Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Meta-analysis

Prevalence and outcomes of malnutrition among hospitalized COVID-19 patients: A systematic review and meta-analysis

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SUMMARY

Background: Malnutrition is inevitable in patients with Coronavirus Disease 2019 (COVID-19) due to its effect on the gastrointestinal system, immune system, and high metabolic activity. However, the prevalence of malnutrition and its outcomes is uncertain. This study aimed to investigate the prevalence and outcome of malnutrition among patients with COVID-19.

Method: A comprehensive search was conducted in PubMed/Medline; Science direct and LILACS from December 29, 2019 to September, 2020 without language restriction. All observational studies reporting the prevalence of malnutrition were included while case reports and reviews were excluded. The data were extracted with two independent authors with a customized format and the disagreements were resolved by the other authors. The methodological quality of included studies was evaluated using a standardized critical appraisal tool.

Results: A total of 511 articles were identified from different databases and 27 articles were selected for evaluation after the successive screening. Fourteen articles with 4187 participants were included. The pooled prevalence of malnutrition among hospitalized patients with COVID-19 was 49.11% (95% CI: 31.67 to 66.54). The odd of mortality among patients COVID-19 with malnutrition was 10 times more likely as compared to those who were well-nourished.

Conclusion: The prevalence of malnutrition and mortality associated with malnutrition among COVID-19 hospitalized patients was very high which entails a mitigating strategy by different stakeholders to prevent and manage malnutrition and its outcomes.

Registration: This systematic review was registered in Prospero's international prospective register of systematic reviews (CRD42020215396).

1. Background

The Coronavirus Disease 2019 (COVID-19) pandemic which is caused by the severe acute respiratory syndrome virus-2 (SARS-CoV-2) infection was identified in Wuhan, Hubei province of China in December 2019 by the Chinese Center for Disease and Prevention from the throat swab of a patient [29]. Though the disease has emerged in China, it widespread worldwide unpredictably and it was declared as a global pandemic by the World Health Organization (WHO) as of March 11, 2020 [13].

The World Health Organization (WHO) situation report showed that there were approximately 50 million laboratory-confirmed cases and more than 1 million deaths globally as of November 6, 2020.

The Coronavirus Disease 2019 (COVID-19) was thought to affect mainly the respiratory system and is presented with fever, dry

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cough, and difficulty of breathing, and lately, the patient may deteriorate associated with pneumonia and acute respiratory distress syndrome [29,34,35,64]. However, recent evidence showed clinical manifestations on the gastrointestinal tract, immune, cardiovascular, dermatologic, and central nervous systems [3,6,21,24,31,43,59,60].

The Coronavirus Disease 2019 (COVID-19) causes significant economic, social, psychological chaos globally due to incompliant to preventive measures, unproven treatment, and the complexity of its transmission [17,45,48,57,62]. These impacts are thought to be disastrous for low-income countries because of very poor health care system, low awareness of the disease and its prevention, lack of skilled health personnel, scarce Intensive Care Unit, a limited number of mechanical ventilators, and prevalence of co-morbidities/infection along with high prevalent chronic malnutrition [8,14,49,62].

Different studies showed that patients with co-morbidities including (Asthma, COPD, Tuberculosis, Pneumonia, Acute respiratory distress syndrome (ARDS), Diabetes mellitus, hypertension, renal disease, hepatic disease, and cardiac disease), history of smoking, and history of substance use, male gender and age greater than 60 years were more likely to die or develop undesirable outcomes [22,44,52,65].

Different systemic reviews and observational studies showed that malnutrition among critically ill patients is as high as 70% which was strongly related to mortality, hospital length of stay, and duration of mechanical ventilation [6,14,20,25,28,31,33–39].

Malnutrition is inevitable in patients with Coronavirus Disease 2019 (COVID-19) due to its effect on the gastrointestinal disorder, immune system, high metabolic activity due to infection, fever, and less oral intake.

Malnutrition during COVID-19 is a 'two-edged sword' particularly in low-income countries where chronic malnutrition is very high. The disease is still very high and it is relapsing to the worst in some countries. However, the prevalence of malnutrition and its outcomes is uncertain and a topic of debate. Therefore, this systematic review and meta-analysis aimed to investigate the prevalence and outcome of malnutrition among patients with COVID-19.

2. Methods

2.1. Protocol and registration

The systematic review and meta-analysis was conducted based on the Preferred Reporting Items for Systematic and meta-analysis (PRISMA) protocols [46], and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) checklist [58]. This systematic review and meta-analysis was registered in Prospero's international prospective register of systematic reviews (CRD42020215396) on October 23, 2020.

2.2. Eligibility criteria

All observational (case series, cross-sectional, cohort, and case–control) studies reporting the prevalence of malnutrition and outcomes among hospitalized patients with coronavirus disease (COVID-19) were included while studies that didn't report the prevalence of malnutrition among hospitalized patients with COVID-19, articles that didn't report full information for data extraction, articles with different outcomes of interest, and Systemic review study design were excluded. The methodological quality of included studies was evaluated with eight item appraisal tool adopted from Joanna Briggs institute as mentioned in methodological quality assessment section and studies with a methodological score less than fifty percent were also excluded. The primary outcomes of interest were the prevalence of malnutrition and mortality among hospitalized patients with COVID-19 worldwide. The prevalence of comorbidities and lengths of hospital stay were secondary outcomes.

