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Ethnic Differences in Adiposity and Metabolic Profiles Among Young Adults in North Sulawesi, Indonesia: Accounting for Diet, Physical Activity, and KCNQ1 rs2237892

Marthina Maryana Sinon[1,2], Nurpudji Astuti Daud[1,2], Andi Yasmin Syauki[1,2], Agussalim Bukhari[1,2], Aminuddin[1], Nur Ashari[1]

[1]Department of Clinical Nutrition, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia
[2] Department of Clinical Nutrition, Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia

ABSTRACT: Cardiometabolic profiles may differ across ethnocultural populations, but data from young adults in Indonesia remain limited. We examined ethnic differences in adiposity and metabolic profiles while accounting for dietary, behavioral, and KCNQ1 rs2237892 variation. This secondary cross-sectional analysis included 300 adults aged 18–25 years from the Minahasa, Sangihe Talaud, and Bolaang Mongondouw ethnic groups in North Sulawesi, Indonesia (100 per group). Anthropometric, lipid, fasting glucose, dietary, physical-activity, and KCNQ1 rs2237892 data were analyzed. A multivariate general linear model evaluated ethnic differences in BMI, waist circumference, HDL-C, fasting plasma glucose, and ln-transformed triglycerides, adjusting for age, sex, physical activity, total energy intake, SFA intake, and C-allele dosage. The combined adiposity–metabolic phenotype differed across ethnic groups (Pillai's Trace=0.189, $F(10,574)=5.992$, $p<0.001$). Ethnicity remained associated with BMI ($p=0.005$) and HDL-C ($p<0.001$), but not waist circumference, fasting plasma glucose, or triglycerides. Adjusted BMI was higher in Minahasa than Sangihe Talaud participants (difference 1.89 kg/m²; $p=0.005$). HDL-C was lower in Bolaang Mongondouw than Minahasa and Sangihe Talaud participants (differences 8.55 and 6.31 mg/dL, respectively; both $p<0.001$). KCNQ1 C-allele dosage was not independently associated with the phenotype panel. Ethnic differences among young North Sulawesi adults were concentrated in BMI and HDL-C and persisted after adjustment for measured dietary, behavioral, and KCNQ1 factors.

1. INTRODUCTION

Obesity and metabolic abnormalities are increasingly relevant early in adulthood, when behavioral patterns that may persist across the life course are being established. Global pooled analyses show that obesity has risen markedly over recent decades, while excess adiposity is closely linked to dyslipidemia, impaired glucose regulation, and subsequent cardiometabolic disease [1,2]. In Indonesia, prospective data from young adults have documented unfavorable metabolic changes accompanying urbanization [3], while a six-year cohort in Bogor identified higher BMI and lower intentional exercise as predictors of metabolic syndrome [4].

The metabolic consequences of adiposity are not uniform across populations. Large multiethnic analyses have demonstrated distinct relationships of BMI, waist circumference, and body composition with cardiovascular risk markers across Malay, Indian, Chinese, and White populations [5]. Ethnic variation in metabolic syndrome has also been demonstrated systematically [6].

Within Indonesia, substantial differences in metabolic syndrome prevalence have been reported across ethnic groups, with low HDL-C being particularly common [7]. Among Indonesian young adults, BMI- and waist-based obesity measures have also shown differing associations with lipid abnormalities [8].

These differences likely reflect intertwined behavioral, environmental, sociocultural, and genetic influences rather than ethnicity itself. Diet and lifestyle are relevant to obesity in young adulthood [9], while longitudinal evidence links lower young-adult physical activity with later diabetes and adverse lipid profiles [10]. Dietary fat quality also influences lipid metabolism [11]. Meanwhile, *KCNQ1* rs2237892 has been associated with type 2 diabetes overall, although evidence in Southeast Asian populations remains limited [12]. We therefore compared adiposity and metabolic profiles across three ethnic groups in North Sulawesi while accounting for diet, physical activity, and *KCNQ1* rs2237892.

2. MATERIALS AND METHODS

2.1 Study Design and Participants

This study was a secondary cross-sectional analysis of data from a population-based nutrigenetic study conducted among young adults from three ethnic groups in North Sulawesi, Indonesia. Participants were recruited from Manado City, North Minahasa Regency, and Kotamobagu, with screening and data collection performed in May 2025. Demographic, anthropometric, dietary, physical activity, biochemical, and genetic data were collected during the study assessment.

