9%)	61 (51.7%)	19 (59.4%)
Elevated Blood Pressure	114 (50.7%)	88 (74.6%)	25 (78.1%)

Table 4: Baseline Prevalence of MetS Components by 5-Year Clinical Outcome

3.5 Risk Stratification by Number of Metabolic Syndrome Traits

A clear dose-response relationship was observed between the number of MetS components at baseline and the 5-year risk for both T2DM and CVEs (Table 5). After adjusting for age and sex, the risk escalated significantly with each additional metabolic abnormality. An individual with all five components had a 13.8-fold increased risk for T2DM and an 8.2-fold increased risk for CVEs compared to someone with zero components.

Number of MetS Components	Participants N (%)	Incident T2DM (n)	Adjusted HR* (95% CI)	Incident CVEs (n)	Adjusted HR* (95% CI)
0	79 (21.1%)	6	1.00 (Reference)	3	1.00 (Reference)
1	82 (21.9%)	11	1.83 (0.69–4.84)	4	1.34 (0.31–5.76)
2	70 (18.7%)	20	3.86 (1.56–9.53)	6	2.53 (0.65–9.86)
3	70 (18.7%)	32	6.47 (2.73–15.33)	8	3.49 (0.94–12.96)
4	55 (14.7%)	33	8.87 (3.73–21.08)	7	4.31 (1.12–16.63)
5	19 (5.1%)	16	13.81 (5.43–35.12)	4	8.21 (1.92–35.09)

Table 5: Adjusted Risk for T2DM and CVEs by Number of MetS Components at Baseline

*Adjusted for age and sex.

Hazard Ratios (HR) calculated using Cox proportional hazards regression.

3.6 Metabolic Syndrome as a Predictor of Incident T2DM and CVEs

The association between baseline MetS status and 5-year risk was evaluated using Cox regression (Table 6 and Table 7). In the fully adjusted model (Model 3), individuals with standard MetS had a 3.95-fold increased risk of incident T2DM (95% CI: 2.63–5.93, $p<0.001$). When using the modified MetS-UA definition, the predictive association was stronger, with a fully adjusted HR of 4.31 (95% CI:

2.91–6.38, p<0.001).

MetS Definition	Model 1 (Unadjusted)	Model 2 (Adjusted for Age, Sex)	Model 3 (Fully Adjusted*)
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Standard MetS	4.62 (3.10–6.88)	4.28 (2.86–6.41)	3.95 (2.63–5.93)
p-value	<0.001	<0.001	<0.001
Modified MetS-UA	5.25 (3.57–7.73)	4.81 (3.25–7.12)	4.31 (2.91–6.38)
p-value	<0.001	<0.001	<0.001

Table 6: Hazard Ratios for Incident T2DM Over 5 Years

*Fully adjusted model includes age, sex, smoking status, and education level.

Similarly, both definitions of MetS were significant predictors of incident CVEs (**Table 7**). The presence of standard MetS at baseline was associated with a 2.3-fold increased risk (HR: 2.33, 95% CI: 1.15–4.71, p=0.019). The MetS-UA definition again demonstrated a stronger predictive capacity, with a fully adjusted HR of 2.78 (95% CI: 1.41–5.48, p=0.003).

MetS Definition	Model 1 (Unadjusted)	Model 2 (Adjusted for Age, Sex)	Model 3 (Fully Adjusted*)
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Standard MetS	2.91 (1.47–5.76)	2.54 (1.27–5.07)	2.33 (1.15–4.71)
p-value	0.002	0.008	0.019
Modified MetS-UA	3.35 (1.74–6.46)	2.96 (1.52–5.78)	2.78 (1.41–5.48)
p-value	<0.001	0.001	0.003

Table 7: Hazard Ratios for Incident CVEs Over 5 Years

*Fully adjusted model includes age, sex, smoking status, and education level.

3.7 Incremental Predictive Value of Including Uric Acid

To formally assess whether including uric acid improved predictive performance, we compared the fully adjusted models (Table 8). For both T2DM and CVEs, adding uric acid to the MetS definition resulted in a statistically significant improvement in risk classification. For T2DM prediction, the MetS-UA model showed a significant increase in the C-statistic (ΔC-statistic=0.024, p=0.025), along with significant and positive IDI and NRI values, indicating better discrimination and reclassification. Similar improvements were observed for the prediction of CVEs, confirming the incremental value of incorporating hyperuricemia into the diagnostic criteria.

