The association of the triglyceride-glucose index and ferritin with hypertension and type 2 diabetes mellitus risk in a wetland environment population

Asociación del índice de triglicéridos-glucosa y la ferritina con el riesgo de hipertensión y diabetes mellitus tipo 2 en una población de humedales

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Abstract

This cross-sectional study aimed to investigate the association of the triglyceride-glucose (TyG) index and serum ferritin levels with type 2 diabetes mellitus (T2DM) in a population residing in the wetland environment of South Kalimantan, Indonesia. The frequent co-occurrence of hypertension and T2DM presents a major public health challenge in this region characterized by unique environmental factors. A total of 151 adults, comprising 73 T2DM cases and 78 non-diabetic controls, were included. Data on fasting plasma glucose, triglycerides, and serum ferritin were collected, and the TyG index was calculated. Analysis using logistic regression, adjusted for age, sex, and body mass index, revealed that both the mean TyG index and median ferritin levels were significantly higher in the T2DM group. After multivariate adjustment, a TyG index of 8.68 or higher and a ferritin level of 129.9 ng/mL or higher were independently associated with T2DM, with adjusted odds ratios of 16.50 and 5.74, respectively. Age of 60 years or older also emerged as a strong independent risk factor. The findings indicate that in this wetland population, an elevated TyG index and high serum ferritin are strongly and independently associated with T2DM. These simple, cost-effective biomarkers could be valuable for early risk stratification of T2DM and its common comorbidity, hypertension, in similar high-risk environmental settings. Integrating these markers into routine screening protocols could enhance preventive healthcare strategies for these communities.

Keywords: Triglyceride-Glucose Index, Ferritin, Type 2 Diabetes Mellitus, Hypertension, Wetland Environment, Insulin Resistance, Iron Overload.

Resumen

Este estudio transversal tuvo como objetivo investigar la asociación del índice de triglicéridos-glucosa (TyG) y los niveles de ferritina sérica con la diabetes mellitus tipo 2 (DM2) en una población residente en humedales de Kalimantan Meridional, Indonesia. La frecuente coexistencia de hipertensión y DM2 representa un importante desafío para la salud pública en esta región, caracterizada por factores ambientales únicos. Se incluyó a 151 adultos, 73 de ellos con DM2 y 78 controles no diabéticos. Se recopilaron datos sobre la glucemia plasmática en ayunas, los triglicéridos y la ferritina sérica, y se calculó el índice TyG. El análisis mediante regresión logística, ajustado por edad, sexo e índice de masa corporal, reveló que tanto la media del índice TyG como la mediana de los niveles de ferritina fueron significativamente mayores en el grupo con DM2. Tras el ajuste multivariado, un índice de TyG de 8,68 o superior y un nivel de ferritina de 129,9 ng/mL o superior se asociaron de forma independiente con la diabetes mellitus tipo 2, con razones de probabilidades ajustadas de 16,50 y 5,74, respectivamente. La edad de 60 años o más también se identificó como un importante factor de riesgo independiente. Los hallazgos indican que, en esta población de humedales, un índice de TyG elevado y una ferritina sérica elevada se asocian de forma sólida e independiente con la diabetes mellitus tipo 2. Estos biomarcadores, sencillos y rentables, podrían ser valiosos para la estratificación temprana del riesgo de diabetes mellitus tipo 2 y su comorbilidad común, la hipertensión, en entornos ambientales de alto riesgo similares. La integración de estos marcadores en los protocolos de cribado rutinario podría mejorar las estrategias de atención sanitaria preventiva para estas comunidades.

Palabras clave: Índice de triglicéridos-glucosa, Ferritina, Diabetes mellitus tipo 2, Hipertensión, Entorno de humedales, Resistencia a la insulina, Sobrecarga de hierro.

Introduction

Hypertension and type 2 diabetes mellitus (T2DM) are leading global public health challenges with intertwined pathophysiological pathways, often co-existing as components of the metabolic syndrome[1]. Indonesia faces a rising burden of both conditions. Notably, South Kalimantan presents a unique demographic and environmental context, as a significant portion of its terrain consists of wetlands[2]. This environment is characterized by water with a naturally high iron content, which may influence population health through dietary exposure[3,4]. The Indonesian Basic Health Research (Riskesdas) in 2018 reported a notable prevalence of T2DM in the region[1].

