 doi:10.20944/preprints202008.0475.v1

The Association Between Presence of Comorbidities and COVID-19 Severity; A Systematic Review and Meta-Analysis

Maryam Honardoost[1,2], Leila Janani[3] ,Rokhsareh Aghili[1], Zahra Emami[1], Mohammad E Khamseh[1*]

[1]Endocrine Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran, Iran.

[2]Cardio-Oncology Research Center, Iran University of Medical Sciences, Tehran, Iran.

[3]Epidemiology and Biostatistics Department, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Running Title: Comorbidities and COVID-19 Severity

***Correspondence:**

Mohammad E Khamseh,

Endocrine Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran,

ORCID: https://orcid.org/0000-0003-4313-8440

 doi:10.20944/preprints202008.0475.v1

Address; No 10, Firoozeh St, Vali-asrSq,Tehran, Iran.

Website;http://www.iums.ac.ir/link/iem

Tel:+982188945246

Email: khamseh.m@iums.ac.ir

Abstract

Aim: Several studies reported the accompaniment of severe COVID-19 with comorbidities. However, there is not a systematic evaluation of all aspects of this association. Therefore, the aim of this meta-analysis was to assess the association between all underling comorbidities in COVID-19 infection severity.

Methods: Electronic literature search was performed via scientific search engines. After the removal of duplicates and selection of articles of interest, 28 studies were included. A fixed-effects model was used; however, if heterogeneity was high (I^2>50%) a random-effects model was applied to combine the data.

Results: A total of 6270 individuals were assessed (1615 severe and 4655 non-severe patients). The median age was 63 (95% CI: 49-74) and 47 (95% CI: 19-63) years in the severe and non-severe groups, respectively. Moreover, about 41% of patients had comorbidities. Severity was higher in patients with history of cerebrovascular disease: OR 4.85 (95% CI: 3.11-7.57). The odds of being in severe group increase by 4.81(95% CI: 3.43-6.74) for history of cardiovascular disease (CVD). This was 4.19 (95% CI: 2.84-6.19) for chronic lung disease and 3.18, 95% CI: 2.09-4.82 for cancer. The odds ratio of a diabetes and hypertension were 2.61 (95% CI: 2.02-3.3), and 2.37(95% CI: 1.80-3.13) respectively.

Conclusions: The presence of comorbidities are associated with severity of COVID-19 infection. The strongest association was observed for cerebrovascular disease, followed by CVD, chronic lung disease, cancer, diabetes, and hypertension.

Keywords: COVID-19, Disease severity, Comorbid conditions

Introduction

On December 31, 2019, a number of cases with pneumonia of unknown etiology were detected in Wuhan City, Hubei Province of China. Different potential causes such as influenza, avian influenza, adenovirus, severe acute respiratory syndrome coronavirus (SARS-CoV), and Middle East respiratory syndrome coronavirus (MERS-CoV) were assessed; however, the pathogen was not identified[1,2]. Consequently, the

 doi:10.20944/preprints202008.0475.v1

causative viral disease called COVID-19 by the World Health Organization (WHO)[1].The 104th COVID-19 Situation Report of WHO reported3 349 786 diagnosed cases with 238 628 deaths around the world until the 3 May 2020 [3]. Older men and those with comorbidities such as cardiovascular disease, diabetes, hypertension, and chronic obstructive pulmonary disease (COPD) were at the highest risk for the disease [4,5]and higher rates of intensive care unit (ICU) admission[6].

Several studies reported the prevalence of comorbidities in COVID-19 patients [4,7,8]; however, a systematic evaluation of comorbidities to compare the relation of underlying medical conditions between severe and non-severe patients is lacking. Previous systematic reviews and meta-analyses explored some but not all aspects of this association. Therefore, the aim of this meta-analysis is to assess the association between all underling comorbidities in COVID-19 infection severity. The results could guide healthcare professionals to encounter properly withCOVID-19. In addition, it will help policy-makers to design a plan for prevention, as well as respond to COVID-19 and its critical outcomes more preparedly.

