PRE-HOSPITAL FACTORS THAT LEAD TO INCREASED MORTALITY AND MORBIDITY IN TRAUMA PATIENTS IN DEVELOPING COUNTRIES: A SYSTEMATIC REVIEW

A thesis submitted to the University of Arizona College of Medicine – Phoenix
in partial fulfillment of the requirements for the Degree of Doctor of Medicine

Gabriella Smith
Class of 2019

David Beyda, MD

Abstract

Background: Trauma is a growing global concern and the WHO estimates that injuries account for one-sixth of the global adult disease burden. Furthermore, there is a disproportionate number of trauma related deaths that occur lower middle-income countries compared to higher income countries. Studies show that deficiencies in care in preventable related deaths include pre-hospital delays, delays in treatment and inadequate resuscitation. Additionally, most trauma related deaths occur in the prehospital setting and it is in the lower to middle income countries where structured emergency medical services are lacking.

Research Question: To identify and categorize the contributing prehospital factors that lead to increased mortality and morbidity in trauma patients in developing countries.

Methods: A systematic review was performed using primary journal articles (written in English) that report pre-hospital interventions and morbidity and mortality outcomes in trauma patients in developing countries. PubMed/MEDLINE and other literature databases were used to locate these primary journal articles by utilizing combinations of search terms "developing countries (MeSH)," "Emergency Medical Services (MeSH)," "pre-hospital emergency response," and "third world countries."

Results: Our analysis found that patients who experienced a prehospital delay had an 86% increase in mortality. Regarding prehospital care, which was not a well-defined factor across all three papers, one papers found that patients who did not experience adequate prehospital care had a 226% increase in mortality while the other papers only included frequency rates of interventions and corresponding data on mortality. Regarding intubation, one study showed that prehospital intubation was associated with increased mortality compared to emergency department intubation. This study adds to the scarce literature how a lack of prehospital infrastructure is associated with an increased likelihood of mortality. It also highlights the importance and necessity of an increase in quality primary research conducted in developing countries.

Conclusion: Only prehospital delay had enough papers with data and thus was the only factor we were able to perform a meta-analysis. Our analysis found that patients who experienced a prehospital delay had an 86% increase in mortality.

Table of Contents

List of Figures and Tables

Introduction

Rationale

Trauma is a growing global concern and the World Health Organization estimates that injuries account for one-sixth of the global adult disease burden[1,2]. According to the global burden of disease study of 2010, injury accounted for 10% of deaths worldwide and 11.2% of all disability-adjusted life years[3,4]. There is a disproportionate number of trauma related deaths that occur in lower middle-income countries compared to high income countries, mostly due to the facts that in LMICs resources to deal with the trauma related disease burden are limited[1,2].

According to a recent estimate, approximately 2 million lives could be saved each year if these countries were to have the same level of trauma care as the developed world[1,2]. Additionally, rising awareness among policy-makers of the burden of injury has led to an increased need for easily quantifiable metrics to improve the allocation of resources for the treatment of injuries[3,4]. Current injury control strategies focus on primary or secondary prevention. An essential tenet of trauma care is the "golden hour," the immediate time after injury when resuscitation and stabilization will be most beneficial to the patient. Unfortunately, the capacity to provide this basic level of care is lacking in many poor countries. The lack of basic infrastructure and the relative isolation of some areas of the world provide additional challenges[5].

Objectives

This systematic review will aim to identify and categorize the contributing prehospital factors that lead to increased mortality and morbidity in trauma patients in developing countries. Variables that will be extracted from primary sources will be as followed: triage, airway management, oxygen administration, intravenous fluid administration, splinting, spinal immobilization, wound care, and patient transport time. We hypothesize that a specific subset of prehospital factors will lead to increased mortality and morbidity in trauma patients in developing countries.

Methods

Databases and Inclusion and Exclusion Criteria

PubMed/MEDLINE, EMBASE, and Cochrane were used to identify relevant peer-reviewed literature describing or evaluating prehospital emergency care in trauma patients in developing countries. The Population, Intervention, Comparison, and Outcome format was used to develop inclusion and exclusion criteria. Specifically, the populations included for analysis included studies that reported prehospital interventions or lack of interventions in trauma patients in developing countries. Interventions included triage, airway management, oxygen administration, intravenous fluid administration, splinting, spinal immobilization, wound care, and patient transport time. The outcome assessed was patient morbidity and mortality.