Eligible participants were men and women aged 18–25 years who self-reported Minahasa, Sangihe Talaud, or Bolaang Mongondouw ethnic ancestry extending for at least two generations. Additional inclusion criteria were body mass index (BMI) ≥18.5 kg/m², willingness to participate, and provision of written informed consent.

Participants were excluded if they had a direct parent–child or sibling relationship with another participant; used medications that inhibit fat absorption; were participating in a weight-loss diet or program; received hormone replacement therapy; had used antibiotics within the preceding month; had a history of HIV infection, tuberculosis, hepatitis or jaundice, diabetes mellitus, cancer, or hypercholesterolemia; used hormonal contraceptives; were pregnant or breastfeeding; or had a history of COVID-19 within the preceding three months.

Participants were recruited using purposive sampling. The analytic sample comprised 300 participants, including 100 participants from each ethnic group, with equal numbers of men and women within each group. The original study targeted approximately 100 participants per ethnic group. Sample size was calculated using the Slovin formula, assuming an estimated population of approximately 25,000 individuals per ethnic group and a 10% margin of error, resulting in a planned total sample of 300 participants.

2.2 Anthropometric, Dietary, Physical Activity, and Biochemical Assessment

Age was determined from the date of birth recorded on the participant's national identity card and expressed in completed years. Body weight and body-fat percentage were measured using a calibrated TANITA RD-953 bioelectrical impedance analyzer (Tanita Corporation, Japan), while standing height was measured using a microtoise. BMI was calculated as body weight in kilograms divided by height in meters squared.

Waist circumference was measured with the participant standing using a non-stretchable measuring tape positioned horizontally at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest. Measurements were obtained at the end of normal expiration without compressing the skin. Two measurements were performed, and the mean value was used for analysis.

Usual dietary intake during the preceding month was assessed using a semi-quantitative food-frequency questionnaire based on foods commonly consumed in the study population. Participants reported the frequency and usual amount of food consumed, and average daily nutrient intake was calculated using NutriSurvey. The present analysis included total energy intake and intakes of saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), and polyunsaturated fatty acids (PUFA). Total energy intake was expressed in kcal/day, while fatty-acid intake was expressed as a percentage of total energy. SFA intake expressed as percentage of total energy was included as a covariate in the adjusted analyses.

Physical activity was assessed by interview using the International Physical Activity Questionnaire (IPAQ) and categorized as low, moderate, or high. Moderate physical activity was defined as vigorous-intensity activity on ≥3 days for at least 20 min/day;

moderate-intensity activity or walking on ≥5 days for at least 30 min/day; or any combination of walking, moderate-intensity, and vigorous-intensity activities totaling at least 600 metabolic equivalent task minutes per week (MET-min/week). High physical activity was defined as vigorous-intensity activity on ≥3 days totaling at least 1500 MET-min/week or any combination of walking, moderate-intensity, and vigorous-intensity activities on ≥7 days totaling at least 3000 MET-min/week. Participants who did not meet these criteria were classified as having low physical activity.

Venous blood samples were collected after an overnight fast of 8–12 h, during which only water was permitted. Fasting plasma glucose was measured enzymatically using a standardized laboratory autoanalyzer and expressed in mg/dL. Total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides were also measured and expressed in mg/dL. Total cholesterol and LDL-C were used for descriptive characterization, whereas HDL-C and triglycerides were included in the primary multivariate metabolic phenotype analysis.

2.3 KCNQ1 rs2237892 Genotyping and Study Variables

Genomic DNA was extracted from buffy-coat samples using a spin-column procedure with the Quick-DNA MiniPrep Plus Kit (Cat. No. D4069) according to the manufacturer's instructions. *KCNQ1* rs2237892 was genotyped using Kompetitive Allele-Specific PCR (KASP) on a real-time quantitative PCR platform. Genotypes were classified as TT, CT, or CC.

For the present analysis, rs2237892 was additionally represented as C-allele dosage, coded as 0 for TT, 1 for CT, and 2 for CC. C-allele frequencies were calculated from the observed genotype distributions. Hardy–Weinberg equilibrium was evaluated separately within each ethnic group using an exact test.

The principal exposure was ethnic group, categorized as Minahasa, Sangihe Talaud, or Bolaang Mongondouw. The primary multivariate phenotype panel comprised BMI, waist circumference, HDL-C, fasting plasma glucose, and triglycerides. Because triglyceride concentrations were right-skewed, values were natural-log transformed before inclusion in adjusted models.

