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Association of Systemic Inflammatory Indices and Adiposity Indices in a Rural T2DM Population of the Mandya Region.

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ABSTRACT:

Background: Low grade inflammation and central obesity plays a key role in development of pathogenesis of T2DM and its vascular complications. Cardiometabolic Index (CMI), closely related metabolic dysfunction and Systemic Immune-Inflammation Index, and Systemic Inflammatory Response Index provides the reflection of inflammatory state and immune response of the body. However, their combined relationship with CVD in T2DM remains inadequately characterized. The study aims to evaluate the association of CMI, SII, and SIRI with cardiovascular disease in patients with T2DM and to assess their diagnostic performance across different levels of glycaemic control.

Methodology: A total 250 study participants were included in this cross-sectional study. Biochemical and haematological parameters were recorded along with the anthropometric data. Standards formulas were used to calculate the indices; CMI, SII and SIRI and their association with cardiovascular risk assessment were analysed by correlation analysis and logistic regressions models. Their discriminative performance was assessed using receiver operating characteristic curve (ROC) analysis, with further evaluation with glycaemic control of the study participants.

Results: Progressive elevation was observed in median CMI, SII and SIRI from controls to T2DM and T2DM+CVD study groups. T2DM participants with poor glycaemic control (HbA1c $\geq 7\%$) exhibited significantly higher CMI compared with good glycaemic control T2DM participants ($p=0.008$). Logistic regression models showed that CMI was independently associated with CVD (OR=1.273, 95% CI: 1.103–1.469, $p<0.001$), combination with SII and SIRI significantly improved model performance, with $\log_{10}(\text{SII})$ (OR=14.58, $p<0.001$) and $\log_{10}(\text{SIRI})$ (OR=8.12, $p<0.001$) making them significant predictors. However, ROC analysis exhibited moderate discriminatory ability

for CMI (AUC=0.711), SII (AUC=0.639), and SIRI (AUC=0.700) among participants with HbA1c $\geq 7\%$.

Conclusion: Combined assessment of CMI, SII and SIRI reflects metabolic and inflammatory pathways associated with cardiovascular risk stratification, in patients with T2DM. These markers are accessible and cost-effective, underscores their potential as early biological indicators.

INTRODUCTION

Cardiovascular disease is the leading of cause of death in diabetic population. Type 2 Diabetes mellitus is characterized by impaired insulin action and sustained insulin resistance linked to various pathological changes in multiple systems (1). The global prevalence of T2DM have been increased over the years affecting around 500 million individuals worldwide (2). It's a systemic cardiometabolic syndrome which includes risk factors such as hyperglycemia, dyslipidemia, hypertension and renal impairment (3). Thus, T2DM contributes to microvascular or macrovascular complications such as coronary artery disease, heart failure, stroke, diabetic nephropathy and retinopathy (3).

In T2DM, one of the key factors is visceral adiposity in development of cardiometabolic dysfunction (4). However, to assess the overall obesity Body Mass Index (BMI) is used, several clinical drawbacks were noted, which mainly included the inability to assess the body fat distribution and also to distinguish between fat and lean muscle mass (5). As a result, those with normal BMI but high visceral fat accumulation also known as normal- weight obesity may be at significant risk for cardiometabolic diseases (5,6). Hence abdominal fat distribution is better captured by central obesity metrics such as waist circumference (WC) and waist-to-height ratio (WHtR) than by BMI (5). Cardiometabolic index is the product of the WHtR and the triglyceride to high density lipoprotein cholesterol ratio which provides an integrated assessment that combines central adiposity with dysregulation of lipid (5). CMI represents both visceral adiposity and metabolic dysfunction by combining the atherogenic dyslipidemia with abdominal fat distribution (5). Studies demonstrated that increased CMI levels are all correlated with insulin resistance, impaired fasting glucose, metabolic syndrome, incident type 2 diabetes, and cardiometabolic morbidity (5).

