

Mortality risk of hypoxaemic acute respiratory failure among Indonesians: A systematic review and meta-analysis

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Abstract

English:

Background: Hypoxaemic acute respiratory failure (ARF) is a life-threatening condition with high global mortality, especially in low- and middle-income countries. In Indonesia, where healthcare access and oxygen infrastructure are unevenly distributed, the mortality burden of hypoxaemic ARF remains poorly quantified.

Objectives: This systematic review and meta-analysis aims to evaluate the mortality risk of hypoxaemic ARF in the Indonesian population across all age groups.

Methods: A systematic search was conducted across MEDLINE, Embase, CENTRAL, Scopus, and manual searches in Garuda and Google Scholar (as of 24 July 2023). Eligible studies included those reporting mortality outcomes among patients with hypoxaemic ARF in Indonesia. The Joanna Briggs Institute checklist for prevalence studies was used for quality assessment. Data were analysed using R-4.3.1 with random-effects meta-analysis, and subgroup analyses were performed based on the pandemic period. The protocol is registered with PROSPERO, CRD42023451225.

Results and discussion: Of 9763 screened records, 8 studies met the inclusion criteria, comprising data from 757 patients. The pooled mortality risk of hypoxaemic ARF was 41% (95% CI: 32–50), with higher mortality during the pre-pandemic era (47%) compared to the pandemic era (24%). The findings are in line with global estimates and reinforce the critical need to strengthen oxygen availability, monitoring and delivery systems in Indonesia.

Conclusion: Hypoxaemic ARF remains a major contributor to in-hospital mortality in Indonesia, particularly where oxygen access is limited. Strengthening oxygen security and investing in early hypoxaemia detection are essential steps to reduce mortality in future respiratory emergencies.

Keywords

acute respiratory failure • hypoxaemia • mortality • Indonesia • oxygen security

Riscul de mortalitate al insuficienței respiratorii acute hipoxemice în rândul populației din Indonezia: referat general și meta-analiză

Rezumat

Romanian:

Background: Insuficiența respiratorie acută hipoxemică (ARF) este o afecțiune amenințătoare de viață, având o mortalitate ridicată la nivel global, în special în țările cu venituri mici și medii. În Indonezia, unde accesul la servicii medicale și infrastructura de oxigen sunt distribuite inegal, povara mortalității prin ARF hipoxemică rămâne slab cuantificată.

Obiective: Acest revizuire sistematică și meta-analiză își propune să evalueze riscul de mortalitate asociat ARF hipoxemice în populația din Indonezia, la toate grupele de vârstă.

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Metode: A fost realizată o căutare sistematică în bazele de date MEDLINE, Embase, CENTRAL, Scopus, precum și prin căutări manuale în Garuda și Google Scholar (până la 24 iulie 2023). Au fost incluse studiile care raportau date privind mortalitatea la pacienți cu ARF hipoxemică în Indonezia. Lista de verificare a Joanna Briggs Institute pentru studiile de prevalență a fost utilizată pentru evaluarea calității. Analiza datelor a fost efectuată în R-4.3.1, utilizând meta-analiza cu efecte random, iar analizele de subgrup au fost realizate în funcție de perioada pandemiei. Protocolul a fost înregistrat la PROSPERO, CRD42023451225.

Rezultate și discuții: Din 9763 de articole evaluate, 8 studii au îndeplinit criteriile de includere, însumând 757 pacienți. Riscul cumulat de mortalitate prin ARF hipoxemică a fost de 41% (IC 95%: 32–50), cu o mortalitate mai mare în perioada pre-pandemică (47%) comparativ cu perioada pandemică (24%). Rezultatele sunt în concordanță cu estimările globale și subliniază necesitatea stringentă de consolidare a disponibilității oxigenului, a sistemelor de monitorizare și de administrare a acestuia în Indonezia.

Concluzie: ARF hipoxemică rămâne un factor major de mortalitate intra-spitalicească în Indonezia, în special în zonele cu acces limitat la oxigen. Consolidarea securității aprovizionării cu oxigen și investițiile în detectarea precoce a hipoxemiei reprezintă pași esențiali pentru reducerea mortalității în viitoarele urgențe respiratorii.

Cuvinte-cheie

insuficiență respiratorie acută • hipoxemie • mortalitate • Indonezia • securitate a oxigenului

Abbreviations: ARDS, acute respiratory distress syndrome; ARF, acute respiratory failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; JBI, Joanna Briggs Institute; LMICs, low- and middle-income countries; PaO_2/FiO_2 , ratio of arterial oxygen partial pressure to fractional inspired oxygen; PaO_2 , partial pressure of oxygen; PRISMA, preferred reporting items for systematic reviews and meta-analyses; SaO_2 , arterial oxygen saturation; SpO_2 , peripheral capillary oxygen saturation; V/Q, ventilation/perfusion.

Introduction

Acute respiratory failure (ARF) is a condition in which the respiratory system fails to provide adequate oxygenation (hypoxaemic) and/or fails to remove carbon dioxide (hypercapnic) (1). Acute hypoxaemic respiratory failure is generally caused by lung damage due to various causes, including infections such as pneumonia, coronavirus disease 2019 (COVID-19), sepsis and tuberculosis; chronic respiratory conditions such as chronic obstructive pulmonary disease (COPD), asthma and heart disease; trauma; emergencies; critical conditions; and anaesthesia during surgeries. Meanwhile, acute hypercapnic respiratory failure occurs when respiratory muscle load exceeds the muscle pump's capacity, often seen in acute COPD exacerbations, neuromuscular diseases, chest wall deformities, and obesity (2, 3).

The incidence and mortality rate of ARF are high. In the United States, the incidence is approximately 1275 cases per 100,000 adults per year, with a high mortality rate of up to 9%–48% (4–7). A study by Rasmin et al. (8) at Persahabatan Hospital, Indonesia, identified infections, particularly pneumonia, as the most common cause of ARF and an intrahospital mortality rate of 53.3%.

Given its high mortality rate and significant financial burden on healthcare systems, effective ARF management is crucial. Treatment primarily relies on oxygenation and ventilation, making access to medical oxygen a critical factor in patient

outcomes. For low- and middle-income countries (LMICs) such as Indonesia, detailed data on ARF mortality risk are essential to guide oxygen supply planning and ensure medical oxygen security. However, to our knowledge, no study has systematically assessed the mortality risk of ARF in Indonesia.