Keyword search strategies

The following search strings were utilized:
1.   "developing countries (MeSH) AND Emergency Medical Services (MeSH)"
2.   "(prehospital emergency response) AND "Developing Countries" [Mesh]"
3.   "prehospital intervention AND Developing Countries [MeSH]"
4.   "Prehospital Emergency Response AND Third World Countries"

Studies that were not conducted in a developing country and non-English articles were excluded after title and abstract review. Only primary journal articles published in English were included in this analysis. Articles were excluded from analysis if they did not contain any pre-hospital data and were not focused on trauma patients. At the beginning of the literature search, we did not differentiate the different types of trauma patients, but once studies were narrowed down, we refined our inclusion criteria to be traumatic injuries, excluding burns, that included patients ages >14. Consequently, there was one study that met all our inclusion criteria at the beginning, but only focused on a subset of burn trauma patients and looked at prehospital burn first aid factors. Since this did not line up with our other studies, it was excluded from this systematic review. Figure 1 is a flowchart demonstrating how articles were found and either excluded or included.
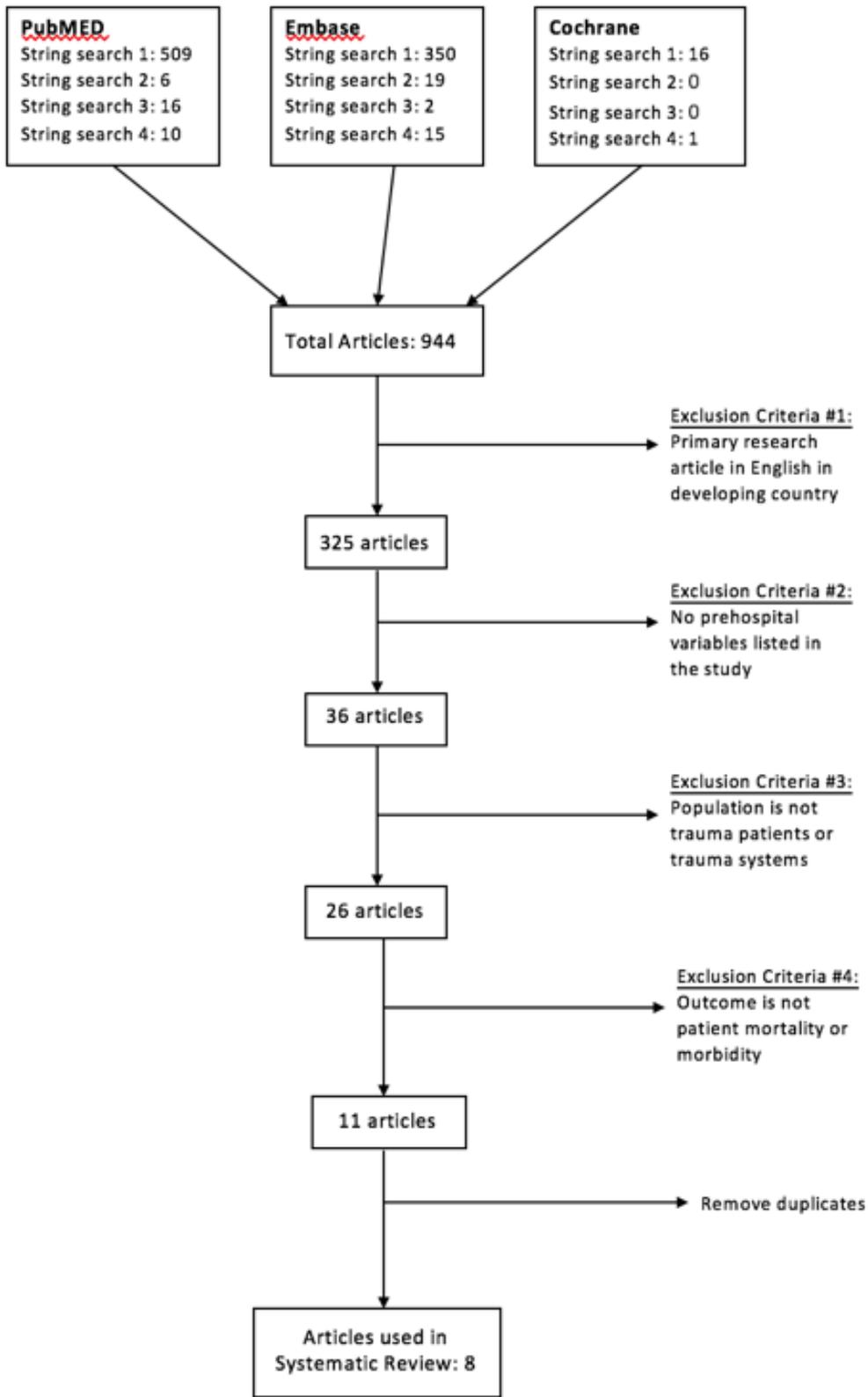
PubMED
String search 1: 509
String search 2: 6
String search 3: 16
String search 4: 10