Chronic low-grade inflammation, a key biological factor that links visceral obesity, cardiometabolic burden and diabetic complications (4). As the visceral fat accumulation increases, dysfunctional adipose tissue and infiltrated macrophages release the pro-inflammatory mediators such as Interleukin-1 (IL-1), Interleukin-6 (IL-6), tumor necrosis factor and monocyte chemoattractant protein-1 (MCP-1) (2). This persistent signaling worse the systemic insulin resistance, by disturbing the insulin receptor pathways in peripheral tissues (2). Endothelial activation, vascular remodeling, pancreatic beta-cell disruption, microvascular damage is all observed with systemic inflammation and oxidative stress (1). This interrelated paradigm offers a biological justification for assessing markers of systemic inflammation in addition to adiposity-metabolic parameters.

Routine complete blood counts (CBCs) comprise of hematological parameters that are considered non-invasive surrogate markers for systemic immune-inflammatory state, using these inexpensive and useful indices such as Systemic Inflammatory Response Index (SIRI) and the Systemic Immune inflammation index (SII) were derived (7). Studies revealed that Insulin resistance, T2DM related microvascular and macrovascular complications are all independently linked to elevated SII and SIRI (7). Hematological parameters -neutrophils, monocytes are incorporated in the indices as they are one of the early innate responders' pro-inflammatory cytokines associated with vascular damage (7). Whereas platelets facilitate thrombosis, inflammatory signaling, endothelial adhesion, and cellular recruitment. Adaptive immunological surveillance is mediated by lymphocytes, and decreased immune protection is indicated by relative lymphopenia (7). By integrating three cell lines, SII and SIRI provide a steady depiction of systemic inflammatory status and are less sensitive to physiological fluctuations than single cell counts or two-cell ratios like NLR and PLR (7).

Although central obesity indices and lipid parameters are assessed independently against inflammatory markers, its association have not been thoroughly described. Therefore, the aim of the study is to investigate CMI in conjugation with SII and SIRI, to know how integrated cardiometabolic-adiposity stress translates onto cell-mediated systemic inflammation because visceral adiposity and metabolic dysregulation are strongly associated with systemic immune activation. Also, to examine whether these

indices are associated with the presence of cardiovascular complications after accounting for relevant demographic and glycaemic factors in T2DM participants.

METHODS AND METHODOLOGY

Study Design and Participants

This cross-sectional study included 250 study participants aged 35 to 65 years. Both men and women were included and categorized into three groups: healthy controls (n=50), patients with T2DM (n=100) and patients T2DM and coexisting with CVD (n=100). Participants with T1DM, autoimmune disorders, psychiatric disorders, primary hypertension, pregnant women and those with gestational diabetes (GDM), also individuals suffering from chronic diseases like cancer, end stage renal disease, thyroid disorders and liver diseases were excluded from the study.

Demographic and anthropometric data, including age, gender, height, and weight were collected. Laboratory investigations included neutrophil count, lymphocyte count, monocyte count, platelet count, glycated haemoglobin (HbA1c), fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Body mass index (BMI) and CMI were calculated from the recorded anthropometric and biochemical parameters. SII and SIRI were calculated using routinely investigated haematological parameters.

Following formulae are used to calculate the indices:

$CMI = TG \text{ (mmol/L)} / HDL-C \text{ (mmol/L)} \times WHtR$. (8) Where, $WHtR = \text{waist circumference (cm)} / \text{height (cm)}$

$SII = \text{platelet count} \times \text{neutrophil count} / \text{lymphocyte count}$ (9).

$SIRI = \text{neutrophil count} \times \text{monocyte} / \text{lymphocyte count}$ (9).