Age, sex, physical activity category, total energy intake, SFA intake expressed as percentage of total energy, and *KCNQ1* rs2237892 C-allele dosage were included as adjustment variables. Body-fat percentage, total cholesterol, LDL-C, MUFA intake, and PUFA intake were used for descriptive characterization but were not included in the primary multivariate phenotype panel.

2.4 Statistical Analysis

Continuous-variable distributions were assessed using the Shapiro–Wilk test. Normally distributed variables were summarized as mean ± standard deviation, whereas non-normally distributed variables were presented as median with first and third quartiles [median (Q1–Q3)]. Categorical variables were presented as frequencies and percentages.

For unadjusted comparisons across ethnic groups, non-normally distributed continuous variables were compared using the Kruskal–Wallis test. SFA intake expressed as percentage of total energy was approximately normally distributed; however, because the homogeneity-of-variance assumption was not satisfied, between-group differences were evaluated using Welch's one-way analysis of variance. Categorical variables, including sex, physical activity category, and *KCNQ1* rs2237892 genotype, were compared using Pearson's chi-square test. Hardy–Weinberg equilibrium was assessed separately within each ethnic group using an exact test.

The primary adjusted analysis used a multivariate general linear model with BMI, waist circumference, HDL-C, fasting plasma glucose, and natural-log-transformed triglycerides as the dependent-variable panel. Ethnic group, sex, and physical activity category were entered as categorical factors, while age, total energy intake, SFA intake (% energy), and *KCNQ1* rs2237892 C-allele dosage were entered as continuous covariates. Type III sums of squares were used.

Equality of covariance matrices was assessed using Box's M test. Pillai's trace was used as the principal multivariate statistic because of its greater robustness to heterogeneity of covariance matrices. Homogeneity of error variances for individual outcomes was evaluated using Levene's test. Multivariate and outcome-specific effects were reported using F statistics, corresponding degrees of freedom, *P* values, and partial eta squared (η^2).

Following the multivariate analysis, Type III between-subject effects were examined for each outcome. For outcomes showing a statistically significant overall ethnic-group effect, adjusted estimated marginal means with 95% confidence intervals were calculated. Pairwise comparisons among ethnic groups were performed using Bonferroni adjustment for multiple comparisons. Adjusted estimated marginal means for BMI and HDL-C were additionally used for graphical presentation.

Analyses were conducted using complete available data, and no missing-value imputation was performed. All statistical tests were two-sided, and $P<0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 30.

3. RESULTS AND DISCUSSION

3.1 Participant Characteristics

The analytic sample included 300 participants, with 100 participants from each of the Minahasa, Sangihe Talaud, and Bolaang Mongondouw ethnic groups. Sex distribution was identical across ethnic groups, whereas physical activity levels differed significantly. KCNQ1 rs2237892 genotype distribution did not differ across ethnic groups.

In unadjusted comparisons, significant ethnic differences were observed for age, BMI, body fat percentage, waist circumference, total cholesterol, HDL-C, LDL-C, fasting plasma glucose, and dietary fatty acid composition. Triglyceride levels and total energy intake did not differ significantly across ethnic groups. Participant characteristics are presented in Table 1.

Table 1. Participant Characteristics According to Ethnic Group

Characteristic	Overall (n=300)	Minahasa (n=100)	Sangihe Talaud (n=100)	Bolaang Mongondouw (n=100)	p-value
Age, years	21.0 (20.0–22.0)	21.0 (20.0–23.0)	21.0 (20.0–22.0)	20.5 (20.0–22.0)	0.031[a]*
Sex, n (%)					1.000[c]
Male	150 (50.0)	50 (50.0)	50 (50.0)	50 (50.0)	
Female	150 (50.0)	50 (50.0)	50 (50.0)	50 (50.0)	
Physical activity, n (%)					<0.001[c]*
Low	136 (45.3)	46 (46.0)	30 (30.0)	60 (60.0)	
Moderate	91 (30.3)	33 (33.0)	37 (37.0)	21 (21.0)	
High	73 (24.3)	21 (21.0)	33 (33.0)	19 (19.0)	
Adiposity measures					
BMI, kg/m²	22.74 (20.42–25.78)	24.29 (21.84–26.91)	22.19 (20.34–24.25)	22.26 (19.93–25.67)	<0.001[a]*
Body fat, %	28.50 (18.63–35.38)	30.75 (21.33–36.25)	25.45 (15.60–35.23)	28.05 (18.83–34.60)	0.017[a]*
Waist circumference, cm	83.25 (77.63–89.38)	86.00 (81.00–90.00)	82.25 (77.13–87.00)	82.25 (76.13–91.63)	0.029[a]*
Metabolic profile					
Total cholesterol, mg/dL	152.5 (131.25–178.00)	159.5 (140.25–184.75)	163.5 (143.00–185.75)	130.5 (112.25–157.75)	<0.001[a]*
HDL-C, mg/dL	36.0 (31.0–44.0)	40.0 (34.0–49.0)	38.0 (34.0–43.0)	32.0 (27.25–37.0)	<0.001[a]*
LDL-C, mg/dL	93.0 (78.0–113.0)	100.5 (85.0–117.75)	96.5 (85.75–114.75)	79.5 (62.5–102.0)	<0.001[a]*
Triglycerides, mg/dL	74.0 (59.0–101.75)	76.5 (62.25–106.75)	71.5 (57.25–99.0)	73.5 (56.5–105.0)	0.665[a]

