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Review Article

Association of Obesity with Coronary Artery Disease, Erosive Esophagitis and Gastroesophageal Reflux Disease: A Systematic Review and Meta-Analysis

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Abstract

Background: We aimed to determine the plausible role of high body mass index (BMI) in the etiopathogenesis of coronary artery disease (CAD), erosive esophagitis (EE) and gastroesophageal reflux disease (GERD) and their complex associations.

Methods: The published literature was retrieved from Cochrane, Google Scholar, Embase, PubMed and Scopus databases until August 2021 based on the inclusion and exclusion criteria. The Newcastle-Ottawa quality assessment scale was used for the risk of bias and publication bias with a funnel plot. Heterogeneity between studies underwent evaluation using the I^2 statistic and Q-test, and a random and fixed-effect model analysed studies with low to moderate heterogeneity.

Results: Out of 3819 studies extracted, 20 studies were studied based on the inclusion and exclusion criteria. The study corroborated the direct association of GERD symptoms and EE among obese Odds Ratio (OR) = 4.25) and overweight subjects (OR 9.75). Separate analyses of the link between GERD symptoms and EE was conducted among the overweight (OR 4.11, OR 4.61) and obesity subjects was statistically significant (OR 12.07, OR 9.95). The corresponding adjusted OR was noted for the association of CAD with overweight and obesity amounted to 3.41 and 3.01, respectively. Separate subgroup analysis was analyzed based on different ethnic populations for the association between GERD symptoms and EE in obesity (OR of 9.38) and overweight (OR of 4.21) subjects were statistically significant ($P<0.05$). For population subgroup analyses the overall OR of 3.32 was noted on the association between CAD and obesity.

Conclusion: Moderate to severe BMI has bene considered as an independent risk factor for GERD symptoms, EE and CAD.

Keywords: Body mass index; Obesity; Acid reflux; Coronary artery disease; Overweight

Background

Obesity has become an increasingly global epidemic, with approximately 1.9 billion adults and 340 million pediatric subjects considered overweight or obese. According to the WHO, the

global burden of obesity has increased three-fold since 1975 (1) and the prevalence of obesity could surpass 50% by 2030 (2). Meanwhile, the estimated prevalence among adults with body mass index BMI>30kg/m^2 was 11.4% in 2010 could increase to 17.5% 2030 (3). Excess adiposity is a key element in persuading the development of various risk factors for cardiovascular diseases: hypertension (4), diabetes (5), dyslipidemia, gastrointestinal (GI) disorders such as inflammatory bowel disease (IBD) (6), GI cancer and pancreatitis (7, 8). Obesity-linked pathological conditions have been identified as the principal cause of mortality among Asian Indians (9). A complex and multifactorial etiopathogenesis of coronary artery disease (CAD) and GI's association is noticed among the subjects with obesity/overweight (10).

Several studies have noted that the impact of obesity on gastrointestinal health may include an increased severity of Crohn's Disease and an elevated risk for cancer and CAD (11). Obesity is considered a risk factor for colorectal cancer and its postoperative recurrence (12). A prospective clinical and endoscopic study by Vaishnav et al. reported increasing frequency, prevalence and severity of symptoms with elevated BMI. The researchers also noted a significant correlation between erosive esophagitis (EE) and dyspeptic symptoms with body mass index (BMI, $P<0.05$) (13). Gastroesophageal reflux disease (GERD) and CAD share metabolic syndrome as a common risk factor (14). Obesity shares a link with a significant increase in the risk of erosive esophagitis, GERD symptoms and esophageal adenocarcinoma (15). The researchers also noted a progressive increase in the risk of these disorders with weight gain (15). Liu et al. noted the common incidence of acid reflux in subjects with CAD and refractory chest pain (16).

The association between obesity and GI can be better explained by the quantitative and qualitative alterations noticed in the gut microbiota of obese patients (17). Currently GERD has been considered as a primarily the disorder of the esophagogastric junction, which is significantly related to esophageal acid exposure (18). To the best of our knowledge, and the literature review shows minimal studies describing the complex associations of GERD, EE and CAD and the common risk factor particularly, obesity.

The present systematic review and meta-analysis explored the plausible role of high BMI, a marker of obesity, in the etiopathogenesis of CAD, EE and GERD and their complex associations. The findings could recognize that obesity is the common risk factor for the development of GERD, EE and CAD.

Methods

This study has proceeded in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (19). Studies underwent extraction from the literature databases based on the inclusion and exclusion criteria. The inclusion criteria for diagnosing CAD comprised health-screening examinations, coronary angiography, Minnesota coded electrocardiogram, and cardiac-gated CT scans for CAC scoring. The inclusion criteria for diagnosis of GERD and EE included gastrointestinal endoscopy, esophagogastroduodenoscopy-validated or telephonic questionnaires and the Los Angeles classification system.

The case-control, cross-sectional or cohort studies with assessment on association of obesity with GERD, EE and CAD were included. In addition, studies that well defined the BMI and outcome of interest with the aforementioned diagnosis were included. The exclusion criteria comprised; abstracts, reviews, *in vitro* animal studies, randomised control trials, literatures with case reports, case-series, and studies with a lack of obesity data and those with insufficient data on BMI, waist-hip ratio and waist circumference (WC) categories for obesity, and other than English language studies were excluded from the current study.

Literature search

The published literature studies until August 2021 were retrieved from the Cochrane, Google Scholar, Embase, PubMed and Scopus databases.

The keywords considered for the search were 'obesity', 'coronary artery disease, 'body mass index', 'waist-hip ratio', 'waist circumference', 'gastroesophageal reflux' and 'erosive esophagitis'. The search MESH terms used for the retrieving articles from PubMed has been listed in the supplemental Table 1 (Supplementary data are not published. Readers may contact the corresponding author for more details).

Data extraction

A preliminary search of various databases selected articles with a title and abstract matching the aforementioned criteria. The abstracts retrieved from electronic databases for selected and eligible studies underwent assessment. In addition, we have searched the bibliographies manually of retrieved articles. Only those studies that helped to calculate the odds ratio (OR) or hazard ratio (HR) of exposure to obesity and CAD and GERD as outcomes were included. The first author, year of publication, cut-off values for defining obesity and odds and hazard ratio for GERD and CAD were noted. Outcomes considered for data extraction included BMI, waist-hip ratio, WC and diagnosis of CAD and GERD. Fig. 1 shows the PRISMA flow diagram of the study selection.