Excessive intake of iron contained in food is associated with an increased risk of T2DM[5]. Increased iron levels in the body can affect the inflammatory process[6]. According to recent clinical data, the pathogenesis of T2DM may be influenced by chronic metabolic inflammation, which disrupts the insulin action mechanism[6-8]. Iron is a strong prooxidant that raises oxidative stress in cells and prevents insulin from being internalized and acting, which results in insulin resistance[9,10]. High ferritin levels were shown to be significantly associated with T2DM in a research by[11]. In T2DM, pro-inflammatory cytokines enhance ferritin release[12,13]. Ferritin is thought to facilitate lipolytic activation and fatty acid mobilization; hence, increased iron accumulation may increase the availability of systemic fatty acids, potentially resulting in insulin resistance[14].

Both ferritin and the triglyceride-glucose index (TyG index) reflect metabolic dysregulation, potentially exacerbated by environmental factors in wetlands. A study in South Kalimantan showed an association between high total cholesterol levels and the prevalence of T2DM[15]. According to a major population-based study conducted in Korea, those who have continuously elevated triglyceride levels are more likely to acquire diabetes within four years[16]. The TyG index is a measure that elucidates the role of triglycerides in the onset of insulin resistance[17]. The TyG index has advantages over other insulin resistance indicators due to its simplicity, user-friendliness, cost-effectiveness, and higher sensitivity and specificity as a potential diabetes mellitus detection signal[17-19]. A study by Maithili et al. found that patients with greater HbA1c had higher TyG index values[20].

To our knowledge, this is the first study to evaluate ferritin and TyG indices in a wetland population with T2DM. This study aims to investigate the relationship between the TyG index, ferritin levels, and the presence of T2DM in a population residing in a wetland area of South Kalimantan. We hypothesize that both elevated TyG index and ferritin levels are independently associated with a

higher risk of T2DM in this environment, potentially offering valuable biomarkers for risk stratification in resource-limited settings.

Study Design and Population

This analytical cross-sectional study was conducted to investigate the association of the triglyceride-glucose (TyG) index and ferritin levels with type 2 diabetes mellitus (T2DM) in a population from a wetland environment. The study utilized secondary data from two sources: medical records of patients attending the Endocrine Polyclinic at Ulin Regional General Hospital, Banjarmasin, and community-based research data collected from Banyu Hirang Village, Gambut District, Banjar Regency, South Kalimantan, in February 2023. This design allowed for the inclusion of both clinically diagnosed individuals and a community sample, providing a broader perspective on T2DM in the wetland context.

Subject Selection

Participants were selected using consecutive sampling. The total sample comprised 151 adults aged 18 years and older, divided into two groups: a T2DM group (n=73) and a non-T2DM control group (n=78). The flow of subject selection is detailed in Figure 1. The inclusion criteria were: (1) Diagnosis of T2DM according to the Indonesian Endocrinology Association (PERKENI) 2021 criteria for the case group, (2) Age ≥18 years, and (3) For the control group, confirmation of non-diabetes status based on random blood glucose <200 mg/dL, fasting plasma glucose <100 mg/dL, or HbA1c <5.7%. The exclusion criteria applied to both groups were: (1) Presence of acute infection with fever, (2) Diagnosis of malignancy, autoimmune disease, chronic kidney disease, liver disorder, or heart failure, (3) History of iron supplementation within the past month, and (4) Diagnosis of type 1 diabetes mellitus.

Data Collection and Variables

Data were extracted from existing medical records and research databases, encompassing demographic and anthropometric variables such as age, sex, height, and weight, with body mass index (BMI) subsequently calculated as weight in kilograms divided by height in meters squared. The clinical and biochemical data collected included fasting plasma glucose (FPG), fasting triglyceride levels, serum ferritin concentrations, and glycated hemoglobin (HbA1c). The diagnosis of type 2 diabetes mellitus (T2DM) was established according to the PERKENI 2021 criteria, defined by an FPG level of 126 mg/dL or greater, a 2-hour post-oral glucose tolerance test plasma glucose of 200 mg/dL or more, a random plasma glucose of 200 mg/dL or higher accompanied by classic symptoms, or an HbA1c value of 6.5% or above. From these primary measurements, the Triglyceride-Glucose (TyG) index was derived using the established formula: TyG index = Ln [Fasting Triglycerides (mg/dL) × FPG (mg/dL) / 2].