Embase
String search 1: 350
String search 2: 19
String search 3: 2
String search 4: 15

Cochrane
String search 1: 16
String search 2: 0
String search 3: 0
String search 4: 1

Total Articles: 944

Exclusion Criteria #1:
Primary research article in English in developing country

325 articles

Exclusion Criteria #2:
No prehospital variables listed in the study

36 articles

Exclusion Criteria #3:
Population is not trauma patients or trauma systems

26 articles

Exclusion Criteria #4:
Outcome is not patient mortality or morbidity

11 articles

Remove duplicates

Articles used in Systematic Review: 8

Figure 6: Study selection

Outcomes and Analytical Approach

Studies were excluded if the title and abstract were not relevant. If title and abstract were relevant, or did not contain enough information for exclusion, then the paper was read to see if it contained all our inclusion criteria. Data from each study was extracted and used to populate an excel table that was then used to initiate analysis. Data collected included country of study, population number, type of prehospital barriers, and types of injuries. The principal outcome measured was mortality amongst the various prehospital factors. The PRIMSA guidelines were utilized in the construction of the manuscript.[22]

Results

There were eight studies that met our predefined inclusion criteria. Table 1 includes a summary of all included studies. Figure 2 shows that seven of the studies included data regarding prehospital transfer times or delays, two studies included data on intubation, and three papers had data on prehospital care, which included measures such as IV fluids, spine immobilization, and splinting. Figure 3 shows that seven of the papers had mortality as one of these outcomes, while two of the papers also included complications or disability as another outcome. Figure 4 shows the location of patient deaths, with one of the papers having data on two developing countries. P-values were calculated using the test of proportion. An asterisk denotes statistical significance following the Bonferroni Adjustment (p<0.008). The paper by Yeboah et al[2] had reported the number of patient deaths in the prehospital setting, the emergency department, the ICU, and the OR. The mortality differences between the prehospital setting and the ICU/Hospital, the ER and the ICU/Hospital, and the ICU/Hospital and OR are all statistically significant. Khan et al[6] excluded mortality data in the prehospital setting but differences between ER and ICU/Hospital mortality were statistically significant. The paper by Mock et al[7] was a comparison paper between emergency medical systems in Seattle, USA, Monterrey, Mexico, and Kumasi, Ghana. Data from Monterrey and Kumasi were included in this study as they are both Mexico and Ghana are characterized as developing economies by the United Nations WESP. Monterrey data showed that mortality differences between the prehospital setting and the ER, the ER and the ICU/Hospital, and the prehospital setting and ICU/Hospital were all statistically significant. In Kumasi, Ghana data showed that mortality differences between the prehospital setting and the ER, the ER and the ICU/Hospital, and the prehospital setting and ICU/Hospital were statistically significant. In the last study by Arreola-Risa et al[8], there was only data on mortality in the prehospital setting and in the ER. The mortality difference between these two locations was statistically significant.

