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Advancing Healthcare Innovation: Multidisciplinary Collaboration and Translational Research

Diabetes mellitus patients with increased death rates and clinical complications in patients with CoV-19 pneumonia: A systematic review

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Abstract Diabetes Mellitus (DM) is a chronic condition that has been associated with Corona virus (CV) sickness and has the potential to cause catastrophic multisystemic consequences. They used a complete meta-analysis and review to examine the connection among DM and a bad prognosis in COVID-19 pneumonia individuals. We searched many online databases for articles assessing the correlation between DM and outcome in COVID-19 pneumonia. This study's principal result was an undesirable interaction of three secondary results: the occurrence of severe cardiovascular disease (CVD), acute respiratory distress syndrome (ARDS), and death. All 17 studies had 6452 participants. After eliminating the duplicates, the number of records remained at 350. After first looking at the titles and abstracts, we discarded 310 articles. After reviewing 43 full-text publications, 13 were ruled ineligible owing to a lack of mortality, interest, or disease progression outcomes, including those for severe ARDS which is disease progression, ARDS, Mortality and COVID-19 severity, were increased in COVID-19 patients with DM.

Keywords: COVID-19, Intensive Care Units (ICUs), diabetes mellitus, pneumonia

1. Introduction

The majority of patients who stay in intensive care units (ICUs) for protracted periods of time are linked to the epidemic. The majority of these individuals need invasive mechanical ventilation. Patients who suffer from viral pneumonia are more vulnerable to bacterial and fungal pneumonia (Stam et al 2020). Additionally, patients are more likely to develop invasive fungal infections during their hospital stay as a result of intubation and corticosteroid medication. In these individuals, ventilation-associated pneumonia (VAP) has been observed as a frequent consequence of negative results (Meawed et al 2021). The pandemic was confirmed by the World Health Organization (WHO). Patients with severe CV pneumonia and ARDS develop chronic aspergillosis as a result of prolonged ICU admission, the use of steroids, and the use of immune modulation devices (Ahmed et al 2022). According to recent findings from Germany, France, and the Netherlands, invasive aspergillosis affects 33%, 19% and 26%, respectively, of patients with severe CV pneumonia. These findings suggest that severe patients be screened for invasive aspergillosis. Antibiotic treatment has been advised for individuals with spergilli detected in their serum or bronchoalveolar lavage fluid, according to a panel of experts (Nasir et al 2020). Viral pneumonia is infrequent, seasonal, and possibly fatal depending on the host's immune status and the presence of comorbid conditions. Importantly, acute viral pneumonia compromises immunological function, endothelial tissues, and alveolar epithelial health (Ahmadikia et al 2021). The government contributed money for medications, negative ventilation in the ICU, and enhancements. Medical staff from inside the Trauma Institute from all the territories of Sindh provided aid to the COVID-19 unit (Sholzberg et al 2021). Patients in Pakistan with drug-resistant COVID-19, especially those in severe condition, are poorly characterized in terms of population, treatment, and fatality rates. The purpose of this research is to gather regional information that will help us better understand the people we treat and better pinpoint individuals who are at a higher risk for contracting a potentially fatal disease (Baqi et al 2021). Bilateral pneumonia, ARDS, and thrombotic vascular disease are complicating factors. Adults with serious underlying conditions, such as heart or lung disease, seem to be more prone to suffering from life-threatening issues (Oriot and Hermans 2022). Figure 1 displays the trends in the incidence and incidence of diagnosed DM among adults aged ≥18 years from 2006 to 2020.

