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The Analysis Study of Underlying Disease, Symptoms and Mortality Rate of COVID-19: A Comprehensive Systematic Review

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ABSTRACT

Background: The prevalence of underlying diseases in 22% of the global population increases their risk of severe COVID-19 outcomes. These conditions, often indicating a decline in physiological systems, compromise health and increase susceptibility to severe complications. A holistic approach is needed to understand their collective influence. **Methods**: This systematic review adhered to PRISMA 2020 guidelines, focusing exclusively on full-text articles published in English between 2014 and 2024. Editorials and review articles without a DOI were excluded to ensure the utilization of high-quality sources. A literature review was conducted utilizing reputable databases including ScienceDirect, PubMed, and SagePub to identify relevant studies. **Result**: The initial database search yielded approximately 1,300 publications relevant to the topic. Following a rigorous three-stage screening process, eight studies met the predefined inclusion criteria and were selected for in-depth analysis. Each study underwent a comprehensive critical evaluation, allowing for a detailed examination of the relationships between underlying diseases, symptoms, and COVID-19 mortality rates. This systematic approach ensured that the analysis was based on high-quality evidence, directly aligned with the study's objectives, and contributed to a more precise and reliable understanding of the subject. **Conclusion**: The study highlights the impact of underlying diseases on COVID-19 outcomes, highlighting the need for proactive management strategies. The study also highlights the global trend in symptomatology and risk factors, emphasizing the need for region-specific healthcare policies. Understanding the interplay between diseases and outcomes is crucial for effective disease management.

Keywords: COVID-19, mortality, risk factor, underlying disease

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The clinical manifestations of COVID-19 range from asymptomatic infections to severe respiratory distress and death.[2,3] Patients with underlying health conditions, such as cardiovascular disease, diabetes, liver disease, and chronic lung disease, have been identified as particularly vulnerable, experiencing worse COVID-19 outcomes and higher mortality rates.[4] Research estimates suggest that approximately 1.7 billion people—22% of the global population—have at least one underlying disease, which may significantly increase their risk of developing severe complications following SARS-CoV-2 infection.[5] The presence of these pre-existing conditions often indicates a functional decline in affected physiological systems, placing individuals in a state of compromised health and heightened susceptibility to severe COVID-19 outcomes.[6] Furthermore, the ongoing emergence of novel SARS-CoV-2 variants, coupled with gaps in vaccination coverage—particularly among high-risk groups—continues to pose a serious threat to global public health and places a significant burden on healthcare systems worldwide.[7]

Previous population-based studies have explored the associations between individual underlying diseases and COVID-19 severity.[8,9] For instance, an umbrella review found that conditions such as diabetes, heart failure, chronic obstructive pulmonary disease (COPD), and dementia were linked to a significantly increased risk of fatal COVID-19, with hazard ratios ranging from 1.2 to 7.7.[9] Some studies have attempted to assess the overall impact of comorbidities in hospitalized COVID-19 patients using comorbidity indices; however, these approaches often obscure system-specific disease effects and fail to provide a comprehensive understanding of the broader population-level risks.[10] Additionally, existing research has not comprehensively examined all potential underlying diseases, with conditions such as mental illnesses and sensory impairments frequently overlooked. Given the complex interactions between human physiological systems, a more

holistic approach is needed to understand how underlying diseases collectively influence COVID-19 outcomes fully.[11]

To advance this field of study, it is essential to investigate the interplay between underlying diseases, COVID-19 symptoms, and mortality rates. A comprehensive, system-based analysis can provide valuable insights into disease interactions and their role in COVID-19 progression. By bridging existing research gaps, this study aims to enhance the understanding of these critical relationships and contribute to developing more effective risk assessment models, preventive strategies, and treatment approaches for high-risk populations.

