Meta-Analysis

Prevalence of co-morbidities and its association with mortality in Indian patients with COVID-19: A meta-analysis

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ABSTRACT

Background and Aims: Coronavirus disease 2019 (COVID 19) has spread to every corner of the world and has led to significant health consequences, especially in patients with co morbidities. This study aimed to estimate the prevalence of co morbidities among COVID 19 patients in the Indian population and their association with mortality. **Methods:** PubMed, Google Scholar, and World Health Organization website were searched for Indian studies on COVID 19 published from February 2020 up to 20 May 2021. English language publications from India, studies reporting epidemiological characteristics, prevalence of co morbidities and in hospital mortality were included in the meta analysis. **Results:** 34 studies were identified with a total of 23,034 patients. The pooled prevalence for co morbidities in COVID 19 patients was 18.1% [95% confidence interval (CI), 13.3 to 24.3%] for hypertension, 17.7% (95% CI, 12.2 to 25.1%) for diabetes, 7.9% (95% CI, 4.6 to 13.4%) for hypothyroidism and 7.7%(95% CI, 4.8 to 12. 1%) for cardiovascular diseases. For chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), cerebrovascular diseases, asthma, chronic liver disease, tuberculosis and cancer, the pooled prevalence was less than 4%. Additionally, the mortality risk was increased significantly in patients with CKD [odds ratio (OR) = 4.1], COPD (OR = 3.9), diabetes (OR = 3.7), cardiovascular diseases (OR = 4.07), tuberculosis (OR = 6.11), chronic liver disease (OR = 8.5), malignancy (OR = 1.89) and hypertension (OR = 2.9). Cerebrovascular diseases, hypothyroidism and asthma were not associated with increased mortality. **Conclusion:** Co-morbidities are more prevalent in COVID 19 hospitalised patients and the presence of co morbidities is associated with increased risk of mortality in Indian COVID 19 patients.

Key words: Co-morbidity, India, prevalence, SARS-CoV-2

INTRODUCTION

Ever since the coronavirus disease 2019 (COVID-19) outbreak started in Wuhan in late December 2019, it has spread to every corner of the world.[1] This disease is transmitted by aerosol droplets, human contact and through fomites, with an incubation period of 5–6 days (ranging from 1 to 14 days).[2,3] The virus is evolving rapidly and spreading exponentially all over the world. Ever since the pandemic has started, a number of studies on COVID-19 have been published in literature. But most of these studies have a small sample size reported from a single centre. Also, earlier studies stated that mortality was higher in older people with co-morbidities because of a weakened immune

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system. But with the passage of time, mortality in the younger generation without significant past medical history was noticed. Hence, whether co-morbidity plays a key role in increasing mortality remains doubtful. Various authors have conducted systematic reviews and meta-analyses on the prevalence of co-morbidities and their association with mortality.[4-12] But as the clinical presentation and outcomes may vary among different ethnic groups, it is important to conduct a meta-analysis of studies from the local population. This study was therefore conducted to estimate the prevalence of co-morbidities and the association of these co-morbidities with mortality in Indian COVID-19 patients.

The primary aim of this meta-analysis was estimating the prevalence of co-morbidities among all categories of included COVID-19 patients in the Indian population, no matter what the severity. The secondary aim was estimating the association of co-morbidities with mortality in Indian COVID-19 patients.

METHODS

Databases and search strategy

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement and checklist. Initially, PubMed search was conducted using Medical Subject Headings (MeSH) index terms and related keywords. Subsequently, analysis of the words within the title, abstract and index terms used to describe the articles was performed. Manual search of cross references was also done. Filter was applied to incorporate only full text articles. Articles with only abstracts were not included within the study. Other databases that were searched included Google Scholar and World Health Organization website. The study included articles published till 20 May 2021 in the above mentioned databases. The search strategy of one of the databases (PubMed) has been provided in Annexure 1. Boolean operators "AND" and "OR" were used as follows:

1) COVID-19 OR 2019-nCoV OR novel coronavirus OR SARS-CoV-2 OR Coronavirus.
2) Prevalence.
3) Co-morbidities OR underlying diseases OR Cardiovascular Diseases OR Neoplasms OR Pulmonary Disease OR Asthma OR Hypertension OR Diabetes Mellitus OR Renal Insufficiency OR Cerebrovascular Disorders OR Hypothyroidism OR Liver Diseases OR Tuberculosis.
4) India.
5) (1) AND (2) AND (3) AND (4).

Inclusion criteria: Studies in English language published online that reported detailed epidemiological characteristics, prevalence of co-morbidities and in-hospital mortality were included. Also, studies that reported the prevalence of co-morbidities without mortality were included only for the meta-analysis of prevalence.

Exclusion criteria: Non-human studies, case reports, systematic reviews with abstract only were excluded from the study. Also, studies with incomplete information, repeated studies, pre-print articles, studies from countries outside India and studies merely classified on survival and death were excluded.

Initial screening of the abstract and title was done by two authors. The full texts of the selected studies were screened by four authors and were retrieved for further review. Whenever the study cohorts overlapped (i.e., cases were reported from same hospital and time period), the largest study was selected for inclusion. If studies had an overlapping cohort but reported the data for different analyses, both were included within the systematic review but were analysed separately. Any confusion during the study selection was resolved by discussion and consensus among the four authors. A detailed PRISMA flow diagram for the search strategy is demonstrated in Figure 1.

Risk of bias and study quality: [Annexure 2]

The Newcastle-Ottawa Scale (NOS), designed to evaluate the quality of non-randomised studies, was employed to assess the risk of bias.[13] The NOS score ranges from 0 to 9 and consists of three categories: selection, comparability and outcome. Two authors independently assessed the studies for risk of bias

Information including authors, duration of clinical observation, the particular hospital and location that the cases came from, sample size, gender, age, proportion of the sample size having at least one co-morbidity, proportion of common clinical symptoms among patients including fever, cough, myalgia, dyspnoea, gastrointestinal symptoms, sore throat, loss of taste and smell, rhinorrhoea and also asymptomatic patients were extracted from the literature. Also, number of patients with specific co-morbidities including hypertension, diabetes mellitus, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD), asthma, chronic liver disease (CLD), chronic kidney disease (CKD), cerebrovascular disease, hypothyroidism, pulmonary

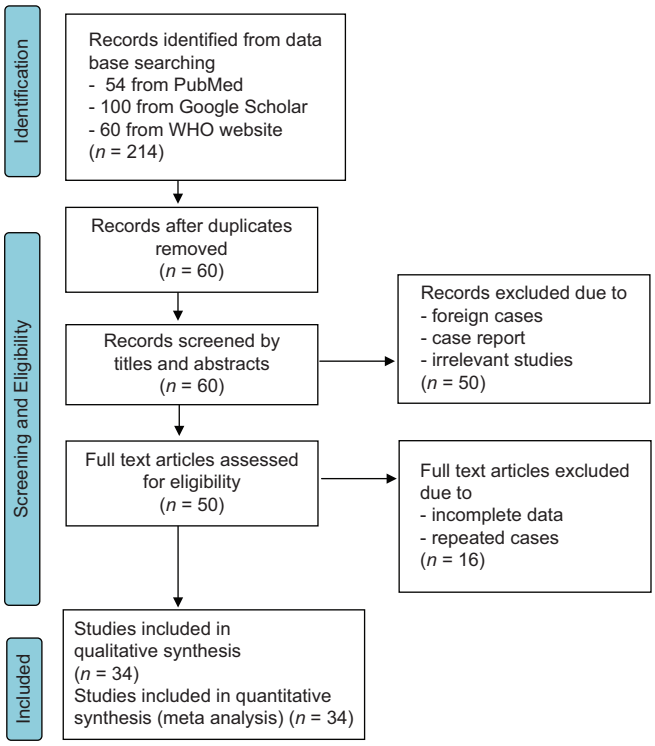

Figure 1: The PRISMA flow diagram of the number of studies screened and included in the meta-analysis. n: number

tuberculosis (TB) and malignancy were retrieved from the studies. Information regarding mortality rate was also noted. The pooled prevalence and 95% confidence intervals (CI) were calculated for each of the selected co-morbidities. Odds ratio (OR) with 95% CIs was also calculated for the estimated pooled risk of mortality with COVID-19 infection as associated with each co-morbidity. Random or fixed-effect model was used based on the degree of heterogeneity of the included studies. Heterogeneity was assessed using Higgins I^2 statistics and was graded as low (I^2 <25%), moderate (I^2 = 25%-50%) or high (I^2 >50%). Random-effects model was used to estimate pooled effects if I^2 >50% and fixed-effects model was applied to calculate pooled effects when I^2 <50%.[14] Between-study heterogeneity was investigated by fitting meta-regression models to assess the associations between study effect size and different covariates. Meta-regression was done using random effects multivariable meta-regression models using restricted maximum likelihood (REML) approach, with the study effect size (i.e., OR) as the dependent variable and the study characteristic of interest which included the mean age of patients (median age was used if the mean was not reported), gender (proportion of males), and all the co-morbidities reported in this meta-analysis as the independent variable. The potential for publication bias within meta-analyses was evaluated by funnel plots and Egger's test.[15] When results from funnel plots and Egger's test contradicted one another, we resorted to the results of Egger's test for reference. For meta-analyses which reported significant publication bias, the pooled effect size was recalculated using the 'trim and fill' adjustment based on the Duval and Tweedle non-parametric method.[16] All analyses were carried out in Comprehensive Meta-Analysis Version 3.[17]

RESULTS

Study characteristics

The search strategy identified 214 studies. After removing duplicates, 60 studies remained, out of which 10 were commentaries, review articles, non-clinical studies, and guidelines. After review of full text, a further 16 studies were excluded. Finally, we included 34 studies which included 23,034 patients totally, of which 14,786 patients were male and 8,208 were females.[18-51] One study did not mention distribution of the sample size between male and female. All the 34 studies were based on Indian population and were performed at different hospitals in India. All the included studies were further sorted by co-morbidities, with 34 studies reporting hypertension, 34 reporting diabetes, 26 reporting cardiovascular diseases, 22 reporting COPD, 22 reporting CKD, 15 reporting hypothyroidism, 13 reporting malignancy, nine reporting asthma, eight reporting CLD, eight reporting cerebrovascular diseases and seven reporting pulmonary TB. Fever (25%) was the most prevalent symptom, followed by cough (24.03%), dyspnoea (14.2%), sore throat (7.7%), myalgia (6.4%), gastrointestinal symptoms (4.2%) and loss of taste and smell (1.8%). Around 16.8% patients were asymptomatic. The age of the patients was distributed around 44 years. Male preponderance (64.1%) was noted in this meta-analysis [Table 1].

Meta-analysis of prevalence of co-morbidities in COVID-19 cases

For pooled prevalence of different co-morbidities among COVID-19 patients refer to Table 2.