This systematic review aims to address this gap by evaluating the mortality risk of ARF, with a particular focus on Indonesia. As a highly populated LMIC in Southeast Asia, Indonesia is expected to share similar healthcare challenges with other nations in the region. This review represents the first comprehensive analysis of ARF mortality in Indonesia across all age groups, providing insights that could inform national healthcare strategies and resource allocation.

Objectives

This systematic review and meta-analysis aims to delineate the mortality risk of hypoxaemic ARF, with a particular focus on Indonesia. As a highly populated country in Southeast Asia and classified as a lower-middle-income country, Indonesia is expected to face similar healthcare challenges to others in the region, particularly in access to medical oxygen. To our knowledge, this is the first comprehensive systematic review

assessing the mortality burden of hypoxaemic ARF among Indonesians across all age groups.

Materials and methods

This systematic review and meta-analysis was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. Following the methodological guidelines for systematic reviews of epidemiological studies, this systematic review utilised the condition, context and population (CoCoPop) approach instead of the population, intervention, comparator and outcome (PICO) structure, as recommended by the methodological guidance from the Joanna Briggs Institute (JBI). This decision was made due to the alignment of this epidemiological study, which focuses on mortality risk, with the CoCoPop framework (9). Eligibility criteria were subsequently applied to match the conditions, context and population.

Within the CoCoPop framework, the condition was hypoxaemic ARF, which is defined using one of the following criteria: (1) $\text{PaO}_2 < 60$ mmHg, (2) SaO_2 or $\text{SpO}_2 < 90\%$ or (3) $\text{PaO}_2/\text{FiO}_2$ ratio < 300 (10). Data obtained from the studies were extracted into Table 1 and Table S1 in Supplementary Materials. The context was Indonesia, so the criteria included all studies conducted in regions within Indonesia, while studies conducted outside Indonesia were excluded. The population included both adults and children, categorised as children (< 18 years) and adults (≥ 18 years), who were included in this study. Patients who were neonates were excluded from this review.

The inclusion criteria for the studies comprised all observational and interventional studies that provided data on mortality among patients with ARF and their control group. The included study outcomes needed to be in the form of mortality risk, or at the very least, calculable using the available data. We only include studies that have been conducted in no more than 20 years, ensuring the relevance of the data. Regarding mortality data, details such as the time interval to death and causes are detailed in Table S1 in Supplementary Materials, ensuring that all studies with potential mortality outcomes for analysis are included in this systematic review.

Studies were excluded if the outcome sought was inappropriate or insufficient to demonstrate mortality risk and if the study types were not relevant to epidemiological outcome syntheses, such as reviews, case reports, case series, animal studies or commentary articles. Restrictions were imposed on the publication year more than 20 years before the literature search, while no restriction was applied to the language of the included studies in this systematic review.

The search strategy encompassed literature searches within international journal databases, specifically MEDLINE,

Embase, CENTRAL, Scopus and manual searches through the national journal databases Garuda and Google Scholar to ensure the inclusion of studies conducted in Indonesia. The literature search was conducted on 24 July 2023. The search keywords included various synonyms for hypoxaemic ARF, mortality risk and Indonesia. The complete list of keywords used for each journal database search is presented in Table S2 in Supplementary Materials. Efforts to locate unpublished reports have also been undertaken. Duplicate articles obtained from the journal databases were removed using EndNote X9 software (Philadelphia, Clarivate Analytics). Studies listed in the references of other systematic reviews with similar clinical questions were also included in this systematic review if they met the eligibility criteria. This systematic review protocol has already been registered with PROSPERO, CRD42023451225. Data extraction was performed independently by three authors (A.F.I., G.A. and S.R.A.). Extracted data included author and year of publication, location, data collection period, sample size, population, mean (SD)/median (range) age, ARF definition, cause of ARF and findings, which consisted of the frequencies of the non-survived and survived groups, along with the percentage of the non-survived group.

Quality assessment of the included studies was also independently conducted by two authors (G.A. and S.R.A.), with discrepancies discussed with the other author (A.F.I.) when they arose. The critical appraisal tool used was the prevalence studies checklist provided by the JBI. This checklist comprised nine items, each with options 'yes', 'no', 'unclear' and 'not applicable' (11). An overall appraisal was also conducted to assess the suitability of the study for inclusion in this systematic review (9, 12, 13).

Meta-analysis was performed using R-4.3.1 (Vienna, R Foundation for Statistical Computing), generating forest plots that displayed cumulative mortality risk values with corresponding 95% confidence intervals (CIs), as well as heterogeneity indicated by I^2 values. The R package 'meta' was used with the command 'metaprop', followed by forest plot visualisation. In general, a random-effects model was used if the results have high heterogeneity, indicated by $I^2 > 50\%$ and a P -value < 0.05 . The common-effect model was applied to the homogenous forest plots, including in our subgroup analysis. Additionally, studies with uncertain or inadequate sample sizes based on critical appraisal were not included in this quantitative analysis.

Results

The results of the study selection process are illustrated in Figure 1. The terms used in this flowchart follow the PRISMA 2020 Statement. 'Record' refers to the title or abstract of a report obtained from a journal database and may include

Table 1. Study characteristics table for included studies assessing mortality risk.