METHODS

Protocol

This study was conducted in strict accordance with the PRISMA 2020 guidelines, ensuring a methodologically robust and high-quality research process. By adhering to these standardized protocols, the review maintained transparency, reproducibility, and scientific rigor throughout. Key procedures—such as comprehensive literature searches, precise data extraction, and systematic synthesis of findings—were meticulously executed to minimize bias and enhance the reliability of results. This rigorous approach strengthens the study's credibility and contributes to the advancement of evidence-based research.

Criteria for Eligibility

This study aims to evaluate the underlying diseases, symptoms, and mortality rate of COVID-19 by systematically reviewing and synthesizing data from a diverse range of studies. By identifying patterns and emerging trends within the existing literature, the research seeks to provide valuable insights that can inform more effective diagnostic approaches and patient care strategies. The ultimate objective is to enhance the understanding of these critical factors, contributing to improved clinical management and public health interventions.

To ensure analytical rigor, the study employed strict inclusion and exclusion criteria. Only peer-reviewed articles published in English between 2014 and 2024

were included, with each study's authenticity verified through DOI validation. Non-research materials, such as reviews, editorials, and duplicate entries, were excluded to maintain a focused and high-quality dataset. This meticulous selection process strengthens the reliability of the findings by ensuring that the analysis is based on credible and relevant sources.

By adopting a systematic and comprehensive methodology, the study guarantees that its conclusions are supported by robust evidence. The anticipated findings aim to deepen the understanding of the relationship between underlying diseases, symptoms, and COVID-19 mortality rates. Ultimately, this research aspires to drive advancements in patient care and contribute to better health outcomes for individuals affected by COVID-19.

Search Strategy

A well-structured search strategy was employed to identify relevant studies for this systematic review, using the key terms "underlying disease," "mortality rate," and "COVID-19." The search was conducted across three major academic databases—PubMed, SagePub, and ScienceDirect—ensuring a comprehensive and thorough investigation of the topic. This systematic approach facilitated the inclusion of diverse, high-quality sources, strengthening the evidence base for analysis and enhancing the reliability and validity of the review's findings.

Table 1. Search Strategy

Database	**Search Strategy**	***Hits***
Pubmed	*("underlying disease" AND "mortality rate" AND "Covid-19")*	37
Science Direct	*("underlying disease" AND "symptoms" AND "mortality rate" AND "Covid-19")*	1.244
Sagepub	*("underlying disease" AND "mortality rate" AND "Covid-19")*	111

Data retrieval

The authors conducted a meticulous preliminary review of each article, systematically screening titles and abstracts to assess their relevance before proceeding with an in-depth evaluation. Only studies that aligned with the research objectives and met the predetermined inclusion criteria were selected for further analysis. This structured and methodical approach facilitated the identification of consistent and meaningful patterns across the literature, ensuring a focus on studies directly relevant to the research question.

To maintain consistency and enhance the comparability of findings, only full-text articles published in English were included. A rigorous screening process was implemented to verify that all selected studies adhered to the established inclusion criteria and effectively addressed the study's objectives. Articles failing to meet these standards were excluded, ensuring a high-quality, precise, and relevant dataset.

The evaluation process involved a comprehensive assessment of multiple factors, including study titles, authorship, publication dates, research locations, and methodologies. This thorough review ensured that only the most relevant and reliable studies were incorporated into the analysis. By employing a systematic and rigorous selection process, the authors strengthened the credibility and validity of the findings, providing a robust foundation for drawing reliable and actionable conclusions.

Quality Assessment and Data Synthesis

The authors employed a meticulous initial screening process, systematically reviewing article titles and abstracts to identify studies relevant for further analysis. Only those that met the predefined relevance and quality criteria progressed to a comprehensive, in-depth evaluation. This rigorous and structured approach prioritized the inclusion of high-quality studies that directly aligned with the research objectives. By refining the selection process, the authors ensured that the final dataset comprised methodologically robust and contextually significant

studies. This strategy not only enhanced the focus and precision of the analysis but also reinforced the overall quality, relevance, and scientific rigor of the review.