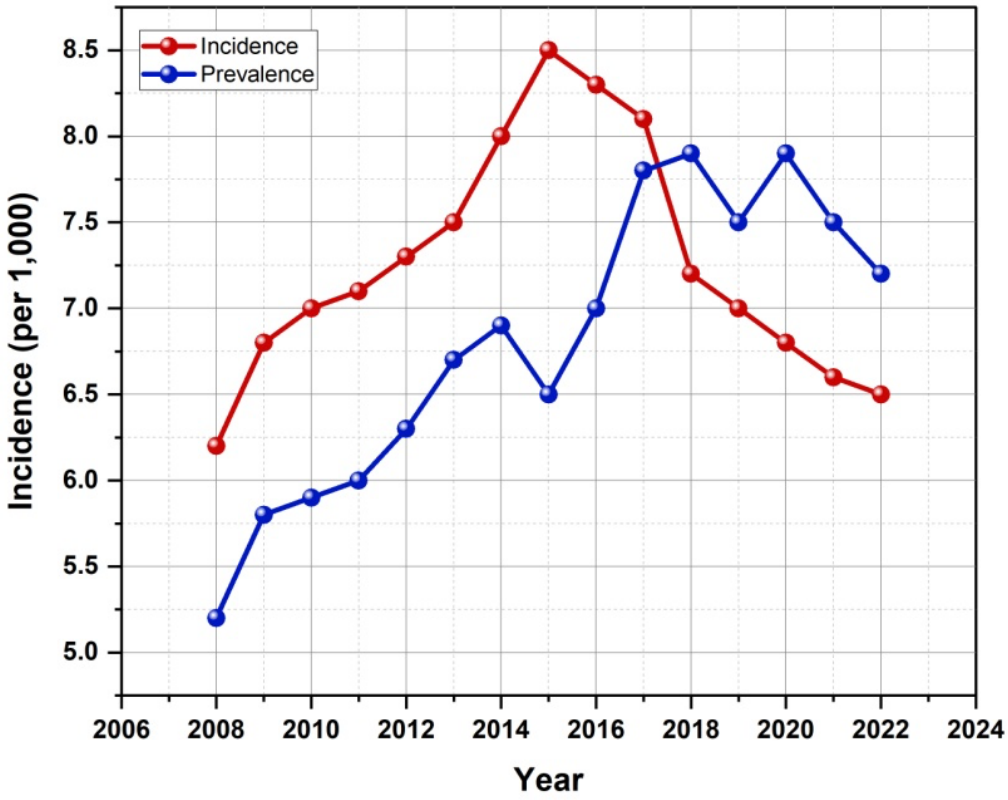

Figure 1 Changes in the incidence and incidence of identified DM with age ≥over 18 years from 2006 to 2020.

The prevalence, development, and severity of peripheral arterial disease (PAD) have been linked to diabetes mellitus. Patients with concomitant DM and PAD are extremely prone to experience serious outcomes, such as amputation. The cause of PAD is caused by atherosclerosis in the arteries that supply the lower extremities, which leads to arterial constriction or occlusion (Barnes et al 2020). CV-TB ranges from mild illness and non-life-threatening problems such as sore throats and headaches to those who need hospitalization for hypoxemia due to pneumonia and those who are critically ill and should be admitted to an ICU (von der Thüsen and van der Eerden 2020). The medical features of COVID-19 pneumonia and coronary artery disease (CAD) patients were compared. The factors associated with a high risk of heart injury were identified in a number of COVID-19 patients. Epicardial adipose tissue (EAT) computed tomography (CT) imaging has demonstrated the myocardial inflammatory response to COVID-19 (Hui et al 2020). Laboratory test findings, clinical presentations, underlying disorders, epidemiological factors, and disease outcomes were gathered and examined. They observed that the in-hospital mortality rate was affected by age, length of illness before admission, LYM (%), and lactate level upon admission (Wang and Wang 2021). The clinical manifestations of pregnancy and vertical transmission are unknown. The possible risks to the fetus during pregnancy and the danger to the newborn after birth were investigated. The patient was then sent to the quarantine area and received further supportive care in addition to an oral dose of chloroquine (Al-kuraishy et al 2020). As the world's population ages and grows and as the incidence of overweight and obesity rises in emerging and developed countries, the number of people diagnosed with diabetes is expected to increase during the coming decades. For people with diabetes, heart disease is a primary cause of death and disability, especially for individuals with type 2 diabetes. The risk of cardiovascular disease is 2-4 times greater in people with diabetes than in people without diabetes, and it increases as glycemic control deteriorates (Dal Canto et al 2019). The relationships between hypertension and CV outcomes were evaluated utilizing information gathered from many sources. Deaths, severe cardiovascular disease, illness progression, acute respiratory distress syndrome, and ICU admission were the main causes of concern (Pranata et al 2020). The prevalence of DM has increased over the last century as the global prevalence of obesity has skyrocketed during the past few decades. Genetic variants have also emerged as a new field of investigation in epidemiology to pinpoint the underlying genetic component of those risk variables and the connection between DM and CVD (Glovaci et al 2019). Complications from diabetes, such as gum disease and tooth loss, are already connected with greater rates of morbidity and death, and this makes matters worse. Periodontal disease is exacerbated by diabetes because of the mutual risk factors for these two conditions. Individuals with diabetes and periodontal gum disease have worse glycemic control, which can lead to serious complications involving coronary artery disease and kidney failure. Metabolic illnesses known as diabetes mellitus are associated with significant mortality and morbidity rates as well as a number of comorbidities, including heart disease, kidney disease, and stroke (Genco et al 2020). New clinical difficulties in the hospital environment develop as the worldwide incidence of CVD has increased worldwide. A serious concern to patients from these difficulties is the elevated