Statistical analysis

Normality was assessed using the Shapiro–Wilk test. Continuous variables were expressed as mean $\pm$ SD or median (IQR), as appropriate. CMI, SII, and SIRI were compared according to CVD status and glycaemic control (HbA1c $<7\%$ vs $\geq 7\%$) using appropriate parametric or non-parametric tests (10). Spearman's correlation was used to assess associations among CMI, SII, SIRI, and cardiometabolic parameters. Binary logistic regression was performed to evaluate their association with CVD, including interaction with HbA1c group. Log10-transformed SII and SIRI were used where appropriate. ROC analysis was performed separately for HbA1c $<7\%$ and $\geq 7\%$ to assess the discriminatory ability of CMI, SII, and SIRI. AUC, sensitivity, specificity, 95% CI, and Youden index were reported. A p-value <0.05 was considered statistically significant.

RESULTS

This cross-sectional study included 250 participants and were categorised into the three study groups, comprising 50 healthy controls, 100 participants with type 2 diabetes mellitus (T2DM), and 100 participants with T2DM with cardiovascular disease (CVD). The descriptive characteristics of the study participants are presented in Table 1. variables are presented as median with interquartile range (IQR).

Table 1: Descriptive characteristics of the study groups

Group/ Variables	Controls (n=50)	T2DM (n=100)	T2DM+CVD (n=100)
Age (Years)	51.5(16.8)	56(16.3)	56(13.3)
Weight (Kg)	71.0 (7.0)	75.0 (11.3)	78.0 (10.0)
Height (cm)	168 (13.0)	164 (17.0)	162 (10.0)
WC (cm)	75.0 (12.0)	92.0 (13.5)	95.5 (15.3)
FPG (mg/dl)	103 (16.8)	166 (89.5)	159 (41.8)

HbA1c (%)	5.50 (0.60)	7.40 (2.53)	8.25 (2.33)
TC (mg/dl)	156 (49.8)	193 (69.3)	219 (46.8)
TG (mg/dl)	112 (40.5)	187 (112)	224 (82.3)
HDL-C (mg/dl)	47(13.3)	39.5(15)	33(9.5)
LDL-C (mg/dl)	106(46.5)	115(65.5)	133(44.5)
CMI	1.10 (0.65)	2.70 (1.85)	4.05 (2.45)
BMI (kg/m ²)	25.6 (3.40)	28.5 (5.80)	29.3 (5.22)
RBC (×10 ⁶ /μL)	4.97 (0.56)	5.16 (0.73)	4.82 (0.92)
Hb (g/dL)	13.6 (2.65)	13.5 (2.75)	13.9 (2.93)
Haematocrit (%)	39.9 (6.88)	43.3 (7.72)	41.5 (7.70)
WBC (×10 ³ /μL)	7.83 (2.70)	8.43 (3.12)	9.12 (2.67)
Platelets (×10 ³ /μL)	267 (138)	271 (119)	297 (127)
Neutrophils (×10 ³ /μL)	4.60 (1.95)	5.20 (2.10)	5.80 (2.13)
Lymphocytes (×10 ³ /μL)	2.45 (1.38)	2.50 (1.60)	2.35 (0.85)
Monocytes (×10 ³ /μL)	0.400 (0.375)	0.500 (0.300)	0.600 (0.300)
SII	527 (416)	541 (366)	720 (558)
SIRI	0.790 (0.650)	0.995 (0.782)	1.41 (1.31)

Note: Data are presented as median (interquartile range). Continuous variables were tested for normality using the Shapiro–Wilk test.

WC=Waist circumference; FPG= Fasting Plasma Glucose; PPPG= Post Prandial Plasma Glucose; HbA1c= Glycated Haemoglobin; TC= Total Cholesterol; TG= Triglycerides; HDL-C= High Density Lipoprotein Cholesterol; LDL-C= Low Density Lipoprotein Cholesterol; CMI= Cardiometabolic Index; BMI= Body mass index; WBC=White Blood Cells; SII= Systemic Immune inflammation index; SIRI= systemic Inflammatory Response Index.

