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REVIEW PAPER

Evaluating the association between blood pressure and mortality in Covid-19 Pneumonia: A systematic review and meta-analysis

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This research sudy evaluates the association between blood pressure and mortality during the Covid-19 epidemic. A software program was employed to manage electronic titles. The 95% confidence interval for the risk ratio, fixed effect method, and Mantel–Haenszel formula were calculated. Meta-analysis in the present study was performed using Stata 16 software. The risk ratio of High blood pressure between poor and good outcomes was 0.73 (RR, 0.73 95 % CI 0.63, 0.83). This result showed High blood pressure had a statistically significant association with increased composite poor outcomes. Meta-analysis showed an association between high blood pressure and increased Mortality, Acute respiratory distress syndrome, Severe COVID-19, ICU care, and disease progression.

KEYWORDS

Blood pressure; hypertension; covid-19; mortality.

Introduction

In December 2019, unexplained cases were detailed in Wuhan, China, due to symptoms similar to severe acute respiratory syndrome (SARS), but more aggressive in symptoms and spread, the World Health Organization (WHO) called it novel coronavirus, which poses significant health threats, especially to people with underlying diseases. Including cardiovascular disorders, diabetes, and high blood pressure [1,2]. According to the latest global statistics (28 November 2021), COVID-19 has infected 261,435,768 million people worldwide to date, of which more than 5,207,634 million have died. And as of 29 November 2021, a total of 7,772,799,316 vaccine doses have been administered [3]. According to studies, most people with COVID-19 have underlying diseases such as hypertension, cardiovascular disorders, and diabetes, and the death rate in these people is higher than in other patients [4-6]. Cardiovascular disease, diabetes, and hypertension alone pose a significant challenge to the global health system, and many die each year from these diseases. With the advent of Covid-19 and its anxiety, a level of excitement has been created between different people, which can have adverse effects on a person's health [7]. Statistics show that high blood pressure is one of the most common chronic diseases affecting about 31.1% of adults worldwide [8]. Angiotensin-converting enzyme 2 (ACE2) is increased in patients with high blood pressure due to related genetic polymorphisms and the use of an angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB). The COVID-19 epidemic is currently controversial, and further studies are needed. In the present study, an attempt was made to

provide sufficient evidence by summarizing the results of the studies. The purpose of this study was evaluating the association between blood pressure and mortality in Covid-19 pneumonia [9].

Method

Search strategy

The current study review of previous studies used the PRISMA checklist to search for the studies [9]. PRISMA protocol consists of five stages: systematic literature search, studies selection, data evaluation, data extraction, and data classification.

Selection criteria

RCT studies, Prospective and retrospective cohort studies (Non-RCT), observational studies were inclusion criteria; case-control, in vitro, reviews and case report studies, and pediatric populations were excluded [10].

Data collection and extraction

Data from selected articles were extracted based on years, study design, many patients, mean of age, underlying diseases. Two blind and independent reviewers extracted the information from the abstract and full content of the articles to extract the data [11]. Before the screening, kappa statistics were performed to confirm the level of agreement between the reviewers with higher kappa values (>0.80).

Data analysis

95 confidence intervals (CI) of risk ratio with fixed effect Model and Mantel-Haenszel procedure were calculated. The random-effects method was used to investigate potential heterogeneity between studies, and I^2 showed heterogeneity. Random effects were used to deal with potential heterogeneity, and I^2 values showed heterogeneity. I^2 values less than 50% indicate low heterogeneity ($p>0.05$), and high values indicate high heterogeneity ($p<0.05$). Statistical analysis and meta-analysis were performed with Software Version 16 (STATA Corporation).

Results

A total of 448 articles were found within the beginning search. After removing duplicates, entry criteria for the titles were applied to the remaining 346 articles, and a summary of the remaining articles was reviewed. In this step, 289 articles were excluded [12]. In the following, the full text of 57 articles were reviewed, and 37 articles were excluded due to lack of access to the complete content of the article and lack of relevance to the title and purpose of the article. Finally, twenty studies were chosen.