possibility of confusion. Complications from diabetes, such as gum disease and tooth loss, are already connected with greater rates of morbidity and death, and this makes matters worse (Segrelles-Calvoetal 2021).

2. Materials and Methods

2.1. Eligibility criteria

Investigations containing adult CV patients were considered if they contained information on severe clinical grouping, CV, diabetes, the result of the validated designation of dying, ICU care, or the course of the disease. Papers with sample sizes of fewer than 20, papers published in Language, nonoriginal research articles, case reports, and series were not eligible for publication.

2.2. Search strategy and study selection

The authors disposed of duplicate findings. The relevance of the abstracts from the remaining papers was assessed. There was no variation in the wording of the remaining articles evaluated for inclusion or deletion. On April 8th, 2020, the investigation was completed. The “Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)” statement served as a reference for the study's methodology.

2.3. Data extraction

The authors used standardized questionnaires that included questions about the name of the study's author, the year it was conducted, the study's design, the subjects' age and sex, as well as questions about their cardiovascular health, blood pressure, diabetes status, need for ICU care, and severity of their CV. The effect of interest was a composite negative result that included the patient's mortality, severe CV, ARDS, need for ICU care, and onset of the illness. The categorization of ARDS was built on the interim WHO guidelines for severe abrupt respiratory infection of CV, which encompasses abrupt onset, oxygenation, cause of pulmonary infiltrates, and chest imaging impairment. Breathlessness, oxygen consumption at rest less than 94%, a comparison between the percentage of oxygen inhaled and exhaled, or PaO2/fiO2 serious complication like breathing multiple organ dysfunction, issues, malfunction failure were signs of severe CV at the time of admission.

2.4. Statistical investigation

Review Supervisor 5.5 and Stata 16 were used to conduct the meta-analysis. Using random effect evaluations, the Mantel–Haenszel technique was utilized to create categorical variables. For categorical variables, the impact estimates are provided as 97% confidence intervals (CIs) and threat ratios (TRs). Hypertension, sex, age, and COPD status were included as independent factors in a restricted-maximum-likelihood MR analysis. All of the composite undesirable results were subjected to subgroup evaluation. They used a regression-based Harbord's test for categorical results to evaluate the impact of a tiny trial.

3. Results and Discussion

3.1. Methods of study selection and demographics

After removing the duplicates, 350 records were obtained from the initial 340. A total of 310 items were disregarded following title/abstract screening. After 43 full-text publications were scrutinized for eligibility, 13 full-text articles were disregarded due to the lack of any outcomes, including mortality, interest, or illness progression, including severe ARDS. In all, 17 studies had 6452 participants. The qualitative synthesis and meta-analysis included 17 studies (Figure 2).

3.2. Complications of diabetes

Multiple studies have shown an association between diabetes and a variety of negative outcomes. The subset included mortality (TR 3.49 [2.89, 2.04], I^2: 63%), mortality (TR 2.13 [1.34, 3.13], I^2: 74%), illness (TR 2.31 [2.08, 9.14], I^2: 0%), ARDS (TR 3.65 [1.87, 10.59], I^2: 8%), and severe CV (TR 3.46 [2.89, 2.36], I^2: 46%). Age and hypertension both had significant associations with a composite adverse outcome according to MR. Tables 1 to 5 indicate that patients with COVID-19 who have diabetes mellitus are at a greater risk for a number of adverse outcomes, including death, ICU admission, ARDS, illness progression and severe COVID-19.

