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BMJ Open Factors associated with prehospital and inhospital delays in acute ischaemic stroke care in Indonesia: a systematic review

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To cite: Wiyarta E, Hidayat R, Kurniawan M, et al. Factors associated with prehospital and in-hospital delays in acute ischaemic stroke care in Indonesia: a systematic review. BMJ Open 2025;15:e095845. doi:10.1136/ bmjopen-2024-095845

Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/ bmjopen-2024-095845).

Received 30 October 2024 Accepted 27 February 2025



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ABSTRACT

Objectives This systematic review examines prehospital and in-hospital delays in acute stroke care in Indonesia. Design Systematic review adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Data sources We conducted a thorough search across 11 databases, ClinicalTrials.gov registries and three preprint repositories up until October 2024.

Eligibility criteria Studies that examined risk variables associated with hospital delays in the treatment of acute stroke in Indonesian individuals were included.

Data extraction and synthesis Two reviewers each carried out the data extraction and risk-of-bias evaluation separately. The quality of the study was evaluated using the Risk of Bias in Non-randomised Studies of Exposures tool. The 'combining p values' approach and albatross plots were used to synthesise the findings.

Results A total of 27 studies with 3610 patients were included. Key factors contributing to prehospital delays included low educational level (p=0.014, 6 studies). low socioeconomic status (p=0.003, 5 studies), cultural beliefs affecting decision-making (p<0.001, 3 studies), significant clinical manifestations such as a low Glasgow Coma Scale score (<8) (p<0.001, 2 studies) and a high National Institutes of Health Stroke Scale score (>16) (p=0.002, 5 studies) and transportation challenges, such as extended travel distance (>15 km) (p=0.009, 5 studies) and lack of ambulance use (p=0.005, 9 studies). Inhospital delays were prominent, with male sex (p=0.046), dyslipidaemia (p=0.045) and arrival time (p=0.007) linked to thrombolysis delays, while CT location affected door-to-CT time (p<0.05).

Conclusion Socioeconomic, cultural, clinical severity and logistical factors were significantly associated with hospital delays in acute ischaemic stroke care in Indonesia. Targeted interventions can mitigate these challenges and improve stroke management and results. PROSPERO registration number CRD42024494954.

INTRODUCTION

Globally, stroke affects approximately 15 million people each year, with 5 million deaths and another 5 million permanently disabled. In Indonesia, the prevalence of stroke is alarmingly high, with an estimated 8.2 per 1000 of the population, translating

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The study employed a thorough search strategy across multiple databases, which ensured a wideranging collection of relevant literature.
- ⇒ Data extraction and risk-of-bias assessments were performed separately by two reviewers, therefore reducing subjective bias and enhancing the reliability of the results.
- ⇒ The study may be subject to publication bias, as only published studies were included.
- ⇒ The quality of included studies varied, which may affect the overall robustness.

to roughly 1.2 million cases annually.2 The primary risk factors for stroke in Indonesia include hypertension, diabetes mellitus, dyslipidaemia, smoking and obesity. A 2018 basic health research study in Indonesia found that 45.9% of patients with stroke had hypertension, 20.3% had diabetes, 29.4% had dyslipidaemia, 28.7% were smokers and 23.1% were obese.

The urgency of timely stroke intervention is underscored by the concept of the 'golden hour', a window of opportunity during which treatment is most effective. This critical period, typically the first 60 min after the onset of stroke symptoms, is when interventions such as intravenous thrombolysis are most beneficial.^{4 5} However, numerous barriers impede prompt medical attention, particularly in regions with limited healthcare infrastructure. In Indonesia, various sociocultural, economic and logistical challenges further complicate timely access to stroke care. Previous studies have highlighted factors such as lack of awareness about stroke symptoms, delays in seeking medical help, transportation issues and inefficiencies within hospital workflows as significant contributors to treatment delays. 78

This systematic review aims to comprehensively analyse the factors associated with prehospital and in-hospital delays in



acute stroke management in Indonesia. By synthesising the available evidence, we seek to identify key areas for intervention to reduce these delays and improve clinical outcomes for patients with stroke.

METHODS

Research question

This study was reported in accordance with the Metaanalysis of Observational Studies in Epidemiology guidelines and is registered in PROSPERO (CRD42024494954). The research question was framed according to the Population-Exposure-Comparator-Outcomes (PECO) framework:⁹

- ► Population: adults (≥18 years) in Indonesia presenting with acute stroke (ischaemic or haemorrhagic).
- Exposure:
 - Prehospital factors, such as lack of awareness about stroke symptoms, delay in decision to seek medical help, inaccessibility of transportation, distance to healthcare facilities, socioeconomic factors and cultural beliefs and practices.
 - In-hospital factors, such as triage processes, availability of stroke specialists, diagnostic delays (eg, waiting times for imaging), hospital protocol workflow efficiency and hospital resource availability.
- ► Comparator: none.
- Outcomes:
 - Duration of prehospital delay: time from symptom onset to arrival at a healthcare facility.
 - Duration of in-hospital delay: time from hospital arrival to the initiation of appropriate medical intervention (eg, thrombolysis, imaging and surgery).
 - Secondary outcomes: impact of delays on clinical outcomes such as stroke severity, recovery rate or mortality.