Characteristics

Twenty observational retrospective studies have been included. The number of patients was 3125 male and 1849 female. A total was 4974 with a mean age of 51.35 years (Table 1).

High blood pressure

Risk ratio of High blood pressure between poor and good outcome was 0.73 (RR, 0.73 95 % CI 0.63, 0.83) and moderate heterogeneity reported (I^2 =53.97%; p=0.00) (Figure 2). This result showed high blood pressure had a statistically significant association with increased composite poor outcomes.

According to the test of group differences, no statistically significant difference was observed between groups (p=0.00) [13].

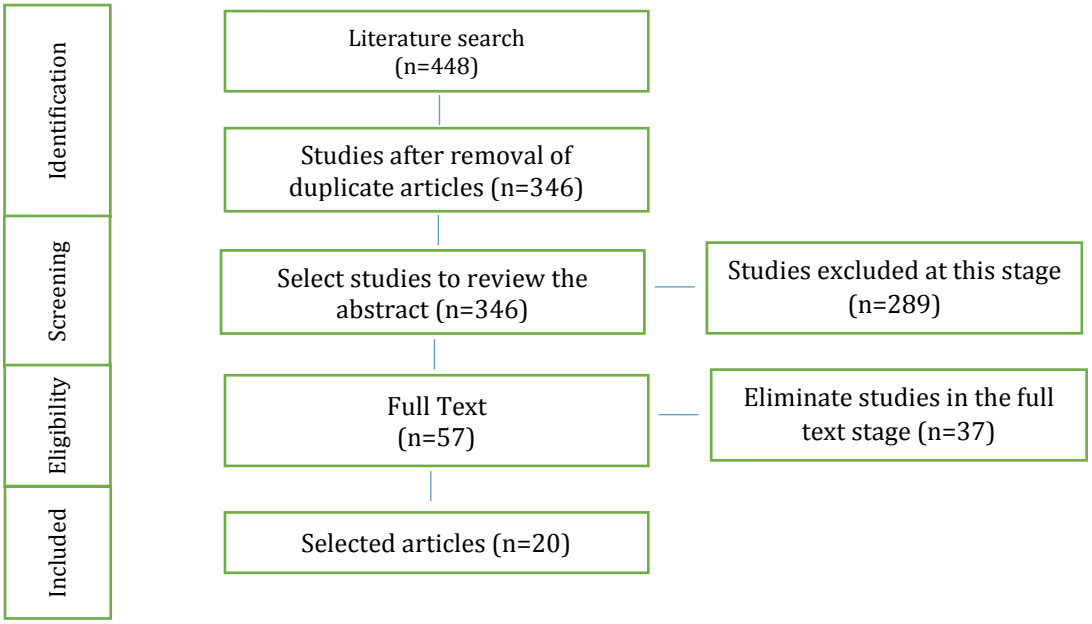

Figure 1 Flowchart of PRISMA

TABLE 2 Characteristics of Included Studies for meta-analysis

n	Study. Years	Study design	Number of patients		Mean of age	Underlying diseases (%)			
			male	female		HTN	CC	D	RC
1	Liu W *et al.*,2020 [10]	OR	39	39	38.8	40	-	25	10
2	Huang *et al.*,2020 [11]	OR	30	11	50	15	15	20	2.5
3	Wu *et al.*,2020 [12]	OR	128	73	51.5	19.4	4	11	2.4
4	Zhang *et al.*,2020 [13]	OR	71	69	49.9	30	5	12	1.5
5	Ma *et al.*,2020 [14]	OR	48	36	48.3	14	6	12	6
6	Hu *et al.*,2020 [15]	OR	162	160	59.9	32.5	13	15	2
