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RESEARCH ARTICLE

Higher body mass index is an important risk factor in COVID-19 patients: a systematic review and meta-analysis

Vivek Singh Malik[1,2] · Khaiwal Ravindra[1] · Savita Verma Attri[2] · Sanjay Kumar Bhadada[3] · Meenu Singh[2]

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Abstract

Globally, both obesity and underweight are severe health risks for various diseases. The current study systematically examined the emerging evidence to identify an association between body mass index (BMI) and COVID-19 disease outcome. Online literature databases (e.g., Google Scholar, PubMed, MEDLINE, EMBASE, Scopus, Medrixv and BioRixv) were screened following standard search strategy having the appropriate keyword such as "Obesity", "Underweight", "BMI", "Body Mass Index", "2019-nCov", "COVID-19, "novel coronavirus", "coronavirus disease". Studies published till 20th April 2020 were included without language restriction. These studies include case reports, case series, cohort, and any other which reported BMI, overweight/obesity or underweight, and its complication with COVID-19 disease. This study observed COVID-19 infection among BMI < 25 kg/m^2 with prevalence of 0.60 (95%CI: 0.34–0.86, $I^2 = -76.77$) as compared to the 0.34 (95%CI: 0.23–0.44, $I^2 = 53.45\%$ heterogeneity) having BMI > 25 kg/m^2. The results of the current study show that BMI plays a significant role in COVID-19 severity in all age groups, especially the older individuals. A panel of doctors and nursing staff should review COVID-19 patients with higher BMI with other co-morbidities (diabetes and hypertension), and they should be given increased vigilance, priority in testing, and treatment to control the associated co-morbidities. Further, the COVID-19 patients whose illness entered 7–10 days, age > 50 years, and elevated CRP levels should be given additional medical considerations. Our finding showed that the population and patients with high BMI have moderate to high risk of medical complications with COVID-19, and hence, their health status should be monitored more frequently including monitoring of blood pressure and blood glucose.

Keywords Age · Body mass index · BMI · COVID-19 · Obesity

Highlights

- The study examines the BMI as a risk factor for COVID-19 infection and severity.
- COVID-19 patients with higher BMI need to be monitored regularly for vital parameters.
- COVID-19 patients with higher BMI needs additional vigilance for associated co-morbidities.
- Blood pressure, blood glucose, and hsCRP levels of COVID-19 patients with higher BMI should be periodically monitored.

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✉ Khaiwal Ravindra
khaiwal@yahoo.com; khaiwal.ravindra@pgimer.edu.in

[1] Department of Community Medicine and School of Public Health, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh 160012, India

[2] Department of Pediatrics, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh 160012, India

[3] Department of Endocrinology, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh 160012, India

Introduction

Being overweight, obese, and underweight may have a major risk factor for multiple disorders in the later stage of life. Earlier studies have shown a relationship between BMI and mortality among diabetic patients (Chang et al. 2016), mental behavioral, neurological (Bhaskaran et al. 2018), and Parkinson's disease (Chen et al. 2014).

Influence of infection on obesity A U-shaped (non-linear relationship) elevated infection rate was seen among overweight/obese and underweight old age persons (Dobner and Kaser 2018), increased CVD risk with greater malignancy rates (Gluvic et al. 2016; Tune et al. 2017; Vucenik and Stains 2012), and obesity with impaired immune responses was seen (Carbone et al. 2016). Overweight/obesity was reported as a risk factor for Clostridium difficile colitis, pneumonia, bacteremia infections (Falagas and Kompoti 2006; Huttunen et al. 2013), and increased surgical site infection (Crabtree et al. 2004; Lillenfeld et al. 1988; Olsen et al. 2003; Thelwall et al. 2015; Tjeertes et al. 2015; Vilar-Compte et al. 2000; Zahr et al. 2011). Similarly, waist circumference was reported as a better predictor of septicemia than BMI (Wang et al. 2013). In a study, adipose tissue serves as a source for human influenza A virus, Trypanosoma gondi, HIV, adenovirus Ad-36, cytomegalovirus, and mycobacterium tuberculosis (Kassir 2020). The elderly population is reported to be more susceptible to infections (Dorner et al. 2010a). Higher mortality risks of influenza were reported among the underweight and obese old population (L. Yang et al. 2013).