Methods

Search strategy

This systematic review and meta-analysis follows the PRISMA guidelines [9]. We searched PubMed, Embase, Scopus, and web of science databases between 1 Jan 2020 and 2 April 2020. The search performed using the following search terms: “Coronavirus”, “Covid-19”, “2019-nCov”, “nCov”, “Severe acute respiratory syndrome”, “SARS-COV-2”, “Clinical Feature”, “Clinical characteristic”, “Cardiovascular disease

 doi:10.20944/preprints202008.0475.v1

(CVD)", "Hypertension", " Diabetes", "Comorbidity", "severity", " Laboratory test", "Biochemical test", "ICU admission", "Acute respiratory distress syndrome (ARDS)", "Paraclinic", "CT scan", "CT finding", "CT image", "Radiologic", "Cerebrovascular disease", "Chronic obstructive pulmonary disease (COPD)", "Chronic lung disease" (see Appendix 1). There was no limitation for language as well as study design and all articles including case-control studies, and cross-sectional studies were assessed. If appropriate information was not reported in the article, it was then excluded. All publications from January 1, 2020 until April 2, 2020 were assessed.

Study selection and data extraction

Inclusion and Exclusion Criteria

We included all relevant articles reporting clinical characteristics and epidemiological information on COVID-19 patients separately in severe and non-severe group. The criteria for severe disease include ICU admission, acute respiratory distress syndrome (ARDS), need for supplemental oxygen, abnormal CT imaging and severe outcome (e.g cardiac decompensation, organ failure or death). Case series with incomplete information as well as review articles, opinion articles and letters not presenting original data as well as any type of published data that only presented total patients were also excluded.

Data extraction

 doi:10.20944/preprints202008.0475.v1

Two authors (M.H and R.A)screened and evaluated the titles and abstracts of citations independently and then, third author (ME.Kh) checked the screening results. Then, full text of potentially eligible articles was obtained and reviewed for further assessment according to the inclusion and exclusion criteria. Data extraction forms including the following items were also filled out: name of the first authors, date of publication, DOI, the number of reported cases, age, sex, and coexisting underlying diseases such as diabetes, as well as the number of patients in severe and non-severe groups.

Risk of bias assessment

Newcastle-Ottawa Scale was used to evaluate quality of the included studies.The Funnel plots were used to investigate possible publication bias.

Statistical analysis

All Statistical analyses were performed using Stata version 14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP.). We employed “metaprop” command to calculate the pooled prevalence estimates of comorbidities with 95% confidence. The associations between comorbidities and severity of disease, were expressed as odds ratios (ORs) and 95% confidence intervals (CIs).Heterogeneity among the primary studies was evaluated by the forest plots, Cochran’s Q statistic, and I^2 statistic. A random-effects model was used if heterogeneity was high (I 2 > 50%); otherwise, a fixed-effects model was applied. Also, the publication bias was formally tested with Egger’s regression asymmetry tests to determine the asymmetry of the funnel plots, where $p < 0.10$ was considered as evidence of bias.

 doi:10.20944/preprints202008.0475.v1

Results

Characteristics of included studies

In the initial search, 559 articles were found in different databases. Two papers were excluded due to being duplicates. All papers were screened by reading their title and abstract and 499 studies were excluded based because of the irrelevant data. Figure1 shows the search details, and table 1 shows details of included studies. In total, 28 studies on 6276 patients (32.2% female) were included (Figure 1) .All studies were conducted between January and April 2020 during the novel coronavirus (SARS-2-CoV) outbreak. The heterogeneity of all selected studies were low (I^2 between 0.0-30) except for hypertension (I^2 =58.6). A total of 1615 individuals were identified as severe disease whereas 4655 individuals had non-severe disease. The median age was 63 (95% CI: 49-74) years in the severe group compared to 47 (95% CI: 19-63) years in the non-severe group.

Prevalence of underlying diseases in COVID-19

We found that 41.1% of patients had associated comorbidities such as hypertension (20.9%), diabetes (9.96%), and cardiovascular disease (4.8%) (Figure 2, Table 2).

Figure 2, illustrates the relationship between associated comorbidities and disease severity. The most strongly associated comorbidities with severity of COVID-19 were cerebrovascular disease(OR 4.85, 95% CI: 3.11-7.57), cardiovascular disease (OR 4.81, 95% CI: 3.43-6.74), and

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 21 August 2020 doi:10.20944/preprints202008.0475.v1

chronic lung disease (OR 4.19, 95% CI: 2.84-6.19) followed by cancer (OR 3.18, 95% CI: 2.09-4.82), diabetes (OR 2.61, 95% CI: 2.02-3.39), and Hypertension (OR 2.37, 95% CI: 1.80-3.13) respectively (Figure 3).

Discussion

Care of COVID-19 patients is presenting a major challenge for health care systems. This include dealing with rapidly growing numbers of patients, inadequate response to current treatments, limited care staffing, and inadequate of medical supplies [35]. Moreover, many factors can lead to severe COVID-19, especially in older adults. Disease severity was defined as need for hospitalization , admission to an intensive care unit, and death [36].Classification of COVID-19 patients into severe and non-severe cases improves patient outcomes[37].Previous studies demonstrated that comorbidities such as diabetes, COPD, hypertension and malignancy may lead to poorer prognosis [35,38-41]. Therefore; in this study we tried to explore the impact of comorbidities on the prognosis of the COVID-19 infection(Figure 3).