Prevalence of hypertension

Based on the random effects model after inclusion of 34 studies, the prevalence of hypertension among the confirmed COVID-19 patients was 18.1% (95% CI, 13.3 to 24.3%). Cochrane Q statistics showed 98.54% heterogeneity among the studies, which was high

Table 1 : Characteristics Of Studies Included In The Meta - Analysis

Study	Location	Sample size	Gender (*n*/%)		Age (mean±SD/ median)	Comorbidity	Comorbidities (*n*/%)			
			M	F		Total(*n*/%)	Hypertension	Diabetes	COPD	CVD
P.Mohandas *et al*. 2020	Miot hosp chennai	3345	2314/69.20%	1031/30.80%	47.58±16.69		974/29.1%	1240/37.1%	7/0.2096%	1103/33%
Mithal A, *et al*. 2020	Max saket new delhi	401	276/68.82%	125/31.18%	54		164/40.9%	189/47.13%	3/0.7%	35/8.7%
Soni, *et al*. 2020	Pgi, chandigarh	114	66/57.8%	48/42.1%	35.9±14.7	34/29.8%	19/16.6%	17/14.9%	2/1.7%	2/1.7%
Singla N, *et al*. 2020	Screening opd, pgi, chandigarh	40				9/10.2%	3/7.5%	5/12.5%		0
Kumar R, *et al*. 2020	Aiims, new delhi	231	181/78.35%	50/21.6%	39.8±13.6	49/21.2%	19/8.2%	28/12.1%		
Sherwal, *et al*. 2020	Rajiv gandhi cancer hopital, new delhi	308	69/22.4%	239/77.5%	48	117/38%	104/34%	107/35%		
Pande D, *et al*. 2020	, V.M.M.C. New delhi	27	13/48.1%	14/51.9%	50±15	22/85%	8/29.6%	9/33.3%	2/7.4%	2/7.4%
Mohan A, *et al*. 2020	Aiims, new delhi	144	134/93.1%	10/7.2%	40±13.1	23/15.9%	3/2.1%	16/11.1%	2/1.4%	1/0.7%
Kayina, *et al*. 2020	Icu, aiims, new delhi	235	160/68.1%	75/31.9%	50.7±15.1		65/28.1%	54/23.3%		
Krishnasamy N, *et al*. 2020	Nandambakkam ccc, chennai	1263	836/66.3%	425/33.7%	35	223/17.7%	396/31.4%	861/68.2%		79/6.3%
Sharma A.K. *et al*. 2020	Designated covid govt hospital, jaipur	234	151/64.5%	83/35.47%	35±16.6		11/4.7%	11/4.7%	12/5.1%	
Saxena, *et al*. 2020	Mamc, new delhi	3745	2254/60.1%	1491/39.81%	42.49±17.26	626/16.7%	129/20.60%	159/25.30%	12/1.91%	62/9.90%
Gupta N, *et al*. 2020	Vmmc, new delhi	21	14/66.7%	7/33.3%	40.3	6/28.6%	5/23.8%	3/14.2%		
Gupta N, *et al*. 2020	Vmmc, new delhi	200	116/58%	84/42%	40.03±17.03	83/41.5%	46/23%	32/16%	1/0.5%	9/4.5%
Gaur A, *et al*. 2020	Bhilwara	26	16/61.54%	10/38.46%	37.6	6/23.07%	4/15.38%	2/7.69%	1/3.84%	2/7.69%
Bhandari S, *et al*. 2020	Sms, jaipur	29	20/68.9%	9/31.03%	38.8±18.9	5/17%	2/7%	2/7%	1/3%	1/3%
Bhandari S, *et al*. 2020	Sms, jaipur	21	14/66.66%	7/33.33%	43.5	3/4.76%	3/14.28%	2/9.5%	1/4.7%	1/4.7%
Jain AC, *et al*. 2020	Apollo hospital, new delhi	425	310/73.38%	113/26.62%	49	217/51.06%	143/33.88%	124/29.41%	12/2.82%	24/5.66%
K Revathishree *et al*. 2020	Tamil nadu	250	177/70.8%	73/29.2%	41.13±9.93	144/57.6%	25/10%	38/15.2%		11/4.4%
Suresh, *et al*. 2020	Aiims, new delhi	116	73/62.9%	43/37.1%	47	68/58.6%	35/30.2%	32/27.6%	3/2.6%	8/6.9%
Charvi Patel, *et al*. 2020	Bvp, pune	413	249/60.29%	164/39.7%	46.13±15.71	159/38.50%	73/17.68%	102/24.7%		
Aggarwal A, *et al*. 2020	Rml, delhi	32	19/59.4%	13/40.6%	54.5	22/68.8%	11/34.4%	11/34.4%	5/15.6%	4/12.5%
Gurtoo A, *et al*. 2020	Lhmc , new delhi	182	107/58.79%	75/41.2%	46.1±16.4	125/68.6%	45/24.7%	53/29.1%	21/11.5%	9/4.9%
Jain P, *et al*. 2020	Rml, new delhi	63	46/73.01%	17/26.9%	47.03±15.4		14/23%	11/17%		11/17%
R. Yadav, *et al*. 2020	Kasturba hosp, mumbai	8103	5312/46.31%	2791/39.14%	47		320/3.9%	348/4.29%		
Tambe MP, *et al*. 2020	Sasoon hosp, pune	197	107/54.31%	97/49.2%	45.8±17.3	93/47.2%	60/30.5%	42/21.3%	10/5.1%	4/2%
Prakash S, *et al*. 2020	Kgmu, lucknow	17	15/8.2%	2/11.7%	40.5	6/35.29%	2/11.76%	5/29.41%	1/5.88%	1/5.88%
Sharma S, *et al*. 2020	Sms, jaipur	75	56/74.6%	19/25.3%	38.46	10/13.3%	5/6.6%	3/4%	1/1.3%	2/2.7%
Dosi R, *et al*. 2020	Aurobindo med clg, indore	329	191/58.66%	136/41.6%	49	154/47.11%	82/24.92%	71/21.58%		11/3.34%
Agarwal N, *et al*. 2020	Aiims, patna	95	79/83.1%	16/16.8%	47.7±15.9	43/45.2%	21/22.1%	22/23.15%	1/1.05%	5/5.2%
Gupta A, *et al*. 2020	Command hospital, kolkatt	710	530/74.6%	180/25.4%	48.4±16.4		87/12%	53/7.2%	21/2.9%	49/6.7%
Marimuthu Y, *et al*. 2020	Esic, bengalaru	854	483/56.6%	370/43.32%	45.3±17.2	348/40.7%	200/23.4%	196/23%	13/1.5%	37/4.3%
Mathur A , *et al*. 2020	Dch, udaipur	100	60/60%	40/40%		14/14%	64/64.2%	21/21.4%		21/21.4%
desouza R *et al*. 20201	Tnmc, mumbai	689	338/49%	351/50.94%	44	129/18.72%	66/9.5%	67/9.7%	11/1.5%	17/2.4%
Total		23034	14786/64.19%	8208/35.63%	44.24					

Study	Comorbidities (*n*/%)							Mortality	Type of study
	Asthma	CKD	Hypothyroidism	CLD	Cancer	TB	Cerebrovascular diseases		
P.Mohandas *et al*. 2020	98/2.90%	52/1.60%	974/29.1%	1240/37.1%	7/0.2096%		98/2.90%	142/4.2%	Retrospective observational
Mithal A, *et al*. 2020	17/4.2%	12/3%	61/15.2%		11/2.7%			15/3.7%	Prospective observational

Contd...

Table 1 : Contd...

Study	Comorbidities (*n*/%)							Mortality	Type of study
	Asthma	CKD	Hypothyroidism	CLD	Cancer	TB	Cerebrovascular diseases		
Soni, *et al*. 2020		3/2.6%		1/0.8%			1/0.8%	3/2.6%	Prospective observational
Singla N, *et al*. 2020		4/10%		0				7/17.5%	Prospective descriptive
Kumar R, *et al*. 2020								0	Retrospective observational
Sherwal, *et al*. 2020								11/3.5%	Prospective observational
Pande D, *et al*. 2020		2/7.4%	2/7.4%		2/7.4%	I/3.7%		16/59.2%	Retrospective case series
Mohan A, *et al*. 2020	1/0.7%		3/2.1%			1/0.7%		2/1.4%	Prospective observational
Kayina, *et al*. 2020		22/9.5%		10/4.3%	26/11%			40/17.02%	Prospective observational
Krishnasamy N, *et al*. 2020								3/0.2%	Retrospective observational
Sharma A.K. *et al*. 2020									Retrospective cohort
Saxena, *et al*. 2020	10/1.59%	91/14.53%		5/0.79%					Retrospective cohort
Gupta N, *et al*. 2020			1/4.7%					0	Descriptive case series
Gupta N, *et al*. 2020		4/2%	6/3%		5/2.5%	11/5.5%	5/2.5%	19/9.5%	Prospective observational
Gaur A, *et al*. 2020	1/3.84%	2/7.69%					1/3.84%	2/7.6%	Descriptive case series
Bhandari S, *et al*. 2020									Retrospective observational descriptive
Bhandari S, *et al*. 2020			2/9.5%						Prospective observational
Jain AC, *et al*. 2020		30/7.06%	22/5.21%		7/1.65%	7/1.65%			Retrospective observational
K Revathishree *et al*. 2020	3/1.2%		3/1.2%					25/10%	Prospective desriptive cross sectional analytical
Suresh, *et al*. 2020	5/4.3%	18/15.5%		8/6.9%	10/8.6%		5/4.3%	51/43.9%	Prospective observational
Charvi Patel, *et al*. 2020		32/7.75%						53/12.83%	Retrospective observational
Aggarwal A, *et al*. 2020	2/6.25%	0	2/6.25%		0	2/6.2%		9/28.13%	Retrospective single center case series
Gurtoo A, *et al*. 2020		1/0.5%	6/3.2%	5/2.7%			8/4.3%	60/32.9%	Retrospective observational
Jain P, *et al*. 2020		2/3%							Cross sectional observational
R. Yadav, *et al*. 2020		43/0.5%						211/2.6%	Prospective cohort
Tambe MP, *et al*. 2020		2/1%		4/2%				58/29.44%	Cross sectional descriptive hospital based
Prakash S, *et al*. 2020								1/5.8%	Retrospective observational cross section
Sharma S, *et al*. 2020		2/2.7%					1/1.3%	3/4%	Prospective observational
Dosi R, *et al*. 2020		6/1.82%	9/2.7%		2/0.6%			31/8.42%	Retrospective observational
Agarwal N, *et al*. 2020		1/1.05%	9/9.47%	0	2/2.1%	2/2.1%		27/28.4%	Observational record based longitudinal.
Gupta A, *et al*. 2020		39/5.3%			50/7.1%		37/5.2%	50/7%	Prospective observational
Marimuthu Y, *et al*. 2020	12/1.4%		45/5.3%		9/1.1%	9/1.1%		87/10.2%	Record based longitudinal
Mathur A , *et al*. 2020			14/14.2%		7/7.14%			1/1%	Observational cross sectional
desouza R *et al*. 20201		20/2.9%		2/0.2%	10/1.4%			156/22.64%	Retrospective observational
Total									