Obesity and coronavirus infection In many countries, the obese population is more vulnerable to most of the non-communicable diseases. Further, the COVID-19 pandemic has put this population at higher risk (Dayal 2020). The measures introduced in some countries, e.g., restriction on leaving home for several weeks even for daily walk, will have an impact on mobility, and these infection control measures resulted in physical inactivity, and even short periods of restriction can increase the risk of metabolic disease in future. Overweight and obesity among severe COVID-19 patients were reported as an independent risk factor (Jose and Manuel 2020). Increased adiposity undermines the pulmonary function contributing the viral pathogenesis as a secondary cause of infection (Dorner et al. 2010) has been reported in obese among older individuals (> 60 years of age) (Andersen et al. 2016). Following the 2009 influenza A virus H_1N_1 pandemic (Sun et al. 2016) and adult respiratory distress syndrome (ARDS) (Ni et al. 2017), obesity was reported as a risk factor. Decreased mortality due to ventilator-induced lung injury resulting in chronic pro-inflammatory status in obese patients has been reported (Repine and Fernandez-Bustamante 2013). Infection of influenza A showed that overweight/obesity risk elevates with virus shedding (42% longer) duration among symptomatic patients with obesity (Milner et al. 2015). In H_1N_1 disease, obesity was reported as a risk factor with increased hospitalization and death rates (Maier et al. 2018). Obesity has been shown to increase vulnerability to infections, serving as a risk factor among COVID-19 patient's mortality rate (Misumi et al. 2019). Potential confounders for obesity and infection risk: smoking (Baik et al. 2000; Nuorti et al. 2000), well-being (Lasselin et al. 2016), physical activity (Krüger et al. 2016), weight loss (Dobner and Kaser 2018), co-morbidities (Pearson-Stuttard et al. 2016), and nutrition (Urwin et al. 2014) are reported independent of age and sex.

Methods

Search strategy PRISMA guideline was used for this meta-analysis (Moher et al. 2009). Boolean operators: (BMI) AND (COVID-19), (Obesity) AND (COVID-19), ((Underweight) AND (COVID-19)) OR (CASRS-Cov-2), (BMI) OR (Body Mass Index) AND (COVID-19) were used for PubMed database and for Google Scholar, MEDLINE, EMBASE, Scopus, Medrixv and BioRixv using appropriate keywords (e.g., "Obesity", "BMI", "Body Mass Index", "2019-nCov", "COVID-19, "novel coronavirus", "coronavirus disease"). The study included published literature without language restriction until 20th April 2020.

Selection criteria (inclusion/exclusion) Studies with the following conditions had included for the meta-analysis: (1) case report, case series, and cohort studies design; (2) BMI assessment > 25 kg/m^2 and < 25 kg/m^2 reported; (3) indicating the risk ratio and/or odds ratio for the obesity risk; (4) studies reporting cross-sectional were excluded; (5) age and gender were not kept as a bar for inclusion; (6) for meta-analysis, we included BMI with reported COVID-19 infections (clinical, laboratory, or both confirmed); and (7) definition of severe COVID-19 was taken (Xu et al. 2020).

Data extraction Details of authors, total sample size, and numbers reported for obesity and other conditions, e.g., comorbidity (obesity) and clinical condition (critical/severe), were extracted and recorded independently. Data extraction was accomplished by two reviewers (Dr. Khaiwal Ravindra and Dr. Neha Chanana). Any disagreement was resolved by joint discussion. To minimize the risk of duplication, data were carefully handled. Continuous variable (BMI) was expressed as mean ± SD/median and IQR (interquartile range). The systematic review include case reports, case series, and observational and any other study types of study design which reported obesity and or underweight or its complication of COVID-19 infection. Studies for meta-analysis were pooled only if the outcome measured in the same way by all studies.

