

# Adiposity indices and bone health amongst Malaysian adults: Evidence from a cross-sectional study

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**Abstract.** The relationship between adiposity and bone health is controversial because of the various direct and indirect bone regulatory functions of adipose tissue. Given the limitations of the body mass index (BMI) as a reliable marker of adiposity, several alternative indices have been developed. The different indices show varying associations with bone health. The present study aimed to determine the association between various adiposity indices and bone health amongst Malaysians. In October and November 2024, this cross-sectional study recruited 320 subjects (231 women and 89 men) from a bone health screening event via purposive sampling. The subjects' body weight, height, and waist and hip circumference were measured, and adiposity indices [BMI, waist-to-hip ratio (WHR), waist-to-height ratio (WtHR), body roundness index (BRI), conicity index (CI) and a body shape index (ABSI)] were derived from these basic parameters. The subjects' bone health was evaluated by using a calcaneal

bone quantitative ultrasonometer-derived osteoporosis index (OI). Linear regression analysis was used to determine the relationship between adiposity indices and bone health after adjustment for potential confounders. The strength of association was indicated as beta coefficient ( $\beta$ ). The results indicated that after adjustment for confounders, a significant relationship existed between the OI and all adiposity indices, with the exception of CI. The BMI ( $\beta=0.172$ ,  $P<0.001$ ), waist circumference ( $\beta=0.184$ ,  $P=0.001$ ), WHR ( $\beta=0.124$ ,  $P=0.025$ ), WtHR ( $\beta=0.160$ ,  $P=0.002$ ) and BRI ( $\beta=0.165$ ,  $P=0.001$ ) showed a positive association with bone health, whereas the ABSI ( $\beta=-0.183$ ,  $P=0.008$ ) showed a negative association. In conclusion, adiposity indices associated with body size showed a positive relationship with bone health, whereas the ABSI, which has already been adjusted for body size, showed a negative relationship with bone health.

## Introduction

Osteoporosis, a metabolic disease affecting millions of older adults globally, is represented by the deterioration of bone mass and microarchitecture, leading to fragility fracture (1). Dual-energy X-ray absorptiometry (DXA) is the gold-standard method for diagnosing osteoporosis. It quantifies bone mineral density (BMD) as a surrogate of bone strength. However, DXA is not portable and emits ionising radiation. Therefore, it is unsuitable for deployment in mass bone health screening. These limitations can be overcome with quantitative ultrasonometry (QUS), which provides alternative measures of bone health (2). Previous studies have established that QUS indices predict osteoporosis/osteopenia (3,4) and fracture risk (5) and may reflect microarchitecture (6).

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Apart from being female and menopausal, being underweight is a major risk factor for osteoporosis (7,8). A low body weight negatively impacts bone health by acting as a surrogate for malnutrition or exerting low mechanical loading on bone (9). Mechanical loading is important to stimulate bone repair and maintain bone health (10). Previous studies have firmly established body weight and the body mass index (BMI) as positive predictors of bone health status (11). Obesity, defined by BMI, is found to decrease the odds of osteoporosis by 70.1% (11). The BMI is reflective of body size but may not reflect adiposity status correctly (12). It underestimates the degree of adiposity in patients with sarcopenia but overestimates that in athletes (12). The relationship between adiposity and bone health remains controversial even after the delineation of the effects of the BMI (13).

Adiposity may be a double-edged sword for bone health. On the positive side, it exerts mechanical loading on bone; such loading stimulates bone mass accrual to support a person's weight (14). Adipose tissue also synthesises oestrogens, which are beneficial for bone health (15). Furthermore, the hyperinsulinaemia that is often associated with obesity can increase bone mass because of the anabolic action of insulin (16).

On the negative side, adiposity is associated with chronic inflammation, a state known to cause bone loss. Adipokines secreted by adipocytes, such as adiponectin and resistin, can actively promote bone loss (17,18). Meanwhile, leptin's role is complex: It can be either pro- or antiosteogenic depending on whether it regulates bone health through central or peripheral pathways (19). Therefore, the net effect of adiposity on bone health remains debatable.