2.3. Search strategy

The search strategy was conducted to explore all available published and unpublished studies among surgical COVID-19 patients admitted to the hospital from December 2019 to September 2020 without language restrictions. A comprehensive search was employed in this review. An initial search on PubMed/Medline, Science Direct, and Cochrane Library was carried out followed by an analysis of the text words contained in Title/Abstract and indexed terms. A second search was undertaken by combining free text words and indexed terms with Boolean operators. The third search was conducted with the reference lists of all identified reports and articles for additional studies. Finally, an additional and grey literature search was conducted on Google scholars. The databases were searched with the following search terms using PICos (population, interest, context and design) strategy by combining with AND, OR Boolean operators as COVID-19 OR novel coronavirus OR SARS-CoV-2 AND malnutrition OR undernutrition OR deficiency OR hunger AND mortality OR death OR outcomes AND comorbidity OR complication AND prevalence OR incidence. The final search results were shown with the Prisma flow diagram (Fig. 1).

2.4. Data extraction

The data from each study were extracted by SA and YC independently with a customized format excel sheet. The disagreements between the two independent authors were resolved by the other authors. The extracted data included: Author names, country, date of publication, sample size, the prevalence of malnutrition, mortality, the number of days in the hospital, presence of co-morbidities, screening/diagnostic malnutrition tools, and determinants. Finally, the data were then imported for analysis in R software version 4.0.2 and STATA 16.

2.5. Assessment of methodological quality

Articles identified for retrieval were assessed by two independent Authors for methodological quality before inclusion in the review using a standardized critical appraisal Tool adapted from the Joanna Briggs Institute (Supplemental Table 1). The disagreements between the Authors appraising the articles were resolved through discussion. Articles with average scores greater than fifty percent were included for data extraction.

2.6. Data analysis

Data analysis was carried out in R statistical software version 4.0.2 and STATA 16. The pooled prevalence of malnutrition, mortality, and length of hospital stay among hospitalized patients with COVID-19 was determined with a random effect model with restricted maximum likely hood (REML) as there was substantial heterogeneity. The Heterogeneity among the included studies was checked with forest plot, $\chi 2$ test, I^2 test, and the p-values. Substantial heterogeneity among the included studies was investigated with subgroup analysis for categorical moderators (nutritional status screening/assessment tools, setting, country, and age group) and meta-regression for continuous covariates (lengths of stay, mean age, and sample size) for outcomes extracted from more than ten studies.

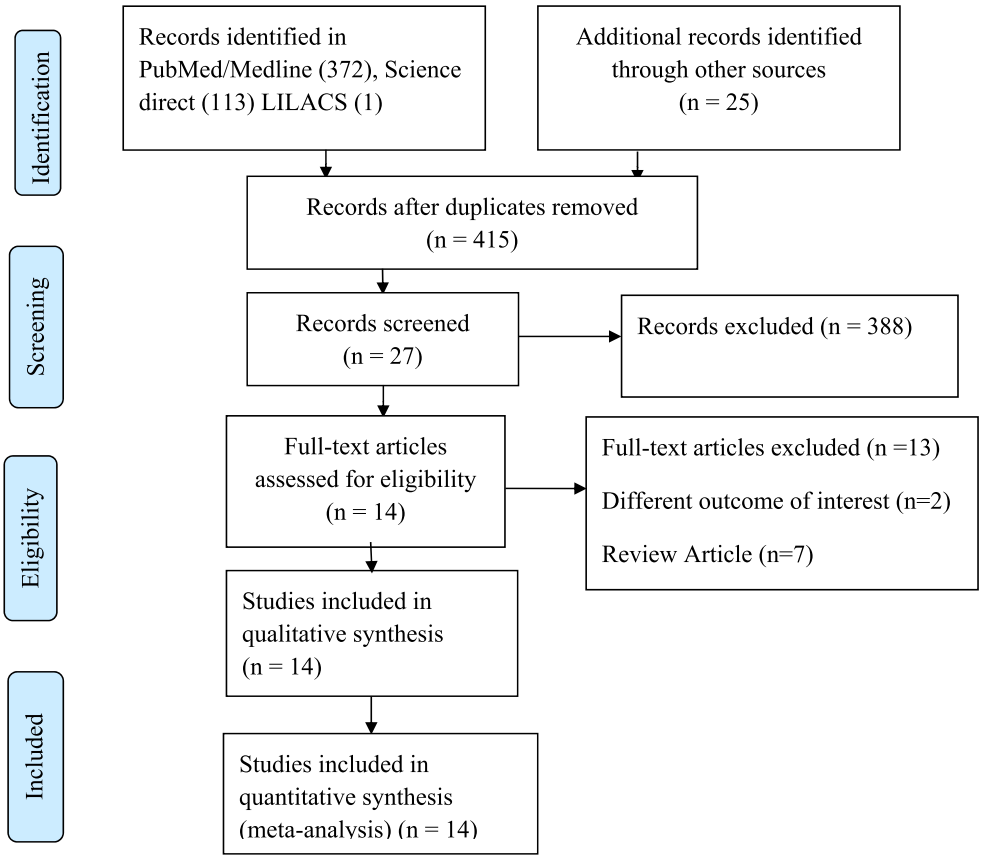

Fig. 1. Prisma flow chart.

Publication bias was checked with a funnel plot and the objective diagnostic test was conducted with Egger's correlation, Begg's regression tests. Furthermore, factor analysis was carried out to identify the independent predictors of malnutrition among hospitalized patients with COVID-19.