No.	Author, year	Location	Data collection time	Sample size (hypoxaemia patients)	Population	Mean (SD)/median (range) age (years)	Definition of ARF	Cause of ARF	Findings		
									Frequency of the non-survived group	Frequency of the survived group	Percentage (%)
1	Amin et al. (2016) (15)	Jakarta	October 2015–August 2016	101	Patients aged >18 years, diagnosed with ARDS by Berlin criteria	52.7 (17.2)	$\text{PaO}_2/\text{FIO}_2 \leq 300$	Not specified	Mild ARDS: 16 Moderate ARDS: 22 Severe ARDS: 15 Total: 53	Mild ARDS: 28 Moderate ARDS: 14 Severe ARDS: 6 Total: 48	Mild ARDS: 36.4 Moderate ARDS: 61.1 Severe ARDS: 71.4 Total: 52.48
2	Elhidi et al. (2021) (16)	Jakarta	January 2017–December 2018	111	Patients aged ≥ 18 years, diagnosed with ARF caused by pulmonary tuberculosis	N/A	$\text{PaO}_2 < 60$ mmHg, $\text{SpO}_2 < 91\%$ and $\text{PaO}_2/\text{FIO}_2 < 300$	Tuberculosis	53	58	47.75
3	Made Reditya Noviyani et al. (2020) (17)	Bali	January 2018–December 2019	60	Children with ARDS admitted in the PICU during the data collection period	ARDSp: 2 (1–180) months ARDSexp: 6 (1–144) months	$\text{PaO}_2/\text{FIO}_2 < 300$	Not specified	ARDSp: 10 ARDSexp: 22 Total: 32	ARDSp: 20 ARDSexp: 8 Total: 28	ARDSp: 33.3 ARDSexp: 73.3 Total: 53.33
4	Nugraha et al. (2022) (18)	East Java	July–December 2020	78	Patients with the age of ≥ 18 years, confirmed COVID-19 by PCR test and the $\text{PaO}_2/\text{FIO}_2$ ratio of < 300 mmHg were included.	47.75 (± 13.39) years	$\text{PaO}_2/\text{FIO}_2 < 300$	COVID-19	Mild ARDS: 1 Moderate ARDS: 9 Severe ARDS: 10 Total: 20	Mild ARDS: 9 Moderate ARDS: 36 Severe ARDS: 13 Total: 58	Mild ARDS: 5 Moderate ARDS: 45 Severe ARDS: 50
5	Nugrahani et al. (2022) (14)	Central Java	November 2020–September 2021	43	Patients diagnosed with COVID-19 during the data collection period	N/A	$\text{SpO}_2 < 90\%$	COVID-19	31	12	72
6	Rasmin et al. (2018) (8)	Jakarta	January–December 2015	69	Patients aged >18 years, diagnosed with ARF	51 (15–92) years	$\text{PaO}_2 < 60$ mmHg, $\text{SaO}_2 < 91\%$, $\text{PaO}_2/\text{FIO}_2 < 300$	Not specified	28	41	40.58
7	Rasmin et al. (2021) (10)	Jakarta East Java West Sumatera Aceh	January–December 2017	228	Patients aged >17 years, diagnosed with ARF	56 (20–90)	$\text{PaO}_2 < 60$ mmHg, $\text{SaO}_2 < 91\%$, $\text{PaO}_2/\text{FIO}_2 < 300$	Not specified	103	125	45.17
8	Valentania et al. (2021) (19)	West Java	May 2020–September 2020	67	Patients aged 1 month–18 years with pneumonia	23.5 (1–210) months	$\text{SpO}_2 < 90\%$	Pneumonia	15	52	22.3

ARDSexp, Extrapulmonary Acute Respiratory Distress Syndrome; ARDS, acute respiratory distress syndrome; ARDSp, Pulmonary Acute Respiratory Distress Syndrome; ARF, acute respiratory failure; COVID-19, coronavirus disease 2019; N/A, Not Applicable; PICU, Pediatric Intensive Care Unit; PCR, polymerase chain reaction; SD, Standard Deviation.

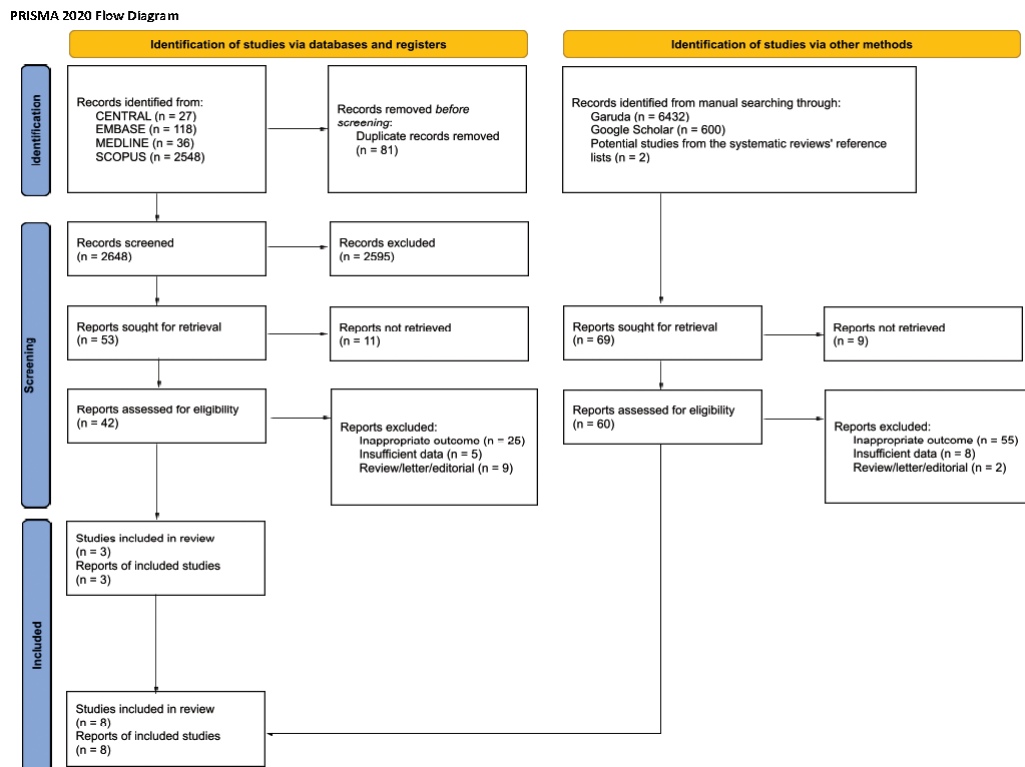


Figure 1. PRISMA 2020 flow diagram of study selection. PRISMA, preferred reporting items for systematic reviews and meta-analyses.

duplicates, 'Report' refers to a document providing information on a specific study, and 'Study' refers to an investigation that may generate multiple reports. From international journal databases, a total of 2729 records were obtained, with 27 records from CENTRAL, 118 records from Embase, 36 records from MEDLINE and 2548 records from Scopus. Duplicates totalling 81 records were removed using EndNote X9 software and resulting in 2648 records. These reports underwent title and abstract screening, yielding 53 reports. Subsequently, 42 retrieved reports were assessed in full-text accordance with the predefined eligibility criteria. Excluded reports encompassed reasons for inappropriate outcomes if the CoCoPop of the studies did not meet the framework (25 reports), insufficient data (5 reports) and forms of reports that were not suitable, such as reviews, letters and editorials (9 reports). Additionally, manual searches were conducted through Garuda (6432 records) and Google Scholar (the first 600 records appearing in keyword searches). Furthermore, two studies identified during the systematic review assessment were considered for study selection. Ultimately, a total of 69 reports were identified, of which 60 reports proceeded to full-text assessment based on eligibility criteria. Consequently, 55 reports were excluded due to inappropriate outcomes, 8 due to insufficient data and 2 due to being in the form of reviews, letters or editorials. The combined identification of studies from international journal

databases and manual searching resulted in a total of eight studies included in this systematic review.