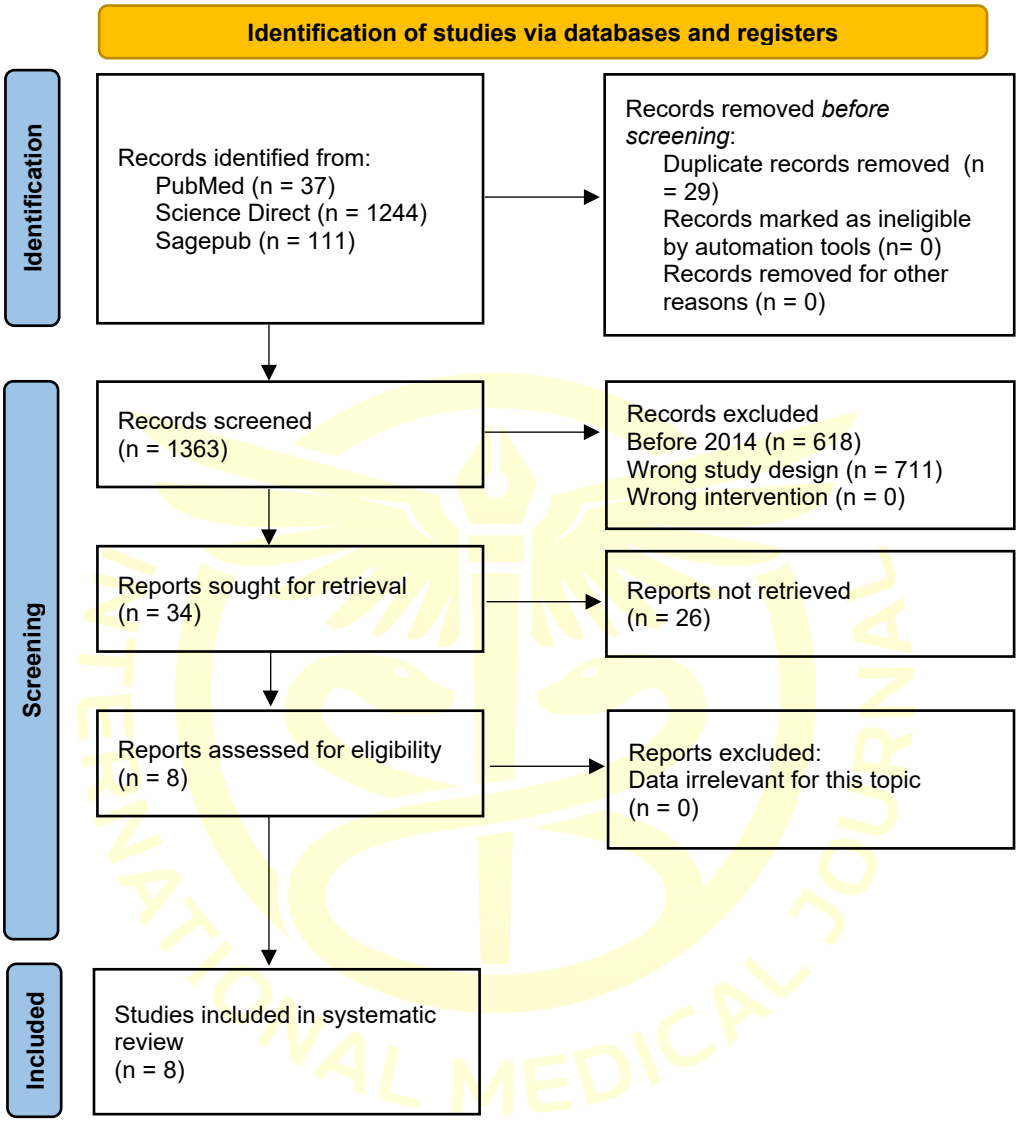

Figure 1. Article search flow chart

Table 2. Critical appraisal of Study

Parameters	(Banarjee et al., 2020)	(Novosad et al., 2020)	(Javanmardi et al., 2020)	(Bhaskaran et al., 2021)	(Choi, W, 2021)	(Elezkurtai et al., 2021)	Shams et al., 2022)	(Wang et al., 2023)
1. Bias related to temporal precedence Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation Was there a control group?	No	No	No	No	No	No	No	No
3. Bias related to confounding factors Were participants included in any comparisons similar?	No	No	Yes	No	No	No	Yes	Yes
4. Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Yes.	Yes.	Yes.	Yes.	Yes.	Yes.	Yes.	No.
5. Bias related to assessment, detection, and measurement of the outcome Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	No	No	No	No	No	No	No	No
Were the outcomes of participants included in any comparisons measured in the same way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Were outcomes measured in a reliable	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

way?								
6. Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Yes	Yes	No	Yes	Yes	Yes	No	No
7. Statistical conclusion validity Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

RESULT

The investigation began with a systematic search of reputable academic databases, including ScienceDirect, PubMed, and SagePub, to identify studies relevant to the review. A rigorous three-stage screening process was employed to meticulously filter and select the most pertinent studies, ultimately narrowing the selection to eight papers that met the predefined inclusion criteria. These studies underwent an in-depth analysis, with key topics carefully extracted for comprehensive examination. To enhance clarity and facilitate effective presentation, the findings are succinctly summarized in Table 3, offering a well-structured and concise overview of the analyzed data.

Table 3. The literature included in this study

Author	Origin	Method	Sample	Result
Banerjee et al.[12] (2020)	United Kingdom	Cohort	Over 3 million participants	The study included 3 862 012 individuals, with over 20% in the high-risk category. The estimated 1-year mortality in this population was 44%. Age and underlying conditions combined significantly influence background risk.
Novosad et al.[13] (2020)	India	Retrospective Study	Over 17 million	The mortality rate in India compared to England is higher due to higher rates of diabetes and chronic

