ASSOCIATION WITH INCIDENCE OF ISCHEMIC HEART DISEASE BASED ON THE ESTIMATED GLOMERULAR FILTRATION RATE IN THE POPULATION OF THE THREE SOUTHERN BORDER PROVINCES OF THAILAND

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Abstract

Background: Declining kidney function, as reflected by a reduced estimated glomerular filtration rate (eGFR), has been associated with an increased risk of ischemic heart disease (IHD). However, limited evidence is available in the population residing in Thailand's three southern border provinces.

Objective: This study aimed to examine the association between estimated eGFR and the incidence of IHD in the population of Thailand's three southern border provinces.

Methods: A retrospective cohort study was conducted using electronic medical records from three government hospitals between October 1, 2018, and September 30, 2023. Adults aged 30 years or older with baseline eGFR data were categorized into five groups based on their eGFR levels. The outcome was incident IHD, identified using ICD-10 codes. Cox proportional hazards regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs), adjusting for relevant covariates.

Results: Among 16,763 participants followed for a total of 53,360 person-years, 746 developed IHD. The cumulative incidence was 4.5% (95% CI: 4.0–5.0%), and the incidence density was 13.98 cases per 1,000 person-years. A significant inverse relationship was observed between eGFR and IHD incidence ($p < 0.001$). Compared with participants with eGFR ≥90.00 mL/min/1.73 m², the adjusted HRs for IHD were 1.89 (95% CI: 1.58-2.25) for eGFR 60.00-89.99, 2.65 (95% CI: 2.16-3.24) for 30.00–59.99, 4.96 (95% CI: 3.62-6.81) for 15.00-29.99, and 3.74 (95% CI: 2.34-5.99) for <15.00 mL/min/1.73 m². A graded increase in IHD risk was observed across lower eGFR groups. Other significant risk factors included older age, males, higher systolic blood pressure, and atrial fibrillation, while higher high-density lipoprotein cholesterol (HDL-C) levels were associated with a reduced risk of IHD.

Conclusion: Reduced eGFR was independently associated with a higher risk of IHD, even among individuals with mildly impaired kidney function. These findings support the potential role of eGFR in cardiovascular risk assessment and the development of targeted prevention strategies in high-risk populations.

Keywords: estimated glomerular filtration rate (eGFR), ischemic heart disease (IHD), chronic kidney disease (CKD), cardiovascular risk, retrospective cohort study

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Introduction

Ischemic heart disease (IHD), or coronary heart disease (CHD), is characterized by reduced myocardial blood flow due to coronary artery narrowing or obstruction.[1] According to the American Heart Association (AHA), over 244 million people were affected by IHD in 2020, resulting in approximately 8.95 million deaths worldwide.[2] The World Health Organization (WHO) also reported that IHD was the leading cause of death globally in 2019, accounting for 16% of all deaths.[3] In the United States, the prevalence of IHD was estimated at 7.1% among adults aged 20 years and older during 2017-2020. In contrast, the United Kingdom and China reported prevalence rates of 4% and over 11 million cases, respectively.[2,4,5] In Thailand, IHD has remained one of the top three causes of death, with Pattani Province recording one of the highest age-adjusted mortality rates at 53.29 per 100,000 population in 2021.[6] More recent age-standardized data show a rising trend in IHD mortality between 2010 and 2021.[7]

The estimated glomerular filtration rate (eGFR) reflects the kidneys' ability to filter waste products from the body through urine. Changes in eGFR, whether transient or chronic, indicate underlying kidney dysfunction.[8] It is now well recognized that eGFR and proteinuria are important predictive factors for cardiovascular disease (CVD).[9–11] Previous studies have indicated that a decline in eGFR to below 60 mL/min/1.73 m² is associated with an increased risk of coronary artery disease.[12–14] Park et al. demonstrated that a lower eGFR was significantly associated with a higher incidence of IHD, with the risk increasing from the second quartile (eGFR: 71.07-83.16 mL/min/1.73 m²; adjusted hazard ratio [aHR] 1.15, 95% confidence interval [CI] 1.04-1.27) to the first quartile (eGFR: ≤71.07 mL/min/1.73 m²; aHR 1.31, 95% CI 1.18–1.44).[15] Conversely, Ichii et al. found that the association between eGFR and coronary artery calcification, a precursor of coronary artery stenosis, remains inconclusive.[16] Additionally, Kirstin et al., involving 10,489 individuals from the general population, indicated that lower eGFR levels were not associated with an increased risk of myocardial infarction, ischemic heart disease, or premature death.[17] Therefore, the prediction of IHD based on changes in eGFR remains inconclusive. Moreover, most previous studies[18–20] have focused on specific populations, such as those with diabetes, CKD, or high cardiovascular risk, which may limit their generalizability.