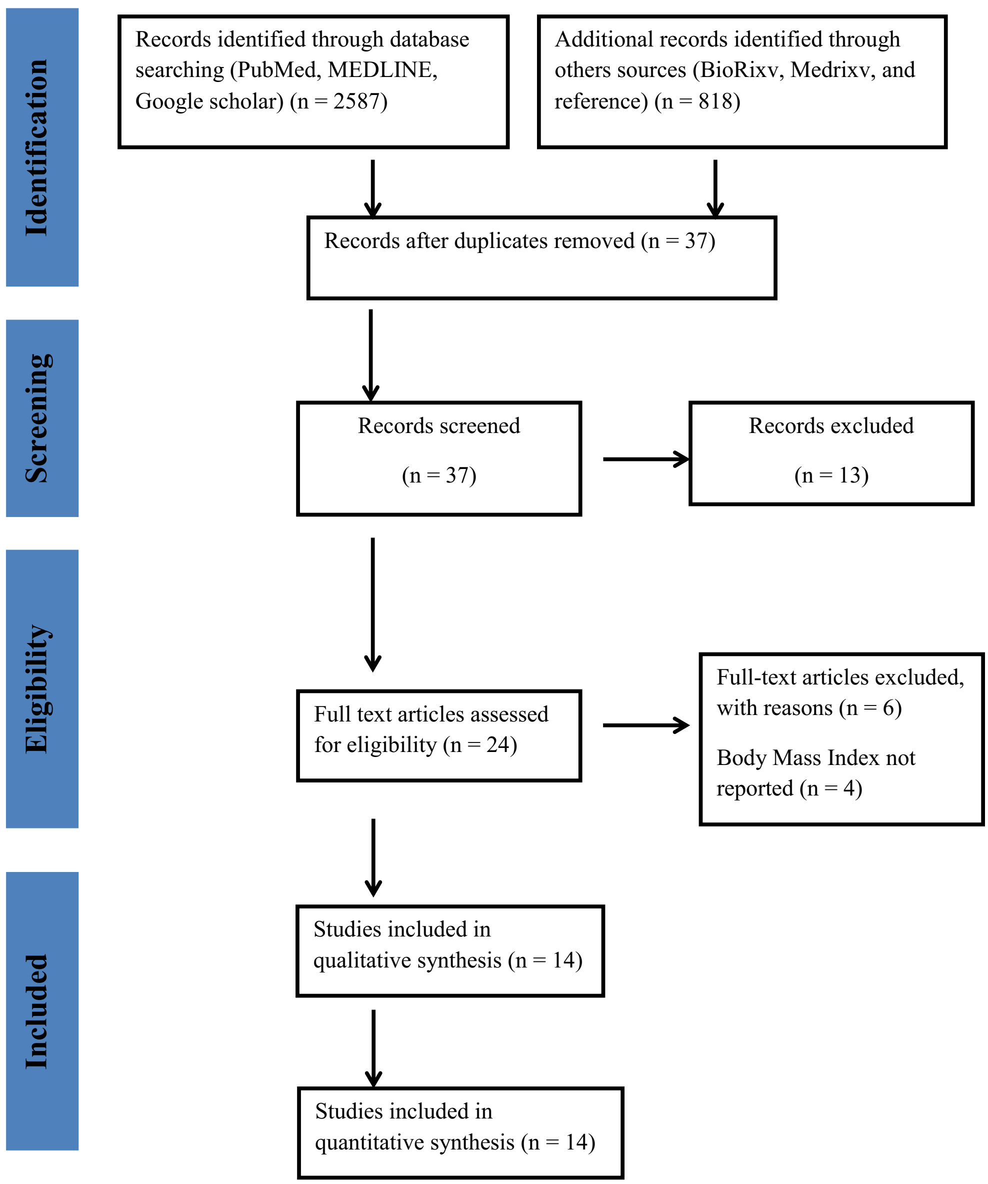
Quality assessment The Newcastle-Ottawa scale for cohort studies was used for quality evaluation of the selected studies (Wells 2014). This scale was applied because most of the studies in this study fall under cohort studies (retrospective), analyzing the other studies by covering broad spectra of study design. However, another study used the modified Newcastle-Ottawa scale for cohort and case-control study design (Codipilly et al. 2018).