We found disease severity was highly associated with presence of cerebrovascular disease (OR 4.85, P<0.01).It seems that the nervous system disease, may be linked to the pathogenesis of COVID-19.In addition to respiratory tract system, nervous system may be invaded by SARS-CoV-2 via hematogenous system or retrograde neuronal route, the same as SARS and MERS viruses leading to wide spectrum of neurological manifestations from taste and smell impairment to acute cerebrovascular diseases and impaired consciousness [42]. Furthermore, lymphocyte counts have been shown to be lower for patients with CNS involvement. This might be explained by immune suppression in patients with

 doi:10.20944/preprints202008.0475.v1

COVID-19 with CNS involvement, especially in severe cases. Moreover, acute cerebrovascular disease with severe infection leads to rapid clinical deterioration contributing to high mortality rate[42].

Pre-existing CVD is also an important Underlying disease for more severe COVID-19 accompanied by worse clinical outcomes [43]. Our meta-analysis revealed that Pre-existing CVD is associated with a nearly 4.8 fold significantly increased risk of severe COVID-19 disease (Figure3). In a meta-analysis on six published studies on 1527 patients with COVID-19 from China, the prevalence of diabetes, cardio-cerebrovascular disease and hypertension were reported to be 9.7%, 16.4% and 17.1%, respectively [43].In addition, diabetes and hypertension were shown to increase the risk of severity or requiring ICU admission by 2-fold while this figure was reported to be 3-fold for cardio-cerebrovascular disease[43]. In addition, in a study by Clerkin et al, CVD Was associated with disease severity and ICU admission by 4.4 times(95% CI 2.64–7.47).Furthermore, disease severity Is associated with higherCFR[43]. In addition, in a study by Shi et al, it was shown that preexisting cardiovascular diseases may predispose COVID-19 patients toCOVID-19–induced heart injury [33].

Our study also showed that chronic lung disease was significantly related to development of severeCOVID-19 infection (OR 4.19 P<0.01) (Figure 3).Severe COPD is also a risk factor for severe COVID-19. In a meta-analysis conducted on seven studies, COPD was shown to increase the risk of developing severe COVID-19 infections[40].In a case series report from Chinese Center for Disease Control and Prevention, the overall case fatality rate (CFR) was 2.3%, while this figure was 6.3% for people with COPD [44].In a study by Jain et al, COPD was shown as the strongest predictive factor for disease severity (OR 6.42, 95% CI 2.44 – 16.9) as well as ICU admission (OR 17.8, 95% CI 6.56 – 48.2)[45].

 doi:10.20944/preprints202008.0475.v1

Malignancy was also a risk factor for COVID-19 severity. The results of our pooled analysis also show that pre-existing cancer is associated with an up to 3.18-fold higher risk of severe COVID-19 (Figure 3). Infections are the leading cause of mortality in malignancy [46]. The underlying disease, malignancy-related treatments as well as accompanied comorbidities are three main reasons in susceptibility to infections in this group of patients. Both malignancy and its related treatment result in compromised immune systems and a higher risk of infection[46]. Moreover, accompanied comorbidities were previously shown to increase the risk of mortality in MERS-CoV infection [46]. Furthermore, Liang et al showed that among patients with malignancy, older age was the only risk factor for severe events (OR 1.43, 95% CI 0.97–2.12; p=0.072)[47].

In this Meta-analysis, we found that diabetes(OR 2.61, 95% CI: 2.02-3.39)and hypertension (OR 2.37, 95% CI: 1.80-3.13) also increase the risk of severity in COVID-19.Diabetes was an important risk factor for mortality in patients infected with Pandemic Influenza A (H1N1), SARS-CoV as well as MERS-CoV[48]. In a study that was conducted by Fadini et al, the pooled rate ratio of diabetes among patients with severe disease compared to those with non-severe disease was 2.26 (95% CI 1.47–3.49)[49].Moreover, diabetes related complications as the indicators of advanced diabetes may increase the risk of mortality in COVID-19 [38].