3.3. Meta regression

Figures 3 to 5 from the MR study reveal that neither sex nor COPD status nor CVD status mitigated the association between DM and adverse composite outcomes. However, they were older and had hypertension. Hypertension *(p=0.101*) and age *(p = 0.339)* were shown to have interdependent effects on two-way multivariable MR.

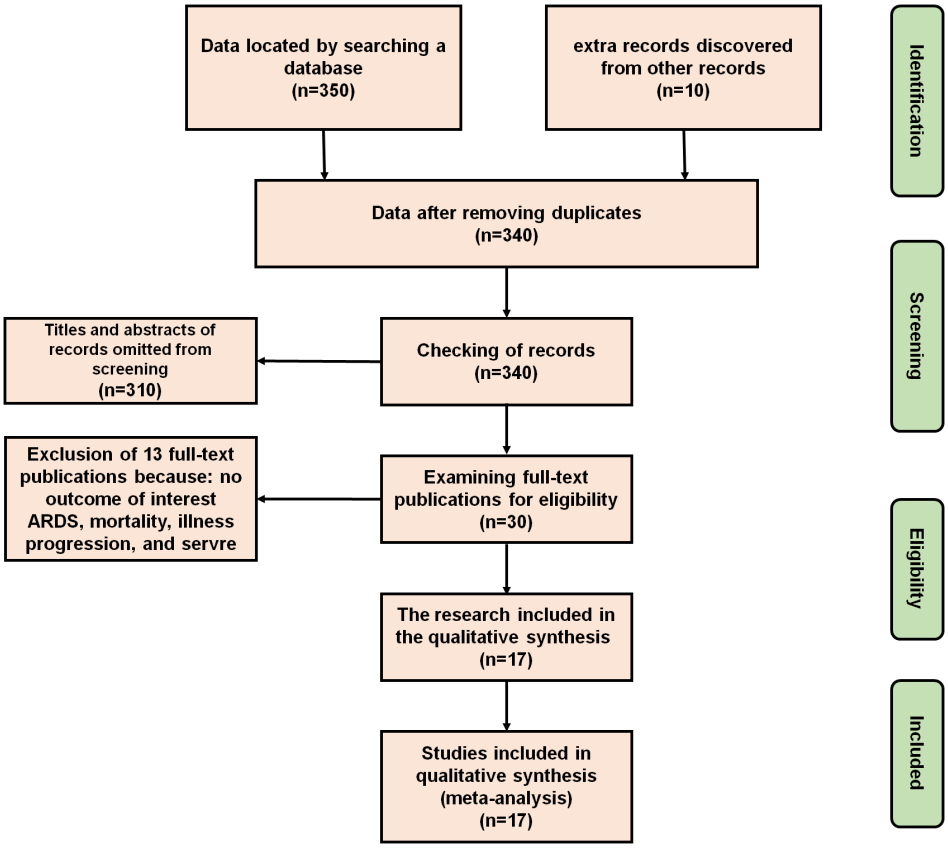

Figure 2 Study selection (using PRISMA).

Table 1 Outcomes of mortality.

Study or Subgroup	Diabetes Mellitus (+)		Diabetes Mellitus (-)		Mass	TR
	Activities	Overall	Activities	Overall		96% CI , Random, M-H,
Mortality						
Yuan M (2020)	7	11	1	18	0.8%	21.24[1.33,34.1.84]
Fu L (2020)	28	35	112	167	6.7%	1.15[0.93,1.40]
Zhou 2020	15	55	20	138	5.1%	2.21[1.29,4.04]
Chen M (2020)	7	33	9	93	3.1%	2.24 [0.85,5.89]
Li K (2020)	8	14	25	88	4.8%	1.70[0.90,3.22]
Subtotal (CI 96%)	-	148	-	504	20.5	2.10[1.41,3.12]
Total events	65		167		-	-
Heterogeneity: chi_2=33.31,Tau^2=0.25; i^2=71%, df=8						
Test for overall effect; Z=3.82						

Table 2 Outcomes of Severe CV.