Prehospital Delay

Seven of the eight papers included data on prehospital delay, with five of the papers having data that we were able to use to calculate odds ratio statistics. Prehospital delay was characterized as a time interval of greater than one hour from time of injury to the emergency department in 4 of the 5 studies. Data on transfer patients were excluded from this study. Figure 5 shows the meta-analysis data for the pooled odds ratio for the likelihood of mortality between people who experienced pre-hospital delay versus those who did not. Overall, patients who experienced a prehospital delay had an 86% increase in mortality.

In the study by Al-Thani et al[9], no data could be extracted from a prehospital time interval greater than one hour with corresponding mortality. However, we did use data that analyzed EMS scene time greater than 20 minutes and a corresponding mortality rate. Group 1 had an average total EMS time of 64.3 +/- 20.9 minutes with mortality percentage of 53%. Group 2 had an average total EMS time of 51.7 +/- 21.9 with mortality percentage of 18.5%.

Two papers did not include proper data to be included in our meta-analysis. Joosse et al[10] reported on prehospital delay as the mean hours from time of injury to ER in survivors and non-survivors. Average time from injury to ER was 8.29 +/- 20.20 hours for survivors and 1.91 +/- 2.12 hours for non-survivors. However, this difference is not statistically significant. Survivors were younger, had less physiologic derangement (as indicated by a lower RTS), and were less severely injured (as indicated by a lower ISS). A significant higher percentage of survivors underwent operation. In Mock et al[7], prehospital times were not analyzed with corresponding mortality, but it was found that 107/239 patients had prehospital delays > 1 hour in Monterrey, Mexico and 85/171 patients had prehospital delays > 1 hour in Kumasi, Ghana.