Statistical analysis and data synthesis After extracting the results of the studies, the effects of BMI on COVID-19 patients were pooled and were examined using the random effects method. For continuous outcome, standard error (SE) with 95%CI was calculated. The heterogeneity (I^2 statistic) was assessed between studies. Higgins and colleagues suggested I^2 values 25% (low), 50% (moderate), and 75% (high), indicating the existence of heterogeneity (Ioannidis et al. 2007; Higgins 2003; Higgins and Thompson 2002). Data analysis was undertaken using Microsoft Excel (Neyeloff et al. 2012).

Results

Literature search Literature searching and screening was done according to PRISMA chart, as shown in Fig. 1. Initially, 3405 published research articles were identified through a database search. After the removal of 3368

Fig. 1 PRISMA chart



publications due to duplicates and not relevant to study criteria, only 37 research papers were taken for the full-text paper. Finally, 14 articles that met the inclusion criteria were included in the quantitative synthesis of the current systematic review.

Study characteristics The main characteristics are summarized in Table 1. All published research papers fall under observational (cohort) study design. Most of the studies are from China, the USA, and France. The study included articles published/available online till 20th April 2020. About the obesity criteria, BMI > 25 kg/m^2 was considered as also described in selected studies.

Quality assessment The Newcastle-Ottawa Scale (for cohort studies) was used for the qualitative evaluation of the included studies (Wells 2014). The risk of bias was assessed based on three domains, i.e., selection, comparability, and outcome, as highlighted in Table 2.

Publication bias This study included published studies, as well as unpublished literature on MedRxiv and Bioxiv, as long as it

Table 1 Patient/study characteristics

Author (Ref. No.)	Country	Study type	Numbers or %	Clinical condition (COVID-19)	BMI (kg/m^2) (mean ± SD/median (IQR)	Outcome
Jose and Manuel (2020)	China, Wuhan	Editorial/ Retrospective	N = 112 (T) N = 15 N = 18	ICU General	25.5 (23.0–27.5) 22.0 (20.0–24.0)	BMI ↑ among ICU and non-survivor group
Wu et al. (2020)	China	Retrospective	N = 280 (T) N = 83 N = 197	Severe Mild	25.8 ± 1.8 23.6 ± 3.2	BMI ↑ among severe COVID-19 group
Liu et al. (2020)	China	Retrospective	N = 30 (T)	Critical General	27.0 ± 2.5 22.0 ± 1.3	BMI ↑ among critical COVID-19 group
Garg et al. (2020)	USA	COVID-NET	N = 151 (T) N = 73		≥ 30 kg/m^2	BMI ↑ Hospitalization rate↑ with age and older adults.
Simonnet et al. (2020)	France	Retrospective	N = 124 N = 107		> 30 kg/m^2	BMI ↑ Invasive Mechanical Ventilation (IMV) requirement ↑
Lighter et al. (2020b)	USA	Retrospective	N = 1370 (T) N = 202		> 30 kg/m^2	Significant difference in admission and ICU care only in patients < 60 years of age with varying BMIs.
Guo et al. (2020)	China	Retrospective	N = 159 N = 02		> 25 kg/m^2	Most death among elder adults and 1.65-fold higher in male than female.
Liao et al. (2020)	China	Retrospective	N = 46 (T) N = 17 N = 24		BMI ≥ 25 BMI < 25	Adolescent and young adult had long COVID-19 incubation period
Qi et al. (2020)	China, Chongqing	Retrospective	N = 267 N = 30 (11.2%)		BMI > 25	Severe were older (71.5 years) and overweight/obese 14 (28%)
Hu et al. (2020)	China, Wuhan	Retrospective	N = 323 (T) N = 141 N = 256	Severe Non-severe	≥ 25 < 25	
Yang et al. (2020)	China	Retrospective	N = 55 (T) N = 21 N = 34	Without pneumonia With pneumonia	24.85(22.86–26.79) 26.12(22.86–27.68) 24.54(22.89–26·27)	
Cai et al. (2020)	China	Retrospective	N = 298 (T) N = 240 N = 58	Non-severe Severe	23.2 (21.1–25.6) 22.9 (20.6–25.2) 24.5 (22.0–27.8)	BMI ↑ among elder
Xu et al. (2020)	China	Meta-analysis	N = 79			WMD 3.38 (0.07–6.69), I^2 = 67.20%
Petrilli et al. (2020)	USA	Cross-Sectional	N = 4103 (T) N = 2104 N = 1999	Not hospitalized Hospitalized	BMI 30–40 BMI 30–40	High BMI had higher hospitalization rate OR 6.2 (4.21–9.25)