Other indices have been developed as alternatives in consideration of the limitations of the BMI in reflecting adiposity. Waist circumference (WC) (20), waist-to-hip ratio (WHR) (21), waist-to-height ratio (WtHR) (22), a body shape index (ABSI) (23), body roundness index (BRI) (24) and conicity index (CI) (25), derived from body anthropometric measurements, can predict cardiometabolic risks well. The relationship between these alternative adiposity indices and bone health has been explored. However, most studies that investigated these relationships are derived from the databases of the National Health and Nutrition Examination Survey on the United States population (26-32), whereas those from other geographical regions are sparse (33-37). Heterogeneous findings, whereby negative and positive relationships between adiposity indicated by the above indices and bone health have been observed, have been obtained. These gaps suggest that additional studies on diverse populations should be implemented.

The present study attempts to address the above research gaps by comparing the associations between various adiposity indices and bone health measured via calcaneal QUS amongst Malaysians. It will help clarify the effect of adiposity on bone health. Its findings are particularly important for Malaysians at two levels. Firstly, Malaysia is rapidly advancing to an ageing society, with 15% of the overall population projected to be aged 60 years or above by 2030 (38). Secondly, Malaysians have a combined obesity and overweight prevalence of 54.4% (39). The compounded effects of ageing and obesity could have an influence on the prevalence of osteoporosis in Malaysia. Therefore, the present study offers insight into adiposity as an interventional target in osteoporosis.

## Patients and methods

*Ethical considerations.* The study protocol was reviewed and approved by the Universiti Kebangsaan Malaysia Ethics Committee (Kuala Lumpur, Malaysia; approval code: JEP-2024-739). Subjects were briefed on the details of the study and provided written informed consent before participating.

*Subject recruitment.* This cross-sectional study was conducted from October 2024 to November 2024 in conjunction with the institutional Osteoporosis Month programme. Subjects were recruited through purposive sampling, in which all individuals who met the selection criteria were invited to participate in the study. The purposive sampling strategy was adopted because of the nature of the health screening event. The screening site was the lobby of Hospital Canselor Tuanku Muhriz, affiliated with Universiti Kebangsaan Malaysia (Kuala Lumpur, Malaysia). The researchers were aware of the biases carried by the recruitment strategy. These biases are discussed amongst the limitations of the study.

The subjects included were adult Malaysians aged 20 years and above. They were excluded if they declared having medical conditions affecting bone health (such as Paget's disease, osteogenesis imperfecta, osteomalacia, rickets, hyper/hypothyroidism, hyper/hypoparathyroidism and chronic kidney diseases) or taking medication that affects bone health [such as glucocorticoids, sex hormones, aromatase inhibitors, androgen deprivation therapy, anticoagulants (heparin and warfarin), loop diuretics, chemotherapeutics, anticonvulsants, antidepressants, thiazolidinediones and antiretrovirals].

*Sample size calculation.* Sample size was calculated by using G\*Power version 3.1.97 (Heinrich-Heine-Universität) with input effect size=0.15 (moderate effect size by convention), alpha error=0.05, power=0.8 and number of predictors (variables of interest and confounders)=16. The calculated minimum sample was 143.

*Confounder measurements.* The subjects answered a demographic, lifestyle and medical history questionnaire that has been used in previous bone health studies (40). Their date of birth and citizenship were identified from their national registration identity card. Their biological sex, ethnicity, household income, pre-existing medical conditions and medical use were self-declared. The lifestyle questionnaire explores the subjects' habits in smoking cigarettes and consuming alcohol, dairy products, tea and coffee. Female subjects answered additional questions on menstrual status.

*Anthropometric measurements.* The subjects' waist circumference at the midpoint between the lowest point of the ribcage and highest point of the iliac crest was determined by using a measuring tape. Hip circumference was measured at the widest part of the gluteal muscle. The subjects' height without shoes was measured with a stadiometer. These three measurements were recorded to the nearest 1 cm. The subjects' body weight while wearing light clothing without shoes was recorded by using a scale (BC353; Accunic) to the nearest 0.1 kg.

Table I. Formula for calculating indices of adiposity.

First author/s, year	Index of adiposity	Formula	(Refs.)
Weir <i>et al</i> , 2023	Body mass index	$\frac{weight (kg)}{squared height (m^2)}$	(41)
Obesity in Asia Collaboration, 2008	Waist-to-hip ratio	$\frac{WC (m)}{hip circumference (m)}$	(42)
Ashwell <i>et al</i> , 2012	Waist-to-height ratio	$\frac{WC (m)}{height (m)}$	(43)
Bertoli <i>et al</i> , 2017	A body shape index	$WC (m)/(BMI^{2/3} \times height^{1/2})$	(23)
Tao <i>et al</i> , 2024	Body roundness index	$364.2 - 356.5 \times \sqrt{1 - \frac{(\frac{WC (m)}{2\pi})^2}{(0.5 \times height (m))}}$	(44)
Martins <i>et al</i> , 2023	Conicity index	$\frac{WC (m)}{(0.109 \times \sqrt{\frac{weight (kg)}{height (m)}})}$	(45)

WC, waist circumference.