Fasting plasma glucose, mg/dL	71.0 (65.0–78.0)	73.0 (67.25–78.0)	72.0 (64.25–78.75)	69.0 (62.0–75.75)	0.032[a]*
Dietary intake					
Total energy, kcal/day	2180.3 (1881.35–2681.73)	2168.9 (1817.33–2650.65)	2201.6 (1712.93–2819.50)	2166.9 (1945.98–2628.15)	0.860[a]
SFA, % energy	9.52 ± 3.25	9.13 ± 3.07	9.20 ± 3.92	10.22 ± 2.53	0.011[b]*
MUFA, % energy	5.57 (4.37–7.20)	5.27 (4.04–6.98)	5.53 (3.96–7.41)	6.03 (5.00–7.27)	0.029[a]*
PUFA, % energy	6.03 (4.65–7.68)	5.60 (4.13–6.85)	5.71 (3.68–7.73)	7.02 (5.75–8.19)	<0.001[a]*
KCNQ1 rs2237892 genotype, n (%)					0.631[c]
TT	142 (47.3)	52 (52.0)	47 (47.0)	43 (43.0)	
CT	132 (44.0)	38 (38.0)	45 (45.0)	49 (49.0)	
CC	26 (8.7)	10 (10.0)	8 (8.0)	8 (8.0)	

Note: Data are presented as median (Q1–Q3), mean ± SD, or n (%), as appropriate. [a]Kruskal–Wallis test; [b]Welch analysis of variance; [c]Pearson chi-square test. *p<0.05. BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

3.2 KCNQ1 rs2237892 Distribution and Hardy–Weinberg Equilibrium

Overall, the KCNQ1 rs2237892 genotype distribution consisted of 142 TT participants (47.3%), 132 CT participants (44.0%), and 26 CC participants (8.7%). Genotype distribution did not differ significantly across ethnic groups (p=0.631). The C-allele frequency was 29.0% among Minahasa, 30.5% among Sangihe Talaud, and 32.5% among Bolaang Mongondouw participants. Within each ethnic group, genotype distributions were consistent with Hardy–Weinberg equilibrium: Minahasa p=0.467, Sangihe Talaud p=0.641, and Bolaang Mongondouw p=0.361. The ethnic-specific genotype distributions are shown in Table 2.

Table 2. KCNQ1 rs2237892 Genotype Distribution and Hardy–Weinberg Equilibrium According to Ethnic Group

Ethnic group	TT, n (%)	CT, n (%)	CC, n (%)	C-allele frequency	HWE p-value
Minahasa	52 (52.0)	38 (38.0)	10 (10.0)	0.290	0.467[c]
Sangihe Talaud	47 (47.0)	45 (45.0)	8 (8.0)	0.305	0.641[c]
Bolaang Mongondouw	43 (43.0)	49 (49.0)	8 (8.0)	0.325	0.361[c]
Overall	142 (47.3)	132 (44.0)	26 (8.7)	0.307	—

Between-ethnic-group genotype comparison: p=0.631[b].

Note: C-allele frequency was calculated as (2×CC + CT)/(2N). [b]Pearson chi-square test for genotype distribution across ethnic groups; [c]exact Hardy–Weinberg equilibrium test within each ethnic group. No ethnic group showed evidence of deviation from Hardy–Weinberg equilibrium. HWE, Hardy–Weinberg equilibrium.