The Medical and Health Data Center of the Ministry of Public Health, Thailand, reported that the three southern border provinces—designated as a special development zone—continue to face a rising burden of non-communicable diseases (NCDs), especially cardiovascular diseases, which remain among the leading causes of death in this region. Pattani Province, in particular, has shown a worrisome trend.[21] Compared to other parts of Thailand, this region is characterized by a relatively high burden of NCDs, limited healthcare accessibility, and socio-political challenges, which may impact disease prevalence and health outcomes. Although eGFR is widely used to predict cardiovascular outcomes, data specific to populations in these provinces remain limited. Therefore, this study aimed to investigate the association between eGFR and IHD in this setting to support risk prediction based on kidney function. The findings could inform targeted screening and prevention

strategies tailored to the high-risk population of Thailand's southern border region.

Methods

Study Design

A retrospective cohort study was conducted to predict the risk of ischemic heart disease (IHD) based on the eGFR among the population of Thailand's three southern border provinces. The study included individuals who received services at government hospitals under the Office of the Permanent Secretary, Ministry of Public Health, between October 1, 2018, and September 30, 2023. All participants were followed until either a diagnosis of IHD was made or until the end of the study period on September 30, 2024. Data were collected from hospital electronic databases. The study was approved by the Human Research Ethics Committee of the Narathiwat Provincial Public Health Office, Ministry of Public Health (approval number 24/2567; June 24, 2024).

Study Population

All patients who received services at government hospitals selected through simple random sampling (SRS) were included between October 1, 2018, and September 30, 2023. The participating hospitals were Naradhiwas Rajanagarindra Hospital (a regional referral hospital), Yaha Crown Prince Hospital (a secondary hospital), and Khokpho Hospital (a community hospital). These hospitals were selected to represent various healthcare levels and geographic coverage across the three southern border provinces. The inclusion criteria were: (1) patients aged over 30 years, (2) availability of complete general examination data, including sex, age, weight, height, and blood pressure, and (3) availability of baseline eGFR data at study initiation. Patients were included regardless of visit type—outpatient department (OPD), inpatient department (IPD), or emergency room (ER)—provided that complete data were available. All participants were alive and free of ischemic heart disease (IHD) at the time of study entry, and all had an eGFR value documented before any IHD diagnosis. The exclusion criterion was a prior diagnosis of IHD before study entry. A total of 16,763 eligible patients were included in the study, and all were analyzed without further sampling.

Data Collection and Measurements

Data were collected from the electronic medical record databases of the participating hospitals using a case record form, which included: (1) baseline patient characteristics (age, sex, smoking history, alcohol consumption history); (2) past medical history and comorbidities diagnosed by a physician or inferred from relevant medication use, including hypertension (ICD-10: I10–I15), diabetes mellitus (ICD-10: E10–E14), dyslipidemia (ICD-10: E78), and atrial fibrillation (ICD-10: I48); (3) physical examination findings (weight, height, systolic and diastolic blood pressure); (4) laboratory data (fasting plasma glucose, glycated hemoglobin [HbA1c], eGFR, triglycerides, total cholesterol, high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C], and urinary microalbumin); (5) medication use (antihypertensive agents, antidiabetic agents, and lipid-lowering agents); and (6) follow-up data (date of enrollment, date of event occurrence, and date of follow-up completion).

The eGFR was calculated by laboratory medical technologists at each hospital using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation[22] as follows: $eGFR = 142 \times \min(SCr/\kappa, 1)\alpha \times \max(SCr/\kappa, 1)\text{-}1.200 \times 0.9938Age \times 1.012$ [if female], where κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of SCr/κ or 1, and max indicates the maximum of SCr/κ or 1.