Table 2 Quality assessment: cohort study quality according to Newcastle-Ottawa Scale

S.No.	Selection******				Comparability**	Outcome*****			Total quality score
	1	2	3	4	5	6	7	8	
Jose and Manuel (2020)	*	0	*	0	0	**	0	0	3
Wu et al. (2020)	*	0	*	0	*	**	0	0	4
Garg et al. (2020)	*	0	*	0	0	**	0	0	3
Simonnet et al. (2020)	*	0	*	*	*	**	0	0	5
Lighter et al. (2020b)	*	0	*	*	0	**	0	0	4
Liao et al. (2020)	*	0	*	*	0	0	0	0	3
Qi et al. (2020)	*	0	*	0	0	**	*	0	4
Hu et al. (2020)	*	0	*	0	*	**	0	0	4
Yang et al. (2020)	*	0	*	0	*	**	*	0	5
Cai et al. (2020)	*	0	*	0	*	**	0	0	4

Note: Selection: (1) representativeness of the exposed cohort, (2) selection of the non-exposed cohort, (3) ascertain exposure, (4) demonstration that outcome of interest was not resent at stat of study; comparability; (5) comparability of cohorts on the basis of the design or analysis controlled for confounders; outcome: (6) assessment of outcome, (7) was followed up long enough for outcomes to occur, (8) adequacy of follow-up of cohorts.

meets study inclusion criteria. Possible publication bias was not calculated due to the limited power among studies, and the outcome was < 10 for funnel plot (Lau et al. 2006).

Meta-analysis The outcomes of the meta-analysis (Table 3) and forest plot (Figs. 2 and 3) are shown. A random-effects model (I^2 = 53.45%) was used on 9 articles for those reported ≥ 25 BMI kg/m^2 for COVID-19 infection involving 689 patients to analyze the risk factors of ≥ 25 BMI kg/m^2 [prevalence, 95%CI: 0.34 (0.23–0.44)] for patients with COVID-19 than those of having < 25 BMI kg/m^2 [prevalence, 95%CI: 0.60 (0.34–0.86)] with random-effect model (I^2 = 0%). BMI < 25 kg/m^2 random effect models I^2 were negative, which indicates no observed heterogeneity for this group (Higgins 2003; Melsen et al. 2014).