3.3 Multivariate Differences in Adiposity and Metabolic Profiles

A multivariate general linear model was used to assess ethnic differences across the combined phenotype panel comprising BMI, waist circumference, HDL-C, fasting plasma glucose, and ln-transformed triglycerides. The model accounted for age, sex, physical activity, total energy intake, SFA intake, and KCNQ1 rs2237892 C-allele dosage. Because Box's test indicated unequal

covariance matrices (Box's M=391.807, p=0.002), Pillai's Trace was used as the principal multivariate statistic. Ethnic group was significantly associated with the combined adiposity–metabolic phenotype (Pillai's Trace=0.189, F(10,574)=5.992, p<0.001, partial η^2=0.095).

Age (p=0.001), total energy intake (p<0.001), and sex (p<0.001) were also associated with the combined phenotype panel. In contrast, SFA intake (p=0.468), KCNQ1 C-allele dosage (p=0.601), and physical activity category (p=0.877) were not statistically significant multivariate predictors (Table 3, Panel A). In the adjusted univariate analyses, ethnicity remained significantly associated with BMI (F=5.393, p=0.005, partial η^2=0.036) and HDL-C (F=21.481, p<0.001, partial η^2=0.129). Ethnic differences were not statistically significant for waist circumference (p=0.125), fasting plasma glucose (p=0.135), or ln-transformed triglycerides (p=0.884) (Table 3, Panel B).

Table 3. Adjusted Multivariate and Univariate Associations With the Adiposity–Metabolic Phenotype Panel

Panel A. Multivariate General Linear Model

Effect	Pillai's Trace	F (df)	p-value	Partial η^2
Age	0.067	4.108 (5, 286)	0.001[d]*	0.067
Total energy intake	0.078	4.864 (5, 286)	<0.001[d]*	0.078
SFA intake, % energy	0.016	0.921 (5, 286)	0.468[d]	0.016
KCNQ1 C-allele dosage	0.013	0.730 (5, 286)	0.601[d]	0.013
Sex	0.070	4.326 (5, 286)	<0.001[d]*	0.070
Physical activity	0.018	0.519 (10, 574)	0.877[d]	0.009
Ethnic group	0.189	5.992 (10, 574)	<0.001[d]*	0.095

Panel B. Adjusted Univariate Effect of Ethnic Group

Outcome	F	df	p-value	Partial η^2
BMI	5.393	2, 290	0.005[e]*	0.036
Waist circumference	2.093	2, 290	0.125[e]	0.014
HDL-C	21.481	2, 290	<0.001[e]*	0.129
Fasting plasma glucose	2.015	2, 290	0.135[e]	0.014
ln(Triglycerides)	0.123	2, 290	0.884[e]	0.001

Note: The multivariate phenotype panel comprised BMI, waist circumference, HDL-C, fasting plasma glucose, and natural-log-transformed triglycerides. Models included age, sex, physical activity category, total energy intake, SFA intake (% energy), KCNQ1 rs2237892 C-allele dosage, and ethnic group. [d]Multivariate general linear model using Pillai's Trace; [e]Type III between-subjects effect from the general linear model. *Statistically significant at p<0.05. BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; SFA, saturated fatty acid.

3.4 Adjusted Ethnic Differences in BMI and HDL-C

Because ethnicity was significantly associated with BMI and HDL-C in the adjusted univariate analyses, Bonferroni-adjusted pairwise comparisons were performed using estimated marginal means. For BMI, the adjusted mean was 24.80 kg/m² (95% CI 23.96–25.64) among Minahasa participants, 22.91 kg/m² (95% CI 22.08–23.73) among Sangihe Talaud participants, and 23.44 kg/m² (95% CI 22.57–24.31) among Bolaang Mongondouw participants. Minahasa participants had an adjusted BMI 1.89 kg/m² higher than Sangihe Talaud participants (95% CI 0.46–3.33; Bonferroni-adjusted p=0.005). Differences between Minahasa and Bolaang Mongondouw (p=0.076) and between Sangihe Talaud and Bolaang Mongondouw (p=1.000) were not statistically significant.