Data extraction results are available in Table 1. The oldest study was published in 2016 and the most recent in 2022, with data collection times varying from 2015 to 2021. The results of the risk of bias assessment for the included studies, using the prevalence studies checklist by the JBI, are presented in Table S3 in Supplementary Materials. Based on the results of the Risk of Bias (ROB) assessment, seven studies received an overall good appraisal and were included in the quantitative analysis. However, the study of Nugrahani and Fauzi (14) was excluded from the quantitative analysis due to inadequate sample sizes. However, the qualitative data were still extracted. The other components of quality assessment varied among the included studies.

We include the quantitative mortality events and the total of ARF patients in the forest plot for the meta-analysis process, as shown in Figure 2. From the seven studies analysed, it is shown that the mortality of ARF is 41% (95% CI: 32–50) in the random effect model. Nevertheless, this result showed a significant heterogeneous distribution ($I^2 = 78.3\%$, $t^2 = 0.2201$), so we did a subgroup analysis to assess the heterogeneity.

From our subgroup analysis, we investigated the source of the heterogeneity in the different studies conducted in the pre-

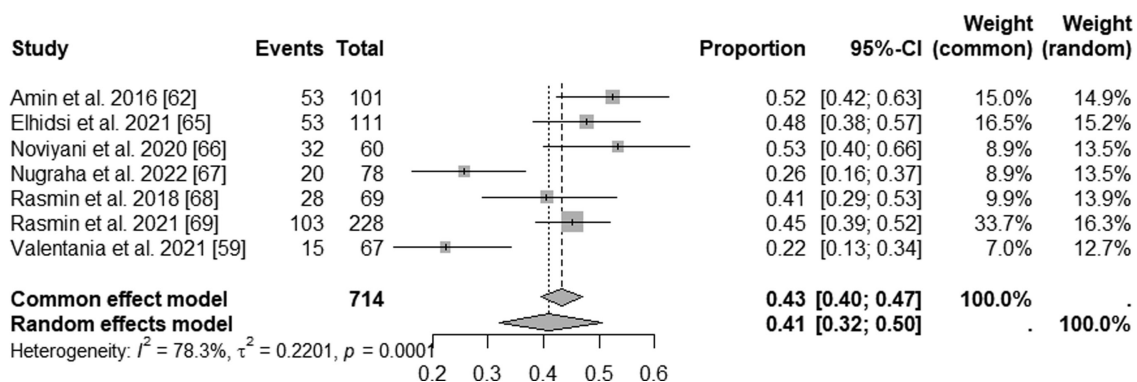


Figure 2. Forest plot of mortality risk among hypoxaemic ARF. ARF, acute respiratory failure; CI, confidence interval.

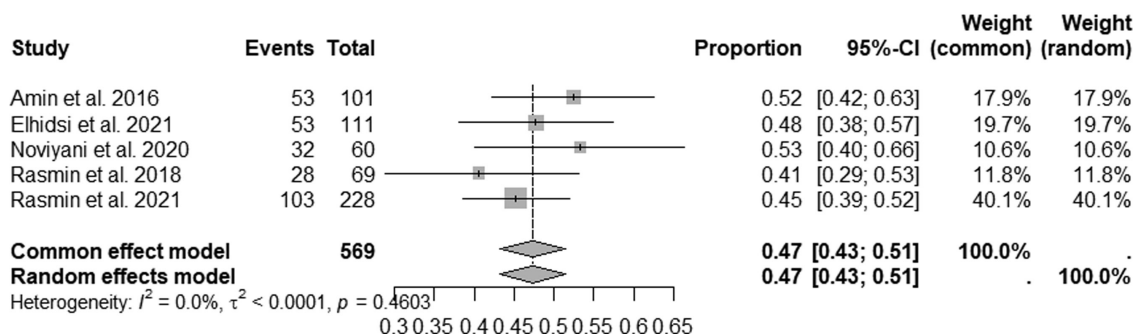


Figure 3. Subgroup analysis of mortality risk among hypoxaemic ARF in the pre-pandemic era. ARF, acute respiratory failure; CI, confidence interval.

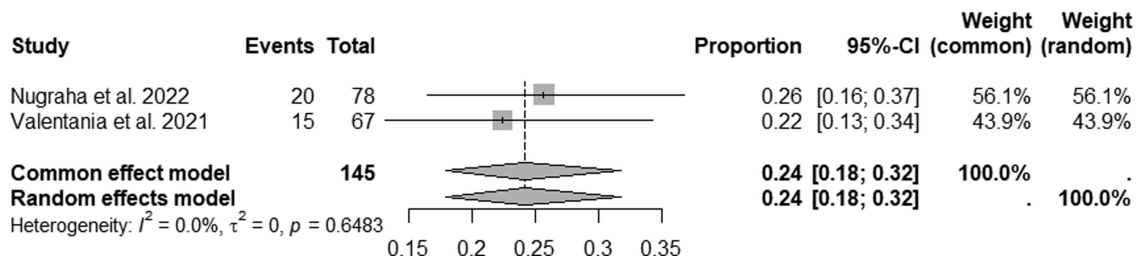


Figure 4. Subgroup analysis of mortality risk among hypoxaemic ARF in the pandemic era. ARF, acute respiratory failure; CI, confidence interval.

pandemic and pandemic periods. The pandemic era started in March 2020 and had a significant influence on patients' conditions and healthcare management around the world (20). Figure 3 shows the subgroup meta-analysis for the only studies analysing the mortality among ARF in the pre-pandemic era. It indicates that the mortality was 47% (95% CI: 43–51) with the homogenous data distribution ($I^2 = 0\%$, $\tau^2 < 0.0001$).