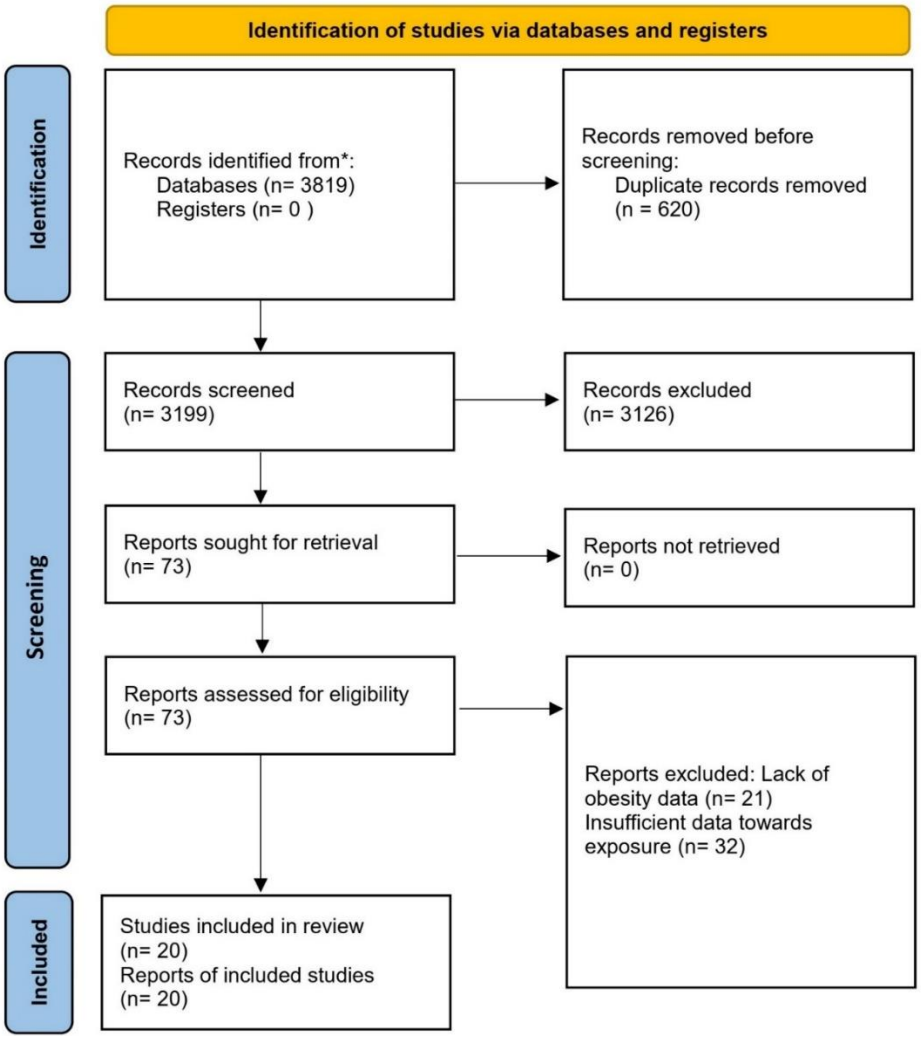


Fig. 1: PRISMA flowchart for the selected studies

Quality assessment of selected studies

The risk of bias was assessed using NOS by broadly categorising the studies as case-control and cohort studies. The NOS instrument evaluates the risk of bias by granting a star for each answer that meets the criteria. In keeping with the instrument, each study can obtain a maximum of nine stars: four for selection, two for comparability and three for the outcome.

Publication bias

The chance of publication bias underwent evaluation through a visual demonstration using a funnel plot with standard error (SE) and mean of each study on the y-axis and x-axis, respectively.

Statistical analysis

The summary OR was estimated using either relative risks or ORs as we considered that OR was a valid estimation of the risk ratio. Heterogeneity between studies was examined using the I^2 statistic and Q-test, whereby P <0.10 and I^2 > 50% indicated high heterogeneity. A random-effect model was applied by calculating pooled HRs and their CIs for meta-analysis. However, a fixed-effect model was also analyzed studies with low heterogeneity (I^2 = 0%). Further analysis took place by categorising the studies based on ethnicity and BMI. Publication bias was visually identified using funnel plots, where the log SE of log HR was plotted against HR and any asymmetric plot suggested a possible publication bias. To determine the statistical significance difference, Egger's and Begg's linear regression tests were conducted. All data analysis occurred using the Open Meta [Analyst] software (http://www.cebm.brown.edu/openmeta) and Review Manager (RevMan) [computer programme] (Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Statistical significance was considered as *P*-value <0.05.

Results

Study selection

The literature search of various databases until August 2021 yielded 3819 studies. Out of these studies, 620 were removed due to duplicate records. Among the 3199 records screened, 3126 did not make the final list, as they existed outside the field of interest, and the studies lacked data on the association of obesity with CAD and GERD. Out of 73 studies assessed for eligibility, 21 were excluded due to lack of obesity data and 32 due to insufficient data on BMI, waist-hip ratio and waist circumference categories for obesity. The inclusion/exclusion criteria meant that 20 studies (20-39) could form part of the meta-analysis.

Tables 1 and 2 illustrate the characteristics of the selected obesity and GERD studies. Among the selected studies, six were case-control, and the remaining were cohort studies. The age group of participants ranged from 32 to 74.1 years. In studies with GERD as the outcome, the exposure underwent assessment-using BMI in 11 studies (20-30). For the studies involving CAD as an outcome of interest, the corresponding number of studies using BMI amounted to nine (31-39). In studies with GERD as an outcome and obesity as exposure, out of 11 studies, eight came from the Asian region (20-24, 26-28), two from the European region (25, 29) and one from the American region (30). In studies with CAD as an outcome and obesity as exposure, out of nine studies, six from the Asian region (31,32,34,35,38,39), one study from the European region (33) , and two from the American region (36,37).