Discussion

This study summarized available studies from retrospective about BMI and COVID-19 infection. We observed prevalence rate from 0.11 (95%CI: 0.07–0.15) to 0.86 (95%CI: 0.69–1.02) among COVID-19 patients having BMI > 25 kg/m^2. Similarly, those having BMI < 25 kg/m^2 show prevalence rate from 0.16 (95%CI: 0.08–0.23) to 0.80 (95%CI: 0.70–0.90) studies included in the meta-analysis. This study observed heterogeneity of 53.45% among COVID-19 patients with BMI > 25 kg/m^2. This might be due to the various variables, age, and gender. The previous study suggests 30% prevalence of obesity in MERS-CoV infection (Badawi and Ryoo 2016) with pooled prevalence in obesity of 16 ± 2% (95%CI: 12–19%). Similarly, other studies observed the relationship between weight gain with pneumonia (Baik et al. 2000), infection rate among weight-reduced patients (Anderin et al. 2015), and thromboembolic risk in obese (Kassir 2020) population. COVID-19 patient with high BMI has moderate to high risk of medical complication with infection; hence, their periodic health status of co-morbidities, e.g., hypertension and diabetes, should be evaluated. Also, there is geographical variation in fatality case rates in South Korea (0.8), China (2.3), and Italy (7.2) that has been reported (Onder et al. 2020) with risk factors of smoking, pollution, and aging. In US patients, < 60 years and with BMI 30–40 (OR (95%CI) 1.8: 1.2–2.7) were more likely to be admitted to acute and critical care to individuals with a BMI < 30 (Lighter et al. 2020a) that has been reported for the first time. In a study, gender (male), age, and heart disease were the main risk factors of COVID-19-related death (Guo et al. 2020). Adolescents and young adults might play a key role in the worldwide spread of COVID-19 disease because they study overseas and frequently travel (Liao et al.

Table 3 The meta-analysis of body mass index for COVID-19 patients

Risk factor	Variable	Number of studies	Size (*n*)	Prevalence (95%CI)	I^2
Body mass index					
< 25 kg/m^2	Continuous	6	769	0.60 (0.34–0.86)	0% (− 76.77)
> 25 kg/m^2	Continuous	9	689	0.34 (0.23–0.44)	53.45%

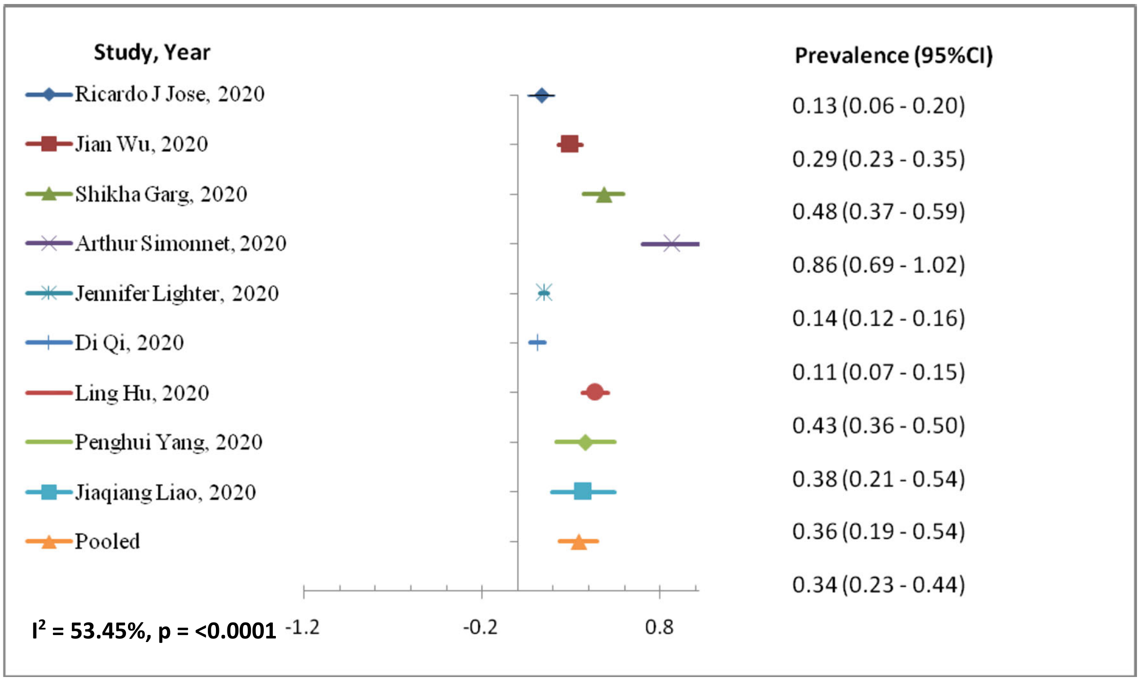


Fig. 2 Forest plot of risk factor BMI > 25 kg/m^2 with COVID-19 patients

2020). Meta-analysis showed that elderly male patients with high BMI have greater chances of being into critically ill patient category (53). This study observed prevalence rate 0.60 (95%CI: 0.34–0.86) of COVID-19 infection among < 25 kg/m^2 BMI population with no heterogeneity as compared to the > 25 kg/m^2 BMI, 0.34, 95%CI: 0.23–0.44 with heterogeneity of 53.4% among study population.