**Calculation of adiposity indices.** The adiposity indices BMI (41), WHR (42), WtHR (43), ABSI (23), BRI (44) and CI (45) were calculated on the basis of the formulas shown in Table I.

**Bone health measurements.** The bone health of the subjects was quantified by using a calcaneal bone sonometer (OSTEOKJ3000; Kejin) and recorded as speed of sound (SOS) and broadband ultrasound attenuation (BUA). The osteoporosis index (OI) was calculated automatically by using the formula  $OI = 0.106 \times SOS + 0.5 \times BUA - 127.4$ , as preset by the manufacturer. The subject inserted their nondominant foot into the holder. Two oil-filled balloon transducers were inflated to touch the lateral sides of the calcaneus, which had been cleaned with alcohol and covered with ultrasonic gel. Ultrasound was transmitted through the calcaneal bone and the device interpreted signals. Each subject was measured two times and a third reading was taken when the previous two readings were inconsistent. The categorisation of subjects based on T-score or Z-score was not performed in the present study because the World Health Organisation's cut-offs apply only to DXA. Therefore, raw OI values were used to reflect the bone health of the subject, in which a high value indicates good bone health.

**Statistical analysis.** The Kolmogorov-Smirnov test was used to test for data normality. The subjects' characteristics were compared between men and women by using an independent-samples t-test for normally distributed parameters and the Mann-Whitney U-test for skewed data. Comparison between categorical variables was conducted by employing the Chi-squared test or Fisher's exact test. Multiple linear regression was used to investigate the association between OI

and bone health, with adjustment for potential confounders, such as age, sex, ethnicity, status of smoking (yes or former/no), status of alcohol use (yes or former/no), status of regular milk/tea/coffee consumption (yes/no), calcium supplements (yes/no), self-reported fracture (yes/no), self-reported parental fracture (yes/no), self-reported height reduction (yes/no), use of medication (yes/no) and presence of comorbidities (yes/no). Cook's distance was employed to identify multivariate outliers, which were subsequently removed to ensure the generalisability of the models. Associations were reported in the form of B and  $\beta$  values. Statistical analysis was performed by utilising SPSS version 26 (IBM, Corp.). The data were expressed as mean standard  $\pm$  deviation and n (%).  $P < 0.05$  was considered to indicate a statistically significant difference.

## Results

**Subject characteristics.** The present study recruited 320 subjects (231 women and 89 men) within the study period. The mean age of the subjects was  $50.1 \pm 16.7$  years. The height, weight, waist circumference, WHR, WtHR, CI, BRI, ABSI, skeletal muscle mass, visceral fat area, BUA and OI of men were significantly higher compared with women ( $P > 0.05$ ). The body fat percentage of women was significantly higher compared with men ( $P > 0.05$ ; Table II). Significantly more men were regular cigarette smokers and alcohol consumers ( $P < 0.05$ ). Significantly more women were regular coffee and calcium supplement consumers ( $P < 0.05$ ). The distributions of ethnicity, regular milk and tea consumption, self-reported fracture history, parental fracture history and height reduction were not significantly different between sexes ( $P > 0.05$ ; Table III).

Table II. Subject's age, body composition and calcaneal quantitative ultrasonometry data.