Definition of Outcomes

The primary outcome of this study was the first occurrence of IHD during the follow-up period. Participants were followed up from the date of cohort entry until the diagnosis of IHD, death from any cause, or the end of the study period on September 30, 2024, whichever occurred first. Newly diagnosed cases of IHD

were recorded by physicians in the hospital electronic medical records. Diagnoses were based on ICD-10 codes I20 to I25, according to the International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10).23 These codes represented the composite outcome and included: I20: Angina pectoris; I21: Acute myocardial infarction; I22: Subsequent myocardial infarction; I23: Certain current complications following acute myocardial infarction; I24: Other acute ischemic heart diseases and I25: Chronic ischemic heart disease.

Statistical Analysis

Participants were categorized into five groups according to the definitions of chronic kidney disease (CKD) stages: Group 1 (eGFR ≥ 90.00 mL/min/1.73 m²), Group 2 (eGFR 60.00–89.99 mL/min/1.73 m²), Group 3 (eGFR 30.00–59.99 mL/min/1.73 m²), Group 4 (eGFR 15.00–29.99 mL/min/1.73 m²), and Group 5 (eGFR < 15.00 mL/min/1.73 m²). Continuous variables with a normal distribution were presented as means and standard deviations, while those with a non-normal distribution were presented as medians and interquartile ranges (IQRs). Categorical variables were summarized using frequencies and percentages. Person-years were calculated as the sum of follow-up time from study entry to the diagnosis of IHD, death, or the end of the study period on September 30, 2024.

The Cox proportional hazards model was used to analyze the association between eGFR categories and IHD incidence. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Group 1 as the reference. Covariates for the multivariable model were selected based on univariable analysis and assessed for multicollinearity using the variance inflation factor (VIF). The final model included age, sex, smoking status, hypertension (HT), atrial fibrillation (AF), systolic blood pressure (SBP), and high-density lipoprotein cholesterol (HDL-C). Fasting blood sugar (FBS) and urinary microalbuminuria were excluded due to a lack of statistical significance; however, they were included in a sensitivity analysis. The sensitivity analysis reintroduced FBS and microalbuminuria into the multivariable model, confirming the robustness of the primary results. The proportional hazards assumption was tested using log-minus-log survival plots, and no violations of the assumption were detected. All analyses were conducted using SPSS version 23.0 (IBM Corp., Armonk, NY). A p-value < 0.05 was considered statistically significant.

Results

A total of 16,763 participants were followed over a cumulative period of 53,360 person-years, with a median follow-up time of 3 person-years (IQR: 1.00–5.00) between 2018 and 2024. During the follow-up period, 746 participants developed ischemic heart disease (IHD), corresponding to a cumulative incidence of 4.5% (95% CI: 4.0–5.0%) and an incidence density of 13.98 cases per 1,000 person-years.

Table 1 presents the baseline characteristics, major comorbidities, and laboratory findings of the study population categorized by eGFR levels into five groups according to chronic kidney disease (CKD) staging. There was a clear trend of older age, higher prevalence of hypertension, diabetes, and atrial fibrillation, and lower HDL-C levels in the lower eGFR groups. The overall mean age of the participants was 57.1 years (SD=12.86), and 60.2% were female. Participants with lower eGFR categories generally exhibited worse laboratory profiles than those with normal kidney function.

Univariable Cox regression analysis revealed a significant inverse association between eGFR and the incidence of IHD ($p < 0.001$), with a graded increase in risk across decreasing eGFR categories. Compared with participants in the reference group (eGFR ≥90.00 mL/min/1.73 m²), the unadjusted hazard ratios (HRs) were significantly higher in the lower eGFR groups: 1.89 (95% CI: 1.58–2.25) for 60.00–89.99, 2.65 (95% CI: 2.16–3.24) for 30.00–59.99, 4.96 (95% CI: 3.62–6.81) for 15.00–29.99 and 3.74 (95% CI: 2.34–5.99) for <15.00 mL/min/1.73 m².