Globally, hypertension is a prevalent disease reported in 26% of population worldwide [41].However, Previous studies showed controversial results regarding on the association between hypertension and COVID-19 severity[41].In a study by Lippi et al., hypertension was shown to increase both severity and mortality of COVID-19 by ~2.5-fold. This effect was mainly demonstrated in people older than the age of 60, in a meta-regression [41]. In addition, Jain et al, showed that hypertension increased disease severity and ICU admission by 3.7 times (95% CI 2.22–5.99) [45].In a meta-analysis by Yang et al. on eight studies, comorbidities such as hypertension (OR 2.36, 95% CI: 1.46-3.83), respiratory system

 doi:10.20944/preprints202008.0475.v1

disease (OR 2.46, 95% CI: 1.76-3.44), and cardiovascular diseases (OR 3.42, 95% CI: 1.88-6.22) were shown to impose higher risk for disease severity[6].However, diabetes did not have statistically significant effect (OR2.07, 95% CI: 0.89-4.82)[6].

In general, our findings indicate that the individuals with associated comorbidities are more susceptible to severe COVID-19 infection. Those at highest risk for severe disease include people with underlying conditions such as cerebro-cardiovascular disease, chronic respiratory disease, cancer , diabetes, and hypertension.

The key strengths of this study are its quality assessments of studies, large sample size, and desirable I^2 of chosen studies. The funnel plot results indicated that our selected studies had high precision which mostly plotted near the average (Figure 4).

One issue with the current study was that the generalizability of findings to other population was unclear because published reports being restricted to China and a few other countries. Moreover, considering uncertainty about data collection methods and consistency,the results should be interpreted cautiously.

Conclusion

The findings clearly indicate that the presence of associated comorbidities are associated with worse outcome in COVID-19 infection.Cerebrovascular disease was the most strongly predictive comorbidity for severe disease, followed by CVD, chronic lung disease, cancer, diabetes and hypertension.

Acknowledgment

This work was supported by Iran University of Medical Sciences (grant # IR.IUMS.REC.1399.070).

References

1. Leung C. Clinical features of deaths in the novel coronavirus epidemic in China. *Reviews in Medical Virology* 2020.
2. Honardoost MG, M.; Khamseh, M.E. Role of Vitamin D in Pathogenesis and Severity of COVID-19 Infection. *Preprints 2020, 2020040355 (doi: 1020944/preprints2020040355v1)*.
3. Coronavirus disease (COVID-2019) situation reports-104 WHO. *https://wwwwhoint/emergencies/diseases/novel-coronavirus-2019/situation-reports* 2020.
4. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *Jama* 2020.
5. Honardoost MA, R.; Khamseh, M.E. . Coronavirus 2019 Infection in People with Associated Co-Morbidities: Case Fatality and ACE2 Inhibitors Treatment Concerns. *Preprints 2020, 2020040331 (doi: 1020944/preprints2020040331v1)* 2020.
6. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. *International Journal of Infectious Diseases* 2020.
7. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 2020; **395**(10223): 497-506.
8. Zhang Jj, Dong X, Cao YY, et al. Clinical characteristics of 140 patients infected by SARS-CoV-2 in Wuhan, China. *Allergy* 2020.
9. Stewart LA, Clarke M, Rovers M, et al. Preferred reporting items for a systematic review and meta-analysis of individual participant data: the PRISMA-IPD statement. *Jama* 2015; **313**(16): 1657-65.
10. Guan W-j, Ni Z-y, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *New England journal of medicine* 2020.
11. Liu Y, Yang Y, Zhang C, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Science China Life Sciences* 2020; **63**(3): 364-74.
12. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine* 2020.
13. Li J, Li S, Cai Y, et al. Epidemiological and Clinical Characteristics of 17 Hospitalized Patients with 2019 Novel Coronavirus Infections Outside Wuhan, China. *medRxiv* 2020.
14. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet* 2020.
15. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. *Clinical Infectious Diseases* 2020.
16. Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. *PLoS One* 2020; **15**(3): e0230548.