Distribution of CMI, SII and SIRI according to glycaemic control

A total of 200 participants were Type 2 diabetic, among them 51 participants had good glycaemic control (HbA1c <7%) and 149 participants had poor glycaemic control (HbA1c ≥7%). CMI was observed to be increased in the in the HbA1c ≥7% group (4.09 ± 2.40; median 3.50) compared to HbA1c <7% group (mean 3.30 ± 2.36; median 2.80). Also mean SII and SIRI were 780.52 ± 517.57 and 1.70 ± 1.53 respectively in the HbA1c ≥7% group compared to good glycaemic control group (SII= 693.88 ± 490.42; SIRI= 1.57 ± 1.26). Normality was assessed using Shapiro-Wilk test in both the groups, CMI, SII and SIRI showed significant departures, whereas BMI was normally distributed in the good glycaemic control group, but showed statistically significant Shapiro–Wilk result in the HbA1c ≥7% group.

Table 2. CMI, BMI, SII and SIRI according to HbA1c category

Variable	HbA1c <7% (n=51)	HbA1c ≥7% (n=149)	Mann–Whitney U / P Value
CMI, mean ± SD; median	3.30 ± 2.36; 2.80	4.09 ± 2.40; 3.50	2854; p= 0.008
BMI, mean ± SD; median	28.12 ± 3.60; 27.90	29.60 ± 4.35; 29.90	2978; p= 0.021
SII, mean ± SD; median	693.88 ± 490.42; 570.80	780.52 ± 517.57; 649.40	3364; p= 0.223
SIRI, mean ± SD; median	1.57 ± 1.26; 1.17	1.70 ± 1.53; 1.21	3557; p= 0.497

p-values are from the Mann–Whitney U output. The alternative hypothesis was HbA1c <7% ≠ HbA1c ≥7%.

Correlation analysis

Spearman correlation analysis among the 200 participants showed a weak positive correlation of HbA1c with CMI ($\rho=0.141$, $p=.046$) and BMI ($\rho=0.190$, $p=.007$). CMI was also positively correlated with BMI ($\rho=0.218$, $p=.002$). No significant correlation was observed between HbA1c and SII ($\rho=0.061$, $p=.390$), HbA1c and SIRI ($\rho=0.060$, $p=.402$), CMI and SII ($\rho=0.048$, $p=.502$), or CMI and SIRI ($\rho=0.111$, $p=.117$). SII and SIRI showed a strong positive correlation ($\rho=0.673$, $p<.001$).

Table 3. Spearman correlation matrix

Pair	Spearman's rho	p-value
HbA1c–CMI	0.141	0.046
HbA1c–BMI	0.190	0.007
CMI–BMI	0.218	0.002
HbA1c–SII	0.061	0.390
HbA1c–SIRI	0.060	0.402
CMI–SII	0.048	0.502
CMI–SIRI	0.111	0.117
BMI–SII	0.043	0.549
BMI–SIRI	0.019	0.791
SII–SIRI	0.673	<.001

Spearman's rank correlation coefficient (ρ) was used to assess correlations between variables. A two-tailed p-value <0.05 was considered statistically significant. CMI, Cardiometabolic Index; BMI, Body Mass Index; SII, Systemic Immune-Inflammation Index; SIRI, Systemic Inflammation Response Index.