Table 1: Basic characteristics of selected obesity and GERD studies

Author	*Year*	*Study design*	*Sample size*	*Age (Mean/ Median/ Range)*	*Gender (M : F)*	*Country*	*Obesity measurements*	*GRED criteria*
Kang et al [20]	2007	Cohort	161	45.3	145:6	South Korea	BMI ≥ 30, waist circum-ference: ≥80 cm in women or ≥90 cm in men	Esophago gastroduodenoscopy and self-administered vali-dated questionnaire
Chung et al [21]	2008	Case-control	3539/3539	47.6	M: 2810/ 2810	South Korea	BMI ≥25	endoscopy
Chua et al [22]	2009	Case-control	427/427	48.3	365:62/ 365:62	Taiwan	BMI >25 waist circumference: ≥80 cm in women or ≥90 cm in men	Esophagogastro duodenoscopy and Los Angeles classifi-cation system
Lee et al [23]	2009	Case-control	100/ 100	52.73/ 50.65	76:24/ 76:24	South Korea	BMI ≥ 30 Waist hip ratio: >0.90 cm	endoscopy and Los Angeles classifica-tion system
Nam et al [24]	2010	cohort	495	50.3	M: 432	South Korea	BMI ≥30.0 Waist circum-ference _≥100.0, Waist-to-hip ratio _≥100.0	Questionnaire and Esophagogastro duodenoscopy
Rubio et al [25]	2004	cohort	2500	40–79	1185: 1315	Spain	BMI ≥30.0	Telephone ques-tionnaire
Hung et al [26]	2014	cohort	1922	49.6	M:1438	Taiwan	BMI ≥27 kg/m2 waist circum-ference: ≥80 cm in women or ≥90 cm in men	Oesophagogastro duodenoscopy
Moki et al [27]	2007	cohort	5159	47.1	3599:1560	Japan	BMI ≥ 25.0	gastrointestinal en-doscopy
Nam et al [28]	2009	cohort	552	48.8	M: 552	South Korea	BMI ≥30.0 Waist circum-ference _≥100.0	Esophagogastro duodenoscopy
Nilsson et al [29]	2003	case-control	M: 1555/ 18814 F: 1598/ 21396	M: 58/48 F: 53/47	Case: 1555: 1598 Control: 18814: 21396	Sweden	BMI ≥30.0	Questionnaire
Locke et al [30]	1999	cohort	1562	50.5	1524	USA	BMI ≥30.0	Questionnaire

Table 2: Basic characteristics of selected obesity and CAD studies

Author	*Year*	*Study design*	*Sample size*	*Age(Mean/ Median/ Range)*	*Gender (M : F)*	*Country*	*Obesity Measurements*	*CAD Criteria*
Choi et al [31]	2018	Cohort	2 611 450	34.3	1 802 408: 809 042	South Korea	BMI ≥30.0	Health screening
Azab et al [32]	2018	Cohort	556	55	M: 395	Jordan	BMI ≥30.0	Coronary angiography
Bechlioulis et al [33]	2013	Cohort	207	62	M: 178	Greece	BMI ≥30.0 Moderate central obesity: WC ≥102 and <110 cm in men and ≥88 and <105 cm in 4women; severe central obesity, WC ≥110 cm in men and ≥105 cm in women.	Coronary angiography
Tseng et al [34]	2008	Cohort	M: 233 F: 267	M: 66.6 F: 66.8	233/267	Taiwan	BMI ≥30.0 Waist-to-hip ratio: ⩾102 cm in males and ⩾88 cm in females WC: ≥80 cm in women or ≥90 cm in men	Minnesota coded electrocardiogram
Lin et al [35]	2015	Cohort	N: 93 O: 218 Mi: 145 M to S: 61	N: 74.1 O: 72.6 Mi: 73.1 M to S: 72.2	M: N: 72 O: 158 Mi: 106 M to S: 33	Taiwan	Mild obesity: BMI: 27.0-29.9 M to S: BMI ≥30.0	Coronary angiography
Zen et al [36]	2012	Case-control	155/221	59.7/ 57.3	M: 114/128	Brazil	BMI ≥30.0 Waist-to-hip ratio: ⩾102 cm in males and ⩾88 cm in females WC: ≥80 cm in women or ≥90 cm in men	Coronary angiography
Jensen et al [37]	2020	Cohort	36509	54.1	M: 23954 F: 12555	New York	BMI ≥30.0	Cardiac-gated CT scans for CAC scoring
Hsu et al [38]	2007	Cohort	48	50.5	37:11	Taiwan	Mi: 27.0–29.9 Obesity: BMI: >30	CAC Score
Park et al [39]	2017	Cohort	1342	59.7	M: 728	South Korea	BMI≥27.5	Coronary angiography

M: Male, F: Female, N: Normal, O: Overweight, Mi: Mild obesity, M to S: Moderate to severe obesity, WC: Waist circumference.

Quality assessment

The quality assessment conducted using NOS scores (Table 3) revealed that six studies had obtained the maximum score of 9. The number of studies with scores 8 and 7 amounted to nine and seven, respectively, whereas only one study had yielded a total score of 6 (25).

Table 3: Newcastle-Ottawa-Scale scores for the quality assessment of including studies

S.No	Author Year	Selection	Comparability	Exposure	Total
Case-control studies					
	Chung et al 2008(21)	★★★★	★★	★★	8
	Chua et al 2009(22)	★★★	★★	★★	7
	Lee et al 2009(23)	★★★★	★	★★	7
	Nilsson et al 2003(29)	★★★★	★	★★★	8
	Zen et al 2012(36)	★★★	★★	★★	7
Cohort studies					
	Nam et al 2010(24)	★★★★	★	★★★	8
	Rubio et al 2004(25)	★★	★★	★★	6
	Hung et al 2014(26)	★★★★	★★	★★★	9
	Moki et al 2007(27)	★★★	★★	★★★	8
	Nam et al 2009(28)	★★★★	★★	★★★	9
	Locke et al 1999(30)	★★★	★★	★★	7
	Choi et al 2018 (31)	★★★	★★	★★★	8
	Azab et al 2018 (32)	★★★★	★★	★★	8
	Bechlioulis et al 2013(33)	★★★★	★★	★★★	9
	Kang et al 2007 (20)	★★★★	★	★★	7
	Tseng et al 2008 (34)	★★★★	★	★★★	8
	Lin et al 2015 (35)	★★★	★	★★★	7
	Jensen et al 2020(37)	★★★	★	★★★	7
	Hsu et al 2007 (38)	★★★	★★	★★★	8
	Park 2017 (39)	★★★	★★	★★★	8