Subgroup or Research	Diabetes Mellitus (+)		Diabetes Mellitus (-)		Mass	TR
	Activities	Overalll	Activities	Overall		96% CI , Random, M-H,
Severe CV						
Wan (2020)	10	72	4	96	2.5%	7.14 [2.04,24.96]
Yuan B (2020)	17	39	17	326	4.7%	3.54[1.85,5.53]
Liu j (2020)	4	16	3	45	1.4%	3.89 [0.71,21.25]
Zhang j (2020)	9	59	10	167	3.9%	1.27 [0.53,3.07]
Li Q (2020)	6	27	26	300	3.6%	2.31[0.97,5.51]
Qin (2020)	54	287	23	167	5.8%	1.41 [0.89,2.22]
Guan (2019)	29	174	54	924	5.8%	2.82[1.85,4.35]
Subtotal (96% CI)	-	674	-	2025	27.7	2.46[1.80,3.36]
Total events	129	-	137	-	-	-
Heterogeneity: chi_2=21.76,Tau^2=0.14; i^2=46%, df=11						
Test for overall effect; Z=5.64						

Table 3 Outcomes of ICU care.

Subgroup or Research	Diabetes Mellitus (+)		Diabetes Mellitus (-)		Mass	TR
	Activities	Overall	Activities	Overall		96% CI , Random, M-H,
ICU care						
Cao M (2020)	3	20	13	180	2.1%	1.46[0.36,5.96]
Wang D (2020)	9	37	7	101	3.3%	3.79[1.42,10.15]
Subtotal (96% CI)	-	57	-	281	5.4%	1.48[0.39,5.68]
Total events	12	-	20	-	-	-
Heterogeneity: chi_2=5.45,Tau^2=0.89; i^2=0%, df=2						
Test for overall effect; Z=0.57						

Table 4 Outcomes of disease progression.

Subgroup or Research	Diabetes Mellitus (+)		Diabetes Mellitus (-)		Mass	TR
	Activities	Overall	Activities	Overall		96% CI , Random, M-H,
Disease progression						
Feng (2020)	3	16	7	127	1.08%	2.81[0.63,12.66]
Liu W (2020)	3	12	4	68	1.7%	4.07 [0.77,21.62]
Subtotal (96% CI)	-	29	-	195	2.78	3.332 [1.09,10.15]
Total events	6	-	11	-	-	-
Heterogeneity: chi_2=0.09,Tau^2=0.01; i^2=0%, df=0						
Test for overall effect; Z=2.08						

Table 5 Outcomes of ARDS.

Subgroup or Research	Diabetes Mellitus (+)		Diabetes Mellitus (-)		Mass	TR
	Activities	Overall	Activities	Overall		96% CI , Random, M-H,
ARDS						
Wu c (2020)	17	85	7	118	3.6%	3.72[1.53.9.10]
Subtotal (96% CI)	-	85	-	118	3.6%	4.65[1.87,12.59]
Total events	17	-	7	-	-	-
Heterogeneity: chi_2=1.11,Tau^2=0.04; i^2=8%, df=2						
Test for overall effect; Z=3.26						