Outcome	Metric	Improvement	95% CI	p-value
Incident T2DM	Δ C-statistic	0.024	0.003–0.045	0.025
	IDI (%)	4.8	1.9–7.7	0.001
	NRI>0 (%)	19.2	8.1–30.3	<0.001
Incident CVEs	Δ C-statistic	0.029	0.001–0.057	0.042
	IDI (%)	3.5	0.8–6.2	0.011
	NRI>0 (%)	16.4	5.3–27.5	0.004

Table 8: Improvement in Prediction Performance by Adding Uric Acid to the MetS Definition

4. DISCUSSION

In this prospective cohort from Kirkuk, baseline MetS was a strong and independent predictor of incident T2DM and CVEs over five years, and risk rose steeply with each additional MetS component. This graded, dose‑response pattern mirrors prior meta‑analyses and consensus statements describing the escalating cardiometabolic hazard conferred by clustered risk factors. [12]. Individuals meeting four to five MetS criteria faced markedly higher hazards for both outcomes compared with those with none, emphasizing that the quantitative burden of metabolic derangement—not merely the presence of the syndrome—matters for prognosis. {13}

Component‑specific patterns were clinically instructive. Elevated fasting glucose at baseline was the most frequent antecedent among those who developed T2DM, while hypertension and hypertriglyceridemia predominated in those with CVEs. These observations align with the pathophysiology linking glucotoxicity to beta‑cell failure and dyslipidemia/hemodynamic load to atherothrombotic events, and they support prioritizing the most deranged component(s) in individualized prevention plans. [14] This means strict blood pressure control and triglyceride‑oriented lifestyle therapy (with consideration of pharmacotherapy when indicated) for patients at heightened vascular risk, alongside intensive glycemic surveillance for those with impaired fasting glucose.

A central hypothesis of our work concerned SUA. Incorporating hyperuricemia into the MetS construct (MetS‑UA) improved risk discrimination for both T2DM and CVEs, as reflected by incremental gains in C‑statistic and reclassification indices. Mechanistic and epidemiologic evidence support a contributory role of SUA in cardiometabolic disease via endothelial dysfunction, oxidative stress, renal microvascular effects, and amplification of insulin resistance and blood pressure. [4,5] These data, together with our findings, suggest that SUA is more than an innocent bystander and that routine SUA assessment may refine primordial and primary prevention strategies in high‑risk settings. [15]

The Kirkuk context also adds external validity. Prior local work from the Baba GurGur Diabetic Center documented a substantial MetS burden among patients with established T2DM, highlighting the regional importance of upstream risk detection. [7] Our study extends this by showing prognostic utility in a cohort free of outcomes at baseline, thereby addressing temporality and supporting actionable screening algorithms that include SUA where resources permit.

This study has several strengths. It was prospective, had a high follow-up rate, used standardized measurements, and directly compared standard MetS with MetS-UA using reclassification metrics. However, there are also limitations. Some cardiovascular events were self-reported, which may have caused misclassification. There may also be residual confounding factors, such as diet. Future research should include larger samples and test whether lowering uric acid can reduce the risks linked to MetS.

This study's Clinical and public‑health implications are immediate. So first, metabolic syndrome is still a simple and cheap tool we can use in primary care to sort out who is at higher risk. And second, the more components a patient has, the higher their risk — so we should use that when explaining things to patients. Third, adding SUA is a pragmatic enhancement where laboratory capacity exists; individuals meeting MetS‑UA criteria warrant intensified lifestyle and pharmacologic prevention targeting blood pressure, triglycerides, weight, and glycemia. Finally, health systems in Iraq could consider including SUA in MetS screening bundles in occupational and community clinics, alongside structured follow‑up pathways, to blunt the rising burden of T2DM and CVD. [16]. Furthermore, and is clear that Noncommunicable diseases (NCDs) represent the leading cause of illness and death in Iraq (Iraqi Ministry of Health, 2019). Current estimates indicate that approximately 30% of the population has hypertension, 14% has diabetes, and over 30% are classified as obese. Tobacco use also remains a major concern, with 38% of adult males reported as smokers, and worrying trends observed among adolescents, where 20% of boys and 9% of girls aged 13–15 years are already using tobacco products.[17] [18] [19]

5. CONCLUSION

In this prospective study of an Iraqi cohort, Metabolic Syndrome was a powerful and independent predictor of both incident Type 2 Diabetes and Cardiovascular Events over five years. The risk demonstrates an apparent dose-response effect, increasing significantly with each additional metabolic abnormality. Our findings strongly support the inclusion of Serum uric acid in the diagnostic criteria for MetS, as it significantly improves risk classification for both diabetic and cardiovascular outcomes in this population. These results highlight an urgent need for aggressive screening and multifaceted risk factor management to mitigatethe rising burden of cardiometabolic disease.

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