Parameter	Total (n=320)	Women (n=231)	Men (n=89)	P-value
Age, years	50.1±16.7	50.0±16.0	50.5±18.5	0.802
Height, cm	159.8±8.4	156.1±5.2	169.4±7.5	<0.001
Weight, kg	66.8±16.4	63.4±14.2	75.6±18.5	<0.001 <sup>a</sup>
Body weight index, kg/m <sup>2</sup>	26.1±5.6	26.0±5.7	26.2±5.5	0.770 <sup>a</sup>
Waist circumference, cm	85.1±12.0	82.1±10.1	92.7±13.2	<0.001
Waist-to-hip ratio	0.89±0.09	0.87±0.07	0.94±0.12	0.009 <sup>b</sup>
Waist-to-height ratio	0.53±0.07	0.53±0.07	0.55±0.07	0.017
Conicity index	1.21±0.06	1.19±0.03	1.28±0.06	<0.001
Body roundness index	4.08±1.46	3.96±1.39	4.39±1.61	0.024 <sup>a</sup>
A body shape index	0.077±0.004	0.075±0.002	0.081±0.003	<0.001 <sup>b</sup>
Skeletal muscle mass, kg	24.9±5.4	22.6±3.3	30.8±5.4	<0.001 <sup>c</sup>
Fat mass, kg	21.6±8.9	22.2±8.5	20.1±9.7	0.060
Body fat percentage, %	31.5±7.2	33.8±5.9	25.3±6.9	<0.001
Visceral fat area, cm <sup>2</sup>	99.1±52.0	90.7±47.2	120.9±57.8	<0.001 <sup>a</sup>
Speed of sound, m/sec	1,530.3±26.5	1,528.9±24.1	1,533.9±31.9	0.183
Broadband attenuation of sound, dB/MHz	25.1±6.1	24.1±5.7	27.5±6.5	<0.001
Osteoporosis index	47.0±5.4	46.4±4.9	48.6±6.2	0.003

<sup>a</sup>The values were normalized using square-root transformation before being compared; <sup>b</sup>the values were compared using Mann-Whitney U-test; <sup>c</sup>the values were normalized using logarithmic transformation before being compared. Values are expressed as the mean ± standard deviation.

*Association between bone health and adiposity indices.* Linear regression revealed a positive association between OI and BMI ( $\beta=0.212$ ,  $P<0.001$ ), waist circumference ( $\beta=0.268$ ,  $P<0.001$ ), WtHR ( $\beta=0.190$ ,  $P=0.001$ ), CI ( $\beta=0.151$ ,  $P=0.007$ ) and BRI ( $\beta=0.203$ ,  $P<0.001$ ) before adjustment for confounders (Table IV, Model 1). After adjustment for confounders (Table IV, Model 2), a significant positive association was found between OI and BMI ( $\beta=0.172$ ,  $P<0.001$ ), waist circumference ( $\beta=0.184$ ,  $P=0.001$ ), WHR ( $\beta=0.124$ ,  $P=0.025$ ), WtHR ( $\beta=0.160$ ,  $P=0.002$ ) and BRI ( $\beta=0.165$ ,  $P=0.001$ ). A significant negative association was found between OI and ABSI ( $\beta=-0.183$ ,  $P=0.008$ ). The changes in the regression coefficient with the increment of confounders are presented in Table SI. The associations between OI and adiposity indices were consistent in each model, showing their robustness.

## Discussion

The present cross-sectional study found a positive association between bone health and BMI, waist circumference, WHR, WtHR, CI and BRI and a negative association between bone health and ABSI amongst Malaysians. It found no significant association between bone health and CI.

In the present study, the BMI was found to be positively associated with bone health. This observation agrees with the authors' previous findings on Malaysian men aged >20 years that revealed a positive relationship between BMI and bone health, as indicated by QUS (46). As mentioned earlier, underweight is well recognised as a strong risk factor for osteoporosis (7,8). A Mendelian randomisation study demonstrated a causal relationship between BMI and BMD; however,

this relationship is site-specific (47). A high BMI was found to causally increase the BMD at the lumbar spine and calcaneus but exerts no effects on forearm and femoral neck BMD (47). This association is likely driven by mechanical loading (11). However, the relationship between the BMI and bone health is highly complex. A meta-analysis reported a low risk of vertebral fracture with a high BMI in men, whereas the inverse was observed in women after adjustment for BMD (48). Another meta-analysis found that an increased BMI was associated with trabecular microarchitecture deterioration (49). Therefore, an increased BMI associated with BMD does not always translate into improved bone quality.

In this work, bone health was positively associated with the waist circumference, WHR, WtHR and BRI. Given that these indices were not adjusted for the BMI, they could act as surrogate measures for body size, reflecting the relationship between mechanical loading and bone health. This observation was supported by other studies that indicated a positive association between the above indices and BMD (37) or a negative association between the above indices and osteoporosis risk (29,31,50). Nevertheless, other studies reported contradictory results (32,34,51). These controversies may be explained by a nonlinear relationship between these indices and bone health (U-shape) and sex differences in this relationship (52). As a result of the limited number of male subjects, a sex-based subanalysis was not performed in the present study.