17. Yuan J, Zou R, Zeng L, et al. The correlation between viral clearance and biochemical outcomes of 94 COVID-19 infected discharged patients. *Inflammation Research* 2020: 1-8.
18. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *Bmj* 2020; **368**.
19. Young B, Ong S, Kalimuddin S, et al. Singapore Novel Coronavirus Outbreak Research T. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. *Jama* 2020; **10**.
20. Wu J, Li W, Shi X, et al. Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19). *Journal of Internal Medicine* 2020.
21. Li K, Wu J, Wu F, et al. The Clinical and Chest CT Features Associated with Severe and Critical COVID-19 Pneumonia. *Investigative radiology* 2020.
22. Guan W-j, Liang W-h, Zhao Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. *European Respiratory Journal* 2020.
23. Gao Y, Li T, Han M, et al. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. *Journal of Medical Virology* 2020.
24. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H. Clinical and immunologic features in severe and moderate forms of Coronavirus Disease. *J Clin Invest* 2019; **137244**.
25. Chen C, Yan J, Zhou N, Zhao J, Wang D. Analysis of myocardial injury in patients with COVID-19 and association between concomitant cardiovascular diseases and severity of COVID-19. *Zhonghua xin xue guan bing za zhi* 2020; **48**: E008-E.
26. Li Y-K, Peng S, Li L-Q, et al. Clinical and transmission characteristics of Covid-19—a retrospective study of 25 cases from a single thoracic surgery department. *Current Medical Science* 2020: 1-6.
27. Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. *Clinical Infectious Diseases* 2020.
28. Wang L, Li X, Chen H, et al. Coronavirus disease 19 infection does not result in acute kidney injury: an analysis of 116 hospitalized patients from Wuhan, China. *American journal of nephrology* 2020: 1-6.
29. Wan S, Xiang Y, Fang W, et al. Clinical Features and Treatment of COVID-19 Patients in Northeast Chongqing. *Journal of medical virology* 2020.
30. Shi Y, Yu X, Zhao H, Wang H, Zhao R, Sheng J. Host susceptibility to severe COVID-19 and establishment of a host risk score: findings of 487 cases outside Wuhan. *Critical Care* 2020; **24**(1): 1-4.
31. Mo P, Xing Y, Xiao Y, et al. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. *Clinical Infectious Diseases* 2020.
32. Liu W, Tao Z-W, Wang L, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chinese medical journal* 2020.
33. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA cardiology* 2020.
34. Peng Y, Meng K, Guan H. Clinical features and outcome of 112 cases of novel coronavirus pneumonia in cardiovascular patients. *Chin J Cardiol* 2020; **48**.
35. Tang X, Du R, Wang R, et al. Comparison of hospitalized patients with acute respiratory distress syndrome caused by COVID-19 and H1N1. *Chest* 2020.

36. Control CfD, Control CfD, Prevention. Morbidity and mortality weekly report: MMWR: US Department of Health, Education, and Welfare, Public Health Service …; 1988.
37. Wang T, Du Z, Zhu F, et al. Comorbidities and multi-organ injuries in the treatment of COVID-19. *The Lancet* 2020; **395**(10228): e52.
38. Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes/Metabolism Research and Reviews* 2020.
39. Deng Y, Liu W, Liu K, et al. Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 (COVID-19) in Wuhan, China: a retrospective study. *Chinese medical journal* 2020.
40. Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). *Respiratory Medicine* 2020.
41. Lippi G, Wong J, Henry BM. Hypertension and its severity or mortality in Coronavirus Disease 2019 (COVID-19): a pooled analysis. *Polish archives of internal medicine* 2020.
42. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA neurology* 2020.
43. Clerkin KJ, Fried JA, Raikhelkar J, et al. Coronavirus disease 2019 (COVID-19) and cardiovascular disease. *Circulation* 2020.
44. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *Jama* 2020.
45. Jain V, Yuan J-M. Systematic review and meta-analysis of predictive symptoms and comorbidities for severe COVID-19 infection. *medRxiv* 2020.
46. Jazieh A-R, Alenazi TH, Alhejazi A, Al Safi F, Al Olayan A. Outcome of oncology patients infected with coronavirus. *JCO Global Oncology* 2020; **6**: 471-5.
47. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *The Lancet Oncology* 2020; **21**(3): 335-7.
48. Gupta R, Ghosh A, Singh AK, Misra A. Clinical considerations for patients with diabetes in times of COVID-19 epidemic. *Diabetes & Metabolic Syndrome* 2020; **14**(3): 211.
49. Fadini G, Morieri M, Longato E, Avogaro A. Prevalence and impact of diabetes among people infected with SARS-CoV-2. *Journal of Endocrinological Investigation* 2020: 1.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 21 August 2020 doi:10.20944/preprints202008.0475.v1