On the other hand, Figure 4 shows the mortality risk of ARF in the pandemic era. The result was lower than in the pre-pandemic era, as the proportion was only 24% (95% CI: 18–32). This result was also homogenous ($I^2 = 0\%$, $\tau^2 < 0.0001$),

showing the potential heterogeneity source of the main forest plot. It is interesting that this review not only shows the mortality risk data regarding ARF mortality in Indonesia but also shows the comparison between the pre-pandemic era and the pandemic era.

Discussion

ARF occurs when disruptions in the respiratory system, whether in the airways, central or peripheral nervous system, chest wall, or respiratory muscles, impair oxygenation

or hinder carbon dioxide elimination (3). In Type 1 ARF, insufficient oxygenation leads to hypoxaemia. The underlying pathophysiology includes alveolar hypoventilation, diffusion impairment, ventilation/perfusion (V/Q) mismatch, right-to-left shunt and reduced atmospheric oxygen pressure (3, 21, 22). Among these various causes, V/Q mismatch is the primary mechanism contributing to hypoxaemic ARF. This mechanism is commonly observed in populations with pneumonia, COVID-19, tuberculosis and acute respiratory distress syndrome (ARDS), aligning with the study populations included in this systematic review and meta-analysis. Acute inflammation due to these various causes leads to alveolar oedema and inflammatory exudates, which create areas with low ventilation but preserved perfusion. Additionally, inflammatory responses trigger pulmonary microthrombosis, causing capillary perfusion loss despite normal ventilation. These combined ventilation and perfusion disturbances drive V/Q mismatch (3, 23). In severe cases, extensive shunting causes V/Q to approach zero, preventing gas exchange at the alveolar-capillary interface. Deoxygenated blood then bypasses the lungs and enters the systemic circulation via a right-to-left shunt, leading to tissue hypoxia, organ ischaemia (especially in the brain and heart) and potentially fatal outcomes (3, 24).

Based on a previous study in Indonesia by Rasmin et al. (8), the intrahospital mortality rate of ARF was reported at 53.3%. However, our systematic review estimates a lower overall mortality risk of ARF at 41% (95% CI: 32–50). This discrepancy may be caused by the fact that the previous single study was conducted in tertiary referral hospitals, which often manage more severe cases with poorer prognoses. Additionally, the incorporation of studies conducted during the pandemic may have contributed to improved clinical management strategies, ultimately leading to reduced mortality rates.

This review found that the overall mortality risk of hypoxaemic ARF in Indonesia was 41% (95% CI: 32–50), with subgroup analysis showing higher mortality in the pre-pandemic period (47%) compared with the pandemic era (24%). ARDS, often considered a more severe subset of ARF, has an even wider reported mortality rate, ranging from 30% to 75%, depending on disease severity and available healthcare resources (25). Recent data in Germany also show that among over 1 million mechanically ventilated patients in 1395 hospitals over 4 years, in-hospital mortality reached 43.3%, with rates increasing with age and peaking above 50% in COVID-19 cases (26). These findings reinforce the serious prognosis of ARF requiring ventilation and the need for context-specific strategies to reduce mortality. The Indonesian data reflect a meaningful part of this spectrum and offer important context for understanding ARF burden in LMICs, where data remain relatively limited.

When viewed regionally, Indonesia's mortality rate appears comparable to those reported in other Southeast Asian settings. In Singapore, ARDS mortality is reported to be around 40%, while Taiwan's long-term data show even higher fatality, with 57.8% in-hospital and 72.1% 1-year mortality (27, 28). A recent study in the United States demonstrates an estimated increase in ARF-related mortality of around 3.4% annually (29). In contrast, Singapore's reported ARDS incidence was much lower at 4.5 per 100,000, suggesting significant variability in reporting practices, surveillance capacity and healthcare system responsiveness (27).

Differences in mortality across settings are likely influenced by a range of factors, including healthcare access, critical care availability and underlying patient characteristics. Globally, older adults, individuals with pneumonia or sepsis and populations exposed to seasonal respiratory viruses tend to have worse outcomes. In high-income countries such as the United States, rising ARF mortality has also been linked to disparities affecting rural residents and racial minorities (29, 30). Although this review did not include granular subgroup data, similar health system limitations may have contributed to higher mortality in the Indonesian pre-pandemic context. Conversely, the reduced mortality observed during the pandemic could reflect improved respiratory illness management, greater awareness and expanded healthcare resources during the COVID-19 response. These findings highlight the evolving nature of ARF outcomes and point to the importance of strengthening respiratory care systems in Indonesia moving forward.

The management of ARF shifted considerably during the COVID-19 pandemic, influenced by emerging evidence, patient load and oxygen supply constraints. Before the pandemic, non-invasive ventilation (NIV) and Continuous Positive Airway Pressure (CPAP) were primarily used for hypercapnic ARF, such as COPD exacerbations (31). However, during the pandemic, their use expanded to hypoxaemic ARF, particularly in COVID-19 cases, despite initial concerns around aerosolisation. Intubation practices also changed; while early intubation was common pre-pandemic, clinicians began favouring delayed intubation and trials of High-Flow Nasal Cannula (HFNC) or CPAP, often out of necessity (31, 32). Oxygen targets became more liberal during the pandemic, with clinicians aiming for $\text{SpO}_2 \geq 90\%$ –95%. These adjustments contributed to a significant rise in oxygen demand (32, 33).

Despite continuity in lung-protective strategies such as low tidal volume ventilation (6 mL/kg), ventilator management had to be tailored to the variable lung compliance seen in COVID-19 ARDS. Prone positioning, previously reserved for moderate-to-severe ARDS in intubated patients, was extended to awake, non-intubated individuals known as 'awake proning'

as a means to improve oxygenation while avoiding intubation (33). These evolving strategies helped reduce ventilator use, but they placed even greater pressure on oxygen supplies, especially in low-resource settings.

The pandemic exposed longstanding weaknesses in the oxygen infrastructure. Prior to COVID-19, around half of hospitals in LMICs lacked reliable oxygen access. During the pandemic, demand surged by 100–200 times in countries such as Nepal, far exceeding supply. While global efforts committed over \$1 billion to support oxygen access, distribution remained uneven due to logistical barriers, geopolitical disruptions and unreliable electricity in rural areas (34). In some LMICs, oxygen shortages forced difficult triage decisions, with resources often directed towards COVID-19 cases at the expense of others, including patients with pneumonia or neonatal emergencies (35).