Table 1. Baseline characteristics of study participants according to quartile groups of eGFR levels (N=16,763)

Characteristics	Overall (n= 16,763)		Group 1 (≥90.00) (n= 8,035)		Group 2 (60.00-89.99) (n= 5,867)		Group 3 (30.00-59.99) (n= 2,173)		Group 4 (15.00-29.99) (n= 396)		Group 5 (<15.00) (n= 292)	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Person-year												
Total	53,360		25,422		18,985		7,307		1,093		555	
Median (IQR)	3.00 (1.00-5.00)		3.00 (1.00-5.00)		3.00 (1.00-5.00)		3.00 (1.00-6.00)		2.00 (1.00-5.00)		1.00 (1.00-3.00)	
Age (year)												
Mean (±SD)	57.06 (12.86)		50.57 (10.37)		61.56 (11.49)		67.54 (11.74)		64.76 (12.69)		56.80 (13.57)	
Gender												
Male	6,664	(39.8)	2,375	(29.6)	2,815	(48.0)	1,151	(53.0)	187	(47.2)	136	(46.6)
Female	10,099	(60.2)	5,660	(70.4)	3,052	(52.0)	1,022	(47.0)	209	(52.8)	156	(53.4)
Smoking												
Yes	14,292	(85.3)	6,803	(84.7)	4,972	(84.7)	1,874	(86.2)	365	(92.2)	278	(95.2)
No	2,471	(14.7)	1,232	(15.3)	895	(15.3)	299	(13.8)	31	(7.8)	14	(4.8)
Alcohol consumption												
Yes	14,300	(85.3)	6,803	(84.7)	4,974	(84.8)	1,873	(86.2)	367	(92.7)	283	(96.9)
No	2,463	(14.7)	1,232	(15.3)	893	(15.2)	300	(13.8)	29	(7.3)	9	(3.1)
Weight (Kg)												
Median (IQR)]	62.80 (54.00-72.00)		63.00 (55.00-72.40)		62.80 (54.40-71.30)		61.00 (53.00-70.00)		61.85 (52.43-70.00)		58.15 (49.73-69.08)	
BMI (kg/m^2)												
Median (IQR)]	24.84 (21.95-28.06)		25.31 (22.27-28.72)		24.62 (21.91-27.56)		24.18 (21.42-27.37)		24.16 (21.46-27.52)		22.82 (20.05-26.64)	
SBP (mmHg)												
Median (IQR)]	137.00 (124.00-149.00)		134.00 (122.00-146.00)		138.00 (126.00-149.00)		140.00 (128.00-153.00)		140.00 (127.00-154.00)		145.00 (127.00-160.00)	
DBP (mmHg)												
Median (IQR)]	78.00 (70.00-87.00)		79.00 (70.00-87.00)		78.00 (69.00-86.00)		77.00 (67.00-85.00)		74.00 (66.00-85.00)		77.00 (69.00-88.75)	
HT												
Yes	10,462	(62.4)	4,185	(52.1)	3,915	(66.7)	1,780	(81.9)	349	(88.1)	233	(79.8)
No	6,301	(37.6)	3,850	(47.9)	1,952	(33.3)	393	(18.1)	47	(11.9)	59	(20.2)
DM												
Yes	4,383	(26.1)	2,282	(28.4)	1,189	(20.3)	651	(30.0)	157	(39.6)	104	(35.6)
No	12,380	(73.9)	5,753	(71.6)	4,678	(79.7)	1,522	(70.0)	239	(60.4)	188	(64.4)
DLP												
Yes	9,334	(55.7)	4,051	(50.4)	3,513	(59.9)	1,413	(65.0)	242	(61.1)	115	(39.4)
No	7,429	(44.3)	3,984	(49.6)	2,354	(40.1)	760	(35.0)	154	(38.9)	177	(60.6)
AF												
Yes	193	(1.2)	44	(0.5)	99	(1.7)	47	(2.2)	2	(0.5)	1	(0.3)
No	16,570	(98.8)	7,991	(99.5)	5,768	(98.3)	2,126	(97.8)	394	(99.5)	291	(99.7)
Total cholesterol (mg/dL) Mean (±SD)	208.51 (48.46)		210.60 (46.82)		207.73 (49.44)		201.86 (50.43)		206.31 (57.78)		212.37 (56.80)	
Triglyceride (mg/dL) Median (IQR)	126.00 (92.00-176.00)		126.00 (91.00-176.00)		124.00 (91.00-173.00)		131.00 (95.00-186.00)		135.50 (101.00-201.50)		145.50 (107.75-215.75)	
HDL (mg/dL) Median (IQR)	49.80 (42.00-58.70)		50.00 (42.70-59.10)		49.90 (42.00-58.80)		47.40 (40.30-56.40)		46.60 (37.05-54.80)		43.60 (34.95-51.35)	
LDL (mg/dL) Mean (±SD)	128.82 (44.24)		130.71 (43.09)		128.24 (45.24)		122.52 (44.38)		127.51 (50.51)		127.80 (50.81)	
FBS (mg/dL) Median (IQR)	103.00 (94.00-121.00)		103.00 (94.00-127.00)		101.00 (93.00-113.00)		105.00 (94.25-125.00)		116.00 (98.00-134.50)		117.00 (91.10-164.00)	
HbA1C (%) Median (IQR)	7.70 (6.50-9.50)		8.19 (6.80-10.30)		7.30 (6.30-8.60)		7.40 (6.30-8.80)		6.60 (5.90-8.05)		6.05 (5.60-7.56)	