Meta-analysis results

Nine studies, considered for the evaluation of the association between GERD symptoms and EE in overweight subjects (BMI ≥25), proved significant (OR = 4.25, 95%CI: 3.16-5.71, I2 81%, *P* <0.00001, Fig. 2A). Four studies that evaluated the relation between GERD symptoms and overweight subjects showed OR 4.11 (95%CI: 3.04-5.56). The I2 statistic noted was 36% (*P* <0.0001, Fig. 2B). The meta-analysis of five studies, which evaluated the association between EE and being overweight based on BMI ≥25, yielded an OR of 4.61 (95%CI: 2.57-8.28, I2=86%, *P* <0.00001, Fig. 2C).

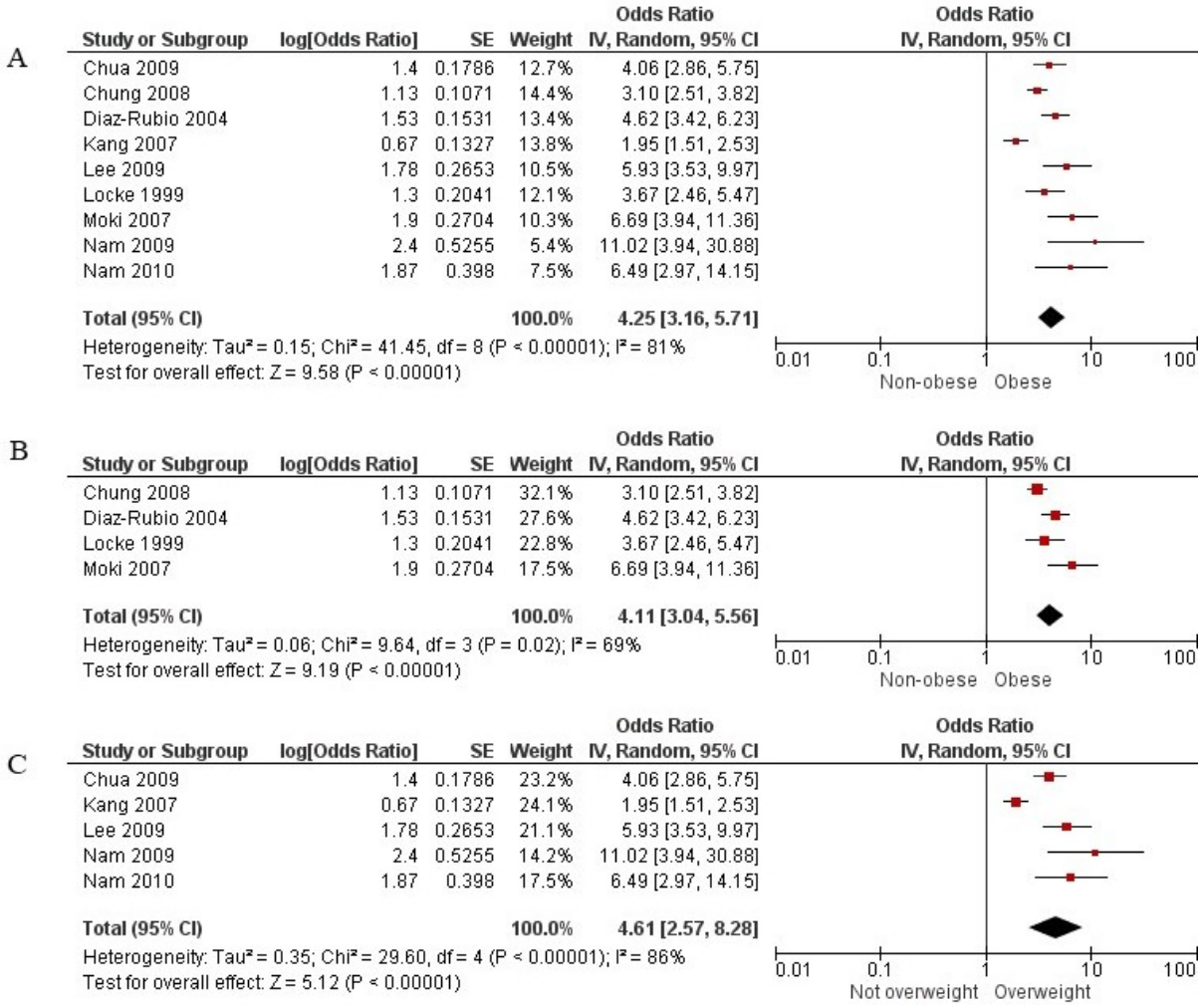


Fig. 2: (A) shows the adjusted odds ratio for the association between GERD symptoms and EE in overweight, (B) association between GERD symptoms and overweight and (C) association between EE and overweight based on BMI ≥25

The association between GERD symptoms and EE in obesity (BMI ≥30), analyzed using six studies, had high significance (OR 9.75, 95%CI: 4.59-20.71, I2=81%, *P* <0.0001, Fig. 3A). Similarly, the association between GERD symptoms and obesity was highly significant upon evaluation of two studies (OR 12.07, 95%CI: 2.39-60.92, I2=87%, *P*-0.006, Fig. 3B). Studies also found that the association between EE and obesity proved substantially significant (OR 9.95, 95%CI: 3.12-31.71, I2=83%, *P*=0.0001, Fig. 3C).

Adjusted OR for the association between CAD and obesity (BMI ≥30) noted amounted to 3.41 (95% CI: 2.13-5.48, I2=98%, *P*<0.00001, Fig. 4A). The funnel plot for the analysis showed that out of five studies, three were outliers (Fig. 4B). Adjusted OR for the association between CAD and overweight subjects (BMI ≥25) amounted to 3.01 (95% CI: 2.89-3.13, I2=0%, *P*<0.00001, Fig. 5A). The funnel plot indicated no publication bias for the studies considered, as all the studies' dispersion fell within the funnel (Fig. 5B).