Search strategy

Published studies from inception until 13 October 2024 were retrieved from PubMed, Cochrane CENTRAL, Ovid Embase, EBSCOhost, Scopus, ProQuest, MedRxiv, bioRxiv, SSRN, ClinicalTrials.gov, Garuda, PsycInfo, PsycNet, Web of Science and Google Scholar. Keywords used included 'stroke', 'cerebrovascular accident', 'prehospital' and 'in-hospital'. The comprehensive search strategies and a complete list of keywords are available in online supplemental file S1. Reference lists were screened to identify additional literature using citation chasing techniques, including reference list scanning of included studies and previous reviews, as well as backward and forward citations of included studies.

Eligibility criteria

Studies were eligible if they met the following criteria: (1) patients aged 18 years or older in Indonesia, (2) patients diagnosed with acute stroke, (3) studies that specifically investigated risk factors affecting prehospital or in-hospital delays in acute stroke management, (4) studies with

an appropriate control group, (5) studies with observational methodological design, including cohort, case-control and cross-sectional studies and (6) studies in Indonesian or English language. The exclusion criteria were: (1) animal studies, (2) duplicate publications, (3) full-text article not available, (4) systematic reviews, meta-analyses, conferences, letters and case reports or series and (5) studies presented in abstract form, without relevant data on prehospital or in-hospital delays.

Data extraction

Titles and abstracts were initially reviewed using EndNote to exclude articles not meeting the eligibility criteria. The remaining articles were examined thoroughly to determine their inclusion in the systematic review or meta-analysis. The screening was conducted independently by two authors (EW and GHPS). Disagreements were resolved through discussion until a consensus was reached. Data from each study were extracted independently using a data extraction sheet covering: (1) baseline demographics (author, year of publication, location and study setting); (2) study population (sample size and characteristics of acute patients with stroke); (3) prehospital and in-hospital risk factors associated with stroke management delays and (4) outcome measures (primary outcome related to stroke management delay and secondary outcomes, including stroke severity, recovery rate or mortality).

Risk of bias assessment

The quality of the included studies was assessed independently by all authors using the preliminary Risk of Bias in Non-randomised Studies of Exposures (ROBINS-E) tool. Seven domains were evaluated: (1) bias due to confounding; (2) bias in selecting participants; (3) bias in exposure classification; (4) bias due to departures from intended exposures; (5) bias due to missing data; (6) bias in outcome measurement and (7) bias in the selection of reported results. Each domain was characterised as low, some concerns, high or very high risk of bias. In case of disagreement between assessors, the rating with the majority approval was assigned.

Data synthesis and statistical methods

Meta-analyses could not be undertaken due to the heterogeneity of interventions, settings, study designs and outcome measures. Albatross plots were created to provide a graphical overview of the data for interventions with more than five data points for an outcome. These plots allow p values to be interpreted in the context of the study sample size. Effect contours show a risk ratio (RR) for a given p value and study size, providing an indication of the overall magnitude of any association. ¹¹

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this systematic review.



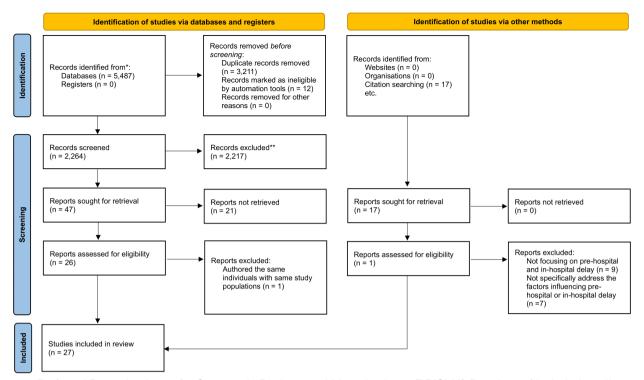


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of included studies. *Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

RESULTS

The initial database search yielded 5487 articles, from which 3211 duplicates were removed and 12 records were marked as ineligible by automation tools, resulting in 2264 studies for initial screening. After screening the titles and abstracts, 2217 studies were excluded, with 21 studies not retrieved, leaving 26 studies assessed for full-text eligibility. Additionally, 17 studies were identified through citation searching. Following full-text reviews, a total of 16 articles were excluded, leaving only 1 article from the citation search included in the final review, resulting in 27 studies that met the criteria for inclusion in the systematic review. A total of 27 studies with 3610 participants were included. The PRISMA flowchart detailing this process is presented in figure 1.

Study demographics

The characteristics of the included studies are detailed in online supplemental file S2. Most studies (18 out of 27) employed a cross-sectional design, with the remainder being retrospective (7 out of 27) and prospective cohort studies (2 out of 27). Sample sizes varied from 30 to 1060 participants. The majority of the studies were conducted on Java Island (17 out of 27), with the rest being carried out in Kalimantan (4 out of 27), Sulawesi (3 out of 27), Sumatra (2 out of 27) and Maluku (1 out of 27). Most studies were conducted in secondary hospitals (12 out of 27), followed by tertiary (9 out of 27) and primary hospitals (3 out of 27). Three studies took place in mixed

settings, combining tertiary and secondary hospitals (3 out of 27).