			participants	respiratory disease, while lower rates of obesity, chronic heart disease, and cancer are observed. Uncontrolled diabetes and chronic respiratory disease increase mortality, while obesity, cancer, and chronic heart disease reduce it. Comorbidities contribute to a 6.26% lower mortality risk in India.
Javanmardi et al.[4] (2020)	Iran	Systematic Review	32 studies	The analysis revealed that underlying disease, such as hypertension and asthma, significantly impact the severity and mortality rate of COVID-19 cases. These diseases, including cardiovascular disease, liver disease, lung disease, malignancy, and cerebrovascular disease, necessitate careful monitoring and awareness of health protocols.
Bhaskaran et al.[14] (2021)	United Kingdom	Cohort	Over 17 million participants	The study found similar associations between factors associated with COVID-19 death and non-COVID death, with older age being more strongly associated with COVID-19 death. Factors such as male sex, deprivation, obesity, and comorbidities had stronger associations with non-COVID death. Non-white ethnic groups had higher odds of COVID-19 death but lower odds of non-COVID death. Identifying unique factors contributing to excess COVID-19 mortality risk is crucial for reducing deaths.

Choi, W.[15] (2021)	Korea	Retrospective Study	566.602 participants	The mortality rate of patients with underlying health conditions was 12%, four times higher than those without such conditions. Women and men with underlying health conditions had rates 5.5 and 3.4 times higher than those without such conditions. Factors such as male sex, age ≥ 41 years, and underlying health conditions were identified as risk factors for mortality.
Elezkurtai et al.[16] (2021)	Germany	Prospective Study	26 participants	The study presented findings on causes of death and comorbidities in 26 decedents who presented with severe COVID-19. The most common immediate cause was septic shock and multi-organ failure, often due to suppurative pulmonary infection. Comorbidities like hypertension, ischemic heart disease, and obesity were present in most patients. The findings suggest that most patients died of COVID-19.
Shams et al.[17] (2022)	Iran	Systematic Review	18 studies	The study found that common symptoms of COVID-19 infection, such as fever and cough, were associated with a higher mortality rate, with underlying diseases such as hypertension, diabetes mellitus, and cardiovascular disease being the most frequent.