For HDL-C, adjusted means were 41.47 mg/dL (95% CI 39.61–43.33) in Minahasa, 39.23 mg/dL (95% CI 37.41–41.05) in Sangihe Talaud, and 32.92 mg/dL (95% CI 30.99–34.85) in Bolaang Mongondouw. HDL-C was 8.55 mg/dL lower in Bolaang Mongondouw than in Minahasa (95% CI 5.32–11.78; p<0.001) and 6.31 mg/dL lower than in Sangihe Talaud (95% CI 3.03–9.60; p<0.001). The adjusted HDL-C difference between Minahasa and Sangihe Talaud was not statistically significant (p=0.272). These adjusted ethnic differences in BMI and HDL-C are summarized in Table 4 and illustrated in Figure 1.

Table 4. Adjusted Estimated Marginal Means and Bonferroni Pairwise Comparisons for BMI and HDL-C

Panel A. Adjusted Estimated Marginal Means

Outcome	Minahasa	Sangihe Talaud	Bolaang Mongondouw
BMI, kg/m²	24.80 (23.96–25.64)	22.91 (22.08–23.73)	23.44 (22.57–24.31)
HDL-C, mg/dL	41.47 (39.61–43.33)	39.23 (37.41–41.05)	32.92 (30.99–34.85)

Values are adjusted estimated marginal mean (95% CI).

Panel B. Bonferroni-Adjusted Pairwise Comparisons

Outcome	Comparison	Adjusted mean difference	95% CI	p-value
BMI, kg/m²	Minahasa vs Sangihe Talaud	1.893	0.457 to 3.329	0.005[f]*
	Minahasa vs Bolaang Mongondouw	1.361	−0.098 to 2.821	0.076[f]
	Sangihe Talaud vs Bolaang Mongondouw	−0.532	−2.017 to 0.953	1.000[f]
HDL-C, mg/dL	Minahasa vs Sangihe Talaud	2.239	−0.936 to 5.415	0.272[f]
	Minahasa vs Bolaang Mongondouw	8.551	5.323 to 11.779	<0.001[f]*
	Sangihe Talaud vs Bolaang Mongondouw	6.312	3.028 to 9.595	<0.001[f]*

Note: Estimated marginal means and pairwise differences were adjusted for age, sex, physical activity category, total energy intake, SFA intake (% energy), and KCNQ1 rs2237892 C-allele dosage. [f]Bonferroni-adjusted pairwise comparison of estimated marginal means. *Statistically significant at p<0.05. BMI, body mass index; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; SFA, saturated fatty acid.

3.5 Role of Dietary Intake, Physical Activity, and KCNQ1 rs2237892

Within the multivariate model, total energy intake was significantly associated with the combined adiposity–metabolic phenotype (Pillai's Trace=0.078, p<0.001), whereas SFA intake was not (p=0.468). Physical activity category was likewise not associated with the combined phenotype panel (p=0.877). KCNQ1 rs2237892 C-allele dosage showed no significant multivariate association with the combined phenotype panel (Pillai's Trace=0.013, p=0.601). In outcome-specific adjusted models, C-allele dosage was also not significantly associated with BMI (p=0.543), waist circumference (p=0.364), HDL-C (p=0.983), fasting plasma glucose (p=0.106), or ln-transformed triglycerides (p=0.967). Thus, the observed ethnic differences in the combined phenotype panel, and specifically in BMI and HDL-C, remained evident after accounting for the measured dietary, behavioral, and KCNQ1 rs2237892 variables.

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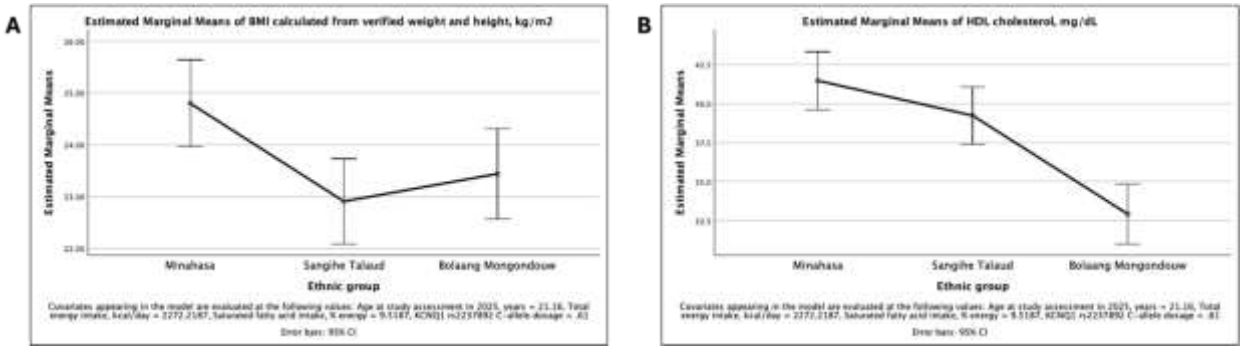