Risk of bias

Online supplemental files S3 and S4 summarise the results of the risk of bias assessment according to the ROBINS-E tool. Among the 27 studies, 2 studies (7.4%) had a very high risk of bias, 15 studies (55.6%) had a high risk of bias, 8 studies (29.6%) had some concerns regarding risk of bias and 2 studies (7.4%) had a low overall risk of bias. Most of the high risk of bias was due to the lack of analysis to adjust for selection between groups. The very high risk of bias was attributed to improperly defined outcome assessments.

Duration of prehospital delay

The included studies have defined prehospital delay using various time intervals, ranging from less than 60 min ¹² to more than 48 hours. ^{13 14} Most studies classify the time interval dichotomously into early and late based on their respective 'golden time' cut-off points at 60 min, ¹² 3 hours, ¹⁵⁻²² 3.5 hours, ²³ 4 hours, ¹⁴ 4.5 hours ²⁴⁻²⁶ or even 24 hours. ²⁷ Several studies also categorised prehospital delay into multiple outcome groups ^{13 14 28-31} or continuous outcomes. ^{10 23} Notably, two studies did not provide a specific time interval. ^{32 33}

The analysis of prehospital delays was conducted across several subgroups: demographic factors, patient background factors, clinical manifestation factors, family

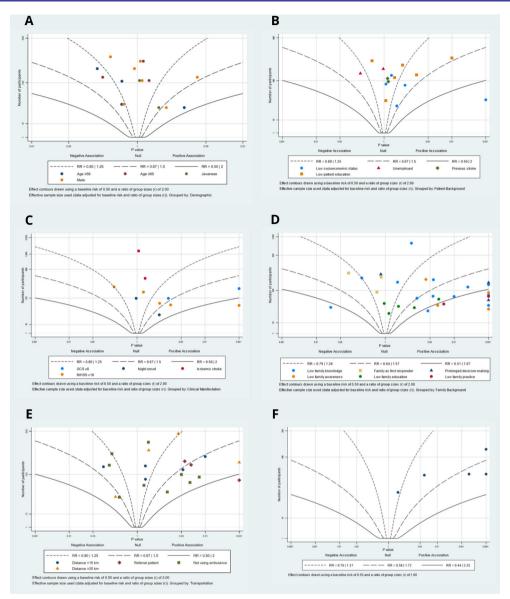


Figure 2 Albatross plots illustrating various associations with hospital delay: (A) demographic factors, (B) patient background, (C) clinical manifestations, (D) family background, (E) transportation risk factors and (F) impact of delays on worsened clinical outcomes. GCS, Glasgow Coma Scale; NIHSS, National Institutes of Health Stroke Scale and RR, risk ratio.

background factors and transportation factors. Due to the heterogeneity of outcome measures, an albatross plot was generated. In this plot, each point represents a single study, with the p value plotted against the total sample size of each study. Contour lines indicate the risk ratio (RR).

The albatross plot for demographic factors showed that all studies clustered around the null line, indicating no significant association between age (≥ 56 or ≥ 65 years), female sex or Javanese ethnicity (figure 2A). When p values were combined, there was no effect of age ≥ 56 years (p=0.554, 4 studies), age ≥ 65 years (p=0.710, 3 studies), female sex (p=0.306, 7 studies) or Javanese ethnicity (p=0.305, 2 studies) in any of the trials.

For patient background factors, most studies clustered around the null line, indicating no significant effect of unemployment (p=0.828, 2 studies) and previous stroke

history (p=0.430, 2 studies). However, significant positive associations were identified between low economic status¹⁷ (p=0.003, 5 studies) and low patient education²⁷ (p=0.014, 6 studies) with prehospital delay (figure 2B). While the combined p value indicated strong evidence of an association, only one study in each category reported a statistically significant effect. Ishak *et al* reported a significantly weak correlation coefficient (-0.452, p<0.01), suggesting that better economic status was associated with shorter delay times to the emergency room. ¹⁷ Conversely, Barahama *et al* reported a significant association between patients who had graduated high school and those who had not, suggesting that low patient education could serve as a predictor for prehospital delay.²⁷

For clinical manifestation factors, most studies clustered around the null line, indicating that most associations were not significant between ischaemic stroke (p=0.395,



2 studies) and night onset (p=0.226, 2 studies). However, there was strong evidence of prehospital delay associated with a Glasgow Coma Scale (GCS) score of less than 8 (p<0.001, 2 studies) and a National Institutes of Health Stroke Scale (NIHSS) score greater than 16 (p=0.002, 5 studies) (figure 2C).