Table 1. Baseline characteristics of study participants according to quartile groups of eGFR levels (N= 16,763) (cont.)

Characteristics	Overall (n= 16,763)		Group 1 (≥90.00) (n= 8,035)		Group 2 (60.00-89.99) (n= 5,867)		Group 3 (30.00-59.99) (n= 2,173)		Group 4 (15.00-29.99) (n= 396)		Group 5 (<15.00) (n= 292)	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
eGFR(mL/min/ 1.73 m²) Median (IQR)	88.77 (69.17-102.21)		102.82 (96.52-110.98)		77.52 (69.92-84.30)		50.48 (42.88-55.54)		23.50 (19.55-26.90)		6.65 (4.17-10.24)	
Microalbuminuria (mg/L) Median (IQR)	20.00 (1.80-50.00)		20.00 (1.80-50.0)		20.00 (1.60-50.00)		20.00 (2.22-100.00)		100.00 (20.00-100.00)		100.00 (20.40-100.00)	
IHD Incident	746	(4.5)	215	(2.7)	302	(5.1)	163	(7.5)	47	(11.9)	19	(6.5)
95%CI	4.0-5.0		2.0-3.0		5.0-6.0		6.0-9.0		9.0-16.0		4.0-10.0	

Data are means (standard deviation), medians (interquartile range), frequencies, or percentages.
BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HT: hypertension; DM: diabetes mellitus; DLP: dyslipidemia; AF: atrial fibrillation; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol; FBS: fasting blood sugar; HbA1c: glycated hemoglobin A1c; eGFR: estimated glomerular infiltration rate.

Multivariable analysis was conducted, adjusting for age, sex, smoking status, alcohol consumption, HT, AF, SBP, HDL-C, FBS, and urinary microalbuminuria. However, multicollinearity was detected between smoking and alcohol consumption variables (VIF=19.61). Given the well-established association between smoking and cardiovascular risk, only smoking status was included in the final model. Additionally, although FBS and urinary microalbuminuria showed associations with IHD in univariable analysis, their hazard ratios did not achieve statistical significance (HR 1.00 [95% CI 1.00–1.01] for FBS and HR 1.00 [95% CI 1.00–1.00] for microalbuminuria), and they were subsequently excluded from the final model.

The final multivariate analysis was performed, adjusting for age, sex, smoking status, HT, AF, SBP, and HDL-C (**Table 2**). The results confirmed that reduced eGFR was independently associated with an increased risk of developing IHD. Adjusted HRs remained statistically significant in all eGFR categories below 90.00 mL/min/1.73 m². Other independent risk factors included older age, males, higher systolic blood pressure, and atrial fibrillation, while higher HDL-C was associated with a reduced risk of IHD. Nevertheless, a sensitivity analysis included fasting plasma glucose and urinary microalbuminuria in the adjusted model, using categorical and continuous variable formats. Across all modeling approaches, including these variables, model stability was reduced, and many previously significant associations, such as eGFR and atrial fibrillation, became statistically nonsignificant. These changes suggested the possibility of multicollinearity or overfitting. The primary model was, therefore, retained as the most stable and parsimonious representation of the relationship between eGFR and IHD.

Discussion

In this study, we found that the incidence of IHD significantly increased from Group 2 (eGFR 60.00–89.99 mL/min/1.73 m²) to Group 5 (eGFR < 15.00 mL/min/1.73 m²) among the population of Thailand's three southern border provinces ($p < 0.001$). This association persisted even after adjusting for potential confounders, including age, sex, smoking status, SBP, HDL-C, HT, and AF. These findings suggest that declining kidney function is an independent risk factor for IHD.