3. Results

3.1. Selection of studies

A total of 511 articles were identified from different databases and 27 articles were selected for evaluation after the successive screening. Fourteen articles with 4187 participants were included and the rest were excluded with reasons [4,5,9–11,19,20,23,26,32,53,55,56](Fig. 1).

3.2. Description of included studies

Fourteen Articles with 4187 participants were included in the review while thirteen studies were included in the meta-analysis for the prevalence of malnutrition and mortality. The Studies with the prevalence of malnutrition and/or prevalence of mortality among hospitalized patients with COVID-19 were included and the characteristics of each included studies were described in (Table 1) and the rest were excluded with reasons.

The included studies were published from January 01 to May 15, 2020, with sample sizes, ranged from 33 to 1115. The mean (±SD) ages of the included studies varied from 54.2 ± 15.9 to 83.38 ± 3.9 years. The mean (±SD) length of hospital stay was varied from 7.63 ± 1.38 to 30.18 ± 11.06 days. The Majority of studies were conducted among hospitalized patients while one study was conducted among malnourished intensive care unit COVID-19 patients.

The included studies used different types of malnutrition screening and diagnostic tools including Nutritional Risk Screening (NRS2000), Global Leadership Initiative on Malnutrition (GLIM), Controlling Nutritional status (CONUT), Mini Nutritional Assessment (MNA), modified Nutritional Risk in the critically Ill (MNUTRIC), Malnutrition Universal Screening Tool (MUST), Geriatric Nutritional Risk Index (GNRI), Anthropometric (Body Mass Index, Mid Upper arm circumference, Skinfolds), and Biological markers (albumin, prealbumin, globulin).

Ten of the included studies were conducted in China while the rest four studies were conducted in France and Italy, two studies in each country.

All of the included studies reported the prevalence of malnutrition among hospitalized patients with COVID-19 which varied from 11.57% to 88.39% while six of the included studies reported the prevalence of mortality among malnourished hospitalized COVID-19 patients. The prevalence of mortality among undernourished patients with COVID-19 from the included studies varied from 10% to 59.09%.

Six of the included studies with 1143 participants reported the prevalence of comorbidity including hypertension, diabetes mellitus, cardiovascular disease, cancer, COPD, and cerebrovascular disease as the major comorbidity among malnourished patients with COVID-19 while five studies with 961 participants reporting the prevalence of gastrointestinal symptoms including nausea, vomiting, diarrhea, anorexia, Anosmia, and dysgueusia.

Table 1
Description of included studies.

Author	Study period	Country	Sample	Setting	Tools	Age group	P (95% CI)
Bedock et al., 2020 [7]	March 21 to April 24, 2020	France	144	Hospital	GLIM	Adult	82.81 [79.17,86.45]
Du et al., 2020 [16]	Jan 1 to Feb 29, 2020	China	155	Hospital	CONUT	Adult	41.13 [33.01,49.26]
Li et al., 2020 [38]	Jan 2 to Feb 15,2020	China	523	Hospital	mNUTRIC	Adult	61.03 [52.83,69.23]
Li et al., 2020 [37]	Jan to Feb, 2020	China	187	Hospital	MNA	>65	82.13 [78.55,85.70]
Lin et al., 2020 [40]	Jan 20 to Feb 23, 2020	China	33	Hospital	Albumin	Adult	52.75 [45.49,60.00]
Liu et al., 2020 [41]	Jan 28 to March 5, 2020	China	141	Hospital	MUST	>65	40.34 [36.14,44.55]
Luo et al., 2020 [42]	Feb to April,2020	China	1115	Hospital	prealbumin	Adult	88.39 [83.34,93.43]
Pironi et al., 2020 [50]	April 2020	Italy	268	Hospital	NRS	Adult	11.57 [9.69,13.45]
Recinella et al., 2020 [51]	March 30 to May 15, 2020	Italy	109	Hospital	GNRI	>65	22.76 [17.74,27.78]
Rouget et al., 2020 [54]	March to April 2020	France	80	Hospital	GLIM	Adult	33.33 [25.63,41.03]
Wang et al., 2020 [63]	Jan to Feb, 2020	China	442	Hospital	CONUT	Adult	60.55 [51.38,69.73]
Zhang et al., 2020 [66]	Jan 28 to Feb 21, 2020	China	136	ICU	mNUTRIC	Adult	39.39 [22.72,56.07]
Zhao et al., 2020 [67]	Jan 29 to Feb 19, 2020	China	413	Hospital	NRS	Adult	37.50 [26.89,48.11]
Zuo et al., 2020 [68]	Jan 17 to Feb 17, 2020	China	446	Hospital	prealbumin	>65	33.18 [28.81,37.55]

4. Meta-analysis

4.1. Prevalence of malnutrition

All of the included studies reported the prevalence of malnutrition among hospitalized patients with COVID-19. The pooled prevalence of malnutrition among hospitalized patients with COVID-19 was 49.11% (95% CI: 31.67 to 66.54, 14 studies, and 4187 participants) (Fig. 2).

The sub-group analysis was conducted by country, setting, Nutritional assessment and screening tools, and age group. The sub-group analysis revealed that prevalence of malnutrition was comparable among elderly patients (>65 years) as compared to adult patients (18–65 years), 46.5% (95% confidence interval (CI):33.97–59.19%) and 49.99% (95% confidence interval (CI):27.10–72.88%) respectively (Fig. 3). The prevalence of malnutrition among hospitalized patients with COVID-19 was found to be higher in China followed by Italy, 53.34% (95% confidence interval (CI): 31.17–75.50%) and 41.45% % (95% confidence interval (CI):4.42 to 78.48) respectively (Supplemental Fig. 1).