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics software version 29.0. Descriptive statistics were used to summarize subject characteristics. Categorical variables were presented as frequencies and percentages, while continuous variables were described as mean ± standard deviation or median (interquartile range, IQR) based on their distribution, assessed using the Shapiro-Wilk test.

The association between variables (TyG index, ferritin, age, sex, BMI) and T2DM incidence was first assessed using bivariate logistic regression, yielding crude odds ratios (OR) with 95% confidence intervals (CI). Subsequently, multivariate logistic regression analysis was conducted, adjusting for potential confounding variables (age, sex, BMI), to determine adjusted odds ratios (Adj. OR). Receiver Operating Characteristic (ROC) curve analysis was employed to determine the optimal cut-off values for ferritin and the TyG index in predicting T2DM. The Youden Index (J = sensitivity + specificity - 1) was used to identify the point maximizing discriminatory ability. Multicollinearity among independent variables in the regression model was assessed using the variance inflation factor (VIF). A two-tailed p-value of less than 0.05 was considered statistically significant for all analyses.

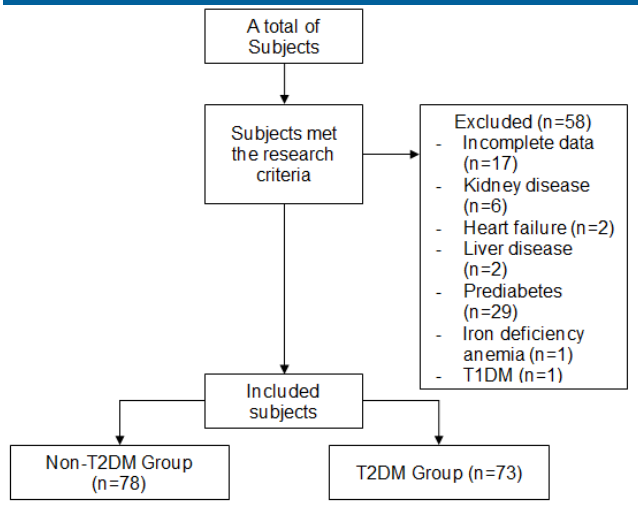
Ethical Consideration

The study protocol received ethical approval from the Health Research Ethics Committee, Faculty of Medicine and Health Sciences, Universitas Lambung Mangkurat (Certificate Number: 027/KEPK-FKIK ULM/EC/VI/2025). Operational permission was also granted by Ulin Banjarmasin Regional General Hospital (Letter Number: 87/PPDS.IPD/Litbang/RSUDU/VI/2025). As this study utilized anonymized secondary data, the requirement for informed consent was waived by the ethics committee. All procedures adhered to the principles of the Declaration of Helsinki.

Results

This study included a total of 151 subjects who met the inclusion and exclusion criteria, comprising 78 individuals in the non-T2DM control group and 73 individuals in the T2DM group. The flowchart detailing subject selection is presented in Figure 1.

Figure 1. Subject selection flowchart



The baseline characteristics of the study participants are summarized in Table 1. The T2DM group was significantly older than the non-T2DM group (mean age 54.10 ± 7.88 years vs. 42.05 ± 10.08 years, p<0.001). A higher proportion of subjects aged 60 years and above were in the T2DM group (90.5%). There was a slight female predominance in both groups. The median BMI was higher in the T2DM group (24.49 kg/m²) compared to the control group (23.45 kg/m²), though this difference was not statistically significant in the initial bivariate analysis. As expected, glycemic parameters (HbA1c and blood glucose) were significantly elevated in the T2DM group. The median ferritin level was more than two-fold higher in the T2DM group (178.5 ng/mL) compared to the control group (80.60 ng/mL). Similarly, the mean TyG index was substantially higher in the T2DM group (9.24 ± 0.76) versus the control group (8.25 ± 0.60).