One plausible biological mechanism underlying this association could involve elevated levels of fibroblast growth factor 23 (FGF23) and impaired phosphate excretion in patients with reduced eGFR. These abnormalities can lead to disturbances in mineral metabolism, particularly calcium, phosphate, and magnesium, and promote vascular calcification, a key pathogenic process in cardiovascular disease (CVD).[24]

Table 2. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the incidence of ischemic heart disease according to the groups of baseline eGFR levels.

Covariates	Per-son-year	Incidence cases	Incidence density (cases/1,000 PY)	Unadjusted HRs (95% CI)	*p*-value	Adjusted HRs (95% CI)	*p*-value
eGFR							
group 1	25,422	215	8.46	1.00		1.00	
group 2	18,985	302	15.91	1.89 (1.58-2.25)	<0.001	1.47 (1.14-1.89)	0.003
group 3	7,307	163	22.31	2.65 (2.16-3.24)	<0.001	1.60 (1.15-2.25)	0.006
group 4	1,093	47	43.00	4.96 (3.62-6.81)	<0.001	3.96 (2.29-6.86)	<0.001
group 5	555	19	34.23	3.74 (2.34-5.99)	<0.001	3.43 (1.08-10.87)	0.036
Age	53,360	746	13.98	1.02 (1.02-1.03)	<0.001	1.01 (1.00-1.02)	0.024
Sex							
Female	32,867	314	9.55	1.00		1.00	
Male	20,493	432	21.08	2.19 (1.89-2.53)	<0.001	1.63 (1.33-2.01)	<0.001
Smoking	44,837	653	14.56	1.31 (1.06-1.63)	0.014	1.14 (0.87-1.51)	0.343
SBP	53,360	746	13.98	1.01 (1.01-1.01)	<0.001	1.01 (1.00-1.02)	0.002
HDL	36,355	395	10.87	0.98 (0.97-0.98)	<0.001	0.98 (0.97-0.99)	<0.001
HT	36,249	571	15.75	1.58 (1.34-1.88)	<0.001	1.10 (0.83-1.45)	0.509
AF	526	18	34.22	2.44 (1.53-3.90)	<0.001	2.49 (1.11-5.61)	0.028
Alcohol consumption	44,842	655	14.61	1.35 (1.08-1.68)	0.008		
Weight (Kg.)	53,360	746	13.98	1.00 (1.00-1.01)	0.320		
BMI (kg/m^2)	53,360	746	13.98	0.99 (0.97-1.00)	0.155		
DBP (mmHg)	53,360	746	13.98	1.01 (1.00-1.01)	0.114		
DM	15,790	239	15.14	1.14 (0.98-1.33)	0.098		
DLP	32,725	461	14.09	1.05 (0.90-1.22)	0.534		
Total cholesterol (mg/dL)	37,861	411	10.86	1.00 (1.00-1.00)	0.721		
Triglyceride (mg/dL)	38,392	416	10.84	1.00 (1.00-1.00)	0.138		
LDL (mg/dL)	36,935	399	10.80	1.00 (1.00-1.00)	0.306		
FBS (mg/dL)	22,330	261	11.69	1.00 (1.00-1.01)	0.025		
HbA1C (%)	11,866	145	12.22	1.05 (0.98-1.12)	0.188		
Urine Microalbumin (mg/L)	24,783	261	10.53	1.00 (1.00-1.00)	0.021		

PY: person-years; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HT: hypertension; DM: diabetes mellitus; DLP: dyslipidemia; AF: atrial fibrillation; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol; FBS: fasting blood sugar; HbA1c: glycated hemoglobin A1c

Consistent with our findings, a retrospective longitudinal observational study by Park et al. involving 206,919 Korean participants demonstrated a significantly higher risk of IHD among those with lower eGFR levels, with adjusted hazard ratios (aHRs) of 1.15 (95% CI: 1.04–1.27) in Quartile 2 and 1.31 (95% CI: 1.18–1.44) in Quartile 1 compared to Quartile 4.15) Similarly, Jin et al. found a significant inverse relationship between eGFR and the Framingham Risk Score (FRS) among healthy Chinese volunteers (r = - 0.658 in 2008 and r = - 0.690 in 2011; $p < 0.01$).[12] A cross-sectional study of 2,308 Chinese participants similarly demonstrated that individuals with eGFR levels between 60–89 and 30–59 mL/min/1.73 m² had a higher risk and prevalence of coronary artery disease compared to those with eGFR ≥90 mL/min/1.73 m².[14] Additionally, Ekici et al. reported an inverse correlation between eGFR and the SYNTAX score, a measure of coronary artery disease severity (r = –0.268, $p < 0.001$).[25]