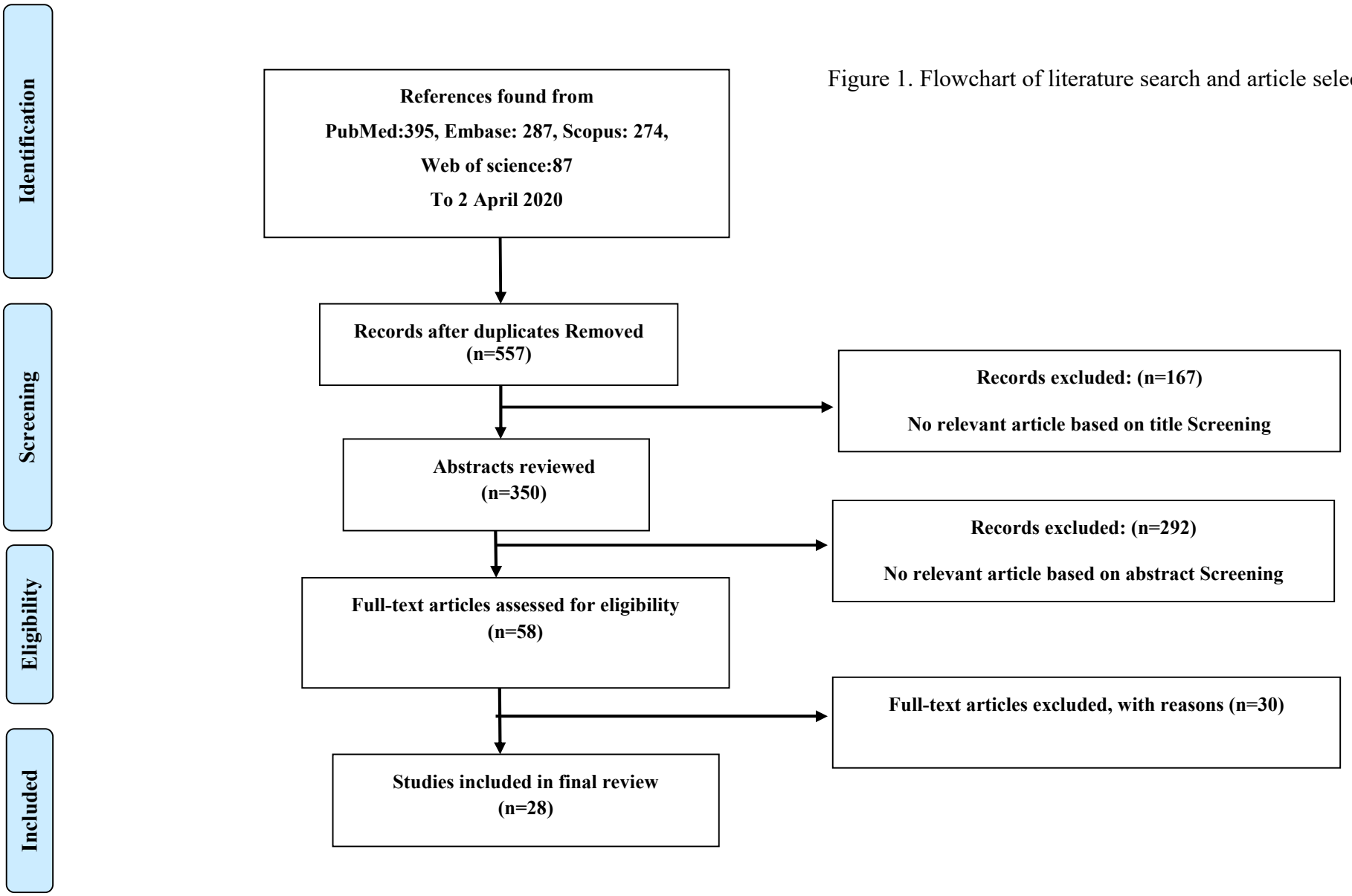


Figure 1. Flowchart of literature search and article selection

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 21 August 2020 doi:10.20944/preprints202008.0475.v1