CI was positively associated with bone health in the adjusted model. However, this association weakened after adjustment for potential confounders. CI primarily reflects central adiposity and, indirectly, the effects of body size and mechanical loading on bone, thereby explaining the above positive association. Nevertheless, this association is weak

Table III. Subject characteristics.

Item	Total (n=320)	Women (n=231)	Men (n=89)	P-value
Ethnicity				0.145
Malay	180 (56.3)	137 (59.3)	43 (48.3)	
Chinese	113 (35.3)	79 (34.2)	34 (38.2)	
Indian	18 (5.6)	10 (4.3)	8 (9)	
Others	9 (2.8)	5 (2.2)	4 (4.5)	
Menstrual status				NR
Regular	105 (45.5)	105 (45.5)	NR	
Irregular	16 (6.9)	16 (6.9)	NR	
Menopausal	110 (47.6)	110 (47.6)	NR	
Regular smoking <sup>a</sup>				<0.001
No	303 (94.7)	227 (98.3)	76 (85.4)	
Yes	17 (5.3)	4 (1.7)	13 (14.6)	
Regular alcohol drinking				0.009
No	304 (95)	224 (97)	80 (89.9)	
Yes	16 (5)	7 (3)	9 (10.1)	
Regular milk consumption				0.845
No	195 (60.9)	140 (60.6)	55 (61.8)	
Yes	125 (39.1)	91 (39.4)	34 (38.2)	
Regular coffee drinking				0.021
No	161 (50.3)	107 (46.3)	54 (60.7)	
Yes	159 (49.7)	124 (53.7)	35 (39.3)	
Regular tea drinking				0.289
No	177 (55.3)	132 (57.1)	45 (50.6)	
Yes	143 (44.7)	99 (42.9)	44 (49.4)	
Regular calcium supplement				0.018
No	228 (71.3)	156 (67.5)	72 (80.9)	
Yes	92 (28.7)	75 (32.5)	17 (19.1)	
Self-reported fracture history				0.962
No	280 (87.5)	202 (87.4)	78 (87.6)	
Yes	40 (12.5)	29 (12.6)	11 (12.4)	
Self-reported parental fracture				0.151
No	273 (85.3)	193 (83.5)	80 (89.9)	
Yes	47 (14.7)	38 (16.5)	9 (10.1)	
Self-reported height reduction				0.238
No	280 (87.5)	199 (86.1)	81 (91)	
Yes	40 (12.5)	32 (13.9)	8 (9)	

<sup>a</sup>Fisher's exact test was used instead of Pearson's Chi-square because >20% of cells have a count <5. Values are expressed as n (%). NR, not relevant.

and not independent of the covariates studied. While CI is a useful cardiometabolic risk marker, it may not effectively predict bone health. Another study comparing the association between various anthropometric indices and osteoporosis risk found that CI did not perform as well as BRI and WtHR (53).

In this research, bone health was negatively associated with ABSI. Similar findings were obtained by previous studies (27,28,30,34-36,54), which reported low BMD and high osteoporosis risk. Given that the calculation of ABSI accounts for BMI, ABSI may accurately reflect the adiposity

status independent of body size. It has been shown to correlate with visceral adiposity without being influenced by body weight (55). Visceral fat has a more significant association with systemic inflammation and metabolic dysregulation than subcutaneous fat (56). These underlying mechanisms could explain the negative association between ABSI and bone health observed in the present study. However, given that inflammatory cytokine and adipokine levels were not determined in the subjects of this research, this mechanistic explanation remains speculative.

Table IV. Association between bone health (osteoporosis index) and adiposity indices.

Parameter	n <sup>a</sup>	Model 1				Model 2			
		B	SE	$\beta$	P-value	B	SE	$\beta$	P-value
Body mass index	300	0.189	0.05	0.212	<0.001	0.152	0.043	0.172	<0.001
Waist circumference	300	0.105	0.022	0.268	<0.001	0.072	0.021	0.184	0.001
Waist-to-hip ratio	302	1.182	3.024	0.022	0.700	6.485	2.874	0.124	0.025
Waist-to-height ratio	302	13.756	4.111	0.190	0.001	11.581	3.625	0.16	0.002
Conicity index	302	14.647	5.367	0.151	0.007	7.106	7.078	0.073	0.316
Body roundness index	302	0.695	0.194	0.203	<0.001	0.566	0.171	0.165	0.001
A body shape index	298	5.529	79.668	0.004	0.945	-251.311	94.264	-0.183	0.008

<sup>a</sup>The number of subjects in each model is <320 due to the removal of multivariate outliers/influential cases. This is to ensure the generalizability of the models. Model 1 is unadjusted.