COPD: Chronic obstructive pulmonary disease, CVD: Cardio vascular disease, CKD: Chronic kidney disease , CLD: Chronic liver disease, TB: tuberculosis, SD: Standard deviation, n: number. M:Male, F:Female

Table 2: Meta-analysis of pooled prevalence of co-morbidities in COVID-19 patients

Disease	*n*	Prevalence	Lower limit	Upper limit	*P*	I^2(%)	Egger's (*P*)		After trim and fill Prevalence (95%CI)
							one-tailed	two-tailed	
Hypertension	34	18.1	13.3	24.3	*P*=0.000	98.54	0.39	0.78	
Diabetes	34	17.7	12.2	25.1	*P*=0.000	99.07	0.14	0.29	
CVD	26	5.6	3.1	9.9	*P*=0.000	98.73	0.000	0.000	7.7 (4.8 to12.1)
COPD	22	2.3	1.3	4.1	*P*=0.000	89.05	0.32	0.65	
Hypothyroidism	15	5.7	2.9	10.8	*P*=0.000	96.86	0.000	0.000	7.9 (4.6 to 13.4)
CKD	22	3.3	2.1	5.2	*P*=0.000	93.47	0.28	0.56	
Asthma	9	2.0	0.9	4.3	*P*=0.000	88.41	0.24	0.48	
CLD	8	2.8	0.5	15.5	*P*=0.000	98.36	0.000	0.000	no change
Malignancy	13	2.8	1.4	5.4	*P*=0.000	92.48	0.03	0.06	no change
Cerebrovascular diseases	8	3.5	2.6	4.9	*P*=0.000	47.59	0.42	0.84	
TB	7	2.3	1.2	4.6	*P*=0.000	67.78	0.46	0.92	

n=Number of studies, CVD=Cardiovascular diseases, COPD=Chronic obstructive pulmonary disease, CKD=Chronic kidney disease, CLD=Chronic liver disease, TB=Tuberculosis, CI=Confidence interval

and significant (Q = 2267.89, P = 0.00, I^2 = 98.54%) [Figure 2].

Prevalence of diabetes mellitus

Based on the random effects model after inclusion of 34 studies, the prevalence of diabetes mellitus among the confirmed COVID-19 patients was 17.7% (95% CI, 12.2 to 25.1%). Cochrane Q statistics showed 99.07% heterogeneity among the studies which was high and significant (Q = 3580.2, P = 0.00, I^2 = 99.07%) [Figure 2].

Prevalence of cardiovascular disease

Based on the random effects model after inclusion of 26 studies, the prevalence of CVD among the confirmed COVID-19 patients was 7.7%% (95% CI, 4.8 to 12. 1%). Cochrane Q statistics showed 98.73% heterogeneity among the studies which was high and significant (Q = 1449.85, P = 0.00, I^2 = 98.73%) [Figure 2].

Prevalence of chronic obstructive pulmonary disease (COPD)

Based on the random effects model after inclusion of 22 studies, the prevalence of COPD among the confirmed COVID-19 patients was 2.3% (95% CI, 1.3 to 4.1%). Cochrane Q statistics showed 89.05% heterogeneity among the studies which was high and significant (Q = 191.91, P = 0.00, I^2 = 89.057%) [Figure 2].

Prevalence of chronic kidney disease

Based on the random effect model after inclusion of 22 studies, the prevalence of CKD among the confirmed COVID-19 patients was 3.3% (95% CI, 2.1 to 5.2%). Cochrane Q statistics showed 93.47% heterogeneity among the studies which was high and significant (Q = 321.69, P = 0.00, I^2 = 93.47%) [Figure 2].

Prevalence of hypothyroidism

Based on the random effect model after inclusion of 15 studies, the prevalence of hypothyroidism among the confirmed COVID-19 patients was 7.9% (95% CI, 4.6 to 13.4%). Cochrane Q statistics showed 96.86% heterogeneity among the studies which was high and significant (Q = 447.106, P = 0.00, I^2 = 96.86%) [Figure 2].

Prevalence of malignancy

Based on the random effects model after inclusion of 13 studies, the prevalence of malignancy among the confirmed COVID-19 patients was 2.8% (95% CI, 1.4 to 5.4%). Cochrane Q statistics showed 92.48% heterogeneity among the studies which was high and significant (Q = 159.62, P = 0.00, I^2 = 92.48%) [Figure 2].

Prevalence of asthma

Based on the random effects model after inclusion of nine studies, the prevalence of asthma among the confirmed COVID-19 patients was 2.0% (95% CI, 0.9 to 4.3%). Cochrane Q statistics showed 88.41% heterogeneity among the studies which was high and significant (Q = 69.035, P = 0.00, I^2 = 88.41%) [Figure 2].

Prevalence of chronic liver disease

Based on the random effects model after inclusion of eight studies, the prevalence of CLD among the confirmed COVID-19 patients was 2.8% (95% CI, 0.5 to 15.5%). Cochrane Q statistics showed 98.36% heterogeneity among the studies which was high and significant (Q = 427.772, P = 0.000, I^2 = 98.36%) [Figure 2].

Prevalence of cerebrovascular disease

Based on the fixed effects model after inclusion of eight studies, the prevalence of cerebrovascular

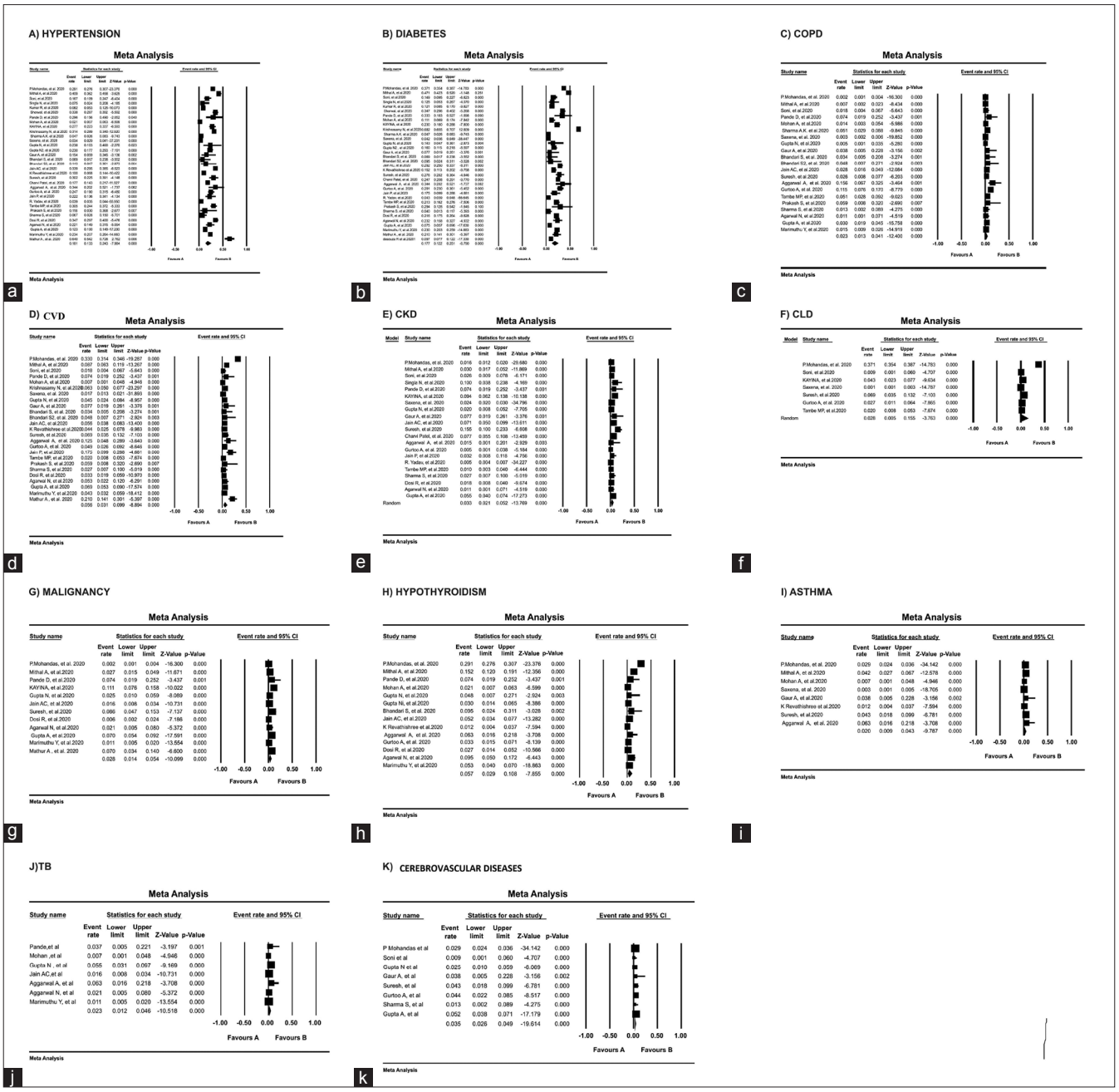

Figure 2: Forest plots of prevalence of co-morbidities in COVID-19 patients. Parts for each co-morbidity are arrayed in the figure orderly as follows: a) Hypertension b) Diabetes c) Chronic obstructive pulmonary disease d) Cardiovascular diseases e) Chronic kidney disease f) Chronic lung disease g) Malignancy h) Hypothyroidism i) Asthma j) Tuberculosis k) Cerebrovascular diseases

disease among the confirmed COVID-19 patients was 3.5% (95% CI, 2.6 to 4.9%). Cochrane Q statistics showed 47.59% heterogeneity among the studies which was moderate and not significant (Q = 13.35, $P = 0.06$, $I^2 = 47.59\%$) [Figure 2].

Prevalence of pulmonary tuberculosis

Based on the random effects model after inclusion of seven studies, the prevalence of pulmonary TB among the confirmed COVID-19 patients was 2.3% (95% CI, 1.2 to 4.6%). Cochrane Q statistics showed 67.78% heterogeneity among the studies which was high and significant (Q = 18.626, $P = 0.01$, $I^2 = 67.78\%$) [Figure 2].

Publication bias for prevalence study:

The risk of publication bias was found significant for prevalence of CVD, hypothyroidism, malignancy and CLD [Figure 3]. However, when trim and fill was applied, point estimates changed only for CVD and hypothyroidism [Table 3].