Table 1. Baseline Characteristics of the Non-T2DM and T2DM Study Groups

Characteristics	Non-T2DM Group (n = 78)	T2DM Group (n = 73)
Gender, n (%)		
Women	46 (49.5%)	47 (50.5%)
Men	32 (55.2%)	26 (44.8%)
Age, mean ± SD (years)	42.05 ± 10.08	54.10 ± 7.88
18-59 years, n (%)	76 (58.5%)	54 (41.5%)
≥60 years, n (%)	2 (9.5%)	19 (90.5%)
BMI, Median (IQR) (kg/m²)	23.45 (21.00 – 26.62)	24.49 (21.88 – 29.13)
HbA1c, Median (IQR) (%)	5.30 (5.10 – 5.50)	8.20 (7.20 – 10.10)
Blood Glucose, Median (IQR) (mg/dL)	80.0 (72.0 – 86.0)	149.0 (113.0 – 208.5)
Ferritin, Median (IQR) (ng/mL)	80.60 (52.40 – 120.50)	178.5 (104.91 – 253.55)
TyG Index, mean ± SD	8.25 ± 0.60	9.24 ± 0.76

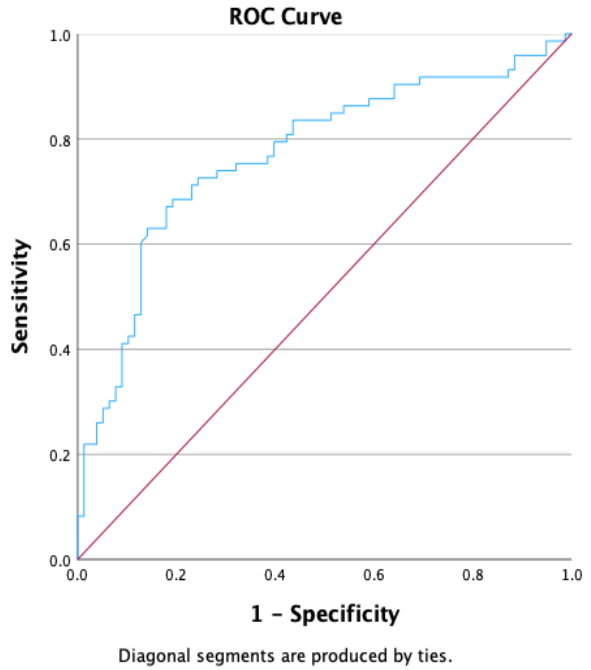
Table 2 presents the results of the bivariate logistic regression analysis examining the association between various factors and the incidence of T2DM. Both ferritin level (as a continuous variable) and the TyG index showed strong, statistically significant associations with T2DM (p<0.001 for both). For every 1 ng/mL increase in ferritin, the crude odds of having T2DM increased by a factor of 1.012. A higher TyG index was associated with a markedly increased crude odds ratio of 7.799. Age ≥60 years was also a significant factor, with a crude OR of 13.370. In this initial analysis, gender and BMI were not significantly associated with T2DM incidence (p=0.495 and p=0.189, respectively).

Table 2. Bivariate Analysis of Factors Associated with T2DM Incidence

Characteristic	T2DM Incidence		Crude OR (95% CI)	p-value
	Non-T2DM	T2DM		
Ferritin (per 1 ng/mL)	80.60 (52.40-120.50)*	178.5 (104.91-253.55)*	1.012 (1.007 – 1.017)	<0.001
TyG Index (per 1 unit)	8.25 ± 0.60**	9.24 ± 0.76**	7.799 (3.992 – 15.238)	<0.001
Gender				
Women	46 (49.5%)	47 (50.5%)	0.795 (0.412 – 1.536)	0.495
Men	32 (55.2%)	26 (44.8%)	1 (Reference)	
Age Group				
18-59 years	76 (58.5%)	54 (41.5%)	1 (Reference)	
≥60 years	2 (9.5%)	19 (90.5%)	13.370 (2.989 – 59.814)	<0.001
BMI (per 1 kg/m²)	23.45 (21.00-26.62)*	24.49 (21.88-29.13)*	1.049 (0.977 – 1.125)	0.189
*Median (IQR); **Mean ± SD				