The meta-analysis also revealed that the prevalence of malnutrition among hospitalized patients with COVID-19 was the highest with CONUT, GNRI, NRS2000 nutritional status screening, and assessment tools while the prevalence of malnutrition was the lowest with GLIM, albumin, and prealbumin (Fig. 4).

The subgroup analysis showed that the pooled prevalence of malnutrition was the highest among critically ill patients as compared to general ward patients; 61.03% (95% confidence

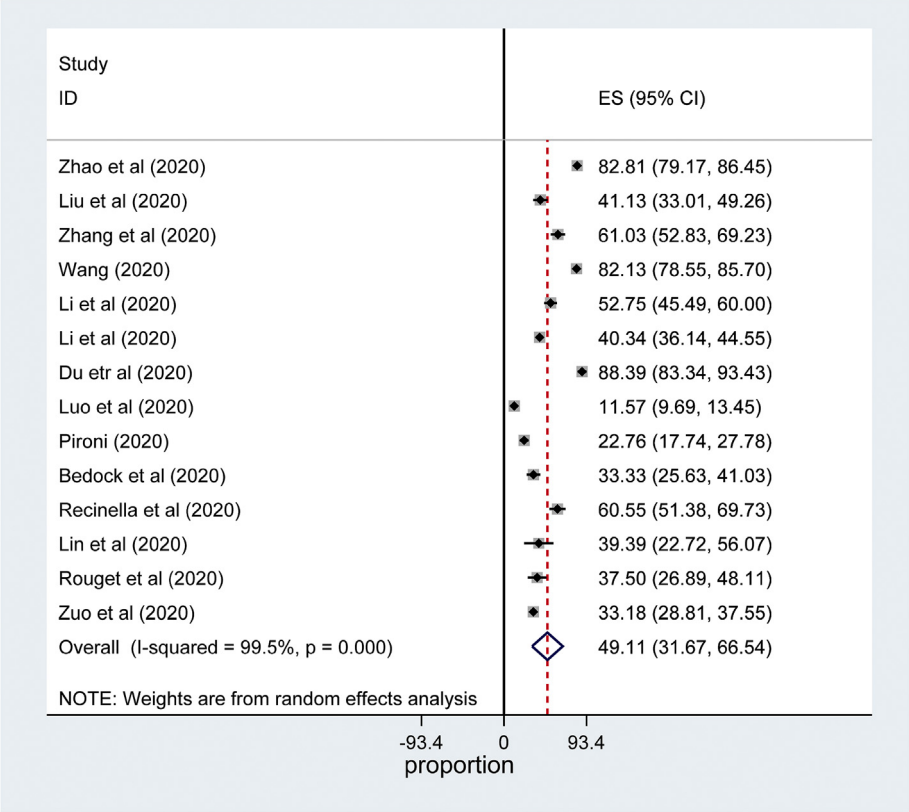

Fig. 2. Forest plot for the prevalence of malnutrition among hospitalized patients with COVID-19: The midpoint of each line illustrates the prevalence; the horizontal line indicates the confidence interval, and the diamond shows the pooled prevalence.

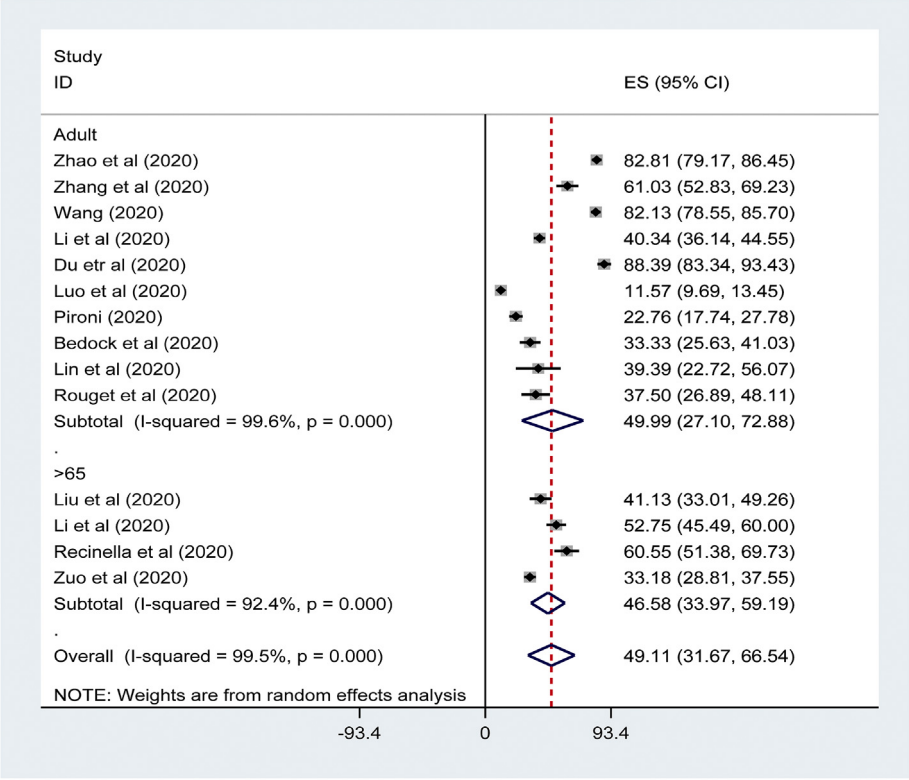

Fig. 3. Forest plot for subgroup analysis of the prevalence of malnutrition among hospitalized patients with COVID-19 by age group: The midpoint of each line illustrates the prevalence; the horizontal line indicates the confidence interval, and the diamond shows the pooled prevalence.

interval (CI):52.83–69.23%) and 48.19% (95% confidence interval (CI): 29.91–66.47%) respectively (Fig. 5).