The prevention and management of hypoxaemic ARF rely on early identification, oxygenation and ventilation, and addressing the underlying cause (1, 2). Since early identification is the essential first step, the simplest approach using a pulse oximeter should be prioritised (25). The next step is correcting hypoxaemia through oxygenation and ventilation, aiming for an oxygen saturation of 90%–96%, which can be delivered via invasive or non-invasive methods depending on the patient's clinical condition (3, 25). However, the use of pulse oximetry in LMICs remains limited, particularly in primary healthcare facilities; its utilisation is often suboptimal, and frequent stockouts and supply interruptions occur. This is concerning, as oxygen therapy is highly acceptable to patients and can be improved through low-cost capacity-building strategies (26).

Oxygen security plays a central role at every stage of ARF management, from detection to treatment. Yet, more than 300 million people who require medical oxygen each year live in LMICs, where basic oxygen services are often unavailable or unreliable. Large coverage gaps persist, with only a fraction of patients receiving adequate therapy. These gaps are often rooted in underinvestment, lack of equipment maintenance and insufficient integration of oxygen systems into routine health services (26).

Many healthcare facilities, particularly at the district and primary care levels, lack essential tools such as pulse oximeters, and even when oxygen devices are present, they are frequently non-functional or improperly used. The inability to monitor and respond to hypoxaemia in a timely manner not only delays care but also leads to poorer outcomes. Addressing oxygen insecurity requires a systemic approach, one that ensures availability, affordability and sustainability across all levels of care, particularly in regions where demand is rising due to population growth and shifting disease burdens (26).

In Indonesia, where health service capacity varies widely between urban and rural regions, ensuring oxygen security is particularly urgent. Despite the clear clinical guidelines for

ARF management, many district-level and remote facilities still struggle with inadequate oxygen supply chains, lack of pulse oximeters and insufficient staff training. These limitations not only compromise care for patients with COVID-19 or pneumonia but also affect surgical safety, neonatal resuscitation and management of sepsis and trauma. Without sustained investment beyond procurement including maintenance, workforce and integration across service levels, oxygen services will remain fragmented. Building resilient and equitable oxygen systems must be a core priority for Indonesia's health security strategy, not only to improve day-to-day critical care but also to prepare for future respiratory pandemics.

Given the high incidence and mortality of ARF, our study highlights the critical role of oxygen in ARF management, particularly in Indonesia. We recommend optimising pulse oximetry use and oxygen therapy, strengthening oxygen supply systems, improving stakeholder coordination and establishing robust market regulations to ensure oxygen security.

Conclusion

In conclusion, the mortality risk of hypoxaemic ARF in Indonesia is considerably high, including in the pre-pandemic and pandemic era. The consistently elevated mortality underscores a broader pattern that may also be seen in other LMICs. These findings reinforce the urgent need to improve oxygen security, ensure early detection of ARF and strengthen system readiness across all levels of care. Addressing these gaps is not only essential to reducing preventable deaths from ARF, but it is central to building a more equitable and resilient healthcare system.

Glossary

Acute Respiratory Failure: Acute impairment of gas exchange between the lungs and blood. Mortality Risk: The proportion of people who die from a medical condition (in this case, hypoxaemia) compared to the total population being studied. Hypoxaemia: A condition in patients characterised by low levels of oxygen in the blood. Systematic Review: A method of literature review conducted systematically to answer a clinical question, involving searching, data extraction, appraisal and analysis. Meta-Analysis: A quantitative statistical method that combines the results of multiple studies to determine an overall effect. Forest Plot: A graphical representation of the combined results of studies in a meta-analysis. Random-Effects Model: A statistical method in meta-analysis that assumes the true effect varies between studies. Common-

Effect Model: A statistical method in meta-analysis that uses a common effect size across studies. **Heterogeneity:** The differences or variability between studies included in a meta-analysis.

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Author contributors

MR and DS: Conceptualisation. AFI, GA and SRA: Data curation. AFI and GA: Formal analysis. AFI, GA and SRA: Investigation. AFI and EW: Methodology. MR and DS: Project administration. MR, DS and AFI: Resources. AFI and EW: Software. MR, DS, EW and EB: Supervision. AFI, GA and SRA: Validation. AFI and EW: Visualisation. AFI, GA and SRA: Writing – original draft. Writing – review and editing by all authors. All authors contributed and approved the submitted version.

Informed Consent Statement

No informed consent was necessary.

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Declaration of interest

The authors declare no conflict of interest.

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Supplementary Materials

Table S1. Hospital setting and details of mortality risk.

No.	Author, year	Hospital setting and measurement process	Definition of mortality
1	Amin et al. (2016) (15)	Hospital setting: Single point, unspecified inpatient setting Treatment prior to measurement: Yes Measurement process: arterial blood gas test Additional information: -	- Mortality type by cause: cause-specific mortality - Mortality type by interval: 28-day mortality
2	Elhidsi and Rasmin (2021) (16)	Hospital setting: unspecified point at ED Treatment prior to measurement: Yes Measurement process: pulse oximetry and arterial blood gas test Additional information: -	- Mortality type by cause: cause-specific mortality, in-hospital mortality - Mortality type by interval: 30-day mortality
3	Made Reditya Noviyani et al. (2020) (17)	Hospital setting: Single point at the PICU Treatment prior to measurement: Yes Measurement process: pulse oximetry or arterial blood gas test Additional information: -	- Mortality type by cause: cause-specific mortality - Mortality type by interval: N/A
4	Nugraha et al. (2022) (18)	Hospital setting: Single point at ICU Treatment prior to measurement: Yes Measurement process: arterial blood gas test Additional information: -	- Mortality type by cause: cause-specific mortality - Mortality type by interval: 28-day mortality
5	Nugrahani and Fauzi (2022) (14)	Hospital setting: unspecified point, Non-ICU and ICU setting Treatment prior to measurement: N/A Measurement process: pulse oximetry Additional information: -	- Mortality type by cause: cause-specific mortality - Mortality type by interval: N/A
6	Rasmin et al. (2018) (8)	Hospital setting: unspecified point, unspecified inpatient setting Treatment prior to measurement: Yes Measurement process: arterial blood gas test Additional information: -	- Mortality type by cause: cause-specific mortality, in-hospital mortality - Mortality type by interval: N/A
7	Rasmin et al. (2021) (10)	Hospital setting: Single point, unspecified inpatient setting Treatment prior to measurement: Yes (initial treatment at the ED) Measurement process: pulse oximetry and arterial blood gas test Additional information: -	- Cause of the mortality: cause-specific mortality, in-hospital mortality - Interval of mortality: unspecified interval
8	Valentania et al. (2021) (19)	Hospital setting: Single point, unspecified inpatient setting Treatment prior to measurement: N/A Measurement process: Pulse oximetry Additional information: -	- Cause of the mortality: cause-specific mortality, in-hospital mortality - Interval of mortality: unspecified interval

ED, Emergency Department; ICU, Intensive Care Unit; N/A, Not Applicable; PICU, Pediatric Intensive Care Unit.