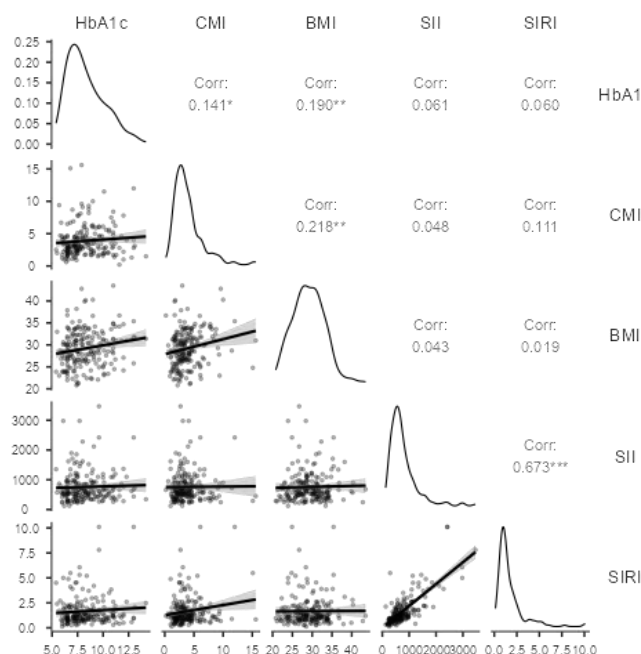


Figure 1: Spearman correlation of CMI with systemic inflammatory indices among T2DM participants.

Binary logistic regression for CVD status

Binary logistic regression was used to examine the association of CMI and inflammatory indices with CVD status (CVD=YES versus NO) among the 200 participants with T2DM. In the model containing CMI alone, CMI was significantly associated with CVD status (likelihood-ratio $\chi^2=13.20$, $df=1$, $p<.001$; McFadden $R^2=0.0476$). The regression coefficient for CMI was 0.241, corresponding to an odds ratio (OR) of 1.273 (95% CI 1.103–1.469; $p<.001$). A model including CMI and HbA1c showed a similar association for CMI (OR 1.266, 95% CI 1.097–1.461; $p=.001$), whereas HbA1c was not independently associated with CVD status (OR 1.079, 95% CI 0.921–1.265; $p=.348$).

In a model containing CMI, log10-transformed SII and HbA1c, both CMI and log10(SII) were significantly associated with CVD status. The CMI coefficient was 0.2524 (OR 1.287; 95% CI 1.113–1.489; $p<.001$), while log10(SII) had a coefficient of 2.6795 (OR 14.58; 95% CI 3.756–56.58; $p<.001$). HbA1c was not significant (OR 1.076; $p=.387$). The corresponding model had McFadden $R^2=0.114$. In the model containing CMI, log10(SIRI) and HbA1c, CMI remained significant (OR 1.253; 95% CI 1.082–1.451; $p=.003$), and log10(SIRI) was also significant (OR 8.117; 95% CI 2.631–25.041; $p<.001$), whereas HbA1c was not significant (OR 1.076; $p=.385$); McFadden $R^2=0.106$.

Table 4. Logistic regression models among T2DM participants

Model / predictor	β	OR (95% CI)	p	McFadden R^2
CMI	0.241	1.273 (1.103–1.469)	<.001	0.0476
CMI + HbA1c: CMI	0.236	1.266 (1.097–1.461)	0.001	0.0508
CMI + HbA1c: HbA1c	0.076	1.079 (0.921–1.265)	0.348	0.0508

Model / predictor	β	OR (95% CI)	p	McFadden R ²
CMI + log ₁₀ (SII) + HbA1c: CMI	0.252	1.290 (1.113–1.489)	<0.001	0.114
CMI + log ₁₀ (SII) + HbA1c: log ₁₀ (SII)	2.680	14.58 (3.756–56.58)	<0.001	0.114
CMI + log ₁₀ (SII) + HbA1c: HbA1c	0.073	1.076 (0.911–1.271)	0.387	0.114
CMI + log ₁₀ (SIRI) + HbA1c: CMI	0.225	1.253 (1.082–1.451)	0.003	0.106
CMI + log ₁₀ (SIRI) + HbA1c: log ₁₀ (SIRI)	2.094	8.12 (2.631–25.04)	<0.001	0.106
CMI + log ₁₀ (SIRI) + HbA1c: HbA1c	0.073	1.076 (0.912–1.271)	0.385	0.106

β , regression coefficient; OR, odds ratio; CI, confidence interval. CVD status was coded as YES versus NO. SII and SIRI were log₁₀-transformed for regression because of their skewed distributions.