7	Zhou *et al.*,2020 [16]	OR	118	73	56.1	30.5	8.1	19.2	3.1
8	Yuan *et al.*,2020 [17]	OR	12	15	60.1	19	11	22	-
9	Luo *et al.*, 2020 [18]	OR	201	202	56.3	28	0	14	7
10	Grasselli *et al.*,2020 [19]	OR	1304	287	63.1	49	21	17	4
11	Fu *et al.*,2020 [20]	OR	101	99	40.8	50.5	-	-	4
12	Jian-ya *et al.*,2020 [21]	OR	31	20	45.1	8	-	8	-
13	Cao *et al.*,2020 [22]	OR	53	49	54.1	27.5	5	11	10
14	Bai *et al.*,2020 [23]	OR	80	47	55.1	29	2.5	12	-
15	Akbari *et al.*,2020 [24]	OR	248	192	48.3	8	6	8	-
16	Feng *et al.*,2020 [25]	OR	71	70	44.3	15	2.2	6	3
17	Wang D *et al.*, 2020 [26]	OR	75	63	56.1	31	14.5	10	3
18	Wang Y *et al.*,2020 [27]	OR	47	63	43	21	-	14	5.5
19	Wan *et al.*,2020 [28]	OR	71	64	47.4	10	5.2	9	0.7
20	Qin *et al.*,2020 [29]	OR	235	217	58.8	30	6	16.5	2.6

HTN: Hypertension; CC: cardiovascular comorbidities; D: Diabetes; RC: Respiratory comorbidities; OR: Observational Retrospective

Subgroup meta-analysis

Mortality

Risk ratio of association between high blood pressure and mortality in Covid-19 pneumonia was 0.75 (RR, 0.75 95 % CI 0.62, 0.89) and heterogeneity was high (I^2 =74.94%; p=0.00) (Figure 2). This result showed High blood pressure increased mortality statistically [14].