Table S2. Full search terms for journal databases.

Database	Keyword
MEDLINE	((("hypoxaemia"[All Fields] OR "hypoxia"[MeSH Terms] OR "hypoxia"[All Fields] OR "hypoxemia"[All Fields] OR "hypoxemias"[All Fields] OR ("hypoxaemia"[All Fields] OR "hypoxia"[MeSH Terms] OR "hypoxia"[All Fields] OR "hypoxemia"[All Fields] OR "hypoxemias"[All Fields]) OR ("hypoxia"[MeSH Terms] OR "hypoxia"[All Fields] OR "hypoxia s"[All Fields] OR "hypoxias"[All Fields]) OR ("hypoxia"[MeSH Terms] OR "hypoxia"[All Fields] OR "anoxemia"[All Fields]) OR ("hypoxia"[MeSH Terms] OR "hypoxia"[All Fields] OR "anoxia"[All Fields]) OR ("hypoxia"[MeSH Terms] OR "hypoxia"[All Fields] OR "oxygen"[All Fields] AND "deficiencies"[All Fields]) OR "oxygen deficiencies"[All Fields]) OR ("hypoxia"[MeSH Terms] OR "hypoxia"[All Fields] OR "oxygen"[All Fields] AND "deficiency"[All Fields]) OR "oxygen deficiency"[All Fields])) AND (Indonesia)) AND (((((((Prevalence) OR (Prevalences)) OR (Period Prevalences)) OR (Period Prevalence)) OR (Point Prevalences)) OR (Point Prevalence)) OR (((((((Incidence) OR (Secondary Attack Rate)) OR (Secondary Attack Rates)) OR (Cumulative Incidence)) OR (Cumulative Incidences)) OR (Attack Rates)) OR (Attack Rate)) OR (Incidence Proportion)) OR (Incidence Proportions)) OR (Incidences)) OR (Person-time Rate)) OR (Incidence Rate)) OR (Person time Rate)) OR (Incidence Rates)) OR (Person-time Rates))) OR (((((((((((Mortality risk) OR (Age-Specific Death Rate)) OR (Age-Specific Death Rates)) OR (Excess Mortality)) OR (Excess Mortalities)) OR (Mortality Determinant)) OR (Mortality Determinants)) OR (Differential Mortality)) OR (Differential Mortalities)) OR (CFR Case Fatality Rate)) OR (Case Fatality Rate)) OR (Case Fatality Rates)) OR (Mortalities)) OR (Crude Death Rate)) OR (Crude Mortality Rates)) OR (Crude Death Rates)) OR (Crude Mortality Rate)) OR (Mortality Rate)) OR (Mortality Rates)) OR (Death Rate)) OR (Death Rates)) OR (Mortality Declines)) OR (Mortality Decline)))
Embase	#1 Hypoxaemia OR Hypoxemia OR Hypoxia OR Anoxemia OR Anoxia OR 'Oxygen Deficiencies' OR 'Oxygen Deficiency' #2 Prevalence OR Prevalences OR 'Period Prevalences' OR 'Period Prevalence' OR 'Prevalence, Period' OR 'Point Prevalences' OR 'Prevalence, Point' OR 'Point Prevalence' #3 Incidence OR 'Secondary Attack Rate' OR 'Rate, Secondary Attack' OR 'Secondary Attack Rates' OR 'Attack Rate, Secondary' OR 'Proportion, Incidence' OR 'Incidence, Cumulative' OR 'Cumulative Incidence' OR 'Cumulative Incidences' OR 'Attack Rates' OR 'Attack Rate' OR 'Incidence Proportion' OR 'Incidence Proportions' OR 'Rate, Attack' OR Incidences OR 'Person-time Rate' OR 'Rate, Incidence' OR 'Incidence Rate' OR 'Rate, Person-time' OR 'Person time Rate' OR 'Incidence Rates' OR 'Person-time Rates' #4 'Mortality risk' OR 'Age-Specific Death Rate' OR 'Death Rate, Age-Specific' OR 'Age-Specific Death Rates' OR 'Age Specific Death Rate' OR 'Rate, Age-Specific Death' OR 'Excess Mortality' OR 'Excess Mortalities' OR 'Mortality, Excess' OR 'Mortality Determinant' OR 'Determinants, Mortality' OR 'Mortality Determinants' OR 'Determinant, Mortality' OR 'Mortality, Differential' OR 'Differential Mortality' OR 'Differential Mortalities' OR 'Rates, Case Fatality' OR 'CFR' OR 'Case Fatality Rate' OR 'Rate, Case Fatality' OR 'Case Fatality Rate' OR 'Case Fatality Rates' OR Mortalities OR 'Crude Death Rate' OR 'Crude Mortality Rates' OR 'Rate, Crude Death' OR 'Crude Death Rates' OR 'Death Rate, Crude' OR 'Mortality Rate, Crude' OR 'Crude Mortality Rate' OR 'Rate, Crude Mortality' OR 'Mortality Rates' OR 'Rate, Death' OR 'Mortality Rates' OR 'Death Rate' OR 'Rate, Mortality' OR 'Death Rates' OR 'Mortality Declines' OR 'Decline, Mortality' OR 'Mortality Decline' #5 #2 OR #3 OR #4 #6 Indonesia #1 AND #5 AND #6
CENTRAL	#1 ((((Hypoxaemia) OR (Hypoxemia)) OR (Hypoxia)) OR (Anoxemia)) OR (Anoxia)) OR (Oxygen Deficiencies)) OR (Oxygen Deficiency) #2 Indonesia #3 ((((Prevalence) OR (Prevalences)) OR (Period Prevalences)) OR (Period Prevalence)) OR (Point Prevalences)) OR (Point Prevalence) #4 ((((((((Incidence) OR (Secondary Attack Rate)) OR (Secondary Attack Rates)) OR (Cumulative Incidence)) OR (Cumulative Incidences)) OR (Attack Rates)) OR (Attack Rate)) OR (Incidence Proportion)) OR (Incidence Proportions)) OR (Incidences)) OR (Person-time Rate)) OR (Incidence Rate)) OR (Person time Rate)) OR (Incidence Rates)) OR (Person-time Rates) #5 ((((((((((((Mortality risk) OR (Age-Specific Death Rate)) OR (Age-Specific Death Rates)) OR (Age Specific Death Rate)) OR (Excess Mortality)) OR (Excess Mortalities)) OR (Mortality Determinant)) OR (Mortality Determinants)) OR (Differential Mortality)) OR (Differential Mortalities)) OR (CFR Case Fatality Rate)) OR (Case Fatality Rate)) OR (Case Fatality Rates)) OR (Mortalities)) OR (Crude Death Rate)) OR (Crude Mortality Rates)) OR (Crude Death Rates)) OR (Crude Mortality Rate)) OR (Mortality Rate)) OR (Mortality Rates)) OR (Death Rate)) OR (Death Rates)) OR (Mortality Declines)) OR (Mortality Decline)