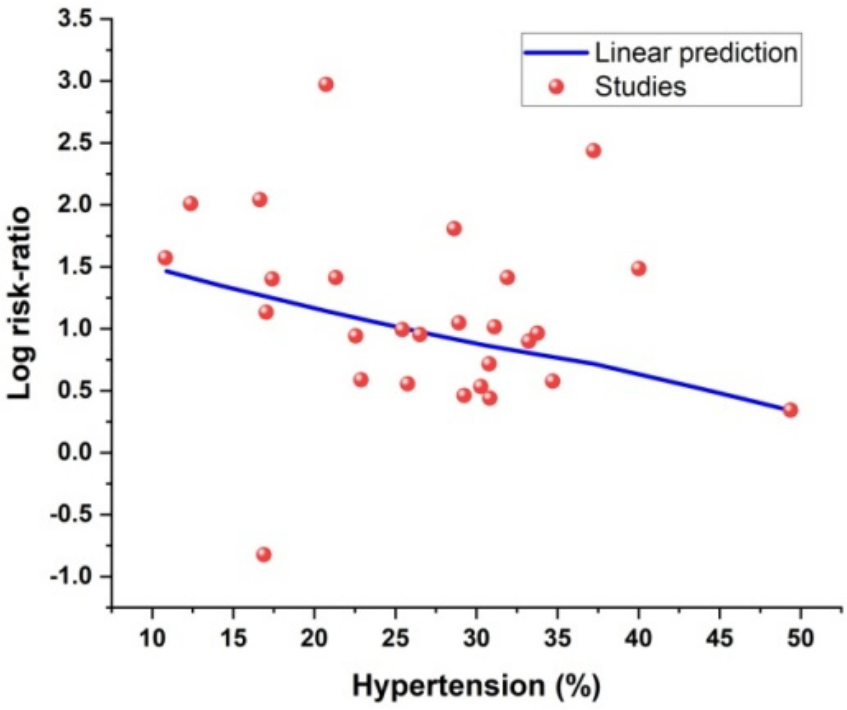

Figure 3 Associations between hypertension and diabetes were found via magnetic resonance (MR) imaging.

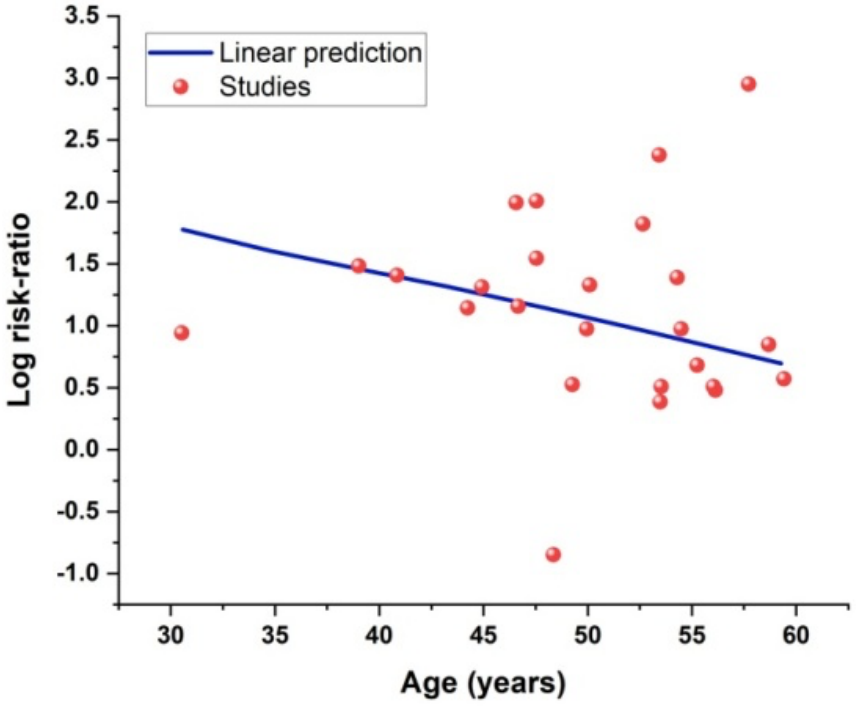

Figure 4 Age-related differences in hypertension and diabetes symptoms were found using magnetic resonance (MR).