The Albatross plot for family background factors (figure 2D) showed that most studies reporting family background factors clustered around the positive segment of the plot, indicating a positive association with higher prehospital delay. However, there was no effect of family as the first responder for prehospital delay in any of the studies (p=0.904, 3 studies). ²¹ ²³ ²⁹

Low family knowledge, defined as a limited family understanding of early stroke symptoms and the risk factors, was strongly associated with prehospital delay (p<0.001, 13 studies). Among the 13 studies that reported low family knowledge, 8 showed a significantly higher risk of prehospital delay. Is 15 17 23 24 32-34 However, Welerubun and Tarihoran found a negative association in the plot. Despite reporting a significant difference between decision-makers' knowledge about early stroke signs and patient arrival times in National Brain Center Hospital (p=0.016), on recalculating the OR for poor knowledge, Welerubun and Tarihoran found an OR of 0.13 (95% CI 0.02 to 0.78, p=0.026), indicating a lower risk of prehospital delay. These contradictory findings may stem from small sample bias in the study.

Low family awareness refers to a lack of attentiveness within a family regarding the severity of symptoms or the need for urgent action in a medical emergency. There was also strong evidence of prehospital delay with low family awareness in at least one study (p<0.001, 4 studies). Among the three out of four studies that reported a significant association between low family awareness and prehospital delay, ¹⁷ ²⁴ ³² Minalloh *et al* initially reported no significant association (p=0.066). However, after adjustment in multivariate logistic regression analysis, unawareness of symptom severity (OR=11.025; p=0.007) was significantly associated with a prehospital delay exceeding 3.5 hours.²³

Low family education refers to the lack of formal education or lower educational attainment within a family. While most studies reported a non-significant association, the combined p value resulted in strong evidence of prehospital delay in at least one study (p=0.028, 5 studies). Only Kurnia *et al* demonstrated a significant association with a prehospital delay exceeding 3 hours when data were transformed to distinguish between those with and without a college degree (OR 3.42, p=0.028). This suggests that the level of education within a family might play a role in determining the promptness of seeking medical care during emergencies.

There was also strong evidence of prehospital delay with prolonged decision-making (p<0.001, 3 studies). Two studies highlighted that prolonged decision-making is linked to longer prehospital delays. Ishak *et al*¹⁷ reported a correlation of –0.816, indicating that better decision-making was associated with shorter delay times, while

Rahmawan *et al*^{β 4} found an immediate correlative score of 0.509, indicating that more stages in decision-making led to longer intervals before patients departed for medical care. Both studies also identified indigenous belief as a major factor for prolonged decision-making, with families often attributing the patient's condition to voodoo magic and opting for alternative medicine experts. ^{17 34} This implicates the importance of understanding cultural influences on healthcare decision-making processes.

Low family practice refers to inadequate health-seeking behaviours, such as not adhering to established guidelines or failing to take necessary steps during a medical emergency. There was also strong evidence of prehospital delay associated with low family practice (p<0.01, 2 studies). Ishak reported that proactive health-seeking behaviours correlated with shorter delay (ratio of group sizes (r)=-0.549, p<0.001),³⁵ while Jusuf *et al* reported that poor health-seeking behaviours had higher odds of prehospital delay (OR=32.14, p=0.02).³²

The albatross plot for transportation is depicted in figure 2E. Several studies are positioned around the positive segment of the plot, indicating a positive association between transportation factors and higher prehospital delay. There was strong evidence of prehospital delay with distances greater than 15 km (p=0.009, 5 studies) and 25 km (p=0.0014, 4 studies). However, Kosasih *et al*²⁹ and Jusuf *et al*²⁰ reported that greater distance from the emergency room correlated with lower prehospital delay. These paradoxical results may be influenced by other significant factors or low sample bias.

All referral patients were also significantly associated with higher prehospital delay (p<0.001, 3 studies). Most patients who were aware of stroke symptoms and arrived at primary centres experienced delays due to the referral system to secondary centres, where thrombolysis treatment is available. ²⁰ ²³ ³¹

The combined p value also revealed strong evidence of prehospital delay with not using an ambulance in at least one study (p=0.0052, 9 studies). Three out of nine studies reported that not using ambulances was significantly associated with prehospital delay. Despite initially reporting no significant difference between ambulance use and patient arrival times at National Brain Center Hospital (p=0.474), on recalculating the OR, Aridamayanti *et al* found an OR of 1.32 (p=0.028) for not using an ambulance, indicating higher odds of prehospital delay. 4

Duration of in-hospital delays

The time interval from the patient's arrival at the health-care facility to the initiation of appropriate treatment is critical for effective care. However, there is very little data available on in-hospital delays compared with prehospital delays, as only three studies reported on this aspect. 8 36 37 Despite this limitation, the existing studies provide valuable insights into specific factors influencing in-hospital delays. Amalia found that male sex (p=0.046), dyslipidaemia (p=0.045) and arrival onset time (p=0.007)

were independent predictors of delayed thrombolysis. These findings highlight specific factors that could influence treatment timing within the hospital.8 Rasyid et al conducted a multivariate analysis showing that the location of the CT scan was the only factor significantly associated with door-to-CT (DTC) time (OR 12.6, 95% CI 6.8 to 23.3). No significant association was found between DTC time and other factors, including sex, symptom onset, NIHSS score at admission and time of admission (whether during working hours or outside working hours). 36 Kurniawan et al analysed the time from stroke onset to puncture and time from stroke onset to recanalisation, finding no significant difference in these time intervals between patients with favourable outcomes (mRS<2) and those with unfavourable outcomes (mRS>2) (p=0.198 and 0.341, respectively). This indicates that these time intervals might not be reliable predictors of patient outcomes.³⁷

Impact of delays on clinical outcomes

There was strong evidence of worsened clinical outcomes, particularly in terms of neurological deficits, with prehospital delay in at least one study (p<0.01, 5 studies). Various grading systems were used to determine the severity of these deficits: two studies used the NIHSS, ^{16 28} two used the modified Rankin Scale(mRS)^{25 37} and one used the GCS. ¹⁸ The albatross plot for the impact of delays on clinical outcomes is depicted in figure 2F.