4.2. Mortality and morbidity

The meta-analysis showed that the prevalence of malnutrition was 26.68% (95% confidence interval (CI): 9.99 to 43.37, 6 studies, 1781 participants) (Fig. 6). The odd of mortality among patients with hospitalized malnutrition patients with COVID-19 was 10 times more likely as compared to those who were not malnourished (Supplemental Fig. 2). The prevalence of individual comorbidity including hypertension, diabetes mellitus, cardiovascular disease were the most common comorbidities respectively but we didn't perform overall prevalence of comorbidity as the included studies didn't report the overall prevalence of comorbidity.

4.3. Mean duration of hospitalization

The pooled mean duration of hospitalization was estimated from the included studies mean duration of hospitalization. The meta-analysis revealed that the mean duration of Hospitalization was 12.18 (95% confidence interval (CI): 8.57–15.79) days (Supplemental Fig. 3).

4.4. Determinants of malnutrition

This study identified different independent predictors of malnutrition including gastrointestinal symptoms (nausea, vomiting, and anorexia), comorbidity (hypertension, cardiovascular disease), and being male gender. The meta-analysis revealed that patients with gastrointestinal symptoms were more than 2 times more likely to develop malnutrition compared to their counterparts (Fig. 7).

4.5. Meta-regression

The meta-analysis showed a substantial heterogeneity between the included studies which entails subgroup analysis and/or meta-regression to identify the sources of heterogeneity. Regression Analysis was run for the prevalence of malnutrition with the only length of hospital stay covariates because the other covariates were reported in less than ten included studies where the meta-regression model fit couldn't be certain. However, it was not possible to explain the source of heterogeneity (I^2 = 99.22, tau^2 = 687, p = 0.000). The model revealed that 99.22% of the residual variation was due to real heterogeneity while only 0.78% of the variation may be due to within-study sampling variability.

4.6. Sensitivity analysis and publication bias

Sensitivity analysis was conducted to identify the most influential study on the pooled summary effect by removing each study at a time and we didn't find a significant influencing summary effect. The funnel plot didn't show significant publication bias. Besides, egger's regression and Begg's correlation rank correlation failed to show a significant difference (p = 0.7634 and p = 1.1733) respectively (Fig. 8).

5. Discussion

This meta-analysis was intended to provide evidence on prevalence, independent predictors, and outcomes of malnutrition

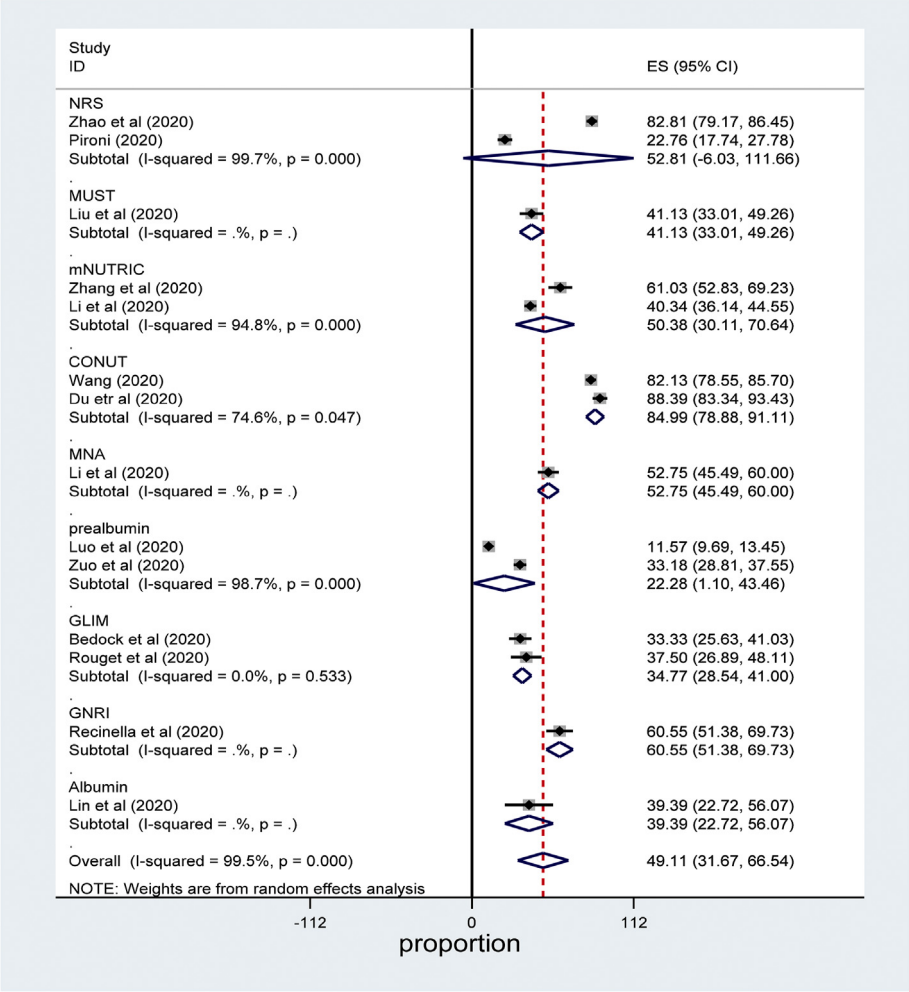

Fig. 4. Forest plot for subgroup analysis of the prevalence of malnutrition among hospitalized patients with COVID-19 by country: The midpoint of each line illustrates the prevalence; the horizontal line indicates the confidence interval, and the diamond shows the pooled prevalence.

among hospitalized patients with COVID-19 for prevention and early intervention in compliance with local guidelines.