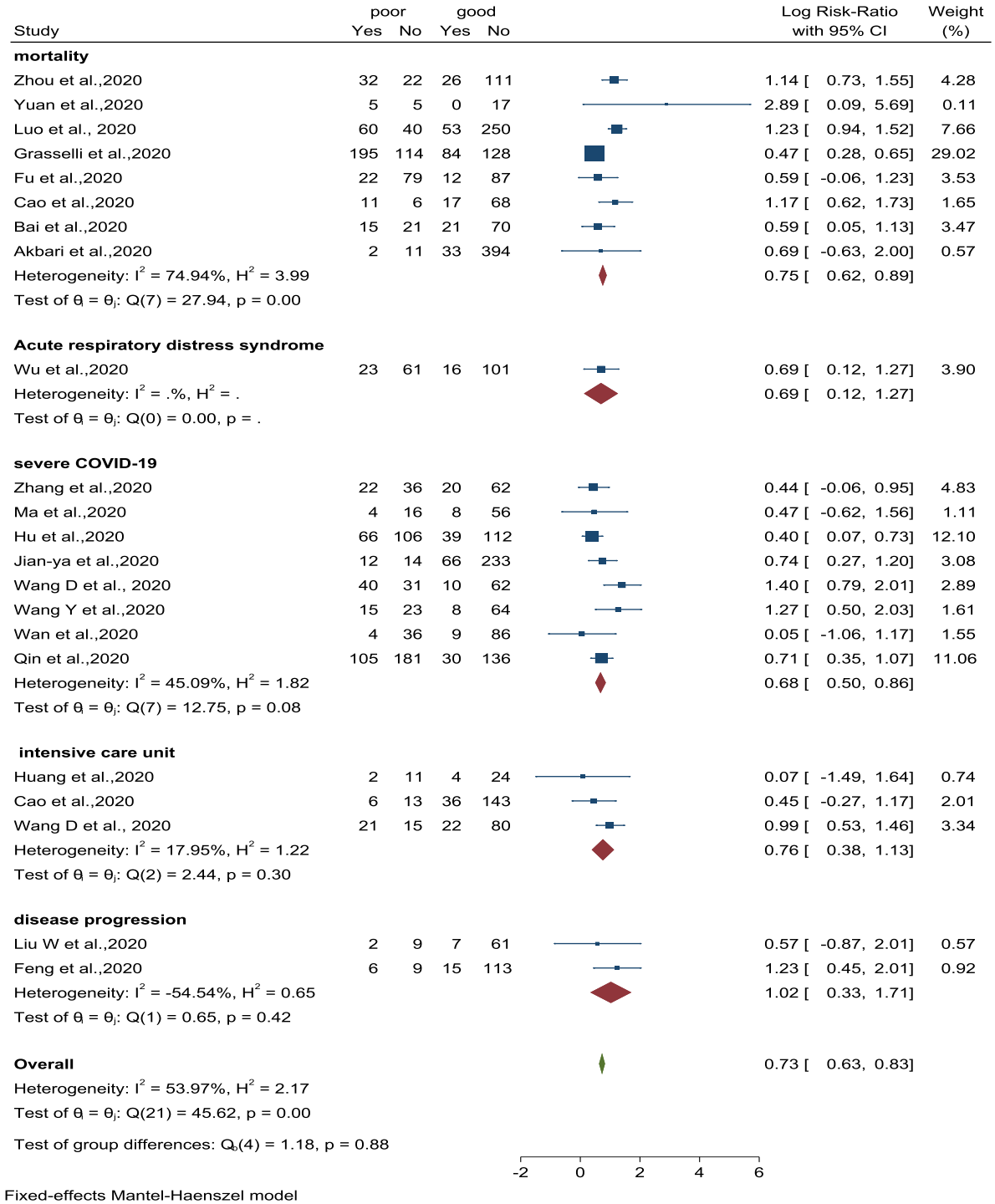

FIGURE 2 The forest plot showed subgroup meta-analysis

Acute respiratory distress syndrome

Risk ratio of association between high blood pressure and Acute respiratory distress syndrome in covid-19 pneumonia was 0.69 (RR, 0.69 95% CI 0.12, 1.27). This result showed high blood pressure increased acute respiratory distress syndrome [15].

Severe COVID-19

Risk ratio of association between high blood pressure and Severe COVID-19 was 0.68(RR, 0.68 95% CI 0.50, 0.86) according to I^2 heterogeneity was low (I^2 =45.09%; p=0.08). This result revealed high blood pressure increased Severe COVID-19.

ICU care

Risk ratio of association between high blood pressure and ICU care was 0.76 (RR, 0.76 95 % CI 0.38, 1.13) low heterogeneity reported (I^2 =17.95%; p=0.30). This result demonstrated high blood pressure increased ICU care.

Disease progression

Risk ratio of association between high blood pressure and ICU care was 1.02 (RR, 1.02 95 % CI 0.33, 1.71) low heterogeneity was found (I^2<0%; p=0.42). This result showed high blood pressure increased disease progression.

Publication bias

Funnel-plot showed an association between high blood pressure and increased Mortality, Acute respiratory distress syndrome, Severe COVID-19, ICU care, and disease progression (Figure 3).

Discussion

The purpose of the current study was to evaluate the association between blood pressure and mortality in covid-19 pneumonia. Meta-analysis showed an association between high blood pressure and increased Mortality, Acute respiratory distress syndrome, severe COVID-19, ICU care, and disease progression [16].