Figure 1. Adjusted BMI and HDL-C According to Ethnic Group. Panel A. Adjusted estimated marginal mean BMI (kg/m²) with 95% confidence intervals among Minahasa, Sangihe Talaud, and Bolaang Mongondouw participants. Panel B. Adjusted estimated marginal mean HDL-C (mg/dL) with 95% confidence intervals among Minahasa, Sangihe Talaud, and Bolaang Mongondouw participants. Estimated marginal means were adjusted for age, sex, physical activity category, total energy intake, saturated fatty acid intake (% energy), and KCNQ1 rs2237892 C-allele dosage. Bonferroni-adjusted comparisons showed higher BMI in Minahasa than Sangihe Talaud participants ($p=0.005$), while HDL-C was lower in Bolaang Mongondouw than both Minahasa and Sangihe Talaud participants (both $p<0.001$).

3.6 Discussion

Among young adults from three ethnocultural groups in North Sulawesi, the combined adiposity–metabolic profile differed after adjustment for age, sex, physical activity, total energy intake, SFA intake, and KCNQ1 rs2237892 C-allele dosage. The separation was concentrated in two traits: Minahasa participants had higher adjusted BMI than Sangihe Talaud participants, whereas Bolaang Mongondouw participants had lower HDL-C than both other groups. By contrast, the unadjusted differences in waist circumference and fasting plasma glucose were attenuated after adjustment, and triglycerides did not differ across groups. Comparable multiethnic Asian studies have also shown that adiposity, lipid, and glycemic characteristics do not necessarily vary in parallel across ethnic populations [5,13,14]. In the HELIOS cohort, for example, visceral adiposity explained some ethnic differences in triglycerides and blood pressure but did not fully account for differences in glycemia, insulin sensitivity, or diabetes susceptibility [14].

The BMI difference between Minahasa and Sangihe Talaud participants should therefore not be interpreted as a complete ranking of adiposity-related metabolic risk. BMI remains useful at the population level, but it does not fully capture body-fat distribution or metabolic risk. Waist circumference and visceral adiposity can provide additional cardiometabolic information beyond BMI alone [15]. Individuals with similar BMI can also have substantially different metabolic profiles and disease risk [16]. This discordance is particularly relevant to our findings. Among young Mauritian adults, Ramessur et al. (2024) found no ethnic difference in either BMI or waist circumference despite clear differences in visceral-to-peripheral fat distribution and lipid profiles [17]. In Indonesian adults, abdominal adiposity has also shown a stronger association with metabolic syndrome than overall adiposity [18]. Thus, the absence of an adjusted between-group difference in waist circumference in our study reflects attenuation of that specific ethnic contrast, rather than evidence that central adiposity is metabolically unimportant.

The clearest metabolic distinction involved HDL-C. Adjusted HDL-C was approximately 8.6 mg/dL lower in Bolaang Mongondouw than in Minahasa participants and 6.3 mg/dL lower than in Sangihe Talaud participants. Low HDL-C is particularly relevant in the Indonesian context: it was the most prevalent metabolic syndrome component in a large multiethnic Indonesian survey, with substantial variation in metabolic profiles across ethnic groups [7]. Obesity indices have also been associated with low HDL-C and other dyslipidemic abnormalities among Indonesian young adults [8]. A similar dissociation between HDL-C and triglycerides was reported in the Singapore Multi-Ethnic Cohort, where ethnic differences in HDL-C persisted after adjustment for socioeconomic, lifestyle, and adiposity measures, whereas differences in fasting triglycerides did not [13]. In our sample, the pattern therefore appears concentrated in HDL-C rather than representing a uniformly adverse lipid profile in the Bolaang Mongondouw group.

The dietary and behavioral findings require a similarly measured interpretation. Total energy intake was associated with the combined phenotype panel, whereas SFA intake and physical-activity category were not significant after multivariable

adjustment. These null coefficients do not indicate that dietary fat or physical activity lacks metabolic relevance. In Indonesian young adults, Kurniawan et al. (2022) found that dietary fat intake contributed to BMI differences and longitudinal BMI change during urbanization [3]. Over 30 years of follow-up, lower physical activity beginning in young adulthood was associated with subsequent diabetes, low HDL-C, and elevated triglycerides [10]. Experimental evidence is more specific for dietary fat quality: replacing palmitic acid with unsaturated fatty acids lowers LDL-C, although effects on HDL-C and triglycerides are less consistent [11]. The SQ-FFQ and categorical IPAQ measures used here may not capture the duration, intensity, or longer-term patterning of these exposures.