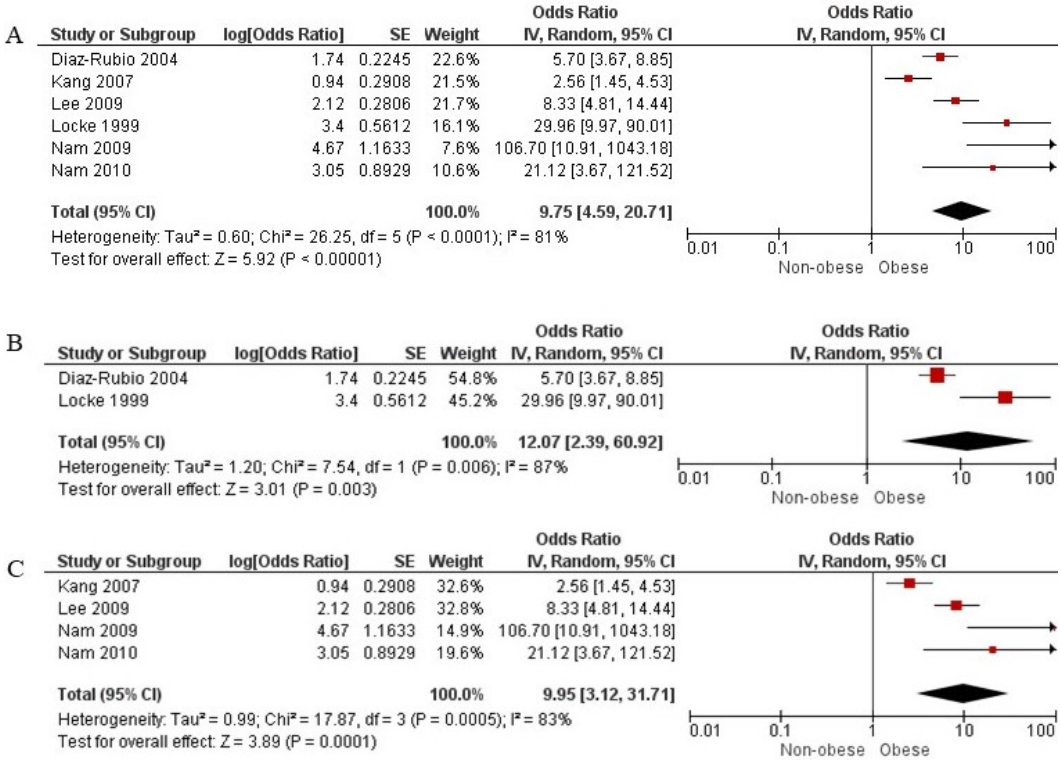


Fig. 3: (A) Adjusted odd ratios for the association between GERD symptom and EE in obesity, (B) association between GERD symptom and obesity and (C) association between EE and obesity based on BMI ≥30

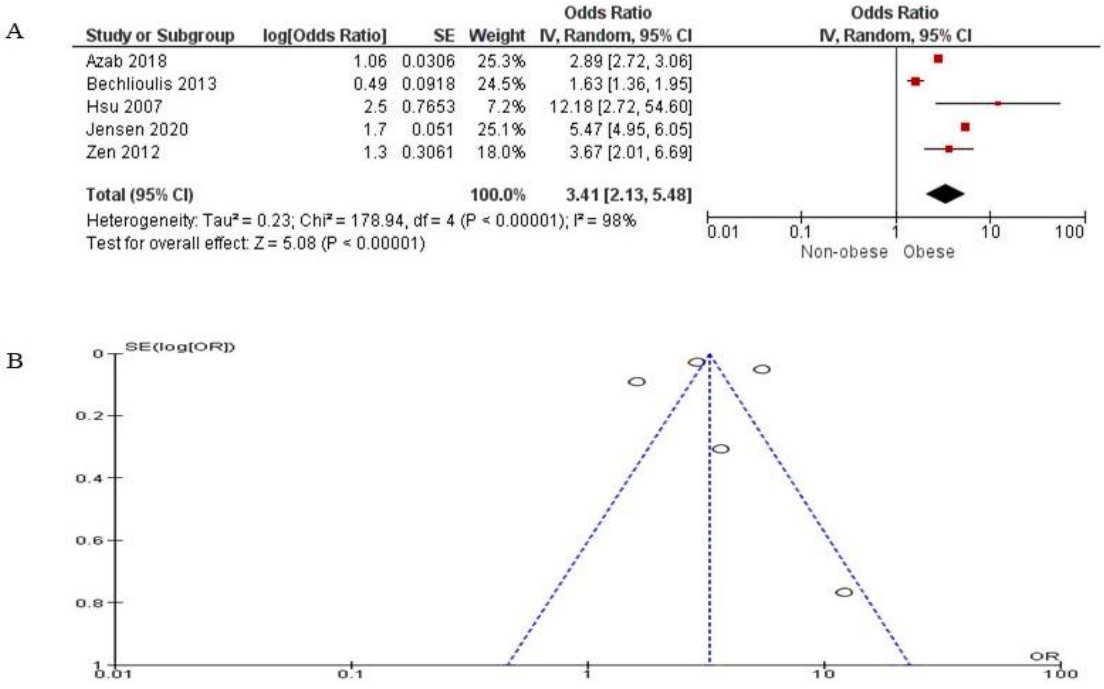


Fig. 4: (A) Adjusted odds ratio for the association between CAD and obesity and (B) Funnel plot for publication bias in the meta-analysis between CAD and obesity based on BMI ≥30