Meta-analysis of association of co-morbidities with mortality in COVID-19 cases

Compared with patients without co-morbidities, mortality risk was significantly increased in those patients with CKD [OR = 4.1 (95%CI 1.53 to 11.05], COPD [OR = 3.96 (95%CI 2.31 to 6.78)], diabetes [OR = 3.7 (95%CI 2.60 to 5.28)], CVD [OR = 4.07 (95%CI (3.02 to 5.47)], TB [OR = 6.11 (95%CI 2.25 to 16.5)], CLD [OR = 8.5 (95%CI 1.92 to 37.8)], hypertension [OR = 2.9 (95%CI 2.07 to 4.0)] and malignancy [OR = 1.89 (95%CI 1.03 to 3.46)]. However, patients with hypothyroidism, asthma and cerebrovascular diseases did not show significant association with mortality [Figure 4, Table 4]. According to Cochran's Q test results, hypertension, diabetes, CKD, asthma and cerebrovascular diseases had $I^2 > 50\%$ ($P < 0.01$) and thus were heterogeneous. No obvious heterogeneity (I^2 ranged from 0 to 24.4%) existed among other co-morbidities. Thus,

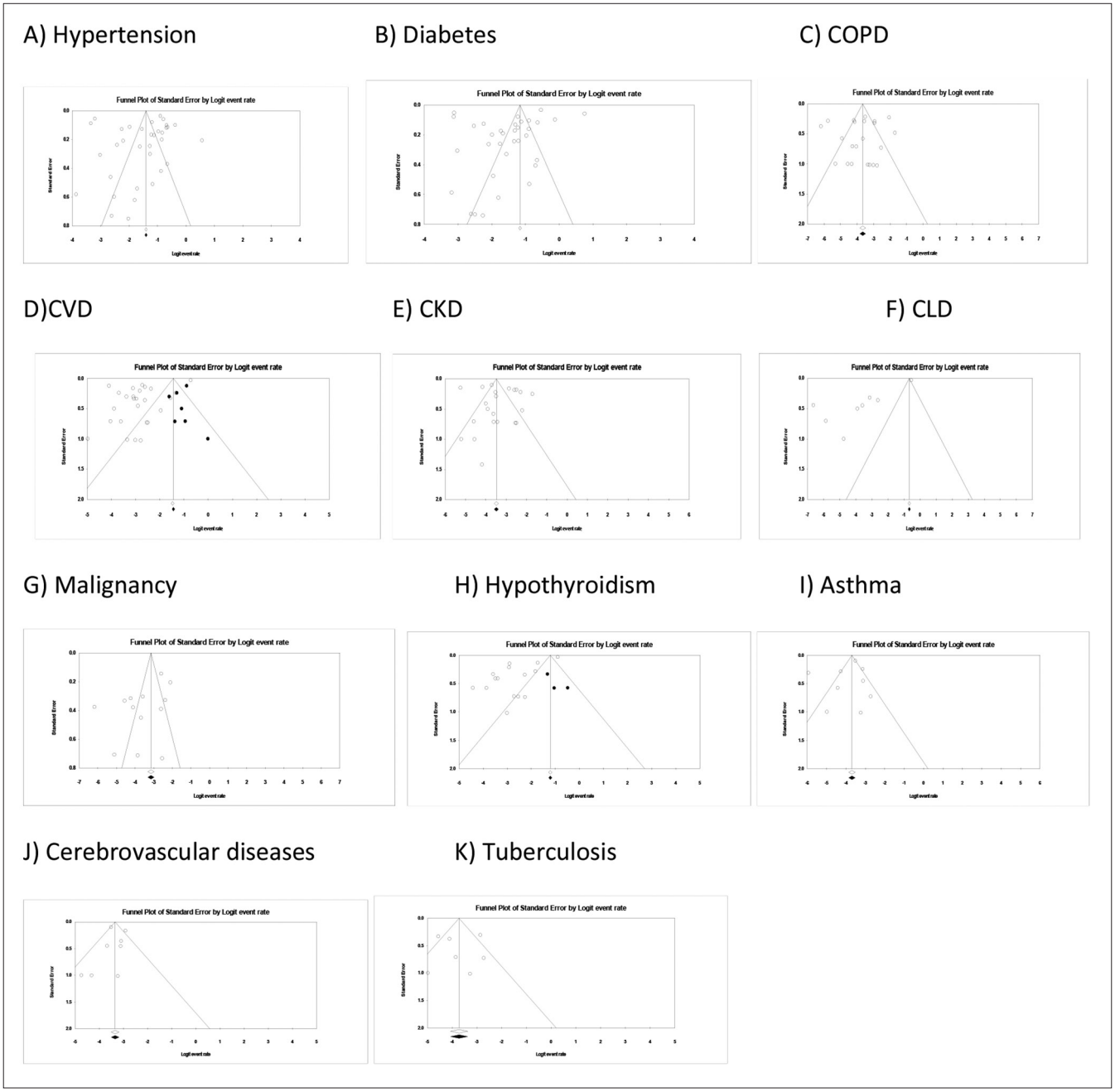

Figure 3: Funnel plots of prevalence of co-morbidities in COVID-19 patients. Parts for each co-morbidity are arrayed in the figure orderly as follows: a) Hypertension b) Diabetes c) Chronic obstructive pulmonary disease (COPD) d) Cardiovascular diseases (CVD) e) Chronic kidney disease (CKD) f) Chronic liver disease (CLD) g) Malignancy h) Hypothyroidism i) Asthma j) Cerebrovascular diseases k) Tuberculosis

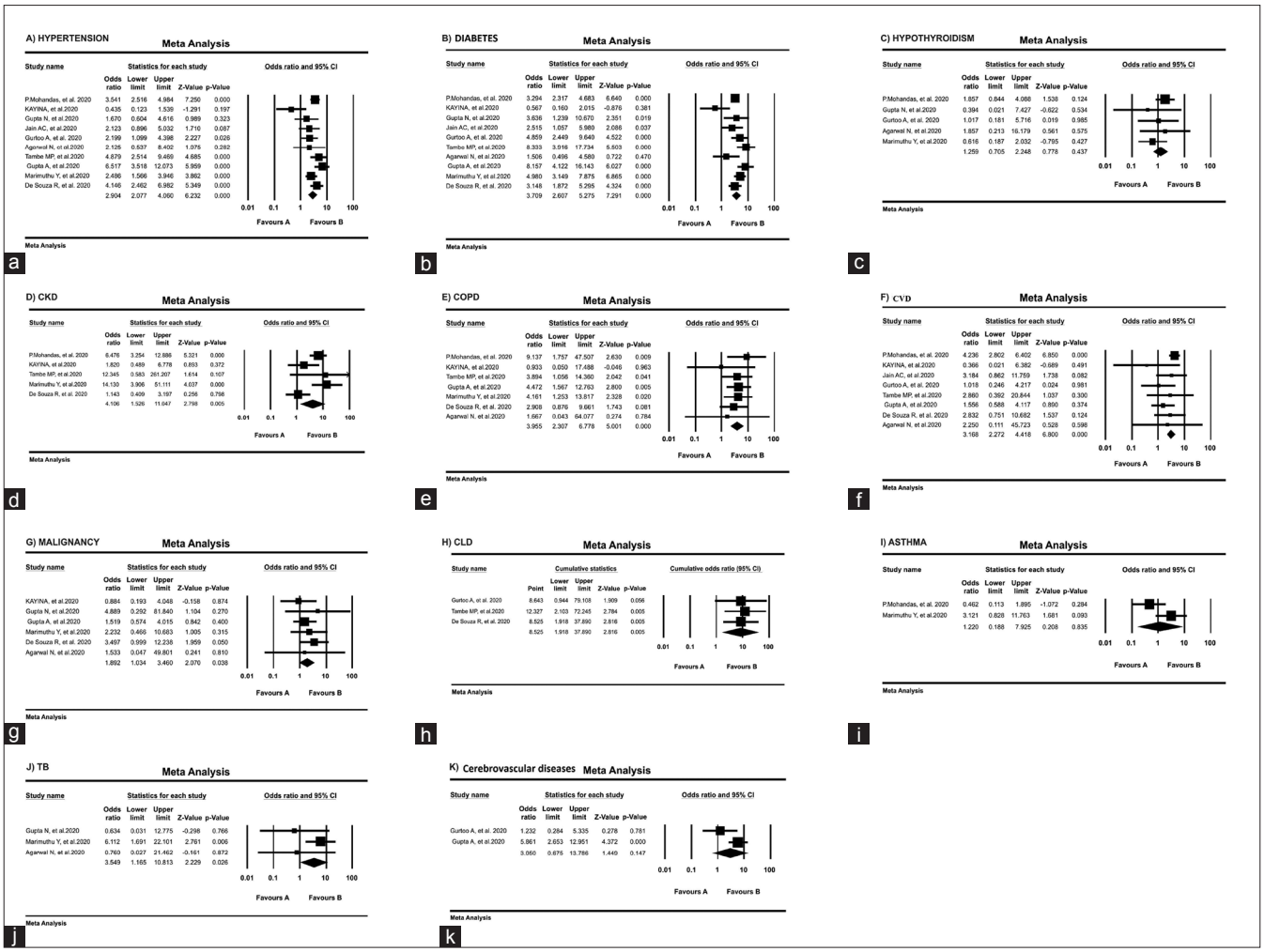

Figure 4: Forest plots of odds ratio of association of mortality with co-morbidities in COVID-19 patients. Parts for each co-morbidity are arrayed in the figure orderly as follows: a) Hypertension b) Diabetes c) Hypothyroidism d) Chronic kidney disease e) Chronic obstructive pulmonary disease f) Cardiovascular diseases g) Malignancy h) Chronic lung disease i) Asthma j) Tuberculosis k) Cerebrovascular diseases

Table 3: Results of trim and fill analyses completed where publication bias was statistically significant

Meta-analysis	Pooled effect size (95% CI)	Egger's test for publication bias (*P*)	Pooled effect size (95% CI), after trim and fill
Prevalence of CVD	5.6 (3.1 to 9.9)	0.000, 0.000	7.7 (4.8 to12.1)
Prevalence of hypothyroidism	5.7 (2.9 to 10.8)	0.000, 0.000	7.9 (4.6 to 13.4)
Prevalence of CLD	2.8 (0.5 to 15.5)	0.000, 0.000	2.1 (0.4 to 11.6)
Prevalence of cancer	2.8 (1.4 to 5.4)	0.030, 0.061	2.6 (1.4 to 4.9)
OR of hypertension and mortality	2.9 (2.08 to 4.06)	0.06, 0.13	3.5 (2.48 to 5.07)
OR of CVD and mortality	3.17 (2.27 to 4.41)	0.02, 0.041	4.07 (3.02 to 5.47)
OR of TB and mortality	3.55 (1.17 to 10.81)	0.04, 0.09	6.11 (2.25 to 16.56)

CVD=Cardiovascular diseases, CLD=Chronic liver disease, TB=Tuberculosis, CI=Confidence interval

there was significant heterogeneity in studies that tested mortality in hypertension, diabetes, CKD, asthma and cerebrovascular disease. However, heterogeneity completely disappeared in studies that tested mortality for hypothyroidism, COPD, CVD, malignancy, CLD and TB. The risk of publication bias was found to be statistically significant in two of the meta-analyses undertaken namely, CVD and TB. Also, publication bias could not be calculated for asthma and cerebrovascular diseases because of inadequate number of studies in both [Figure 5]. When trim and fill analyses were applied, both CVD and TB showed changes in point estimates [Table 3]. As heterogeneity (I^2 >50%) was observed in the meta-analysis of association of some co-morbidities with mortality, a meta-regression analysis was