Kurniawan *et al* reported no significant difference in outcomes between patients with an mRS score of ≤ 2 and those with a score > 2 in relation to the time from stroke onset to treatment.³⁷ This contrasts with the findings of Okraini *et al*, who reported that longer prehospital delays were significantly associated with worse outcomes, as indicated by higher mRS scores.²⁵ The discrepancy may be due to different methods of categorising the stroke onset, with Okraini *et al* using a golden time cut-off of 4.5 hours and Kurniawan *et al* using continuous data.

Patient and healthcare provider perceptions

The study does not include the perceptions of patients and healthcare providers.

DISCUSSION

This systematic review highlights the significant factors contributing to prehospital and in-hospital delays in acute stroke management in Indonesia. The analysis of prehospital delays revealed that socioeconomic factors, cultural beliefs and lack of awareness significantly contribute to delays in seeking medical care. Socioeconomic factors, such as low educational levels and economic status, were strongly associated with prehospital delays, as patients with limited resources often faced challenges in accessing timely care. Cultural beliefs and practices, including reliance on traditional healers and prolonged decision-making processes, further exacerbated delays, particularly in rural areas. Clinical severity, indicated by low GCS and high NIHSS scores, was also linked to longer

prehospital delays, likely due to the need for specialised care and transportation. Family-related factors, such as low knowledge and awareness of stroke symptoms, played a significant role in delaying hospital arrival, as did logistical challenges, including long travel distances and the underutilisation of ambulances.

In this review, five studies identified low economic status as a significant factor associated with prehospital delay (p=0.003). Similarly, six studies found that low education levels significantly contributed to longer prehospital delays (p=0.014). These findings align with previous studies in other low and middle income countries, where socioeconomic disparities have been shown to impede timely access to stroke care.^{38 39} Cultural beliefs and practices also played a crucial role in prehospital delays. Prolonged decision-making processes, often influenced by indigenous beliefs and complementary medicine practices, were identified as significant factors. Two studies in this review reported a strong correlation between prolonged decision-making and prehospital delays (p<0.001). Ishak et al highlighted the impact of cultural beliefs on delaying medical care, where families attributed stroke symptoms to supernatural causes, opting for traditional healers before seeking hospital care. This finding is consistent with similar reports from other low to middle income countries indicating the pervasive influence of cultural practices on healthcare-seeking behaviour. ¹² Additionally, a study by Saudin et al in rural Indonesia found that 30% of patients with stroke sought alternative treatments before visiting a hospital, resulting in critical delays in receiving appropriate medical care.² These delays are comparable to those observed in other low- to middle-income countries, where cultural and socioeconomic factors often lead to significant prehospital delays.⁶

Among the clinical manifestations, there was strong evidence indicating that more severe clinical manifestations were associated with longer prehospital delays. A GCS score of less than 8 (p=0.0003, 2 studies) and an NIHSS score greater than 16 (p=0.0018, 5 studies) were significantly associated with delays. These findings suggest that patients with more severe symptoms may face additional barriers in accessing timely care, possibly due to the need for immediate and specialised transportation and care, which may not be readily available in all settings. A study by Aref et al found that higher NIHSS scores were associated with longer delays in reaching a hospital, likely due to the increased need for specialised medical transport and the challenges in recognising the urgency of the situation by family members and bystanders.⁴¹ This is consistent with our review's findings that patients with severe stroke symptoms, such as those with low GCS scores, experience significant delays in receiving care. In contrast, less severe symptoms, such as those seen in patients with minor strokes or transient ischaemic attacks, were not significantly associated with prehospital delays. This could be attributed to the less urgent perception of these symptoms by patients and their families, leading to



delays in seeking care. Nguyen-Huynh and Johnston highlighted that patients with minor stroke symptoms often underestimated the severity of their condition, resulting in delays in presentation to emergency services. 42

Strong evidence indicates that low family knowledge is associated with prehospital delays. Among the 13 studies reporting on family knowledge, eight studies showed a significantly higher risk of prehospital delay due to poor knowledge about stroke symptoms (p<0.001). For instance, Welerubun and Tarihoran reported a significant difference between decision-makers' knowledge of early stroke signs and patient arrival times at National Brain Center Hospital (p=0.016).³³ Minalloh et al initially reported no significant association (p=0.066), but after adjustment in multivariate logistic regression analysis, unawareness of symptom severity was significantly associated with prehospital delays exceeding 3.5 hours (OR=11.025, p=0.007). 43 These findings are consistent with other studies from various regions. A study by Pandian et al in India found that low family awareness and education were significant predictors of prehospital delays, similar to the findings in this review. Additionally, Mellor et al emphasised that improving family knowledge and awareness through targeted educational interventions could reduce delays and improve stroke outcomes. 44 These findings highlight the critical need for public education to improve stroke symptom recognition and response.