Limitations Population, continuous variable, clinical condition, and statistical methods have the potency to differ and may cause heterogeneity among studies included for the meta-analysis. Further, the study reviewed only the risk of BMI (> 25 kg/m^2 and < 25 kg/m^2) of COVID-19 subjects and their severity.

Conclusion

The BMI plays a significant role in COVID-19 infection and severity at all ages, especially elderly population. COVID-19 patients with higher BMI should be reviewed by a panel for the risk factors. Further, there should be a procedure for

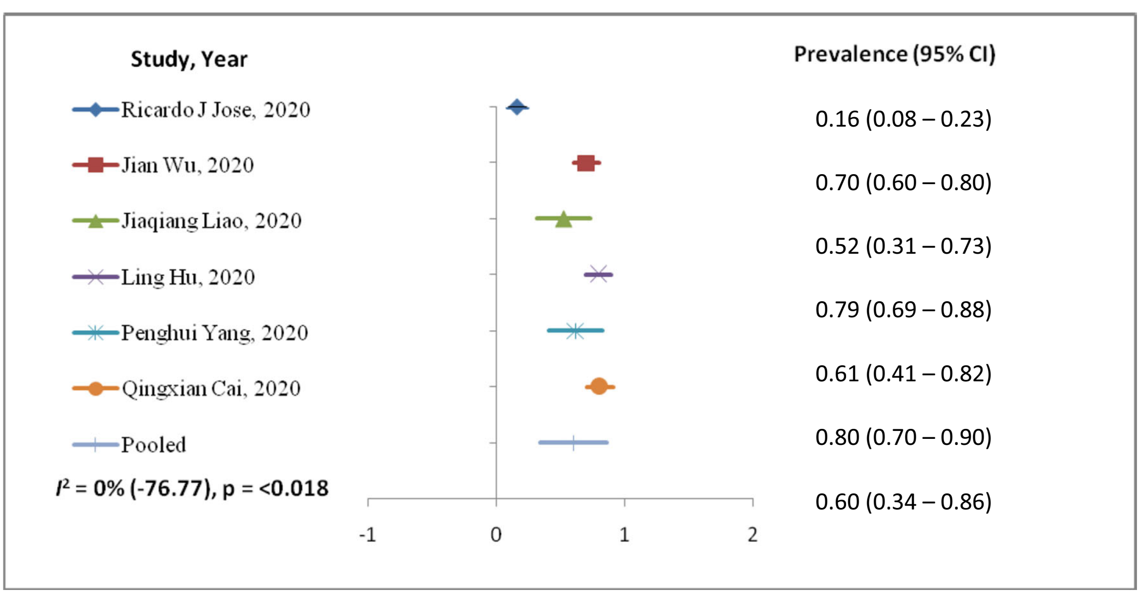


Fig. 3 Forest plot of risk factor BMI < 25 kg/m^2 with COVID-19 patients

increased vigilance, testing priority, and therapy for patients with obesity and COVID-19 disease, whose illness has entered 7–10 days, having age > 50 years, and elevated CRP levels. The severity of COVID-19 found has a significant burden on intensive care resources in hospitals worldwide and specifically in lower-and-middle income countries due to lack of health finance and resources. Hence, the patients having higher BMI with other comorbidities should be given special attention to reduce morbidity and mortality associated with COVID-19 infection.

Compliance with ethical standards

Conflict of Interest The authors declare that they have no conflict of interest.

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