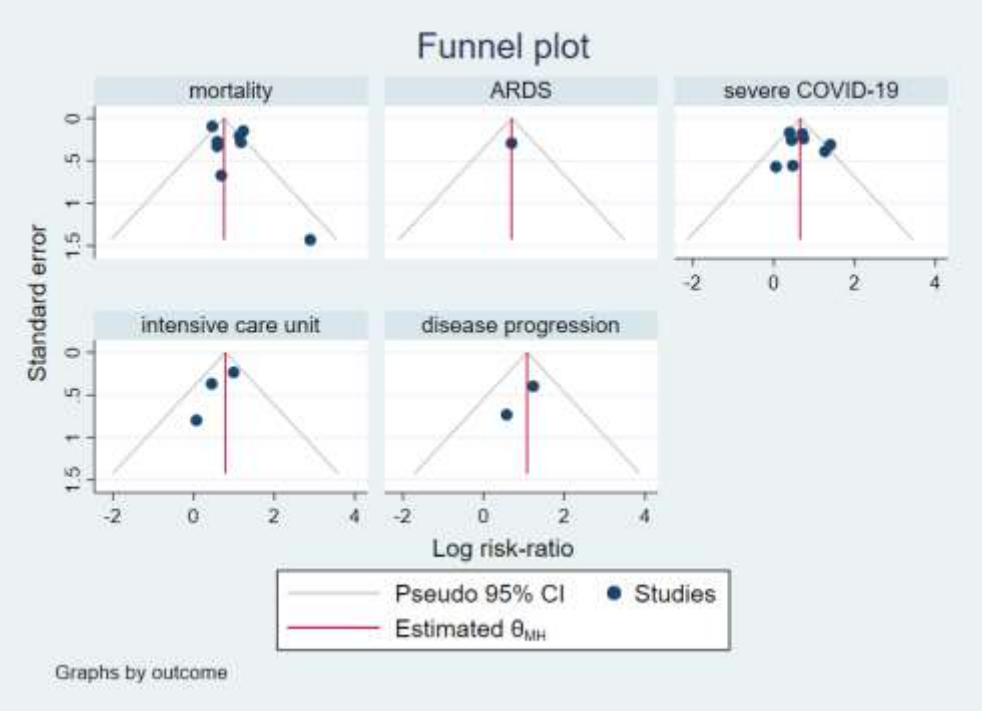

FIGURE 3 Publication bias analysis

However, due to the high heterogeneity in most studies, there is insufficient evidence that patients with high blood pressure have a high hazard of developing COVID-19. Evidence suggests that COVID-19 can be fatal. Increase patients with hypertension. Further studies are needed in this area. Studies have shown that the presence of ACE2 may counteract the inflammatory effects of angiotensin II, thereby reducing the level of the proinflammatory cytokine interleukin-6 [17]. In patients, high blood pressure activates the renin-angiotensin system in the tissues, resulting in increased mortality. Recent studies showed a significant relationship between gender, blood pressure, and mortality; female patients with hypertension who develop COVID-19 have a higher mortality rate. In female patients with hypertension, angiotensin II receptor type 2 activity is higher than angiotensin II type I, resulting in increased mortality. Studies have shown that estrogen causes 'good' Renin-angiotensin-aldosterone in women [18].

None of the studies looked at menopausal age in women and the incidence of COVID-19 in women. However, the mean age in the study was high and focused on the elderly. This cannot be commented on. It is suggested that further studies be performed to provide sufficient evidence to support the available results and hypotheses. At present, there is no scientific evidence that ending ACEI and ARB is beneficial in COVID-19 patients, and authorities continue to advise these patients to continue their common antihypertensive drugs. High blood pressure is often associated with other risk factors such as cardiovascular disease and diabetes, increasing the chance of Covid-19. The presence of underlying diseases such as hypertension, diabetes, and cardiovascular disorders can increase the risk of developing Covid-19 disease and the death rate from these diseases. Studies have shown that COVID-19 reduces ACE2 expression and inhibits its protective effect. Reports indicate that blood pressure control is significant in preventing cardiovascular complications. Given that no studies have been found in this regard, it is suggested that future studies be performed in this range to supply an appropriate answer to the existing hypotheses.

Conclusion

The present study's findings appear that in patients with high blood pressure, if they develop COVID-19, the mortality rate increases and an increase in acute respiratory distress syndrome. These patients need more ICU care than other patients. The meta-analysis showed that the progression of the disease also increased significantly in patients with high blood pressure.

The present had limitations, including that it may differ from country to country in the baseline hypertension studies. The history of hypertension should be considered, and the drugs used should be carefully examined. Gender should be examined separately for better evidence to be presented. The age of patients should be done by gender. Given that high heterogeneity was observed, it is suggested that similar studies be conducted in this range to supply strong proof.

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