Interaction with glycaemic control

Interaction models examined whether the association between the indices and CVD status differed according to HbA1c category (<7% versus $\geq$ 7%). The CMI $\times$ HbA1c-group interaction was not statistically significant (β =0.0604, SE=0.165, p =.714). The log₁₀(SII) $\times$ HbA1c-group interaction was also not significant (β =−1.25, SE=1.57, p =.427), and the log₁₀(SIRI) $\times$ HbA1c-group interaction was not significant (β =1.219, SE=1.150, p =.289). Thus, the supplied models did not demonstrate statistically significant effect modification by HbA1c category.

Receiver operating characteristic analysis

Among participants with HbA1c $\geq$ 7% (n =149), CMI showed an AUC of 0.711 (95% CI 0.625–0.797; p <.001), SII an AUC of 0.639 (95% CI 0.550–0.728; p =.002), and SIRI an AUC of 0.700 (95% CI 0.614–0.786; p <.001). The corresponding Youden-derived cut-offs were 2.85 for CMI, 543.1 for SII, and 1.29 for SIRI.

Among participants with HbA1c <7% (n =51), CMI had an AUC of 0.700 (95% CI 0.549–0.851; p =.009), while SII had an AUC of 0.729 (95% CI 0.586–0.872; p =.002). SIRI had an AUC of 0.610 (95% CI 0.448–0.773; p =.183). The corresponding cut-offs were 3.5 for CMI, 565.45 for SII, and 2.27 for SIRI.

Table 5. ROC characteristics stratified by HbA1c category

HbA1c group	Marker	AUC (95% CI)	p value	Cut-off	Sensitivity	Specificity	Accuracy
$\geq$ 7% (n =149)	CMI	0.711 (0.625–0.797)	<.001	2.85	83.75%	55.07%	70.47%
	SII	0.639 (0.550–0.728)	0.002	543.1	73.75%	49.28%	62.42%

HbA1c group	Marker	AUC (95% CI)	p value	Cut-off	Sensitivity	Specificity	Accuracy
	SIRI	0.700 (0.614–0.786)	<.001	1.29	63.75%	73.91%	68.46%
<7% (n=51)	CMI	0.700 (0.549–0.851)	0.009	3.50	50.00%	83.87%	70.59%
	SII	0.729 (0.586–0.872)	0.002	565.45	80.00%	67.74%	72.55%
	SIRI	0.610 (0.448–0.773)	0.183	2.27	35.00%	93.55%	70.59%

Cut-offs were selected using the Youden index. AUC, area under the ROC curve; CI, confidence interval.

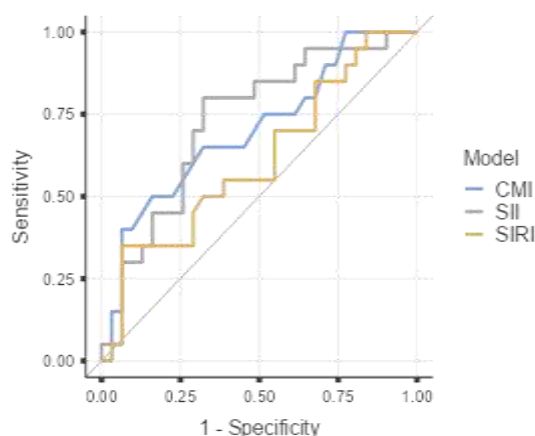


Figure 2A

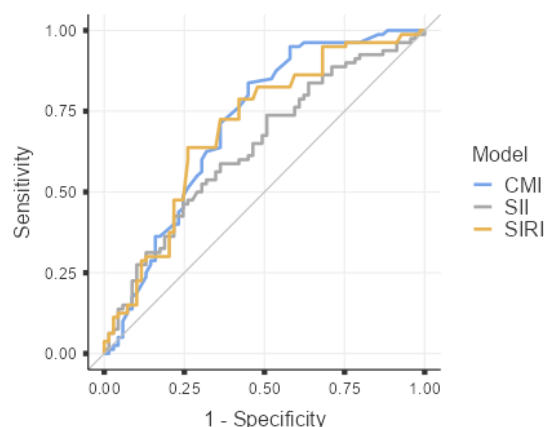


Figure 2B

Figure 2A: ROC curves of CMI, SII and SIRI for discrimination of CVD status among participants with HbA1c <7% (n=51).