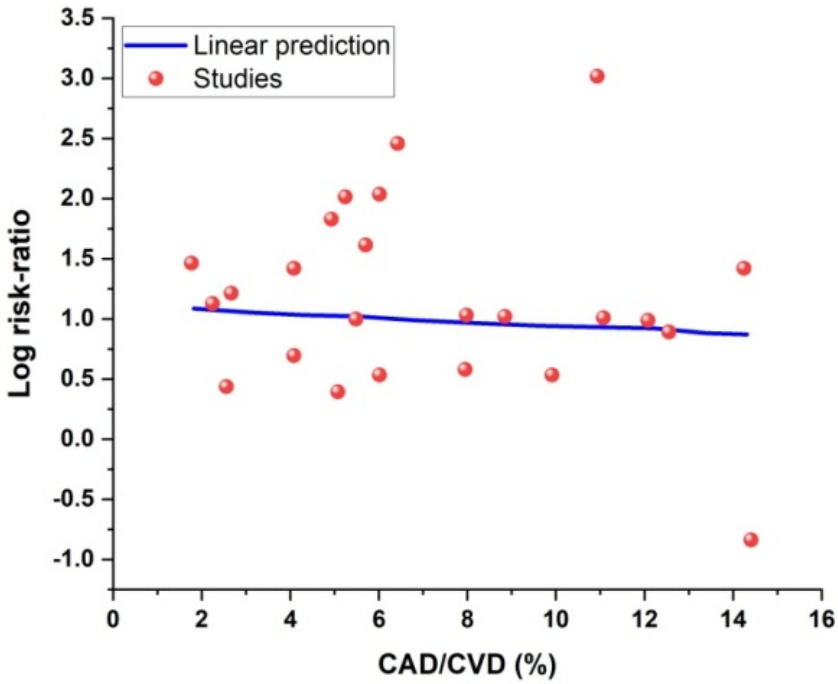

Figure 5 A relationship between hypertension and diabetes symptoms without cardiac disease was found via magnetic resonance (MR) imaging.

3.4. Subgroup analysis

Compared to studies in which the median participant age was 57 years (TR 4.49 (1.67, 5.79), I^2: 23%), the TR for a composite adverse outcome was lower in studies with a median age of 57 years (TR 2.9 (2.66, 3.47), I^2: 11%). In comparison to studies where the incidence of hypertension was less than 27% (TR 1.96 (1.49, 2.54), I^2: 59%), the TR for a combined adverse outcome was lower in studies where the incidence of hypertension was 28% (TR 3.09 (2.20, 4.29), I^2: 35%). Subgroup analysis revealed an association between BMI and worse outcomes in studies where the median participant age was 57 and the incidence of hypertension was 27%.

DM patients with CV had severe CV, severe ARDS, mortality, and illness progression according to this detailed meta-analysis of 17 assessments. This relationship was affected by aging and diabetes. The quality of risk associated with DM as a single feature has been shown to be greater in studies of teenagers and nonhypertensive adolescents, although this association continues to be unexplained by the current study. According to further analysis based on MRI, although it is unknown whether those who have diabetes are more prone to developing CV, several studies have shown that diabetic patients are more likely to experience severe CV (Zhou et al 2020).

Angiotensin II is transformed into angiotensin by the lung, brain, heart, kidney, and gastrointestinal epithelial cells, which express ACE2, a type 1 integral membrane glycoprotein (Chen et al 2019). The aggressive cytokine interleukin (IL)-6 is decreased, whereas angiotensin 1-7's anti-inflammatory and antioxidant properties are increased, surfactant protein D levels are increased, and vascular dilatation is encouraged (Li et al 2020). According to predictions, the newly discovered CV would act in a manner similar to that of SARS-CoV, which is responsible for severe acute respiratory syndrome. Through ACE2, both adhere to and penetrate host pneumocytes (Wan et al 2020). As mentioned above, our MR research demonstrated that age and diabetes status were mediators of the connection between DM and unfavorable findings (Feng et al. 2020). Medication usage, specifically the use of ACEIs or ARBs in hypertensive people, is one of the potential causes of this effect. The benefits and dangers of ACEI/ARB medication for CV patients are unclear (Wu et al 2020). In those with diabetes, severe CV might cause a malfunctioning proinflammatory cytokine response. In addition, diabetic patients have been shown to have elevated levels of the proinflammatory cytokines tumor necrosis factor (TNF)-β, IL-6, and IL-1. Therefore, this may lead to severe illness by exacerbating the cytokine storms observed in CV (Liu et al 2020).

4. Final considerations

The use of a prediction model for diabetes risk was the main goal of the present study. As previously mentioned, a large number of people worldwide suffer from diabetes. It is a major threat to the entire world if it is allowed and uncontrolled. Our findings demonstrated that hypertension, DM, and older age contributed to an elevated risk of mortality in those with CV. In the multivariate study, only diabetes mellitus (DM) was independently related to greater mortality. More studies may be necessary to determine the relationships between perceived risk factors and CV mortality. In the future, we hope to develop a trustworthy website that will help medical professionals identify diabetes early by utilizing the recommended DL algorithm.

Ethical Considerations

Not Applicable.

Conflict of Interest

The authors declare no conflicts of interest.

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