Table 1: Summary Table of Studies

| Author	Year of Publication	Study Design	Population	Types of Barriers	Injuries
Yeboah, et al	2014	Retrospective	Ghana n = 84	prehospital delay	blunt and penetrating injuries
Hashmi, et al.	2013	Prospective	Pakistan n = 1227	prehospital delay	blunt and penetrating injuries
Khan, et al.	2009	Retrospective	Pakistan n = 978	prehospital delay	blunt and penetrating injuries
Husum, et al.	2003	Prospective	Cambodia and Iraq n = 1061	prehospital trauma life support	penetrating injuries, GSW, blunt injuries, burns
Sethi, et al.	2002	Prospective	Malaysia n = 484	prehospital delays	Blunt and penetrating injuries
Joosse, et al.	2001	Prospective	Indonesia n = 97	prehospital delay and care	blunt and penetrating injuries
Mock, et al.	1998	Retrospective	USA, Mexico, Ghana n = 1348	prehospital delay, IV fluids, intubation	blunt and penetrating injuries
Al-Tahani, et al.	2014	Retrospective	Qatar n = 482	transfer time, intubation	trauma requiring intubation
Arreola-Risa, et al.	2007	Retrospective	Mexico n = 3786	IV fluid resuscitation, spinal immobilization, airway intervention	blunt trauma
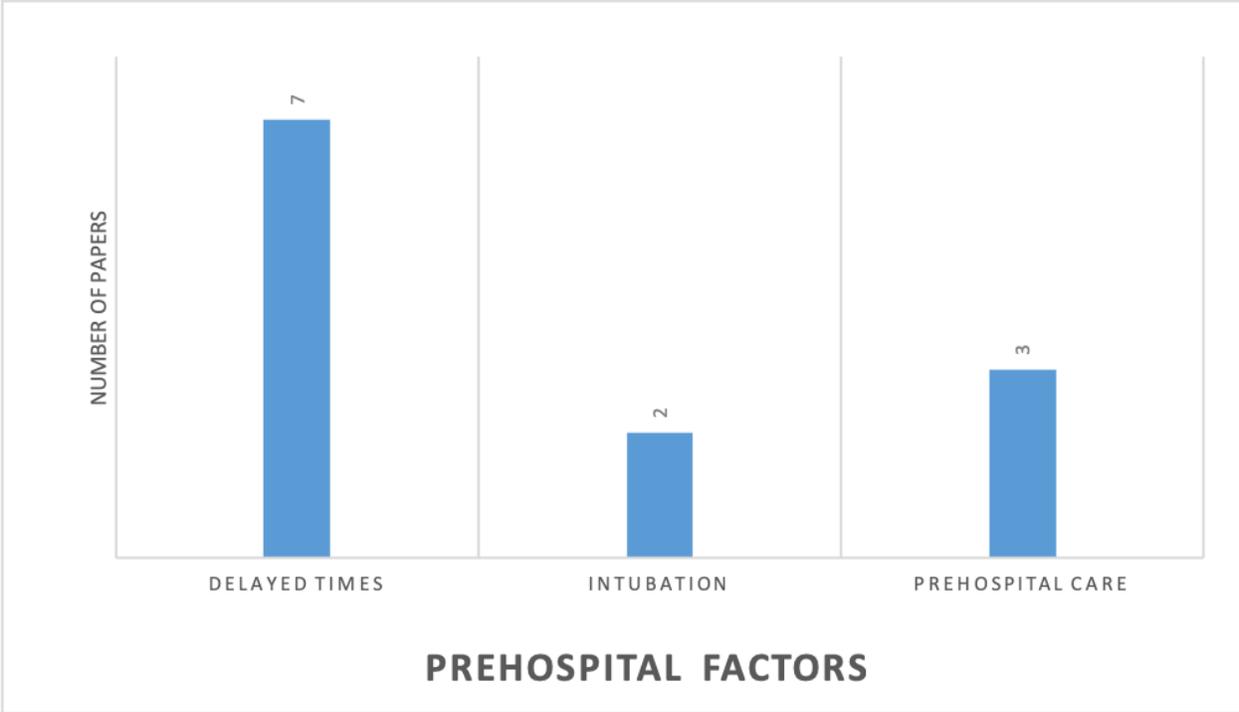
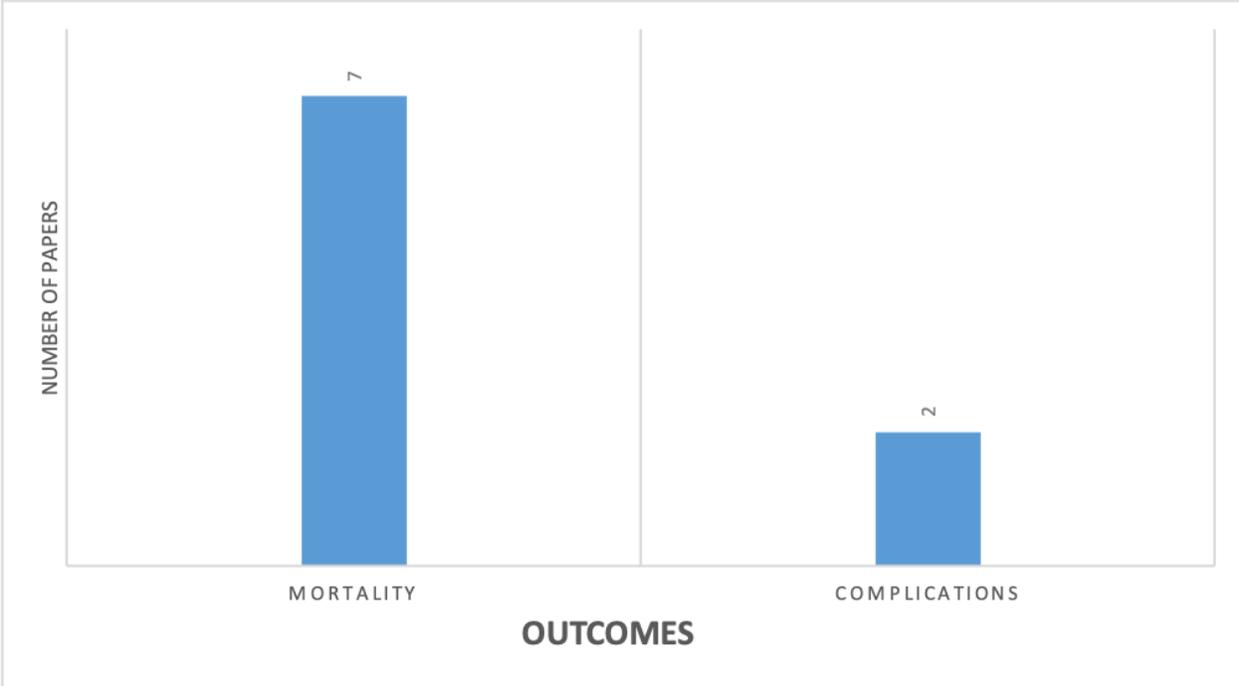*Figure 7: Prehospital factors listed as variables in papers*