Wang et al.[18] (2023)	China	Cross Sectional	28.204 participants	The study found that underlying diseases were associated with higher odds of COVID-19, severe symptoms, loss of smell, and taste among 28,204 participants. Sensory impairments, cardiovascular diseases, neuropsychiatric diseases, and endocrine diseases also showed independent associations with these symptoms. These findings highlight the importance of understanding the underlying causes of diseases.

DISCUSSION

This systematic review aimed to evaluate the prevalence of underlying diseases, symptoms, and mortality rates associated with COVID-19. The findings reaffirm that COVID-19 is a highly transmissible disease with the potential for rapid spread within communities. Given its high transmission rate, strict adherence to public health measures and safety protocols remains essential to controlling the pandemic. The review further underscores the significance of underlying health conditions in determining disease severity and outcomes, emphasizing the need for targeted interventions to protect vulnerable populations.

Our analysis revealed that hypertension, heart disease, diabetes mellitus, respiratory diseases, and cerebral disorders were the most frequently reported comorbidities in COVID-19 patients. Several studies have demonstrated that deceased COVID-19 patients often had pre-existing conditions such as hypertension, a history of angiography, and diabetes mellitus. The presence of these underlying diseases, particularly cardiac and cerebral conditions, combined with a weakened immune system, facilitates the systemic spread of the virus and

significantly increases the risk of mortality.[19-21] These findings highlight the critical role of pre-existing health conditions in influencing COVID-19 outcomes, reinforcing the need for proactive screening and management strategies for high-risk individuals.

Regarding symptom prevalence, the study found that fever, cough, fatigue, dyspnea, and sputum production were the most common clinical manifestations in COVID-19 patients. These findings align with previous research on hospitalized COVID-19 patients, where fever, cough, and dyspnea were among the most frequently reported symptoms.[22,23] Given their high prevalence, these symptoms should be considered primary indicators of COVID-19 infection. Individuals exhibiting such symptoms should seek immediate medical attention to ensure early diagnosis and timely intervention, which can help mitigate disease progression and reduce mortality rates.

The findings of this study are consistent with early reports on COVID-19 clinical features in Iran. Studies have shown that cardiovascular diseases, hypertension, diabetes mellitus, malignancies, kidney injuries, and chronic lung diseases were the most common risk factors among deceased COVID-19 patients in Iran. Additionally, symptoms such as dyspnea, cough, fatigue, and abnormal chest X-ray findings were frequently observed in Iranian COVID-19 patients.[24,25] These similarities suggest a global trend in COVID-19 symptomatology and risk factors, highlighting the need for region-specific healthcare policies that address the burden of comorbidities in different populations.

Overall, this review underscores the importance of understanding the interplay between underlying diseases and COVID-19 outcomes. The presence of comorbid conditions significantly influences disease severity and mortality rates, necessitating a more comprehensive approach to disease management. Future research should focus on expanding the scope of studies to include a broader range of underlying diseases, such as mental health disorders and sensory impairments, which have been largely overlooked. Additionally, more in-depth analyses of region-specific variations in COVID-19 presentation and outcomes could provide valuable insights for developing tailored public health interventions.

CONSCLUSION

The study reveals that COVID-19 is a highly transmissible disease, with underlying diseases such as hypertension, heart disease, diabetes mellitus, respiratory diseases, and cerebral disorders significantly influencing disease severity and mortality rates. These comorbidities, combined with a weakened immune system, facilitate the virus's spread and increase mortality rates. Symptoms such as fever, cough, fatigue, dyspnea, and sputum production are common clinical manifestations in COVID-19 patients, emphasizing the need for proactive screening and management strategies. The findings also suggest a global trend in COVID-19 symptomatology and risk factors, highlighting the need for region-specific healthcare policies. Understanding the interplay between underlying diseases and COVID-19 outcomes is crucial for effective disease management. Future research should include a broader range of underlying diseases and analyze region-specific variations in COVID-19 presentation and outcomes for tailored public health interventions.

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