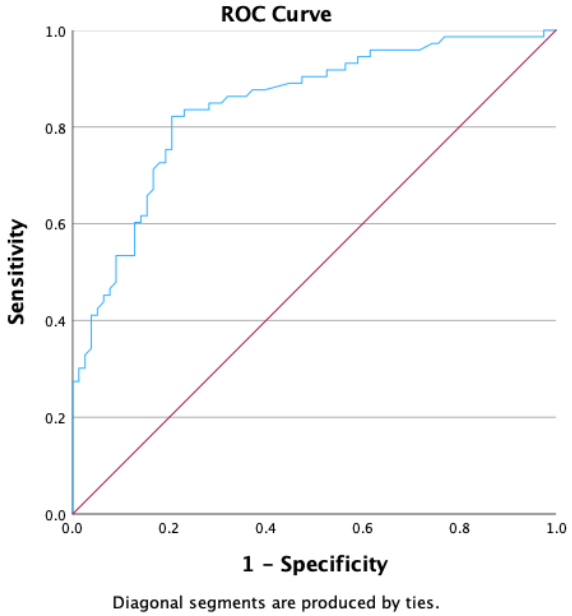
ROC curve analysis was performed to determine the optimal cut-off values for ferritin and the TyG index in discriminating T2DM cases from controls. The Youden Index identified the optimal cut-off for ferritin as 129.9 ng/mL, with an area under the curve (AUC) of 0.801, sensitivity of 68.5%, and specificity of 80.8% (Figure 2).

Figure 2. ROC curve for optimal cut-off value of ferritin. ROC=receiver operating characteristics



For the TyG index, the optimal cut-off was 8.68, with an AUC of 0.873, sensitivity of 82.2%, and specificity of 79.5% (Figure 3). These dichotomized variables were used in subsequent multivariate analysis.

Figure 3. ROC curve for optimal cut-off value of TyG index. ROC=receiver operating characteristics



A multivariate logistic regression model was constructed, adjusting for age, gender, and BMI, to assess the independent association of high ferritin (≥129.9 ng/mL) and a high TyG index (≥8.68) with T2DM. The results are shown in Table 3. After adjustment, both variables remained strongly and independently associated with T2DM. Subjects with high ferritin had 5.74 times higher odds of having T2DM compared to those with lower ferritin (Adj. OR = 5.74; 95% CI: 2.15 – 15.33; p<0.001). The association was even stronger for a high TyG index, with an adjusted odds ratio of 16.50 (95% CI: 5.96 – 45.63; p<0.001). Age ≥60 years remained a highly significant independent risk factor (Adj. OR = 37.14; p<0.001). Gender became a significant factor in the adjusted model, with women having higher adjusted odds for T2DM. BMI was not a significant independent factor in the final model.

Table 3. Multivariate Analysis of Factors Independently Associated with T2DM Incidence

Characteristic	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Ferritin ≥129.9 ng/mL	9.130 (4.32 – 19.31)	<0.001	5.742 (2.15 – 15.33)	<0.001
TyG Index ≥8.68	17.885 (7.93 – 40.34)	<0.001	16.495 (5.96 – 45.63)	<0.001
Age ≥60 years	13.370 (2.99 – 59.81)	<0.001	37.136 (5.20 – 265.16)	<0.001
Gender (Women vs. Men)	1.258 (0.65 – 2.43)	0.495	2.835 (1.00 – 8.02)	0.049
BMI (per 1 kg/m²)	1.049 (0.98 – 1.13)	0.189	1.034 (0.93 – 1.15)	0.547

Discussion

This cross-sectional study investigated the association of two metabolic biomarkers, the TyG index and serum ferritin, with type 2 diabetes mellitus in a unique wetland environment population of South Kalimantan, Indonesia. The key finding is that both elevated TyG index and high serum ferritin are strongly and independently associated with T2DM, even after adjusting for age, gender, and BMI. These results underscore the significant role of insulin resistance, as captured by the TyG index, and iron-related metabolic dysregulation in the pathogenesis of T2DM, potentially heightened in a high-iron environmental context.