KCNQ1 rs2237892 did not account for the ethnic differences observed in this study. Genotype distributions were similar across groups, each group was consistent with Hardy–Weinberg equilibrium, and C-allele dosage was not independently associated with the combined phenotype or individual outcomes. This does not necessarily conflict with the reported association between rs2237892 and type 2 diabetes susceptibility [12], because our outcomes were intermediate anthropometric and metabolic traits measured in generally young adults rather than incident diabetes. Genetic associations are also variant- and phenotype-specific: a recent Asian meta-analysis identified multiple obesity- and diabetes-associated loci, including another KCNQ1 variant, rs2283228, rather than rs2237892 [19]. Common obesity itself is highly polygenic, involving many variants of individually modest effect interacting with environmental exposures [20]. Accordingly, the null result for one SNP cannot exclude broader inherited contributions, but neither does it support a genetic explanation for the ethnic differences observed here.

The balanced sample sizes across the three groups, identical sex distribution, and concurrent assessment of anthropometry, diet, physical activity, biochemical markers, and genotype allowed a joint multivariable assessment of a defined phenotype panel. Several limitations remain. The cross-sectional design precludes temporal inference, and purposive sampling limits population-level generalizability. Dietary intake and physical activity were self-reported, while bioelectrical impedance cannot characterize regional adiposity with the precision of DXA or imaging-based methods. Ethnicity was based on self-reported familial background and should not be interpreted as genomic ancestry; ancestry-informative markers or genetic principal components were unavailable. More broadly, ethnic differences in metabolic health can reflect intertwined socioeconomic, cultural, behavioral, environmental, and biological influences, leaving residual confounding unavoidable in observational comparisons [6].

Overall, the between-group differences that remained after adjustment were concentrated in BMI and, more prominently, HDL-C. These findings identify phenotypic heterogeneity among young adults from three North Sulawesi ethnocultural groups, rather than evidence of an inherent biological hierarchy between them. Longitudinal studies incorporating more detailed dietary assessment, direct measures of regional adiposity, socioeconomic and environmental exposures, and ancestry-informed genomic data would help clarify why these metabolic profiles diverge [14,17].

4. CONCLUSION

Among young adults from three ethnic groups in North Sulawesi, adiposity–metabolic profiles differed after adjustment for age, sex, physical activity, energy intake, SFA intake, and KCNQ1 rs2237892 C-allele dosage. The clearest differences were higher BMI in Minahasa than Sangihe Talaud participants and lower HDL-C in Bolaang Mongondouw than in both other groups, whereas waist circumference, fasting plasma glucose, and triglycerides did not differ after adjustment. KCNQ1 rs2237892 was not independently associated with these phenotypes, indicating that the observed intergroup differences were not explained by this single variant.

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AUTHOR CONTRIBUTIONS

MMS: Conceptualization, Methodology, Investigation, Data Curation, Formal Analysis, and Writing – Original Draft.

NAD: Conceptualization, Methodology, Supervision, Validation, and Writing – Review & Editing.

AYS: Methodology, Supervision, Validation, and Writing – Review & Editing.

AB: Methodology, Supervision, Formal Analysis, Validation, and Writing – Review & Editing.

A: Methodology, Supervision, Validation, and Writing – Review & Editing.

NA: Methodology, Supervision, Validation, and Writing – Review & Editing.

All authors critically reviewed the manuscript, approved the final version, and agreed to be accountable for the integrity of the work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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ETHICS STATEMENT

The study protocol was approved by the Research Ethics Committee of Hasanuddin University (Approval No. 263/UN4.6.4.5.31/PP36/2025; Protocol No. UH25040288) on 30 April 2025. The approval covered genetic, anthropometric, lipid-profile, and fasting-glucose assessments among young adults from the Minahasa, Sangihe Talaud, and Bolaang Mongondouw populations in North Sulawesi. Written informed consent was obtained from all participants before study procedures. The study is reported in accordance with the STROBE guidance for cross-sectional observational studies.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and institutional restrictions.

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