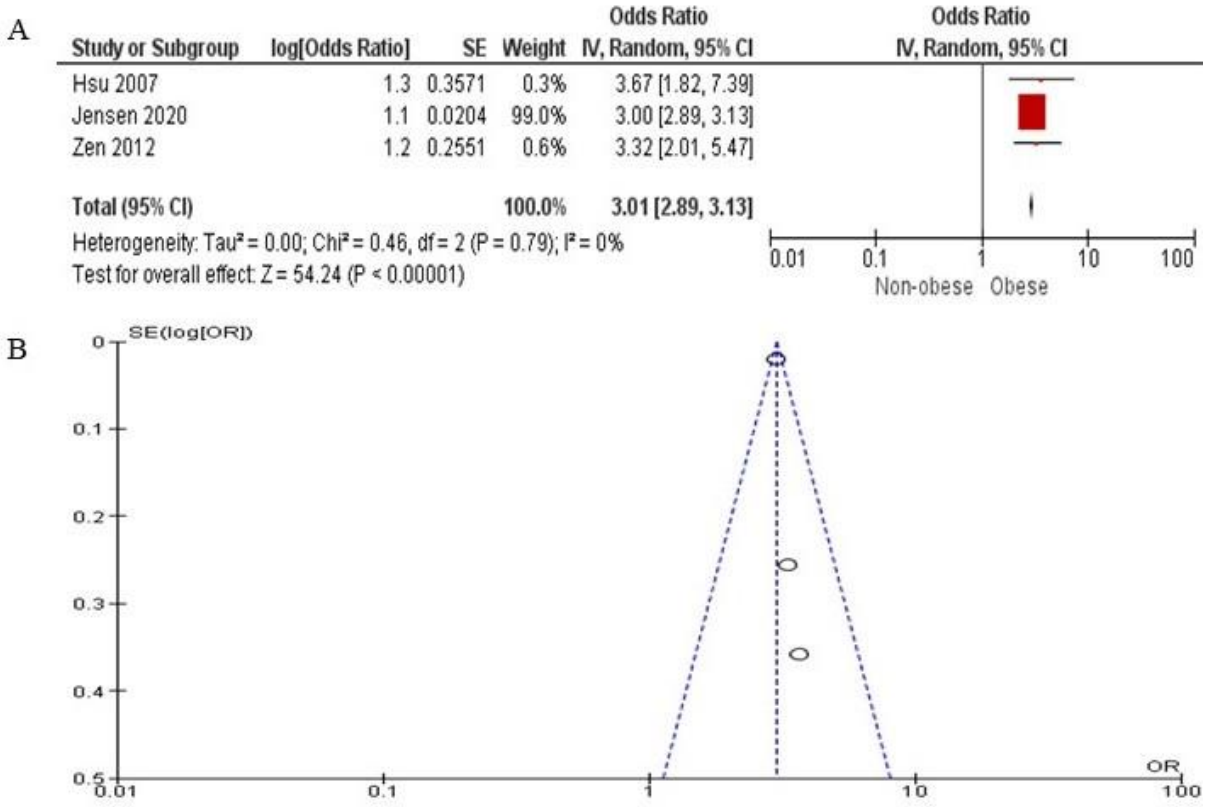


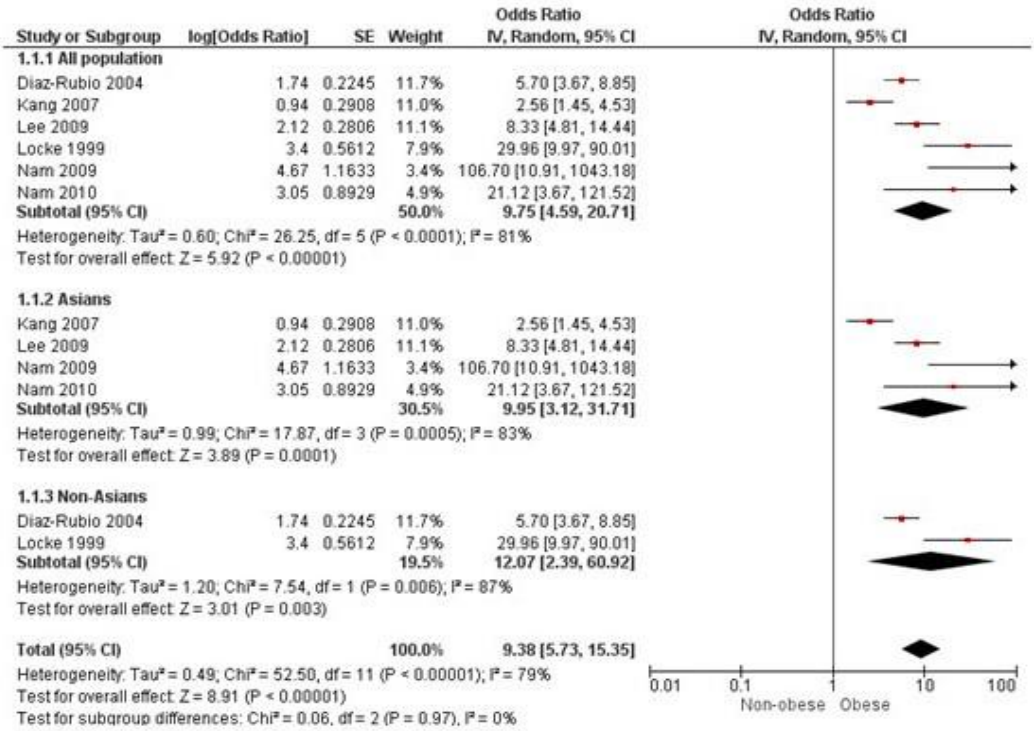
Fig. 5: Adjusted odds ratio for the association between CAD and overweight and (B) Funnel plot for publication bias in the meta-analysis between CAD and overweight based on BMI ≥25

Subgroup analysis

The subgroup analysis based on different ethnic populations for the association between GERD symptoms and EE in obesity (BMI≥30) showed an adjusted OR of 9.38 (95% CI: 5.73-15.35, I2=79%, *P*<0.00001, Fig. 6A). Meta-analysis of two studies considered for the non-Asian group demonstrated that the association proved significantly high with an OR of 12.07 (95% CI: 2.39-60.92, I2=87%, *P*=0.006, Fig. 6A). The meta-analysis involving four studies showed that the association also proved significant in the Asian population (OR 9.95, 95% CI: 3.12-31.71, I2=83%, *P* <0.00001). The analysis of all populations showed an adjusted OR of 9.75 (95% CI: 4.59-20.71, I2=81%, *P* <0.00001, Fig. 6A).