(Continued)

Table S2. Continued

Database	Keyword
	#6 (((((Prevalence) OR (Prevalences)) OR (Period Prevalences)) OR (Period Prevalence)) OR (Point Prevalences)) OR (Point Prevalence)) OR (((((((((((Incidence) OR (Secondary Attack Rate)) OR (Secondary Attack Rates)) OR (Cumulative Incidence)) OR (Cumulative Incidences)) OR (Attack Rates)) OR (Attack Rate)) OR (Incidence Proportion)) OR (Incidence Proportions)) OR (Incidences)) OR (Person-time Rate)) OR (Incidence Rate)) OR (Person time Rate)) OR (Incidence Rates)) OR (Person-time Rates))) OR (((((((((((((((Mortality risk) OR (Age-Specific Death Rate)) OR (Age-Specific Death Rates)) OR (Age Specific Death Rate)) OR (Excess Mortality)) OR (Excess Mortalities)) OR (Mortality Determinant)) OR (Mortality Determinants)) OR (Differential Mortality)) OR (Differential Mortalities)) OR (CFR Case Fatality Rate)) OR (Case Fatality Rate)) OR (Case Fatality Rates)) OR (Mortalities)) OR (Crude Death Rate)) OR (Crude Mortality Rates)) OR (Crude Death Rates)) OR (Crude Mortality Rate)) OR (Mortality Rate)) OR (Mortality Rates)) OR (Death Rate)) OR (Death Rates)) OR (Mortality Declines)) OR (Mortality Decline)) #1 AND #2 AND #6
Scopus	((ALL((Hypoxaemia OR Hypoxemia OR Hypoxia OR Anoxemia OR Anoxia OR (Oxygen Deficiencies) OR (Oxygen Deficiency))) AND ALL((Prevalence OR Prevalences OR (Period Prevalences) OR (Period Prevalence) OR (Prevalence, Period) OR (Point Prevalences) OR (Prevalence, Point) OR (Point Prevalence) OR Incidence OR (Secondary Attack Rate) OR (Rate, Secondary Attack) OR (Secondary Attack Rates) OR (Attack Rate, Secondary) OR (Proportion, Incidence) OR (Incidence, Cumulative) OR (Cumulative Incidence) OR (Cumulative Incidences) OR (Attack Rates) OR (Attack Rate) OR (Incidence Proportion) OR (Incidence Proportions) OR (Rate, Attack) OR Incidences OR (Person-time Rate) OR (Rate, Incidence) OR (Incidence Rate) OR (Rate, Person-time) OR (Person time Rate) OR (Incidence Rates) OR (Person-time Rates) OR (Mortality risk) OR (Age-Specific Death Rate) OR (Death Rate, Age-Specific) OR (Age-Specific Death Rates) OR (Age Specific Death Rate) OR (Rate, Age-Specific Death) OR (Excess Mortality) OR (Excess Mortalities) OR (Mortality, Excess) OR (Mortality Determinant) OR (Determinants, Mortality) OR (Mortality Determinants) OR (Determinant, Mortality) OR (Mortality, Differential) OR (Differential Mortality) OR (Differential Mortalities) OR (Rates, Case Fatality) OR (CFR) OR (Case Fatality Rate) OR (Rate, Case Fatality) OR (Case Fatality Rate) OR (Case Fatality Rates) OR Mortalities OR (Crude Death Rate) OR (Crude Mortality Rates) OR (Rate, Crude Death) OR (Crude Death Rates) OR (Death Rate, Crude) OR (Mortality Rate, Crude) OR (Crude Mortality Rate) OR (Rate, Crude Mortality) OR (Mortality Rate) OR (Rate, Death) OR (Mortality Rates) OR (Death Rate) OR (Rate, Mortality) OR (Death Rates) OR (Mortality Declines) OR (Decline, Mortality) OR (Mortality Decline))) AND ALL(Indonesia)))

Table S3. JBI risk of bias assessment of prevalence studies.

No.	Author, year	Outcome	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there an appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall appraisal
1	Amin et al. (2016) (15)	Mortality risk	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
2	Elhidi et al. (2021) (16)	Mortality risk	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
3	Made Reditya Noviyani et al., (2020) (17)	Mortality risk	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
4	Nugraha et al. (2022) (18)	Mortality risk	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
5	Nugrahani and Fauzi (2022) (14)	Prevalence/incidence, mortality risk	Yes	Yes	No	Yes	Yes	Unclear	Unclear	Yes	Yes	Excluded from quantitative analysis due to inadequate sample size
6	Rasmin et al. (2018) (8)	Mortality risk	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
7	Rasmin et al. (2021) (10)	Mortality risk	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
8	Valentania et al. (2021) (19)	Prevalence/incidence, mortality risk	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include

JBI, Joanna Briggs Institute.