Model 2 is adjusted for age, sex, ethnicity, status of smoking (yes or former/no), alcohol use status (yes or former/no), regular milk/tea/coffee consumption status (yes/no), calcium supplements (yes/no), self-reported fracture (yes/no), self-reported parental fracture (yes/no), self-reported height reduction (yes/no), medication use (yes/no), presence of co-morbidities (yes/no). SE, standard error.

Several limitations should be noted before generalising the results of the present study. The cross-sectional nature of this work prevents causal inference between adiposity and bone health. The subjects' recruitment from a health screening programme is prone to suffering from selection and volunteer biases. Therefore, the characteristics of these subjects might differ from those of the general population. For example, the subjects who volunteered for the present study may be more health-conscious than the general population. Conversely, they may have specific health concerns that motivated them to participate in the research. The nonrandomised sampling approach also prevented the authors from comparing the baseline characteristics of the subjects with those of a national representative cohort, such as the cohort included in the National Health and Morbidity Survey of Malaysia, to verify the extent of sampling bias. The small sizes of subgroups (based on sex, ethnicity and BMI status) also prevented the authors from investigating the relationship between variables in different contexts. Certain studies have demonstrated that the association between the adiposity index and bone health can be influenced by sex and diabetes status (28,52), and most have revealed consistent associations (26,31,32). A study found that the connection between adiposity and bone health differs by sex in older adults (52). For postmenopausal women, the relationship is U-shaped: Both very low and very high adiposity levels are associated with poor bone health. This may be because low body fat limits their postmenopausal oestrogen production (57), which supports bone health, while high body fat promotes chronic inflammation that damages bones. For older men, the relationship is linear, meaning bone health simply declines as adiposity increases, likely due to the damaging effects of chronic inflammation.

Regarding the bone health assessment tool, QUS is not the gold standard for diagnosing osteoporosis despite its portability and safety features. Its T- and Z-scores cannot be used interchangeably with the values generated by DXA because of differences in reference values and technology. In the present study, the physical activity levels of the subjects

were excluded from the analysis because the subjects had difficulty in accurately recalling their physical activities. Bone health biochemical markers, such as circulating vitamin D, calcium and phosphorus levels, were not determined in this research because blood collection was not performed in the health screening session. Nevertheless, this work provides novel insights into the relationship between adiposity and bone health and affirms that ABSI could be considered as a risk factor for osteoporosis in the general population.

In conclusion, amongst Malaysians, adiposity indices unadjusted for body size, such as the BMI, waist circumference, WHR, WtHR, CI and BRI, are positively associated with the bone health index measured by QUS. By contrast, ABSI, which accounts for body size, shows a negative association with the bone health index. The findings of this work suggest that ABSI may be a useful marker for identifying individuals at risk of poor bone health in the Malaysian population. However, its critical value and clinical effectiveness still require further substantial validation before it can be reliably used as a routine risk assessment tool.

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### Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

### Authors' contributions

KYC, NM, SKW, TRJ and SA were involved in the conceptualisation of the study and acquired funding. KYC, WjZ, YW, XJ and YG performed data curation. KYC performed formal analysis, project administration and supervision. WjZ, WzZ, KYC, XM, HSTS, SOE, YW, XJ and YG performed investigations. KYC, NM, SKW, TRJ and SA were responsible for methodology. WjZ, WzZ and XM provided resources. WjZ, WzZ and KYC wrote the original draft. NM, SKW, TRJ and SA reviewed and edited the manuscript. KYC and WjZ confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

### Ethics approval and consent to participate

The Universiti Kebangsaan Malaysia Ethics Committee approved the present study (Kuala Lumpur, Malaysia; approval no: JEP-2024-739) and participants provided informed consent prior to participation.

### Patient consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

### Use of artificial intelligence tools

During the preparation of this work, artificial intelligence tools [ChatGPT 3.0 (OpenAI)] were used to improve the readability and language of the manuscript, and subsequently, the authors revised and edited the content produced by the artificial intelligence tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

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