Population subgroup analyses on the association between GERD symptom and EE in overweight subjects (BMI ≥25) was found to be significant with an OR of 4.21 (95% CI: 3.45-5.15, I2=79%, *P*=0.37, Fig. 6B). The association was substantially significant for the non-Asian group with an OR of 4.25 (95% CI: 3.34-5.40, I2=0%, *P* <0.00001, Fig. 6B). The meta-analysis involving two studies showed a significant association in the Asian population (OR 4.38, 95% CI: 2.98-6.44, I2=84%, *P*=0.06, Fig. 6B). The analysis of all populations indicated an adjusted OR of 4.25 (95% CI: 3.16-5.71, I2=81%, *P* <0.00001, Fig. 6B).

A



B

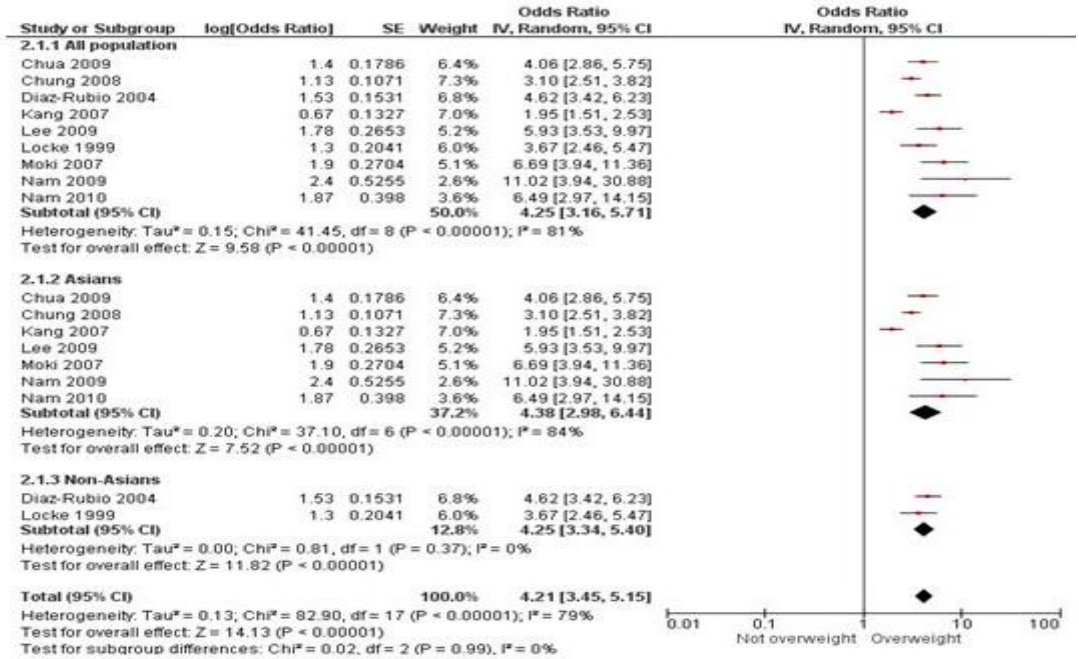


Fig. 6: (A) Population subgroup analyses on the association between GERD symptom and EE in obesity based on BMI≥30, and (B) Population subgroup analyses on the association between GERD symptom and EE in overweight based on BMI ≥25

Population subgroup analyses on the association between CAD and obesity (BMI ≥30) proved significant with an OR of 3.32 (95% CI: 2.52-4.38, I2=97%, *P* <0.00001, Fig. 7A). The association was substantially significant for the non-Asian group with an OR of 3.19 (95% CI: 1.24-8.17, I2=98%, *P* <0.00001, Fig. 7A). The meta-analysis involving two studies showed a significant association in the Asian population (OR 4.84, 95% CI: 1.25-18.74, I2=72%, *P*=0.06, Fig. 7A). The analysis of all populations indicated an adjusted OR of 3.41 (95% CI: 2.13-5.48, I2=98%, *P* <0.00001, Fig. 7A).

The funnel plot for publication bias in the population subgroup meta-analysis between CAD and obesity (BMI ≥30) showed three outliers (one Asian and two all population studies) out of four studies considered (Fig. 7B). Substantial heterogeneity among the study estimates was noted for all the aforementioned meta-analyses with significant *P*-values and/or high I^2 statistics.

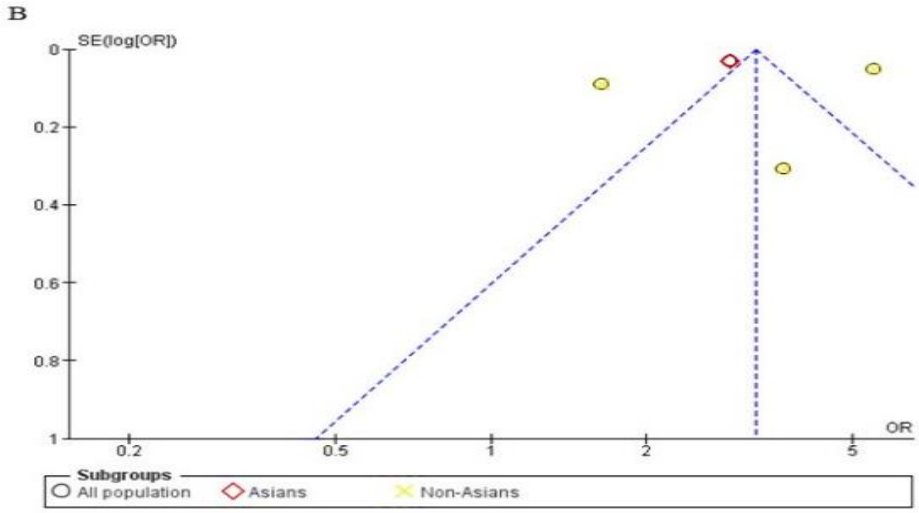


Fig. 7: (A) Population subgroup analyses on the association between CAD and obesity and (B) Funnel plot for publication bias in the population subgroup meta-analysis between CAD and obesity based on BMI ≥30