The meta-analysis revealed that the prevalence of malnutrition was 49.11% (95% CI: 31.67–66.54) which was comparable with the included studies. However, studies conducted among hospitalized patients before the COVID-19 era showed that the prevalence of malnutrition was lower than this meta-analysis which varied from 22 to 40% [1,15,30,61]. This discrepancy might be explained by the impact of COVID-19 disease on the gastrointestinal tract and immunity besides high metabolic rate and decreased oral intake.

Body of evidence showed that malnutrition is very high among elderly hospitalized patients [1,12,25,27,28,33,39], unlike this systematic review and meta-analysis where the prevalence of malnutrition between elderly and adult patients is comparable. The possible explanation might be because of the inclusion of a small number of studies conducted on the elderly; only four studies were conducted on the elderly from a total of 14 studies.

The meta-analysis showed that the prevalence of malnutrition among hospitalized patients with COVID-19 was the highest with CONUT, GNRI, and NRS2000 nutritional status screening and assessment tools while the prevalence of malnutrition was the lowest with GLIM, albumin, and prealbumin which is in line with studies conducted on the predictability of nutritional screening and assessment tools. Studies showed that biological markers are a poor predictor of nutritional status as these indices might be affected by critical illness, infection, liver, and renal disease in which case albumin and prealbumin will rise irrespective of nutritional status [2,18,47].

The subgroup analysis revealed that malnutrition is the highest among ICU critically ill patients when compared to general ward patients which are comparable with studies conducted in ICU among non-COVID-19 patients [12,30,36]. These patients are critically ill with a high metabolic rate due to the inflammatory process, fever, prolonged length of stay, inadequate calorie intake.

The systematic review found out independent predictors of malnutrition among hospitalized patients with COVID-19 including hypertension, gastrointestinal symptoms, being male, and cardiovascular disease. This study showed that patients having gastrointestinal symptoms were 2.26 times more likely to be malnourished as compared to their counterparts.

5.1. Quality of evidence

The methodological quality of included studies was moderate to high quality as illustrated with the Joanna Briggs Institute assessment tool for meta-analysis of observational studies. However, substantial heterogeneity associated with dissimilarities of included studies in nutritional screening/assessment tools, study

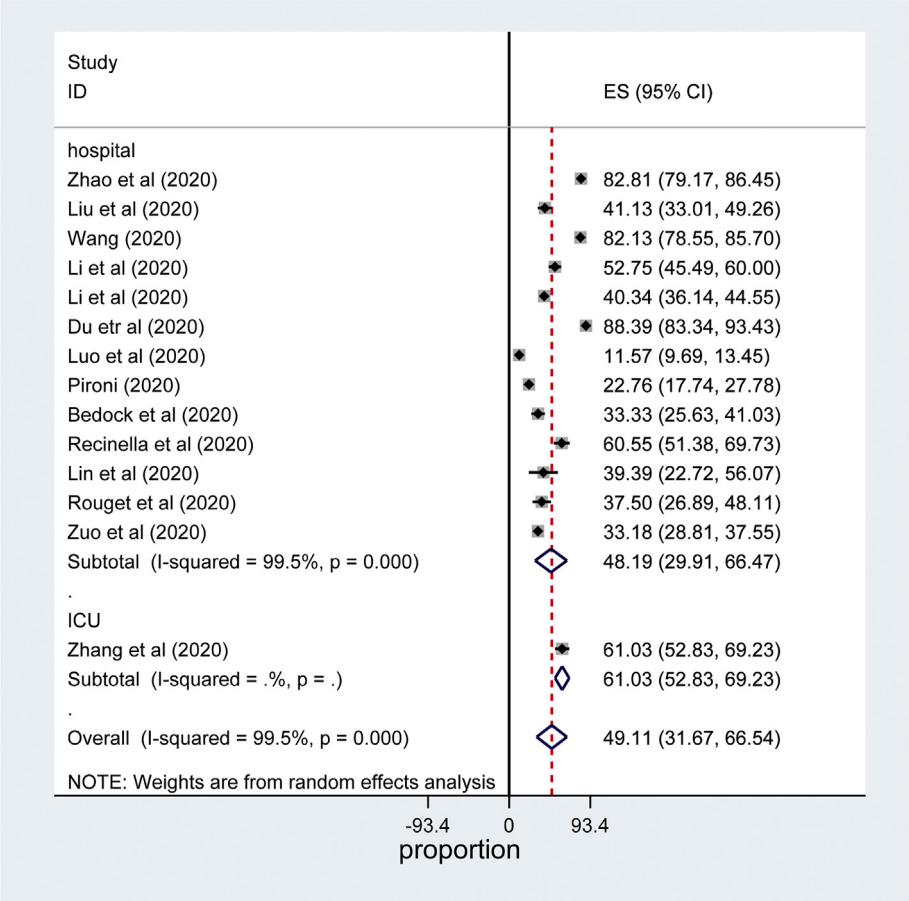

Fig. 5. Forest plot for the prevalence of perioperative complication among surgical patients with COVID-19: The midpoint of each line illustrates the prevalence; the horizontal line indicates the confidence interval, and the diamond shows the pooled prevalence.