Transportation factors are crucial determinants of prehospital delays in acute stroke management. Interestingly, Kosasih *et al*²⁹ and Jusuf *et al*² reported paradoxical findings where greater distances from the emergency room correlated with lower prehospital delays. These contradictory results may be influenced by other significant factors, such as the availability of faster transportation methods or better infrastructure in more distant areas, or they might be due to low sample bias in the studies. Referral patients were also significantly associated with higher prehospital delays (p<0.001, 3 studies). Machin and Hamdan noted that patients aware of stroke symptoms who arrived at primary centres experienced delays due to the referral system for secondary centres, where thrombolysis treatment was available. 31

Three out of nine studies reported significant associations between not using ambulances and increased delays. Aridamayanti et al initially reported no significant difference between ambulance use and patient arrival times at National Brain Center Hospital (p=0.474). However, on recalculating the OR, they found an OR of 1.32 (p=0.028) for not using an ambulance, indicating a higher risk of prehospital delay.45 These findings are consistent with other studies in different settings. A study by Evenson et al found that patients using private transport experienced significant delays compared with those who used emergency medical services (EMSs).46 Similarly, a study by Fassbender et al demonstrated that patients transported by EMSs had significantly shorter prehospital times, emphasising the importance of using ambulances for patients with stroke.4

The time interval from a patient's arrival at a healthcare facility to the initiation of appropriate treatment, often referred to as the door-to-treatment time, is critical for effective stroke care. Rasyid et al conducted a multivariate analysis and found that the location of the CT scan was the only factor significantly associated with DTC time (OR=12.6, 95% CI 6.8 to 23.3). 36 This indicates that logistical factors within the hospital, such as the physical location of critical diagnostic equipment, play a crucial role in determining how quickly patients receive necessary imaging. Interestingly, no significant associations were found between DTC time and other factors like sex, symptom onset, NIHSS score at admission or the time of admission. Previous studies emphasise the critical role of hospital processes and infrastructure in determining treatment times. A study by Meretoja et al found that streamlined in-hospital protocols and having dedicated stroke teams significantly reduced door-to-needle times for thrombolysis, thereby improving patient outcomes.⁴⁷ Additionally, a systematic review by Emberson et al highlighted that every 15 min reduction in door-to-needle time was associated with an increase in the likelihood of a favourable outcome for patients with stroke.⁴⁸

There were several limitations within this review, such as having considerable heterogeneity in terms of study designs, populations, settings and outcome measures. Assessment of risk of bias also highlighted the significance of bias in this review, with 55.6% of the studies included having high risk of bias. Most of the studies included were also from Java Island, which might not represent the general population, culture and healthcare infrastructure in other Indonesian regions. Several of the outcomes measured were also relied on self-reported data, which are susceptible to recall and cultural bias. Future studies should apply standardised definitions and measures of time intervals for prehospital and in-hospital delays. A multicentre study with a larger sample would also improve the accuracy and representability of the studies.

The heterogeneity of study sites, including both urban and rural settings, presents a significant limitation in this review. Urban centres typically have more advanced stroke care facilities, established EMSs and greater awareness of stroke symptoms, whereas rural areas often lack these resources. These disparities likely contribute to variations in prehospital and in-hospital delays and should be explored in future studies. Future studies should stratify findings by urbanisation level, population size and strokecapable centre availability to better understand how geographical and infrastructural disparities affect prehospital and in-hospital delays. Multicentre studies in diverse settings are essential to identify factors specific to urban and rural areas and improve representativeness.

CONCLUSIONS

This systematic review comprehensively examined the factors associated with prehospital and in-hospital delays in acute stroke management in Indonesia. The findings



highlight several critical areas where targeted interventions can significantly improve stroke outcomes. Addressing the identified factors contributing to prehospital and in-hospital delays in stroke management requires a multifaceted approach. By improving public education, transportation infrastructure and hospital protocols, significant strides can be made in reducing delays and enhancing the quality of stroke care in Indonesia. Policy makers, healthcare providers and researchers must collaborate to implement and evaluate effective interventions, ultimately improving outcomes for patients with stroke.

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Acknowledgements We would like to express our gratitude to Risetku, a research consulting and data analytics organisation, for their invaluable support in facilitating this study. Their assistance in data acquisition, methodology refinement and technical guidance greatly contributed to the completion of this systematic review.

Contributors Conceptualisation, EW, RH, MK; methodology, EW, GHPS; software, EW, GHPS; validation, RH, MK; formal analysis, EW, GHPS, RAB; investigation, EW, GHPS; resources, EW; data curation, EW, RH, GHPS; writing—original draft preparation, EW, GHPS, RAB; writing—review and editing, all authors; visualisation, EW, GHPS; supervision, RH, MK; project administration, EW; funding acquisition, EW. All authors have read and agreed to the published version of the manuscript. EW is the quarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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REFERENCES

- 1 Feigin VL, Forouzanfar MH, Krishnamurthi R, et al. Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. The Lancet 2014;383:245–55.
- 2 Kusuma Y, Venketasubramanian N, Kiemas LS, et al. Burden of stroke in Indonesia. Int J Stroke 2009;4:379–80.
- 3 Health Mo. Basic Health Research 2018 (Riskesdas). Jakarta Ministry of Health, 2018.
- 4 Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med 2008;359:1317–29.