Publication bias

According to the funnel plot for publication bias in the meta-analysis between GERD symptoms and EE among overweight subjects out of nine studies; three were outliers. For GERD symptoms and overweight, it was one out of four outliers (Suppl. Fig. 1A and 1B) (Supplementary data are not published. Readers may contact the corresponding author for more details). For the meta-analysis between EE and overweight (BMI ≥25), out of five studies, three were outliers (Suppl. Fig. 1C). The funnel plot for studies on the association between GERD symptoms and EE in obesity showed three outliers out of six studies and for GERD symptoms and obesity, it was one out of two outliers (Suppl. Fig. 1D and 1E). The funnel plot for the meta-analysis between EE and obesity (BMI ≥30) demonstrated two studies with publication bias out of four (Suppl. Fig. 1F). The funnel plot for publication bias in the population subgroup meta-analysis between GERD symptom and EE in obesity showed that two Asian studies and one non-Asian study were outliers, whereas the plot for GERD symptom and EE in overweight (BMI≥25) showed three Asian studies as outliers. The small number of studies considered for the evaluation of specific associations also potentially contributed to publication bias.

Discussion

The study has corroborated the direct association between GERD symptoms and EE in obese (OR

= 4.25) and overweight subjects (OR 9.75). Obesity has gained recognition as a major health hazard resulting in gastrointestinal or cardiovascular complications (40).

The current study has also validated previous literature findings suggesting the increased likelihood of GERD and EE in obese and overweight subjects. Another meta-analysis by Corley et al. reported a positive association between GERD and increased BMI. In concurrence with the current study results, the studies from the US also demonstrated a direct association between elevated BMI and GERD (95% CI: 1.36-1.80, *P*= 0.10). However, research revealed significant heterogeneity in Europe-based studies despite the stratification for several factors (41). In alignment with the present study results, retrospective cross-sectional research by Baeg et al. (10,338 subjects) noted obesity's connection to the elevated risk of erosive esophagitis, irrespective of the metabolic status of the subjects. The corresponding prevalence of EE noted in metabolically healthy non-obese, healthy obese, unhealthy non-obese and unhealthy obese amounted to 6.5%, 12.6%, 9.3% and 14.3%, respectively (42).

A meta-analysis by Hampel et al. noted the positive association between obesity and GERD symptoms, esophageal adenocarcinoma and erosive esophagitis. The corresponding increase in the pooled adjusted odds ratios noted for BMI of 25-30 kg/m^2 and BMI >30 kg/m^2 amounted to 1.43 (95% CI, 1.158 to 1.774) and 1.94 (CI, 1.468 to 2.566). Based on the findings, the researchers underscored the need to conduct counselling for overweight subjects presenting with GERD-related symptoms regarding weight loss to ease symptoms (15).

Literature studies also corroborate the role of obesity as an independent factor and its interaction with related multiple risk factors for developing CAD (43). Such a development concurs with current study findings (44). The largest meta-analysis on obesity and CVD end-points concluded the association between obesity and CAD, emphasising the significance of weight loss to prevent cardiac sequelae (45). Central obesity, measured by waist circumference and waist-hip ratio, also bears an association with CAD. Central obesity had an association with mortality (HR: 1.70, 95% confidence interval CI: 1.58 to 1.83), whereas BMI had an inverse association in patients with CAD (HR: 0.64, 95% CI: 0.59 to 0.69) (46). A prospective study involving 3275 white and black adults aged 18-30 noted that subclinical coronary heart disease and its progression shares a link with the duration of abdominal and obesity. This association is noted throughout midlife, irrespective of the degree of adiposity. Researchers have observed more rates of coronary artery calcification per 1000 person-years in subjects who had > 20 years as opposed to zero years of overall obesity (16.0 vs 11.0, respectively) (47).

In this study, the association between CAD and obesity proved significant for Asian and non-Asian groups. The findings by the Asia Pacific Cohort Studies Collaboration corroborated the growing burden of overweight and obesity in the Asia–Pacific region. In this region, the attributable population fractions of mortality due to overweight and obesity amounted to the following: 0.2% to 2.9% for hemorrhagic stroke mortality, 0.8% to 9.2% for coronary heart disease mortality and 0.9% to 10.2% for ischemic stroke mortality (48).

The current subgroup analysis based on different ethnic populations showed that in Asian and non-Asian populations, the association between GERD symptoms and EE in obesity proved significantly high. Wu et al. reported the compatibility of GERD's risk factors and pathophysiological mechanisms in the Asian GERD subjects and their Western counterparts (49).

The main strength of this present study is that it has carried out the first investigation of the risk of erosive esophagitis, GERD and CAD among obesity and overweight subjects through meta-analysis. The study adds to the literature evidence suggesting the progressive increase in the risk of these disorders with increased BMI. Moreover, none of the studies considered has reported a negative association. However, the heterogeneity tests also indicated statistically significant degrees of heterogeneity among studies. Another notable limitation of the study is the lack of evaluation

regarding the effect of metabolic health status or amount and type of dietary intake on the risk of developing these diseases. Based on the scores obtained in the NOS, the quality of the majority of the studies could be considered reasonable. However, substantial heterogeneity among the study estimates appeared in each meta-analysis, and funnel plot analyses revealed that some studies had publication bias.

Conclusion

The present meta-analysis has corroborated the role of obesity and being overweight in developing GERD, EE and CAD. Even a moderate to a significant increase in BMI can cause or exacerbate reflux symptoms. Future studies should explore the underlying complex mechanisms linked to the elevated risk and the possible benefits of weight loss. The study has also underscored the significance of counselling overweight and obese subjects regarding the elevated risks of these diseases and the potential benefits of weight loss in improving the associated symptoms.

Abbreviations

BMI: Body Mass Index; CAD: Coronary artery Disease; CI: Confidence Interval; CVD: Cardiovascular Disease; GERD: Gastroesophageal Reflux Disease; GI: Gastrointestinal Disease; HR: Hazardous Ratio; NOS: Newcastle-Ottawa Score; WC: waist circumference

Ethics Journalism considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there are no conflicts of interest

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