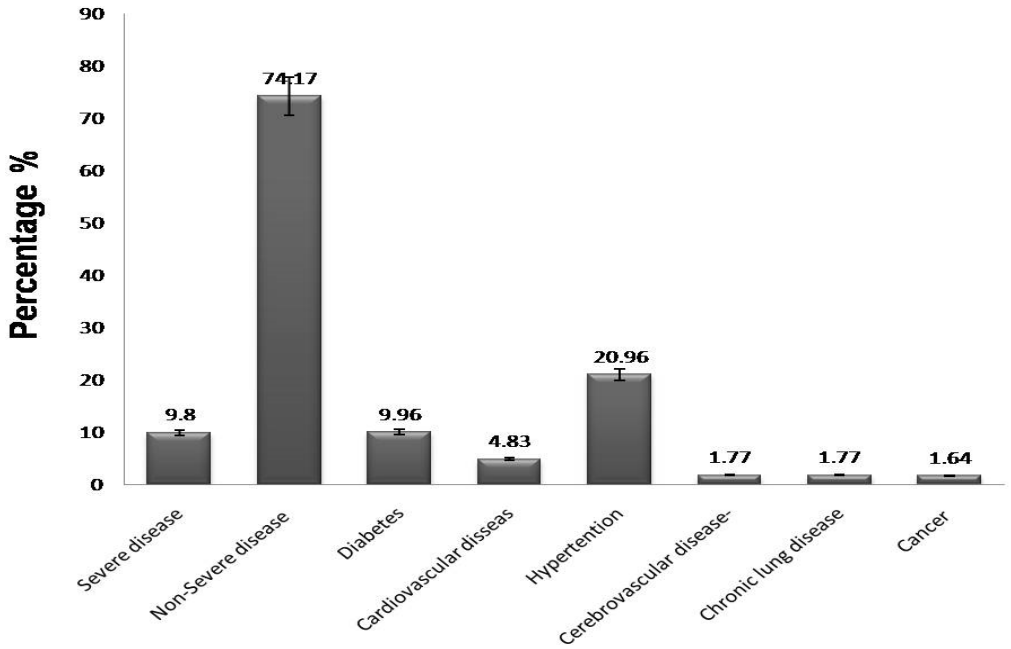
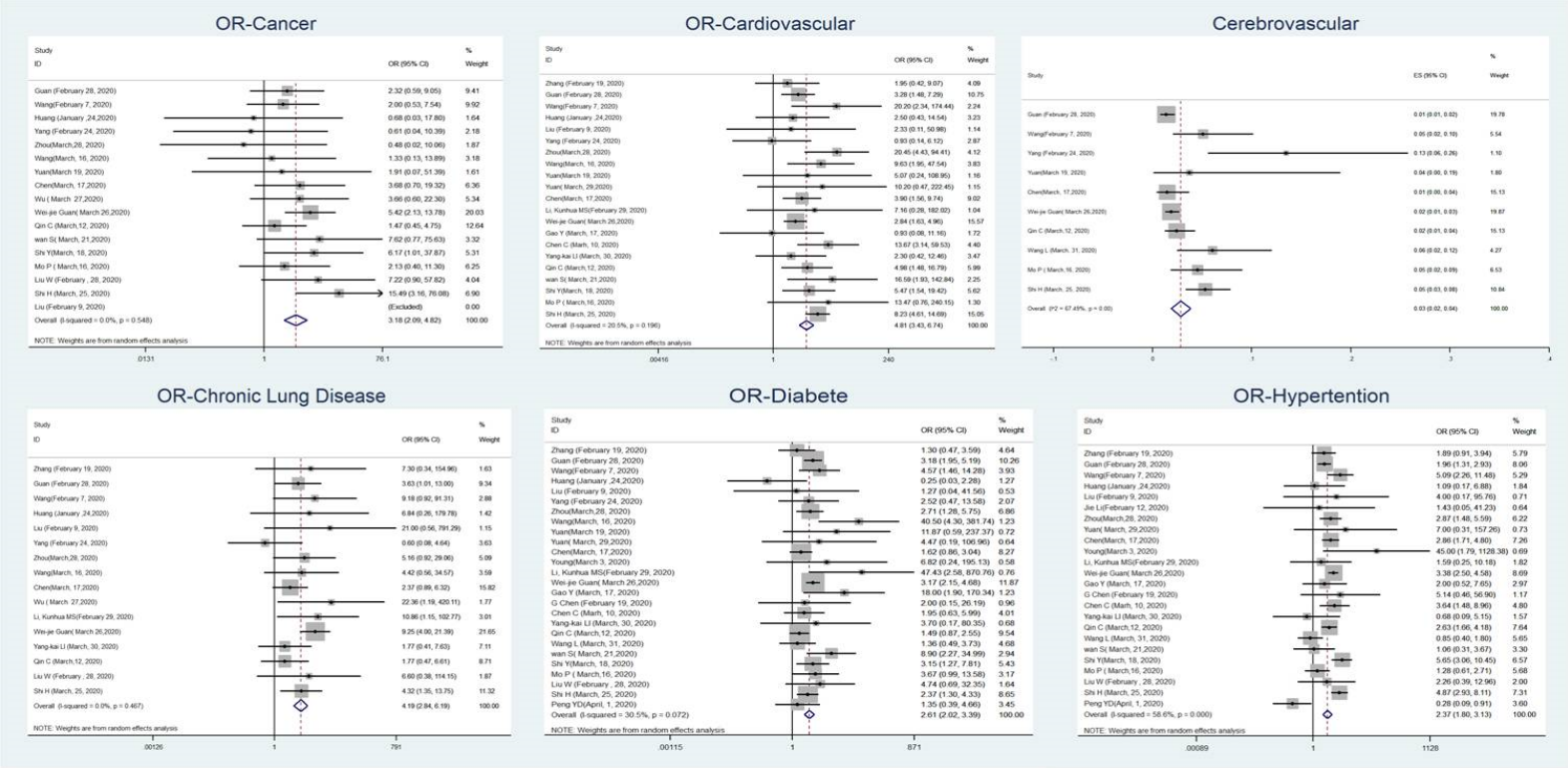