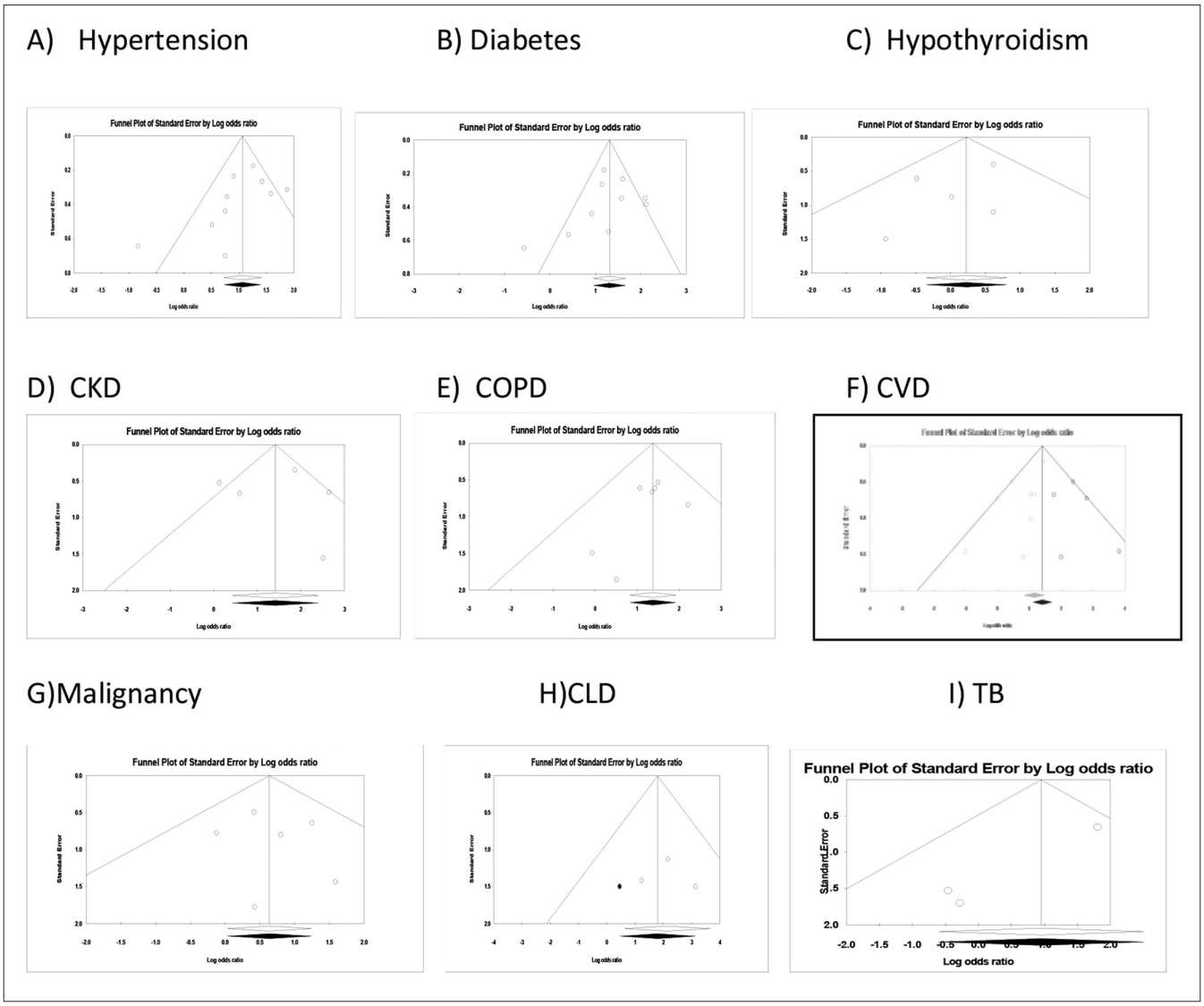

Figure 5: Funnel plots of odds ratio of association of mortality with co-morbidities in COVID- 19 patients. Parts for each co-morbidities are arrayed in the figure orderly as follows: a) Hypertension b) Diabetes c) Hypothyroidism d) Chronic kidney disease (CKD) e) Chronic obstructive pulmonary disease(COPD) f) Cardiovascular diseases (CVD) g) Malignancy h) Chronic liver disease (CLD) i) Tuberculosis (TB)

Table 4: Meta-analysis of association of co-morbidities with mortality (pooled OR) in COVID-19 patients

Disease	*n*	OR	Lower limit	Upper limit	*P*	I^2 (%)	Egger's (*P*)		After trim and fill OR (95%CI)
							one-tailed	two-tailed	
Hypertension	10	2.90	2.07	4.06	*P*=0.00	60.17	0.07	0.13	
Diabetes	10	3.71	2.61	5.28	*P*=0.00	62.64	0.24	0.48	
Hypothyroidism	5	1.26	0.71	2.25	*P*=0.44	0	0.18	0.37	
CKD	5	4.1	1.53	11.05	*P*=0.005	69.51	0.49	0.98	
Asthma	2	1.22	0.19	7.93	*P*=0.83	73.22	**	**	
COPD	7	3.96	2.31	6.78	*P*=0.00	0	0.15	0.3	
CVD	8	3.17	2.27	4.42	*P*=0.00	19.35	0.02	0.041	4.07 (3.02 to 5.47)
Malignancy	6	1.89	1.03	3.46	*P*=0.04	0	0.354	0.71	
CLD	3	8.53	1.92	37.89	*P*=0.005	0	0.44	0.89	
Cerebro vascular diseases	2	3.05	0.68	13.79	*P*=0.15	70.29	**	**	
TB	3	3.55	1.17	10.81	*P*=0.03	27.76	0.04	0.09	6.11 (2.25 TO 16.56)

n=Number of studies, CVD=Cardiovascular diseases, COPD=Chronic obstructive pulmonary disease, CKD=Chronic kidney disease, CLD=Chronic liver disease, TB=Tuberculosis, OR=Odds ratio, CI=Confidence interval

done to estimate the effect of covariates (mean/median age of the patients, % males in the study, co-morbidities) on mortality with COVID-19. As most of the co-morbidities often co-exist, it was necessary

to perform multivariate meta-regression to find out if the co-morbidities independently influenced the mortality or not. We considered all covariates which were identified among study groups such as age, gender, co-morbidities like hypertension, diabetes, COPD, CKD, CLD, asthma, malignancy, CVD, TB, cerebrovascular diseases and hypothyroidism for meta-regression. All meta-regressions were done using the application of REML approach and random effects. For all, statistical significance was set at $P < 0.05$ (two-tailed). As hypertension and diabetes were present in all the patients of all the study groups, their influence on the outcome could not be assessed by meta-regression. Although covariates like percentage of males in the study, patients with asthma, malignancy and cerebrovascular diseases showed negative coefficient, their *P* values were all statistically non-significant. Similarly, covariates like age, patients with COPD, heart diseases, CKD, hypothyroidism, CLD and TB showed positive coefficient, but their *P* values were again statically non-significant. The multivariate meta-regression results showed no statistically significant association between either mean age or the proportion of males or co-morbidities in the study population with estimated OR for mortality which means the covariates were not independently associated with mortality. Thus, from the results of meta-regression, we may conclude that co-morbidities are not independently associated with mortality in COVID-19, but are influenced by co-existing factors like age of the study population, percentage of males in the population and the presence of other co-morbidities in the study population [Table 5].

DISCUSSION

Although systematic reviews and meta-analyses have been previously done by various authors, this study is the first one to be done exclusively in the Indian population. Most of the other meta-analyses have been done in the Chinese population or global population as a whole.

The meta-analysis included 34 studies with 23034 patients, all from the Indian subcontinent. The mean age of the patients was distributed around 44 years. This may be due to the fact that the younger population does not show severe symptoms and hence is not referred to the hospitals thereby remaining undiagnosed. The meta-analysis showed male preponderance (64.1% males and 35.6% females) towards COVID-19 infection, a finding which is consistent with other meta-analyses.[4,6,8,9] The meta analysis also identified hypertension and diabetes as the most common co-morbidities in COVID-19 patients, followed by CVD and hypothyroidism. According to the National Family Health Survey 5, the prevalence of diabetes was 13.5 and 15.6 in males and females, respectively, while the prevalence of hypertension was 21.3 and 24.0 in males and females, respectively. Baradaran A *et al*.,[4] Singh *et al*.,[5] Li B *et al*.,[7] Yin *et al*.,[8] Emami *et al*.[9] and J. Yang *et al*.[12] also unanimously reported hypertension to be the most prevalent co-morbidity in COVID-19 patients followed by diabetes and CVD. However, prevalence rates reported by Espinosa *et al*. were higher as compared to our study [Table 6]. This could be due to the fact that Espinosa *et al*.[10] obtained prevalence rates from the entire COVID-19 positive population, whereas in other

Table 5: Results of meta-regression analyses of odds ratio (association of co-morbidity with mortality)

Covariate	Coefficient	Standard error	95%		*Z*	Two-sided *P*
			Lower	Upper		
Intercept	-9.21	3.03	-15.16	-3.26	-3.04	0.00
Age	0.13	0.07	-0.07	0.26	1.86	0.06
Male	-0.0004	0.00	-0.0009	0.0001	-1.72	0.08
COPD: YES	0.19	1.06	-1.88	2.27	0.18	0.85
CVD: Yes	0.50	1.11	-1.67	2.69	0.46	0.64
Asthma: Yes	-0.55	0.71	-1.94	0.83	-0.78	0.43
CKD: Yes	1.37	0.86	-0.30	3.05	1.6	0.10
Hypothyroidism: Yes	0.27	0.84	-1.37	1.91	0.33	0.74
CLD: Yes	0.54	0.60	-0.64	1.72	0.9	0.36
Cancer: Yes	-0.85	0.67	-2.16	0.47	-1.26	0.20
TB: Yes	0.93	0.93	-0.90	2.76	1	0.31
Cerebro vascular diseases: Yes	-0.68	0.74	-2.12	0.77	-0.92	0.35

Age was mean age of study population where reported, otherwise median was used. CVD=Cardiovascular diseases, COPD=Chronic obstructive pulmonary disease, CKD=Chronic kidney disease, CLD=Chronic liver disease, TB=Tuberculosis

studies, the prevalence rates were calculated only from those COVID-19 patients who were admitted in hospitals. The prevalence of diabetes is higher in Indian COVID-19 patients compared to other countries which can be explained by the overall higher prevalence of diabetes in the Indian population as compared to the prevalence worldwide.[52]

The higher prevalence of these co-morbidities in COVID-19 patients may be explained by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cell entry mechanism. SARS-CoV-2 contains a receptor-binding domain (RBD) that recognises angiotensin-converting enzyme 2 (ACE2) as its receptor.[53] ACE2 receptor is commonly identified in the epithelial cells of the lungs, intestine, kidney and blood vessel.[54] ACE inhibitors (ACE-I) and angiotensin II type 1 receptor blockers (ARBs) are commonly used for treating diabetes, CVD and hypertension.[55] Consequently, increased expression of ACE2 receptor may promote the internalisation of SARS-CoV-2, which in turn may increase the chances of developing COVID-19. In the current meta-analysis, CKD, cerebrovascular diseases and malignancy were found in around 3% of the patients, while respiratory disorders (COPD and TB) were found in 2% of the population. CLD was also found in 2% of the patients. The lowest prevalence was found for asthma.