Figure 2B: ROC curves of CMI, SII and SIRI for discrimination of CVD status among participants with HbA1c ≥7% (n=149).

DISCUSSION

The present study evaluated the relationship of the CMI with the systemic inflammatory indices SII and SIRI in relation to CVD status among patients with T2DM, with further assessment according to glycaemic control. The principal findings were that CMI was significantly associated with CVD status and showed a progressive increase with cardiometabolic severity, while SII and SIRI reflected an additional inflammatory component.

Firstly, significant elevation of CMI was observed in participants with HbA1c ≥7%, confirming its biological relationship with visceral adiposity and atherogenic dyslipidaemia. As there is integration of waist-to-height ratio with TG/HDL-C in CMI, this shows the adiposity and lipid related metabolic abnormalities. Here CMI exhibited a progressive increase across the study

groups and was significantly associated with CVD status in univariate logistic regression ($OR = 1.273$, $p < .001$). This finding is consistent with the observations of Huang et al. (2025), who reported associations between combined lipid-adiposity indices, including TyG-WHTR and TG/HDL-C-related measures, and cardiovascular events, stroke, and mortality across the UK Biobank, US NHANES (11). Marra et al. (2024) also reported elevated lipid-HDL ratios and cardiometabolic scores among individuals with metabolic syndrome (12).

The relationship between atherosclerosis and T2DM are linked by persistent inflammatory activation. Haematological parameters- Neutrophils, monocytes and lymphocytes contributes to changes in immune regulation system and vascular injury, as these are the main components used to compute SII and SIRI that provides information on systemic cellular inflammation. This aligns with study by Kong et al. (2023) and Xia et al. (2023), reported the association of SII, SIRI with adverse cardiovascular outcomes (13,14).

In the present study, CMI demonstrated only weak and non-significant correlations with SII ($\rho = 0.048$, $p = .502$) and SIRI ($\rho = 0.111$, $p = .117$). SII and SIRI were also not significantly correlated with HbA1c. These findings suggest that CMI and the haematological inflammatory indices may capture different biological components of cardiovascular risk. CMI primarily reflects the visceral adiposity-lipid metabolic axis, whereas SII and SIRI reflect the systemic cellular inflammatory axis. Thus, the absence of a strong correlation between these indices does not preclude their simultaneous association with CVD. Instead, it may indicate that metabolic dysfunction and systemic inflammation operate as partially independent components of cardiometabolic pathology (15). This interpretation is consistent with Kong et al. (2023), who reported minimal relationships between SII/SIRI and baseline metabolic characteristics (13). Baş Aksu et al. (2024) similarly reported no significant association between SII and HbA1c or BMI in patients categorized according to glycaemic control (15), while Marra et al. (2024) observed differences between the metabolic associations of lipid-HDL indices and SII (12). The present findings therefore support the assessment of metabolic and inflammatory indices as complementary rather than interchangeable markers.

Also, findings from multivariable logistic regression showed addition of Log10_SII to CMI and HbA1c increased McFadden's R^2 from 0.051 to 0.114, with both CMI ($OR = 1.290$, $p < .001$) and Log10_SII ($OR = 14.580$, $p < .001$) remaining significant. Similarly, incorporation of Log10_SIRI increased McFadden's R^2 to 0.106, while CMI ($OR = 1.253$, $p = 0.003$) and Log10_SIRI ($OR = 8.117$, $p < 0.001$) remained significant. These findings indicate that SII and SIRI contributed additional information to models containing CMI and HbA1c. Importantly, this complementary contribution occurred despite the weak correlations between CMI and the inflammatory indices. This supports the concept that metabolic and inflammatory measurements capture different dimensions of the underlying cardiovascular phenotype. The findings are compatible with observations from Huang et al. (2025), in which systemic inflammatory markers were reported to contribute to the relationship between metabolic abnormalities and cardiovascular outcomes (11). However, because the present study is cross-sectional, the observed associations should be interpreted as statistical associations rather than evidence that CMI or inflammatory indices independently cause or temporally precede CVD.