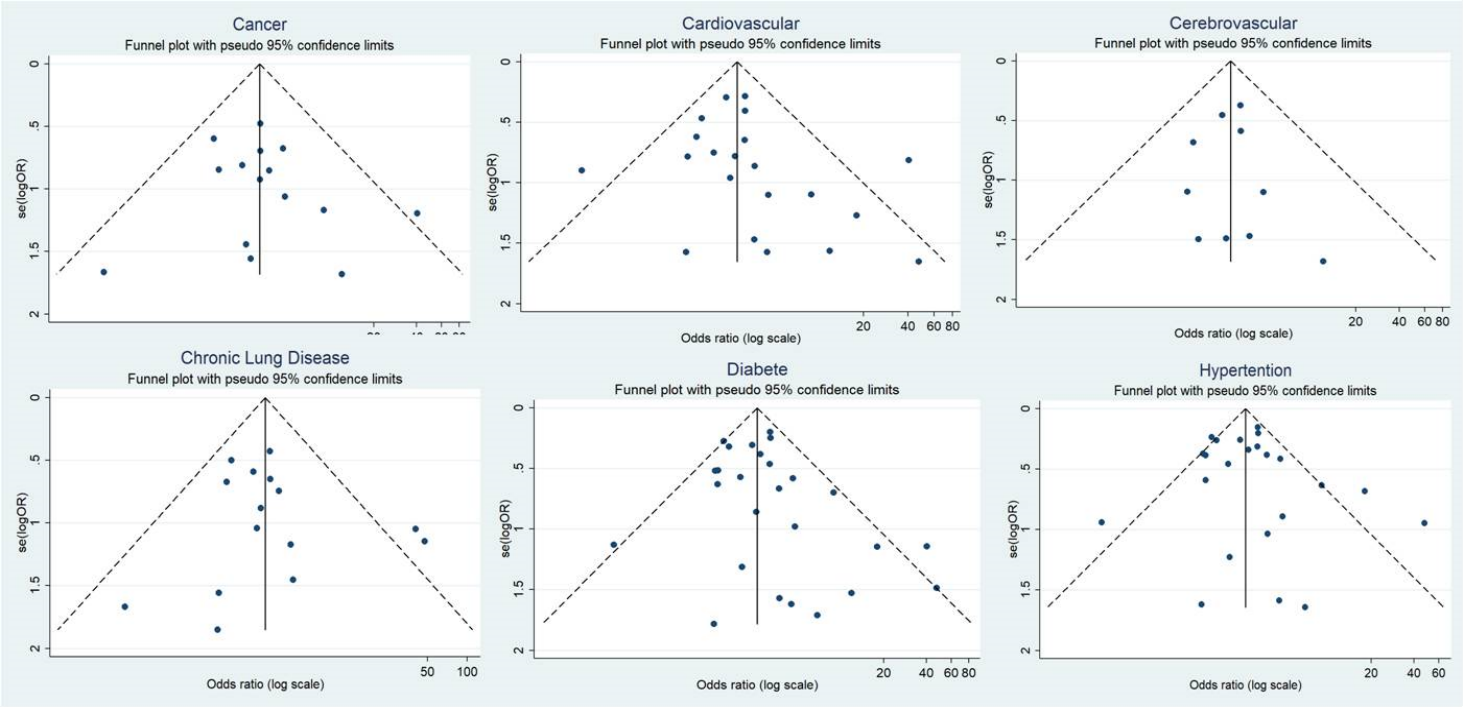
Figure 2.Prevalence of Comorbidities in total Studies

 doi:10.20944/preprints202008.0475.v1



Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 21 August 2020 doi:10.20944/preprints202008.0475.v1

Figure 3.Prevalence of comorbid conditions among patients with severe COVID-19 compared with non-severe patients



 doi:10.20944/preprints202008.0475.v1

Figure 4.Funnel plot for meta-analysis of the prevalence of comorbidity in COVID-19 patients