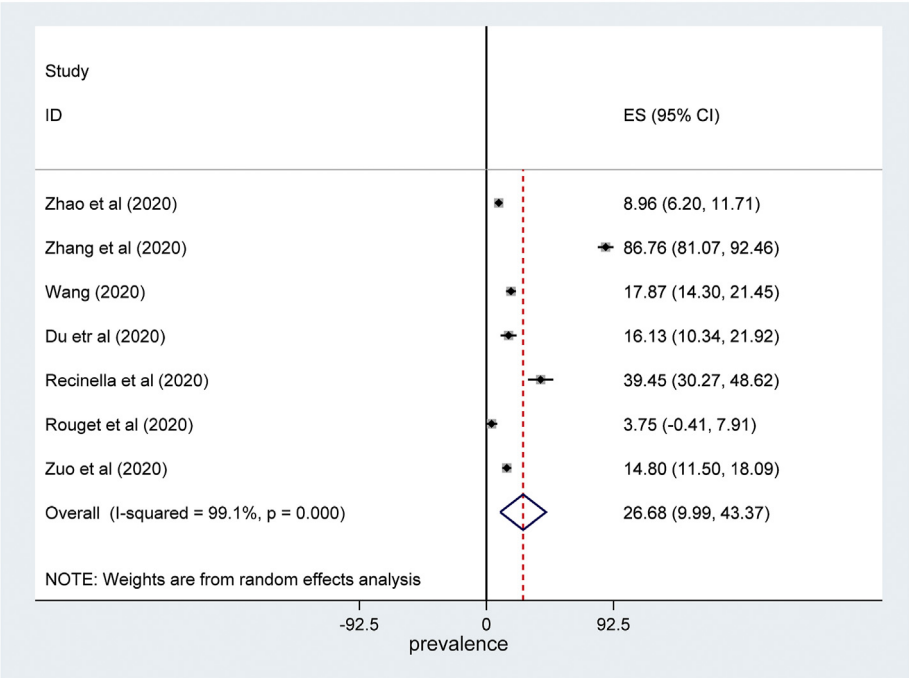

Fig. 6. Forest plot for the prevalence of mortality among hospitalized malnourished patients with COVID-19: The midpoint of each line illustrates the prevalence; the horizontal line indicates the confidence interval, and the diamond shows the pooled prevalence.