- Saver JL. Time is brain--quantified. Stroke 2006;37:263-6.
- 6 Pandian JD, William AG, Kate MP, et al. Strategies to Improve Stroke Care Services in Low- and Middle-Income Countries: A Systematic Review. Neuroepidemiology 2017;49:45–61.
- 7 Yang N, Hartanto YB. Characteristics and reasons for delayed presentation in acute ischemic stroke: single-centered study in Indonesia. Egypt J Neurol Psychiatry Neurosurg 2024;60:67.
- 8 Amalia L. Factors Affecting the Delay of intravenous Thrombolysis in Hyperacute Ischemic Stroke Patients: A Single Centre Study. Int J Gen Med 2023;16:2157–63.
- 9 Morgan RL, Whaley P, Thayer KA, et al. Identifying the PECO: A framework for formulating good questions to explore the association of environmental and other exposures with health outcomes. Environ Int 2018;121:1027–31.
- 10 Morgan RL, Thayer KA, Santesso N, et al. A risk of bias instrument for non-randomized studies of exposures: A users' guide to its application in the context of GRADE. Environ Int 2019;122:168–84.
- Harrison S, Jones HE, Martin RM, et al. The albatross plot: A novel graphical tool for presenting results of diversely reported studies in a systematic review. Res Synth Methods 2017;8:281–9.
- 12 Sumarsono E. Analisis Faktor Determinan Yang Mempengaruhi Keterlambatan Kedatangan Pasien Stroke Di Rumah Sakit Umum Daerah (RSUD) Bangil. Malang: Sekolah Tinggi Ilmu Kesehatan Widyagama Husada, 2019.
- 13 Rachmawati D, Andarini S, Ningsih DK. Pengetahuan Keluarga Berperan terhadap Keterlambatan Kedatangan Pasien Stroke Iskemik Akut di Instalasi Gawat Darurat. JKB 2017;369–76.
- 14 Ningsih DK, Andarini S, Rachmawati D. Incident Location Distance and Transportation to Hospital Delayed Arrival Patients Post-Acute Ischemic Stroke Attack in Emergency Department East Java-Indonesia. *Indian J Public Health Res Dev* 2011;11:244–9.
- 15 Ainiyah N, Izzah SR, Zahroh C, et al. FAMILY KNOWLEDGE ON PREHOSPITAL STROKE DETECTION CORRELATES WITH HOSPITAL ARRIVAL TIME IN STROKE PATIENTS AT THE NAVAL HOSPITAL DR. RAMELAN, SURABAYA. NHC 2021;1:73–81.
- 16 Astina. Hubungan Antara Waktu Rujukan Dan Tingkat Defisit Neurologis Pada Pasien Stroke Di RSUD Sultan Imanuddin Pangkalan Bun Tahun 2020. Pangkalan Bun: Sekolah Tinggi Ilmu Kesehatan Borneo Cendekia Medika, 2020.
- 17 Ishak SJ, Yueniwati Y, Kapti NRE. Factors Related about Family Delay Bring Stroke Patient to Emergency Departments of Labuha Hospital. *IJSOC* 2020;2:657–72.
- 18 Julianto J, Firdaus M, Solikin. Hubungan Prehospital Delay Dengan Tingkat Keparahan Pada Pasien Stroke Di Rumah Sakit Banjarmasin. Jour, Nurs, Invent 2022;3:108–16.
- 19 Kurnia V, Pauzi M, Gustin RK, et al. Faktor Penunjang dengan Waktu Kedatangan Keluarga Membawa Pasien Post Serangan Stroke Iskemik ke IGD RS Otak DR.drs.M. Hatta Bukittinggi Jurnal Keperawatan Cikini 2023;4:216–28.
- 20 Kusyani A. Hubungan Pengetahuan Keluarga dengan Lama Waktu Kedatangan Pasien Stroke Iskemik ke IGD RSUD Jombang. Well Being 2019;4:21–8.
- 21 Prasetyo E. Faktor-faktor yang Mempengaruhi Keterlambatan Pasien Stroke Akut Datang ke Lima Rumah Sakit Pemerintah di DKI Jakarta. MKP 2017;9:040.
- 22 Saudin D, Agoes A, Rini IS. Analisis Faktor yang Mempengaruhi Keterlambatan dalam Penanganan Pasien Stroke saat Merujuk ke RSUD Jombang. *Jurnal Hesti Wira Sakti* 2016;4:1–12.
- 23 Minalloh RH, Machin A, Mardiana W, et al. Pre-Hospital and In-Hospital Delay in Acute Ischemic Stroke Patients in Indonesia: A Multi-center Study. Indonesian Journal of Pharmacy 2022;33.
- 24 Aridamayanti B, Wahid A, Hafifah I, eds. Factors That Contribute on Golden Hour Patient Stroke (Review on the Family). 2020.
- 25 Okraini N. Hubungan Antara Ketepatan "Golden Period" Dan Derajat Kerusakan Neurologi Pada Pasien Stroke Iskemik Di Instalasi Gawat Darurat RS Stroke Nasional Bukittinggi Tahun 2018. Bukittinggi: Sekolah Tinggi Ilmu Kesehatan Perintis Padang, 2018.
- 26 Rahmina Y, Wahid A, Agustina R. TINGKAT PENDIDIKAN KELUARGA TERHADAP GOLDEN HOUR PASIEN STROKE DI RSUD ULIN BANJARMASIN. DK 2017;5:68.
- 27 Barahama DV, Tangkudung G, Kembuan M. Faktor-faktor yang Berhubungan dengan Keterlambatan Kedatangan Pasien Stroke di RSUP Prof. Dr. R. D. Kandou Manado. eCL 2019;7.
- 28 Ishariani L, Rachmania D. Hubungan Respon Time Keluarga dalam Membawa Pasien Stroke ke Pelayanan Kesehatan dengan Tingkat Keparahan Pasien Stroke. IJHS 2021;13:35–43.
- 29 Kosasih MI, Firdausi N, Yektiningsih E, et al. The Effect Of Determinant Factors In The Family On The Arrival Time Of Patients Stroke In Emergency Installation. Sjik 2020;9:44–53.