Although previous studies have consistently shown a trend toward increased incidence of IHD with declining eGFR, several limitations

have been noted. Differences in study design, the formulas used to estimate eGFR, and racial and ethnic variations in study populations may influence the observed associations.[26,27] Thus, this study contributes to the important confirmation of the inverse association between eGFR and IHD incidence in the population of Thailand's three southern border provinces. Notably, even a mild reduction in eGFR was significantly associated with an increased risk of IHD, consistent with previous findings.

Furthermore, increasing age was associated with a 1% increase in the risk of IHD per year (HR: 1.01, 95% CI: 1.00-1.02; $p = 0.024$), supporting longstanding evidence that age is a significant risk factor for IHD.[28,29] Male participants had a 1.6-fold higher risk of IHD than females (HR: 1.63, 95% CI: 1.33-2.01; $p < 0.001$), consistent with numerous previous studies.[28–32] SBP was also a significant factor, with each mmHg increase associated with a 1% increase in IHD risk (HR: 1.01, 95% CI: 1.00-1.02; $p = 0.002$), aligning with findings by Razo et al., who observed that IHD risk increases starting at an SBP of 120 mmHg.[33] Participants with AF exhibited a 2.5-fold increased risk of IHD (HR: 2.49, 95% CI: 1.11-5.61; $p = 0.028$), in agreement with evidence linking AF with coronary embolism and impaired coronary blood flow.[34]

Additionally, higher HDL-C levels were found to have a protective effect against IHD. Each 1 mg/dL increase in HDL-C was associated with a 2% reduction in IHD risk (HR: 0.98, 95% CI: 0.97–0.99; $p < 0.001$), consistent with the study by Barter et al., which demonstrated lower coronary artery disease severity in participants with higher HDL-C quintiles.[35]

The findings of this study highlight the association between kidney function, as measured by eGFR, and the incidence of IHD. These results could inform the development of screening strategies to identify individuals at risk of IHD based on kidney function and support the implementation of prevention programs tailored to the local context of the high-risk population in Thailand's three southern border provinces. Health promotion interventions aim at slowing the decline in kidney function may also effectively reduce cardiovascular risk in these vulnerable groups.

However, several limitations of this study should be noted. First, eGFR was calculated using the CKD-EPI equation; however, differences may arise when using other formulas, such as the MDRD or Cockcroft-Gault equations. Additionally, using serum creatinine, which is influenced by muscle mass, may lead to over- or underestimation of the true kidney function. [36,37] Future studies using alternative eGFR formulas are needed to strengthen the findings. Second, the median follow-up duration of only three years may be insufficient to fully capture the long-term risk of IHD, suggesting the need for studies with more extended follow-up periods. Third, the reliance on secondary data from electronic medical records may have introduced limitations due to missing information for some variables. Fourth, this dataset did not capture deaths during follow-up and admissions to hospitals outside the study facilities; this may have resulted in an underestimation of the true incidence of IHD. Fifth, data on other major cardiovascular risk factors—such as peripheral artery disease (PAD), transient ischemic attack (TIA)/stroke, and end-stage renal disease (ESRD) requiring dialysis—were not available in this study. The absence of these variables may have led to residual confounding. Sixth, although sensitivity analyses included fasting plasma glucose and urinary microalbuminuria, the resulting models exhibited instability and loss of statistical significance for several key predictors. These issues may reflect multicollinearity or overfitting, suggesting that the primary model may better represent the true associations.

Conclusion

This retrospective cohort study demonstrated a significant association between reduced eGFR and increased risk of IHD in Thailand's three southern border provinces. After adjusting for key confounders, the association remained even among individuals with mildly reduced eGFR (60.00–89.99 mL/min/1.73 m^2). These findings suggest the potential utility of eGFR in identifying individuals at risk; however, confirmation

through prospective studies is warranted, given the study's observational nature and limited clinical data. The results may inform preventive strategies and targeted screening in high-risk or underserved populations, with future research needed to refine IHD prediction models incorporating broader cardiovascular risk factors.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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