The study further evaluated whether the diagnostic characteristics of these indices differed according to glycaemic control. Among participants with HbA1c $\geq 7\%$ ($n = 149$), CMI at a cut-off of ≥ 2.85 demonstrated a sensitivity of 83.75% and an accuracy of 70.47%. Among participants with HbA1c $< 7\%$ ($n = 51$), SIRI at a cut-off of ≥ 2.27 demonstrated a specificity of 93.55% and a positive likelihood ratio of 5.425. These findings demonstrate differences in the operating characteristics of the indices across the two glycaemic strata. However, formal interaction testing did not demonstrate statistically significant effect modification. The interaction terms for CMI $\times$ HbA1c group ($p = .714$), Log10_SII $\times$ HbA1c group ($p = .427$), and Log10_SIRI $\times$ HbA1c group ($p = 0.289$) were all non-significant. Amalia et al. (2023) similarly reported that while poor glycaemic control exacerbates inflammatory and lipid parameters, cellular risk markers remain associated with cardiovascular risk across glycaemic categories (16,17).

Thus, although different cut-offs and diagnostic characteristics were observed within the HbA1c strata, the present data do not provide statistical evidence that the association between these indices and CVD status is significantly modified by the HbA1c threshold of 7%. The subgroup findings should therefore be interpreted as exploratory differences in diagnostic performance rather than evidence of a statistically established interaction.

Clinical relevance and interpretation

Taken together, the findings indicate that CMI, SII, and SIRI provide information on distinct but complementary aspects of cardiometabolic risk. CMI reflects visceral adiposity and atherogenic lipid burden, whereas SII and SIRI capture systemic cellular inflammatory activity. The weak correlations between these indices, together with the improved logistic regression model fit after incorporating inflammatory indices, support their complementary nature.

At the same time, the absence of significant differences in ROC AUCs indicates that the present study does not establish one index as superior to another for discriminating CVD status. Their potential value may therefore lie in their combined characterization of metabolic and inflammatory burden rather than in the use of any single index as a standalone marker.

Strengths and limitations

The major strength of the study is the simultaneous assessment of metabolic and inflammatory indices within the same T2DM cohort, together with evaluation according to glycaemic control. The use of multivariable logistic regression, correlation analysis, interaction testing, and formal DeLong AUC comparisons provides a comprehensive assessment of the relationships among CMI, SII, SIRI, glycaemic control, and CVD status.

The study also has limitations. Its cross-sectional design prevents assessment of temporal or causal relationships. The single-centre sample of 200 participants may limit the ability to detect smaller interaction effects or differences between AUCs, particularly in the smaller HbA1c <7% subgroup. In addition, CBC-derived inflammatory indices may be influenced by acute or subclinical infection, physiological stress, and medication use, which may introduce variability in SII and SIRI.

CONCLUSION

Overall, the present findings support the relevance of CMI, SII, and SIRI as complementary markers of metabolic and inflammatory burden in T2DM patients with CVD. CMI demonstrated a significant association with CVD, while SII and SIRI provided additional information when incorporated into multivariable models. However, the lack of significant differences in ROC AUCs and the absence of significant HbA1c interaction effects indicate that these findings should be interpreted as evidence of complementary association rather than superiority or differential performance according to glycaemic control. Prospective multicentre studies are required to determine whether combined assessment of these readily available indices provides incremental cardiovascular risk prediction beyond established clinical risk factors.

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