The present study also evaluated the association between co-morbidities and mortality in COVID-19 patients. It was found that TB had the strongest association with mortality in COVID-19 patients despite having low prevalence. Tamuzi *et al*.[56] too showed similar findings in their meta-analysis. The current meta-analysis showed that hypertension, diabetes, CVD, CLD and cancer also have significant association with mortality. Also, although patients had a lower prevalence of TB, CKD and COPD, the association with mortality was found to be high. Hypothyroidism, asthma and cerebrovascular diseases did not show significant association with

Table 6: Comparison of prevalence of co-morbidities in COVID-19 patients in different studies

Disease	Baradaran A *et al*.[4]	Singh *et al*.[5]	Li B *et al*.[7]	Yin *et al*.[8]	Emami *et al*.[9]	Espinosa *et al*.[10]	Yang J *et al*.[12]	Our study
	Prevalence (%), (95%CI)							
Hypertension	21%	22.9%	17.1%	19%	16%	32%	21.1%	18.1%
Diabetes	11%	11.5%	9.7%	9%		22%	9.7%	17.7%
CVD	5.8%	9.7%		6%	12.11%	13%	8.4%	7.7%
COPD	2%	3.1%		3%	0.95%	8%	1.5%	2.3%
Hypothyroidism								7.9%
CKD	3.6%	2.4%		2%	0.83%	5%		3.3%
Asthma						3%		2%
CLD	2.9%			3%		2%		2.8%
Cancer	2.7%	3.9%		1%	0.92%	3%		2.8%
Cerebrovascular diseases	2.4%	3.0%		3%		2%		3.5%
TB								2.3%

CVD=Cardiovascular diseases, COPD=Chronic obstructive pulmonary disease, CKD=Chronic kidney disease, CLD=Chronic liver disease, TB=Tuberculosis, CI=Confidence interval

Table 7: Comparison of meta-analyses for association of mortality with co-morbidities in different studies

Disease	Singh *et al*.[5](RR)	Ng *et al*.[11]	Biswas *et al*.[6](RR)	Our study (OR)
	OR/RR/HR (95%CI)			
Hypertension	1.53 (0.86-2.71)	HR 2.1 (1.50-2.90)	1.95 (1.58-2.40)	2.904 (2.07-4.06)
Diabetes	1.83 (0.89-3.73)	HR 1.94 (1.54-2.46)	1.97 (1.48–2.64)	3.7 (2.60-5.27)
CVD	1.88 (1.41-2.51)		3.05 (2.20–4.25)	4.07 (3.02-5.47)
COPD	1.53 (1.03-2.28)		2.74 (2.04–3.67)	3.95 (2.3 to 6.77)
Hypothyroidism				1.26 (0.7 to 2.24)
CKD	1.84 (1.03-3.30)	HR 1.28 (0.89-1.67)	4.90 (3.04–7.88)	4.1 (1.52 to 11.04)
Asthma				1.22 (0.18 to 7.9)
CLD			1.64 (0.82-3.28)	8.5 (1.91 to 37.89)
Cancer	1.77 (1.08-2.88)	OR 1.63 (1.01-2.00).	1.89 (1.25-2.84)	1.89 (1.03 to 3.46)
Cerebrovascular diseases	2.48 (2.14-2.86)		4.78 (3.39–6.76)	3.5 (0.67 to 13.7)
TB				6.11 (2.25-16.56)

CVD=Cardiovascular diseases, COPD=Chronic obstructive pulmonary disease, CKD=Chronic kidney disease, CLD=Chronic liver disease, TB=Tuberculosis, CI=Confidence interval. OR=Odds ratio, RR=Relative Risk, HR=Hazard ratio

mortality. We compared three recent meta-analyses on the association of co-morbidities with mortality in COVID-19 infection [Table 7]. All the authors of these meta-analyses have agreed that hypertension, diabetes, CVD and cancer are associated with increased mortality in COVID-19 patients. Singh *et al*.[5] and Biswas *et al*.[6] found high association of CKD and COPD with mortality similar to our study. The higher association of mortality with diabetes, hypertension and CVD can be due to the induction of cytokine storm, a weakened immune system and hypercoagulability induced by these co-morbidities.[57,58] Similarly, the use of immunosuppressive drugs in cancer patients could be the reason for the increased mortality associated with it.[59] We found an OR of 4.1 and 3.95 in CKD and COPD patients respectively which indicates that they are strongly associated with mortality once infected. Elevated ACE-2 expression in bronchial epithelial cells might be the reason for this exacerbated progression in COPD patients.[60] Also, COPD causes systemic hypoxia and hence can cause exaggerated cytokine storm. Alterations in ACE-2 receptor expression and altered immune system may also be the reason for increased risk of mortality with CKD.[61] Also, increased ACE-2 expression at both mRNA and protein levels has been found in patients with heart failure. Therefore, if patients with CVD become infected with SARS-CoV-2, they have a higher risk of poor outcome, a finding which has been observed in the present study.[62]

None of the meta-analyses have mentioned the impact of hypothyroidism on COVID-19. However, individual studies done in some centres did not get significant association of mortality with hypothyroidism.[63] In the present study too, we did not get significant association of mortality with hypothyroidism. Therefore, we might conclude that no additional precaution is required for patients with hypothyroidism. Also, obesity is being speculated to have an important association with mortality in COVID-19 patients as per some reports.[64] Nevertheless, in the current meta-analysis, only one study by Dosi *et al*.[46] has mentioned body mass index and hence we could not investigate this association.

Although this systematic review and meta-analysis was based on a comprehensive search strategy of multiple databases, there are certain limitations. The cases selected for individual studies might not be representative of the entire infected population, especially the asymptomatic cases, because of local policies for testing COVID-19, and the fact that most of the studies only included cases admitted to hospital. Also, values of prevalence and OR reported in this review may not reflect true population rates and hence need to be interpreted with caution. A further limitation is that most of the studies reported in India are from apex institutes of major cities like Delhi, Chandigarh, Chennai, Mumbai and Jaipur. Also, studies from north-eastern, hilly regions and rural populations of India are lacking in literature which again limits generalisability of the results. Another limitation of the review is that we did not include studies from the Indian population outside India. This is because we wanted to study the mortality from COVID-19 with respect to the socio-economic conditions prevalent in India. Additionally, although studies with overlapping cohorts were carefully removed, it was not possible to identify every possible overlap among all the studies. Although many co-morbidities are co-existing, very few studies have given us data on co-existent co-morbidities. So again, data is lacking on this aspect of co-morbidities which would otherwise be a useful factor to assess. Nevertheless, persons with co-morbidities like diabetes, hypertension, CKD and cancer are at high risk of mortality even in the absence of COVID-19.[65-68] These limitations may contribute to the overestimation or underestimation of the prevalence of co-morbidities and its role in the exacerbation of SARS-CoV-2 leading to fatal outcomes. Another limitation of the present study was that we were not able to find the correlation between co-morbidities and severity of COVID-19 infections because of lack of sufficient studies reporting the same. Also, we could not report post-COVID-19 complications (pulmonary fibrosis, fungal infections, etc.) in patients with co-morbidities again because of lack of literature in this regard. In meta-analyses, it is recommended that publication bias is always assessed by statistical methods. However, currently available methods, such as the funnel plot and the Egger's regression test, are not considered useful tools in studies on proportions.[69] Finally in our study, seven co-morbidities were statistically significant for publication bias using Egger's test. When trim and fill was applied, study estimates changed for prevalence of CVD and hypothyroidism, and OR of hypertension, CVD and TB. Results from the meta-analysis where publication bias was significant, and study estimates changed after trim and fill should be reported with caution. Also, publication bias for OR of asthma and cerebrovascular diseases could not be assessed due to insufficient studies and hence, its point estimates should again be reported with caution.

The results of this meta-analysis will help to identify high risk cases which can be used as admission criteria to hospitals in order to minimise the burden of an already overwhelmed health infrastructure. Also, this information can be used to educate the high-risk groups and encourage them to practise social distancing and self-isolation. The higher mortality in COVID-19 associated with these chronic conditions also warrants development of vaccination policies for this group. The perioperative challenges posed by the association of co-morbidities like diabetes and hypertension in COVID-19 and post-COVID-19 patients have already been reported and discussed in previous literature.[70] Nevertheless, this meta-analysis provides evidence on the risk of mortality associated with co-morbidities and this can help improve clinical decision-making in a world that is currently facing difficulty in the practice of evidence-based medicine.[71]

CONCLUSION

Co-morbidities such as hypertension, diabetes mellitus, hypothyroidism and CVD are more prevalent in COVID-19 hospitalised patients and the presence of co-morbidities with COVID-19 is associated with increased risk of mortality in the Indian population. Patients with hypertension, diabetes, CVD, malignancy, TB, CLD, CKD and COPD are at a high risk for mortality whereas patients with hypothyroidism, cerebrovascular diseases and asthma do not have an increased risk when compared to the general population.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: A modelling study. Lancet 2020;395:689-97.
2. Malhotra N, Joshi M, Datta R, Bajwa SJ, Mehdiratta L. Indian society of anaesthesiologists (ISA National) advisory and position statement regarding COVID-19. Indian J Anaesth 2020;64:259-63.
3. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, *et al*. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: Estimation and application. Ann Intern Med 2020;172:577–82.
4. Baradaran A, Ebrahimzadeh MH, Baradaran A, Kachooei AR. Prevalence of comorbidities in COVID-19 patients: A systematic review and meta-analysis. Arch Bone Jt Surg 2020;8:247-55.
5. Singh AK, Gillies CL, Singh R, Singh A, Chudasama Y, Coles B, *et al*. Prevalence of co-morbidities and their association with mortality in patients with COVID-19: A systematic review and meta-analysis. Diabetes Obes Metab 2020;22:1915-24.
6. Biswas M, Rahaman S, Biswas TK, Haque Z, Ibrahim B. Association of sex, age, and comorbidities with mortality in COVID-19 patients: A systematic review and meta-analysis. Intervirology 2021;64:36-47.
7. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, *et al*. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol 2020;109:531-8.
8. Yin T, Li Y, Ying Y, Luo Z. Prevalence of comorbidity in Chinese patients with COVID-19: Systematic review and meta-analysis of risk factors. BMC Infect Dis 2021;21:200.
9. Emami A, Javanmardi F, Pirbonyeh N, Akbari A. Prevalence of underlying diseases in hospitalized patients with COVID-19: A systematic review and meta-analysis. Arch Acad Emerg Med 2020;8:e35.
10. Espinosa OA, Zanetti ADS, Antunes EF, Longhi FG, Matos TAD, Battaglini PF. Prevalence of comorbidities in patients and mortality cases affected by SARS-CoV2: A systematic review and meta-analysis. Rev Inst Med Trop São Paulo 2020;62:257–61.
11. Ng WH, Tipih T, Makoah NA, Vermeulen J-G, Goedhals D, Sempa JB, *et al*. Comorbidities in SARS-CoV-2 patients: A systematic review and meta-analysis. mBio 2021;12:e03647-20. doi: 10.1128/mBio. 03647-20.
12. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, *et al*. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: A systematic review and meta-analysis. Int J Infect Dis 2020;94:91-5.
13. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, *et al*. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2014. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp [Last accessed on 2021 Jun 19].
14. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539-58.
15. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, *et al*. Updated guidance for trusted systematic reviews: A new edition of the Cochrane Handbook for Systematic reviews of interventions. Cochrane Database Syst Rev 2019;10:ED000142.
16. Carpenter CJ. A trim and fill examination of the extent of publication bias in communication research. Commun Methods Meas 2012;6:41-55.
17. Borenstein M, Hedges LV, Higgins JP, Rothstein H. Comprehensive Meta-Analysis (Version 3.0). Englewood, NJ: Biostat; 2013.
18. Mohandas P, Periasamy S, Marappan M, Sampath A, Sundaram VKG, Cherian VK. Clinical review of COVID-19 patients presenting to a quaternary care private hospital in South India: A retrospective study. Clin Epidemiol Glob Health 2021;11:100751.
19. Mithal A, Jevalikar G, Sharma R, Singh A, Farooqui KJ, Mahendru S, *et al*. High prevalence of diabetes and other co-morbidities in hospitalized patients with COVID-19 in Delhi, India, and their association with outcomes. Diabetes Metab Syndr 2021;15:169-75.
20. Soni SL, Kajal K, Yaddanapudi LN, Malhotra P, Puri GD, Bhalla A, *et al*. Demographic and clinical profile of patients with COVID-19 at a tertiary care hospital in north India. Indian J Med Res 2021;153:115-25.
21. Singla N, Gowda R, Mohindra R, Suri V, Dhibar DP, Sharma N. Clinical spectrum and outcome of patients visiting coronavirus screening centre in North India and clinical predictors for COVID-19. J Family Med Prim Care 2021;10:454-61.
22. Kumar R, Bhattacharya B, Meena VP, Aggarwal A, Tripathi M, Soneja M, *et al*. Characteristics and outcomes of 231 COVID-19 cases admitted at a tertiary facility in India:

An observational cohort study. J Family Med Prim Care 2020;9:6267-72.
23. Sherwal BL, Makkar N, Jain A, Dogra V, Prasad S, Sachan A, *et al*. Trends and clinico-epidemiological profile of COVID-19 patients at a designated COVID-19 hospital in Delhi, North India. J Family Med Prim Care 2020;9:6261-6.
24. Pande D, Kochhar A, Saini S, Ganapathy U, Gogia AR. An update on initial epidemiological profile, clinical course, and outcome of COVID-19 patients at a tertiary care center in India. Indian J Palliat Care 2020;26:S36-9.
25. Mohan A, Tiwari P, Bhatnagar S, Patel A, Maurya A, Dar L, *et al*. Clinico-demographic profile & hospital outcomes of COVID-19 patients admitted at a tertiary care centre in north India. Indian J Med Res 2020;152:61-9.
26. Kayina CA, Haritha D, Soni L, Behera S, Nair PR, Gouri M, *et al*. Epidemiological & clinical characteristics & early outcome of COVID-19 patients in a tertiary care teaching hospital in India: A preliminary analysis. Indian J Med Res 2020;152:100-4.
27. Krishnasamy N, Natarajan M, Ramachandran A, Vivian Thangaraj JW, Etherajan T, Rengarajan J, *et al*. Clinical outcomes among asymptomatic or mildly symptomatic COVID-19 patients in an isolation facility in Chennai, India. Am J Trop Med Hyg 2021;104:85-90.
28. Sharma AK, Ahmed A, Baig VN, Dhakar P, Dalela G, Kacker S, *et al*. Characteristics and outcomes of hospitalized young adults with mild Covid -19. J Assoc Physicians India 2020;68:62-5.
29. Saxena S, Manchanda V, Sagar T, Nagi N, Siddiqui O, Yadav A, *et al*. Clinical characteristic and epidemiological features of SARS CoV -2 disease patients from a COVID- 19 designated hospital in New Delhi. J Med Virol 2021;93:2487-92.
30. Gupta N, Agrawal S, Ish P, Mishra S, Gaind R, Usha G, *et al*. Clinical and epidemiologic profile of the initial COVID-19 patients at a tertiary care centre in India. Monaldi Arch Chest Dis 2020;90:193-6.
31. Gupta N, Ish P, Kumar R, Dev N, Yadav SR, Malhotra N, *et al*. Evaluation of the clinical profile, laboratory parameters and outcome of two hundred COVID-19 patients from a tertiary centre in India. Monaldi Arch Chest Dis 2020;90:675-82.
32. Gaur A, Meena SK, Bairwa R, Meena D, Nanda R, Sharma SR, *et al*. Clinico-radiological presentation of COVID-19 patients at a tertiary care center at Bhilwara Rajasthan, India. J Assoc Physicians India 2020;68:29-33.
33. Bhandari S, Bhargava A, Sharma S, Keshwani P, Sharma R, Banerjee S. Clinical profile of COVID-19 infected patients admitted in a tertiary care hospital in North India. J Assoc Physicians India 2020;68:13-7.
34. Bhandari S, Shaktawat AS, Sharma R, Dube A, Kakkar S, Banerjee S, *et al*. A preliminary clinico-epidemiological portrayal of COVID-19 pandemic at a premier medical institution of North India. Ann Thorac Med 2020;15:146-50.
35. Jain AC, Kansal S, Sardana R, Bali RK, Kar S, Chawla R. A retrospective observational study to determine the early predictors of in-hospital mortality at admission with COVID-19. Indian J Crit Care Med 2020;24:1174-9.
36. Revathishree K, Shyam Sudhakar S, Indu R, Srinivasan K. Covid-19 demographics from a tertiary care center: Does it depreciate quality-of-life? Indian J Otolaryngol Head Neck Surg 2020;15:1-8.
37. Suresh S, Tiwari A, Mathew R, Bhaskararayuni J, Sahu AK, Aggarwal P, *et al*. Predictors of mortality and the need of mechanical ventilation in confirmed COVID-19 patients presenting to the emergency department in North India. J Family Med Prim Care 2021;10:542-9.
38. Patel C, Palkar S, Doke P, Deshmukh R. A study of the clinico-epidemiological profile of covid-19 patients admitted in a tertiary care hospital in India. J Clin Diagn Res 2021;15:OC09-13.
39. Agarwal N, Biswas B, Lohani P. Epidemiological determinants of COVID-19 infection and mortality: A study among patients presenting with severe acute respiratory illness during the pandemic in Bihar, India. Niger Postgrad Med J 2020;27:293-301.
40. Gurtoo A, Agrawal A, Prakash A, Kaur R, Jais M, Anand R, *et al*. The syndromic spectrum of COVID-19 and correlates of admission parameters with severity-outcome gradients: A retrospective study. J Assoc Physicians India 2020;68:43-8.
41. Jain P, Sinha N, Prasad MK, Padole V. Clinical and laboratory profile of COVID-19 patients admitted at a tertiary care center in New Delhi and assessment of factors predicting disease severity. Indian J Med Spec 2021;12:59-63.
42. Yadav R, Acharjee A, Salkar A, Bankar R, Palanivel V, Agrawal S, *et al*. Mumbai mayhem of COVID-19 pandemic reveals important factors that influence susceptibility to infection. EClinicalMedicine 2021;35:100841.
43. Tambe MP, Parande MA, Tapare VS, Borle PS, Lakde RN, Shelke SC, *et al*. An epidemiological study of laboratory confirmed COVID-19 cases admitted in a tertiary care hospital of Pune, Maharashtra. Indian J Public Health 2020;64:S183-7.
44. Prakash S, Agrawal MM, Kumar R, Yadav S. Clinical and epidemiological profile of patients infected by COVID-19 at a tertiary care centre in North India. Monaldi Arch Chest Dis 2020;90:508-11.
45. Sharma S, Keswani P, Bhargava A, Sharma R, Shekhawat A, Bhandari S. Overview of early cases of coronavirus disease 2019 (COVID-19) at a tertiary care centre in North India. Ann Acad Med Singap 2020;49:449-55.
46. Dosi R, Jain G, Mehta A. Clinical characteristics, comorbidities, and outcome among 365 patients of coronavirus disease 2019 at a tertiary care centre in Central India. J Assoc Physicians India 2020;68:20-3.
47. Aggarwal A, Shrivastava A, Kumar A, Ali A. Clinical and epidemiological features of SARS-CoV-2 patients in SARI ward of a tertiary care centre in New Delhi. J Assoc Physicians India 2020;68:19-26.
48. Gupta A, Nayan N, Nair R, Kumar K, Joshi A, Sharma S. Diabetes mellitus and hypertension increase risk of death in novel corona virus patients irrespective of age: A prospective observational study of co-morbidities and COVID-19 from India. SN Compr Clin Med 2021;3:937–44.
49. Marimuthu Y, Kunnavil R, Anil NS, Nagaraja SB, Satyanarayana N, Kumar J, *et al*. Clinical profile and risk factors for mortality among COVID-19 inpatients at a tertiary care centre in Bengaluru, India. Monaldi Arch Chest Dis 2021;91:295-301.
50. Mathur A, Fatehpuriya C, Mehta S, Mathur V, Fatima A, Priyadarshani S. Epidemiologic profile of initial covid-19 patients at a tertiary care centre in southern Rajasthan. Glob J Res Anal 2020;9:31-3.
51. Souza RD, Mhatre S, Qayyumi B, Chitkara G, Madke T, Joshi M, *et al*. Clinical course and outcome of patients with COVID-19 in Mumbai city: An observational study. BMJ Open 2021;11:e042943.
52. Lin X, Xu Y, Pan X, Xu J, Ding Y, Sun X, *et al*. Global, regional, and national burden and trend of diabetes in 195 countries and territories: An analysis from 1990 to 2025. Sci Rep 2020;10:14790.
53. Shang J, Ye G, Shi K, Wan Y, Luo C, Aihara H, *et al*. Structural basis of receptor recognition by SARS-CoV-2. Nature 2020;581:221–4.
54. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by the novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS coronavirus. J Virol 2020;94:e00127-20. doi: 10.1128/JVI.00127-20.
55. Li XC, Zhang J, Zhuo JL. The vasoprotective axes of the renin-angiotensin system: Physiological relevance and therapeutic implications in cardiovascular, hypertensive and kidney diseases. Pharmacol Res 2017;125:21–38.
56. Tamuzi JL, Ayele BT, Shumba CS, Adetokunboh OO, Uwimana-Nicol J, Haile ZT, *et al*. Implications of COVID-19 in high burden countries for HIV/TB: A systematic review of