The strong independent association between the TyG index and T2DM aligns with a growing body of literature validating it as a robust surrogate marker for insulin resistance. Our findings are consistent with other studies which demonstrated significant correlations between the TyG index, HbA1c, and diabetes risk. The pathophysiological link likely involves the dual components of the index. Elevated triglycerides reflect increased free fatty acid flux, which promotes hepatic gluconeogenesis and impairs insulin signaling in muscle and liver. Concur-

rent hyperglycemia further exacerbates this cycle. The high adjusted odds ratio in our study suggests that the TyG index is a potent discriminator of diabetes status in this population, potentially offering a simple, cost-effective screening tool in resource-limited wetland settings where advanced tests may be unavailable. The optimal cut-off identified in our population, with good sensitivity and specificity, provides a practical threshold for risk assessment.

Equally important is the significant association we found between elevated serum ferritin and T2DM. This supports the hypothesis that iron overload contributes to diabetes risk, a concern particularly relevant to populations in wetland areas with potentially high environmental iron exposure. Our findings corroborate previous studies which reported higher ferritin levels in individuals with T2DM. Iron acts as a pro-oxidant, catalyzing the formation of reactive oxygen species that induce oxidative stress, damage pancreatic beta-cells, and impair insulin sensitivity in peripheral tissues. Furthermore, ferritin functions as an acute-phase reactant, and its elevation may reflect the chronic low-grade inflammation characteristic of T2DM and its frequent comorbidity, hypertension. The identified cut-off could serve as a useful clinical reference point for identifying individuals at increased metabolic risk in similar environments.

In our multivariate model, older age emerged as the strongest risk factor, consistent with the well-established epidemiology of T2DM. The significant association with female gender after adjustment warrants further investigation, as it may reflect sex-specific differences in body composition, hormonal influences on iron metabolism, or healthcare-seeking behavior in this region. The lack of a significant independent association with BMI in the final model suggests that in this population, the pathophysiological processes reflected by the TyG index and ferritin—insulin resistance and iron-mediated oxidative stress/inflammation—may be more direct determinants of diabetes risk than overall adiposity per se. This highlights the value of these biomarkers over simple anthropometry.

This study has several limitations that must be acknowledged. The cross-sectional design precludes any inference of causality; we cannot determine whether high ferritin and TyG index precede or result from diabetes. The use of secondary data limited our ability to control for all potential confounders, such as detailed dietary habits, physical activity, genetic factors, or precise measures of environmental iron exposure. The sample was drawn from two specific locations in South Kalimantan, which may affect the generalizability of the findings to other wetland or non-wetland populations. Furthermore, reliance on a single measurement of ferritin and lipids may not reflect long-term exposure.

Despite these limitations, this study presents novel insights as the first, to our knowledge, to concurrently evaluate the TyG index and ferritin in a T2DM population from a wetland environment. It strengthens the evidence for the utility of these accessible biomarkers. The findings suggest that in regions like South Kalimantan, integrating the TyG index and ferritin into routine health screenings could improve early identification of individuals at high risk for T2DM and its cardiovascular complications, including hypertension. Future prospective studies are needed to validate these cut-off values and to explore the causal pathways linking environmental iron exposure, systemic inflammation, insulin resistance, and the development of both T2DM and hypertension.

Conclusions

This study demonstrates that both an elevated triglyceride-glucose (TyG) index (≥8.68) and high serum ferritin levels (≥129.9 ng/mL) are significantly and independently associated with the presence of Type 2 Diabetes Mellitus in a population inhabiting a wetland environment in South Kalimantan. These biomarkers, reflecting underlying insulin resistance and iron-related oxidative stress/inflammation, respectively, offer valuable, simple, and cost-effective tools for assessing metabolic risk. The findings underscore the potential impact of unique environmental factors, such as high iron content in wetland ecosystems, on population health. Implementing routine screening with these indices could enhance early detection and preventive strategies for T2DM and its associated complications, including hypertension, in similar resource-limited settings. Further longitudinal research is warranted to confirm the predictive value of these cut-offs and to elucidate the causal mechanisms linking environmental exposures to metabolic dysregulation.

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