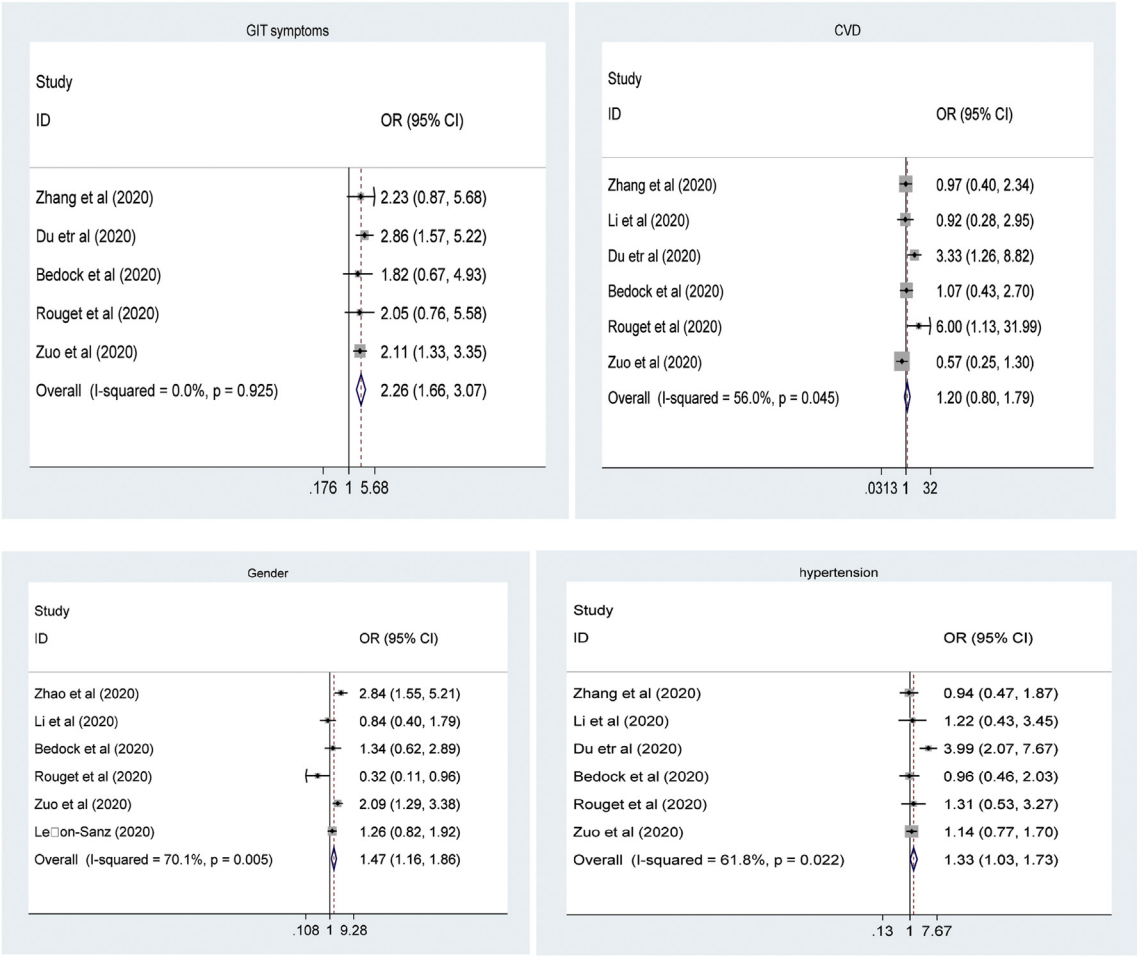

Fig. 7. Forest plot showing pooled odds ratio (log scale) of the associations between malnutrition and its determinants (GIT symptoms; Gender; CVD; Hypertension).

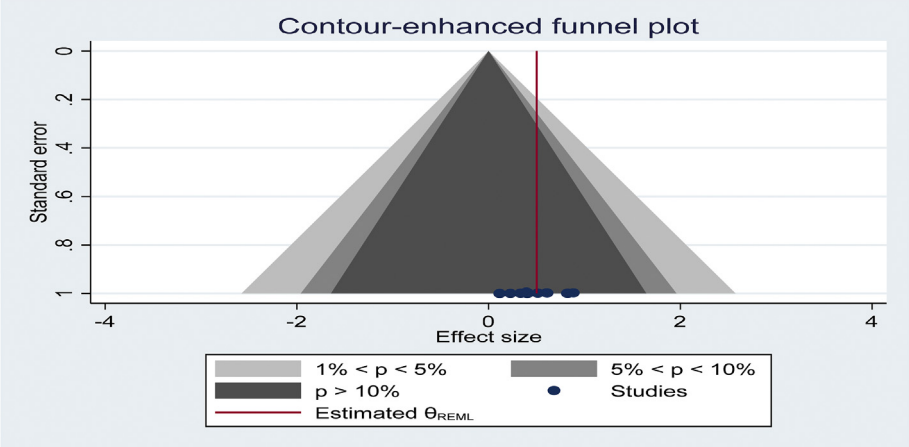

Fig. 8. Funnel plot to assess publication bias. The vertical line indicates the effect size whereas the diagonal line indicates the precision of individual studies with a 95% confidence interval.

setting, age group, and sample size, could affect the allover quality of evidence.

5.2. Implication for policy

Body of evidence revealed that the prevalence of malnutrition and its outcomes was very high among hospitalized patients with COVID-19. Hospital malnutrition in patients with COVID-19 is a huge challenge particularly in low and middle-income countries because of prevalent chronic malnutrition, poverty, inadequate and or no nutritional support at all in some countries, and lack of local nutritional support protocol. Therefore, a mitigating strategy is required by different stakeholders to prevent and manage malnutrition and its and its consequences by screening/assessing

nutritional status, involving the nutritionist/dietitian, and adopting nutritional support guidelines.

5.3. The implication for further research

The meta-analysis revealed that the prevalence of malnutrition and its outcomes was very high among hospitalized COVD-19. However, the included studies were too heterogeneous, low powered and cross-sectional studies also don't show a temporal relationship between malnutrition, mortality, and its determinants. Therefore, further observational and randomized controlled trials with more validated nutritional status screening and assessment tools are required.

5.4. Limitation of the study

The meta-analysis included studies with moderate to high methodological quality. However, some of the included studies were low-powered and the majority of studies included in this review didn't report data on outcomes of malnutrition, comorbidity, and risk factors to investigate the independent predictors. Besides, the included studies used different types of screening and assessment nutritional tools and it would be difficult to provide conclusive evidence.

6. Conclusion

This meta-analysis showed that the prevalence of malnutrition was very high among hospitalized patients with COVID-19. The meta-analysis showed that mortality among hospitalized patients with COVID-19 was more than 10 times more likely as compared to those who were well-nourished. This entails a mitigating strategy by different stakeholders to prevent and manage malnutrition and its outcomes.

Ethics approval and consent to participate

Ethical clearance and approval were obtained from the ethical review board of the College of Health Science and Medicine.

Consent for publication

Not applicable.

Availability of data and materials

Data and material can be available where appropriate.

Funding

No funding was obtained from any organization.

Authors' contributions

SA and MB conceived the idea design of the project. SA, YC, HA, RH, and KH were involved in searching strategy, data extraction, quality assessment, analysis, and manuscript preparation. All authors read and approved the manuscript.

Declaration of competing interest

The authors declare that there are no competing interests.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2021.03.002.

Abbreviations

ARDS	Acute Respiratory Distress Syndrome
CI	Confidence Interval
CONUT	Controlling Nutritional status
COPD	Chronic Obstructive Pulmonary Disease
CVD	Cardiovascular Disease
GIT	Gastrointestinal Tract
GLIM	Global Leadership Initiative on Malnutrition
GNRI	Geriatric Nutritional Risk Index
ICU	Intensive care Unit
MNA	Mini Nutritional Assessment
mNUTRIC	modified Nutritional Risk in the critically Ill
MOOSE	Meta-Analysis of Observational Studies in Epidemiology
MUST	Malnutrition Universal Screening Tool
NRS2000	Nutritional Risk Screening 2000
OR	odds Ratio
PRISMA	Preferred Reporting Items for Systematic and meta-analysis
SD	Standard Deviation
WHO	World Health Organization

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