evidence. BMC Infect Dis 2020;20:744.
57. Sun X, Wang T, Cai D, Hu Z, Chen J, Liao H, *et al*. Cytokine storm intervention in the early stages of COVID-19 pneumonia. Cytokine Growth Factor Rev 2020;53:38–42.
58. Ranucci M, Ballotta A, Di Dedda U, Bayshnikova E, Dei Poli M, Resta M, *et al*. The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome. J Thromb Haemost 2020;18:1747–51.
59. Liang W, Guan W, Chen R, Wang W, Li J, Xu K, *et al*. Cancer patients in SARS-CoV-2 infection: A nationwide analysis in China. Lancet Oncol 2020;21:335–7.
60. Mahajan L, Singh AP, Gifty. Clinical outcomes of using remdesivir in patients with moderate to severe COVID-19: A prospective randomised study. Indian J Anaesth 2021;65(Suppl 1):S41-6.
61. Oyelade T, Alqahtani J, Canciani G. Prognosis of COVID-19 in patients with liver and kidney diseases: An early systematic review and meta-analysis. Trop Med Infect Dis 2020;5:80.
62. Chen L, Li X, Chen M, Feng Y, Xiong C. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. Cardiovasc Res 2020;116:1097–100.
63. Gerwen MV, Alsen M, Little C, Barlow J, Naymagon L, Tremblay D, *et al*. Outcomes of patients with hypothyroidism and COVID-19: A retrospective cohort study. Front Endocrinol (Lausanne) 2020;11:565.
64. Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A, *et al*. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Obesity 2020;28:1195-9.
65. Guembe MJ, Rigo F, Tormo-Díaz MJ, Moreno-Iribas C, Cabré JJ, Segura A, *et al*. Risk of cause specific death in individuals with diabetes: A competing risks analysis. Diabetes Care 2016;39:1987-95.
66. World Health Organization. Cancer. Geneva, Switzerland: World Health Organization; 2018. Available from: https://www.who.int/news-room/fact-sheets/detail/cancer.
67. Arima H, Barzi F, Chalmers J. Mortality patterns in hypertension. J Hypertens 2011;29:S3–7.
68. Wang HE, Gamboa C, Warnock DG, Muntner P. Chronic kidney disease and risk of death from infection. Am J Nephrol 2011;34:330-6.
69. Murad MH, Chu H, Lin L, Wang Z. The effect of publication bias magnitude and direction on the certainty in evidence. BMJ Evid Based Med 2018;23:84-6.
70. Kuttarmare SM, Bhalerao PM, Chavan VA, Kadam BA. A case of post-COVID-19 mucormycosis with permanent pacemaker posted for functional endoscopic sinus surgery: Anaesthetic challenges. Indian J Anaesth 2021;65:703-4.
71. Kotur PF, Kotur P. Challenges for the practice of evidence-based medicine during COVID19 pandemic (practice of evidence-based medicine in the new normal). Indian J Anaesth 2022;66:290-3.

Annexure 1: Search Strategy for PUBMED

Search	Actions	Details	Query	Results	Time
#6	...		Search: (((COVID-19[MeSH] OR 2019-nCoV[MeSH] OR novel coronavirus[MeSH] OR SARS-CoV-2[MeSH] OR Coronavirus [MeSH]) AND (Prevalence[MeSH])) AND (Comorbidities[MeSH] OR underlying diseases[MeSH] OR Cardiovascular Diseases [MeSH] OR Neoplasms [MeSH] OR Pulmonary Disease[MeSH] OR Asthma[MeSH] OR Hypertension[MeSH] OR Diabetes Mellitus[MeSH] OR Renal Insufficiency[MeSH] OR Cerebrovascular Disorders[MeSH] OR Hypothyroidism[MeSH] OR Liver Diseases[MeSH] OR Tuberculosis[MeSH])) AND (India[MeSH]) Filters: Full text	54	09:01:37
#5	...		Search: (((COVID-19[MeSH] OR 2019-nCoV[MeSH] OR novel coronavirus[MeSH] OR SARS-CoV-2[MeSH] OR Coronavirus [MeSH]) AND (Prevalence[MeSH])) AND (Comorbidities[MeSH] OR underlying diseases[MeSH] OR Cardiovascular Diseases [MeSH] OR Neoplasms [MeSH] OR Pulmonary Disease[MeSH] OR Asthma[MeSH] OR Hypertension[MeSH] OR Diabetes Mellitus[MeSH] OR Renal Insufficiency[MeSH] OR Cerebrovascular Disorders[MeSH] OR Hypothyroidism[MeSH] OR Liver Diseases[MeSH] OR Tuberculosis[MeSH])) AND (India[MeSH])	56	09:01:29
#4	...		Search: India[MeSH]	112,878	08:57:53
#3	...		Search: Comorbidities[MeSH] OR underlying diseases[MeSH] OR Cardiovascular Diseases [MeSH] OR Neoplasms [MeSH] OR Pulmonary Disease[MeSH] OR Asthma[MeSH] OR Hypertension[MeSH] OR Diabetes Mellitus[MeSH] OR Renal Insufficiency[MeSH] OR Cerebrovascular Disorders[MeSH] OR Hypothyroidism[MeSH] OR Liver Diseases[MeSH] OR Tuberculosis[MeSH]	7,619,957	08:57:15
#2	...		Search: Prevalence[MeSH] “prevalence”[MeSH Terms]	322,625	08:55:59
#1	...		Search: COVID-19[MeSH] OR 2019-nCoV[MeSH] OR novel coronavirus[MeSH] OR SARS-CoV-2[MeSH] OR Coronavirus [MeSH] “covid 19”[MeSH Terms] OR “sars cov 2”[MeSH Terms] OR “sars cov 2”[MeSH Terms] OR “sars cov 2”[MeSH Terms] OR “coronavirus”[MeSH Terms]	140,910	08:55:10

Annexure 2: Study quality assessment using the Newcastle-Ottawa tool

Study - author name,year (study design)	Selection				Comparability	Outcome			Total Stars
	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow-up of cohort	
P.Mohandas et al. 2020(RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Mithal A, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Soni, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Singla N, et al.2020 (PROSP DESCRI)	★	★	★	★	★	★	★	★	8; good
Sherwal, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Pande D, et al.2020 (RETRO CASE SERIES)	★	★	★	★	★	★	★	★	8; good
Mohan A, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
KAYINA, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Krishnasamy N, et al.2020 (RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Sharma A.K. et al.2020 (RETRO COHORT)	★	★	★	★	★	★	★	★	8; good
Saxena, et al. 2020 (RETRO COHORT)	★	★	★	★	★	★		★	7; good
Gupta N, et al.2020 (DESCRI CASE SERIES)	★	★	★	★	★	★	★	★	8; good
Gupta N, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Gaur A, et al.2020 (DESCRI CASE SERIES)	★	★	★	★	★	★		★	7. good
Bhandari S, et al. 2020 (RETRO	★	★	★	★	★	★	★	★	8; good

Contd...

OBSERV DESCRI)									
Bhandari S, et al. 2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Jain AC, et al.2020 (RETRO OBSERV)	★	★	★		★	★	★	★	7; good
K Revathishree et al.2020 (PROSP DESCRI)	★	★	★	★	★	★	★	★	8; good
Suresh, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Charvi Patel, et al. 2020 (RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Aggarwal A, et al. 2020 (RETRO CASE SERIES)	★	★	★	★	★	★	★	★	8; good
Gurtoo A, et al. 2020 (RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Sherwal, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Pande D, et al.2020 (RETRO CASE SERIES)	★	★	★	★	★	★	★	★	8; good
Mohan A, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
KAYINA, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Krishnasamy N, et al.2020 (RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Sharma A.K. et al.2020 (RETRO COHORT)	★	★	★	★	★	★	★	★	8; good
Saxena, et al. 2020 (RETRO COHORT)	★	★	★	★	★	★		★	7; good
Gupta N, et al.2020 (DESCRI CASE SERIES)	★	★	★	★	★	★	★	★	8; good
Gupta N, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Gaur A, et al.2020 (DESCRI CASE	★	★	★	★	★	★		★	7. good

SERIES)									
Bhandari S, et al. 2020 (RETRO OBSERV DESCRI)	★	★	★	★	★	★	★	★	8; good
Bhandari S, et al. 2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Jain AC, et al.2020 (RETRO OBSERV)	★	★	★		★	★	★	★	7; good
K Revathishree et al.2020 (PROSP DESCRI)	★	★	★	★	★	★	★	★	8; good
Suresh, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Charvi Patel, et al. 2020 (RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Aggarwal A, et al. 2020 (RETRO CASE SERIES)	★	★	★	★	★	★	★	★	8; good
Gurtoo A, et al. 2020 (RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Sherwal, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Pande D, et al.2020 (RETRO CASE SERIES)	★	★	★	★	★	★	★	★	8; good
Mohan A, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
KAYINA, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Krishnasamy N, et al.2020 (RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Sharma A.K. et al.2020 (RETRO COHORT)	★	★	★	★	★	★	★	★	8; good
Saxena, et al. 2020 (RETRO COHORT)	★	★	★	★	★	★		★	7; good
Gupta N, et al.2020 (DESCRI CASE SERIES)	★	★	★	★	★	★	★	★	8; good
Gupta N, et al.2020 (PROSP	★	★	★	★	★	★	★	★	8; good

OBSERV)									
Gaur A, et al.2020 (DESCRI CASE SERIES)	★	★	★	★	★	★		★	7. good
Bhandari S, et al. 2020 (RETRO OBSERV DESCRI)	★	★	★	★	★	★	★	★	8; good
Bhandari S, et al. 2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Jain AC, et al.2020 (RETRO OBSERV)	★	★	★		★	★	★	★	7; good
K Revathishree et al.2020 (PROSP DESCRI)	★	★	★	★	★	★	★	★	8; good
Suresh, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Charvi Patel, et al. 2020 (RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Aggarwal A, et al. 2020 (RETRO CASE SERIES)	★	★	★	★	★	★	★	★	8; good
Gurtoo A, et al. 2020 (RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Jain P, et al.2020 (CROSS SECTIONAL OBSERV)	★	★	★	★	★	★	★	★	8; good
R. Yadav, et al.2020 (PROSP COHORT)	★	★	★	★	★	★	★	★	8; good
Tambe MP, et al.2020 (CROSS SECTIONAL DESCRI)	★	★	★	★	★	★	★	★	8; good
Prakash S, et al.2020 (RETRO OBSERV CROSS SECTIONAL)	★	★	★	★	★	★	★	★	8; good
Sharma S, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★		7; good
Dosi R, et al.2020 (RETRO OBSERV)	★	★	★	★	★	★	★	★	8; good
Agarwal N, et al.2020 (OBSERV	★	★	★	★	★	★		★	7; good
LONGI)									
Gupta A, et al.2020 (PROSP OBSERV)	★	★	★	★	★	★	★	★	8; good
Marimuthu Y, et al.2020 (RECORD BASED LONGI)	★	★	★	★	★	★	★	★	8; good
Mathur A , et al. 2020 (OBSERV CROSS SECTIONAL)	★	★	★	★	★	★		★	7. good
desouza R et al.2020 (RETRO OBSERV)	★	★	★	★		★	★	★	7; good

RETRO=Retrospective, OBSERV=Observational, PROSP=Prospective, LONGI=Longitudinal, DESCRI=Descriptive