- 30 Situmorang RYS, Basuki A. Waktu Kedatangan Pasien Stroke di Bagian Penyakit Saraf Rumah Sakit Hasan Sadikin Bandung. *Journal* of Medicine and Health 2020;2.
- 31 Machin A, Hamdan M. Factors associated with onset to hospital delay among stroke patients in the emergency department. *Ind Jour of Publ Health Rese & Develop* 2018;9:1782.
- 32 Jusuf MI, Pomalango Z, Suleman I. Faktor-Faktor yang Berhubungan dengan Keterlambatan Keluarga Membawa Pasien Stroke. *Jambura Nursing Journal* 2023;5:26–38.
- 33 Welerubun IC, Tarihoran DE, eds. A study of factors that delay hospital arrival of patients with acute stroke. In: 1 st ICGH International Conference on Global Health; 2016
- 34 Rahmawan FA, Yueniwati Y, Suharsono T. PERCEPTION OF SEVERITY LEVEL AND DECISION MAKING OF FAMILY CORRELATION TOWARD DEPARTING INTERVAL OF PATIENT SUFFERING ISCHEMIC STROKE. MNJ 2020;6:63–8.
- 35 Ishak SJ. Hubungan antara faktor ekonomi dan keterlambatan keluarga dalam membawa pasien stroke ke IGD RSUD labuha kabupaten halmahera selatan.
- 36 Rasyid A, Kurniawan M, Mesiano T, et al. Performance of door-to-CT time of code stroke in Indonesian tertiary referral center hospital. Egypt J Neurol Psychiatry Neurosurg 2022;58:144.
- 37 Kurniawan M, Mulya Saputri K, Mesiano T, et al. Efficacy of endovascular therapy for stroke in developing country: A singlecentre retrospective observational study in Indonesia from 2017 to 2021. Heliyon 2024;10:e23228.
- 38 Berkhemer OA, Fransen PSS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015;372:11–20.
- 39 Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis

- of individual patient data from five randomised trials. *The Lancet* 2016;387:1723–31.
- 40 Ishak SJ, Yueniwati Y, Kapti NsRE. Factors Related about Family Delay Bring Stroke Patient to Emergency Departments of Labuha Hospital. *IJSOC* 2020;2:657–72.
- 41 Aref HM, Shokri H, Roushdy TM, et al. Pre-hospital causes for delayed arrival in acute ischemic stroke before and during the COVID-19 pandemic: A study at two stroke centers in Egypt. PLoS One 2021;16:e0254228.
- 42 Nguyen-Huynh MN, Johnston SC. Evaluation and management of transient ischemic attack: an important component of stroke prevention. *Nat Clin Pract Cardiovasc Med* 2007;4:310–8.
- 43 Rizqi Haqqum M, Abdulloh M, Wida M, et al. Pre-Hospital and In-Hospital Delay in Acute Ischemic Stroke Patients in Indonesia: A Multi-center Study. Indones J Pharm 2022;33.
- 44 Mellor RM, Bailey S, Sheppard J, et al. Decisions and delays within stroke patients' route to the hospital: a qualitative study. Ann Emerg Med 2015;65:279–87.
- 45 Aridamayanti B, Wahid A, Hafifah I, et al., eds. Factors That Contribute on Golden Hour Patient Stroke (Review on The Family). 2020.
- 46 Evenson KR, Rosamond WD, Morris DL. Prehospital and in-hospital delays in acute stroke care. Neuroepidemiology 2001;20:65–76.
- 47 Fassbender K, Balucani C, Walter S, et al. Streamlining of prehospital stroke management: the golden hour. Lancet Neurol 2013;12:585–96.
- 48 Emberson J, Lees KR, Lyden P, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. The Lancet 2014;384:1929–35.