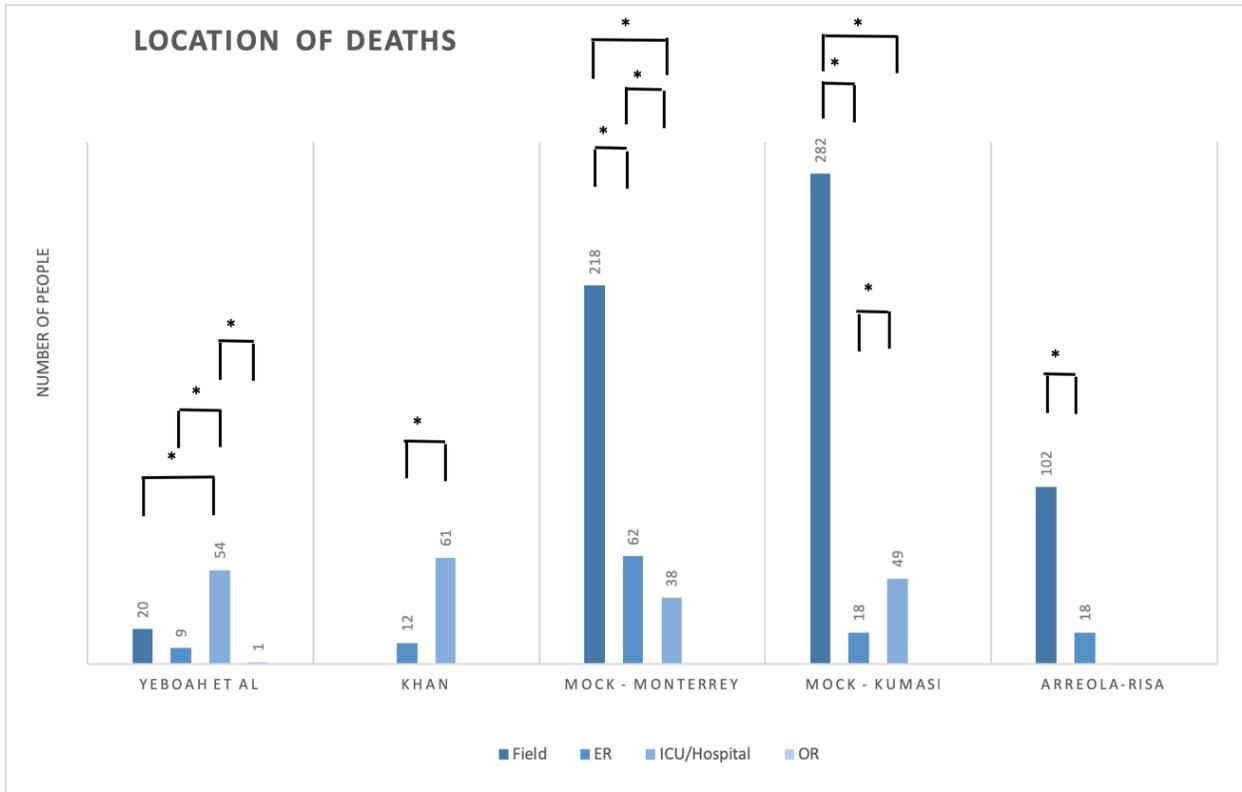*Figure 8: Number of papers that discussed patient mortality or morbidity as outcomes*
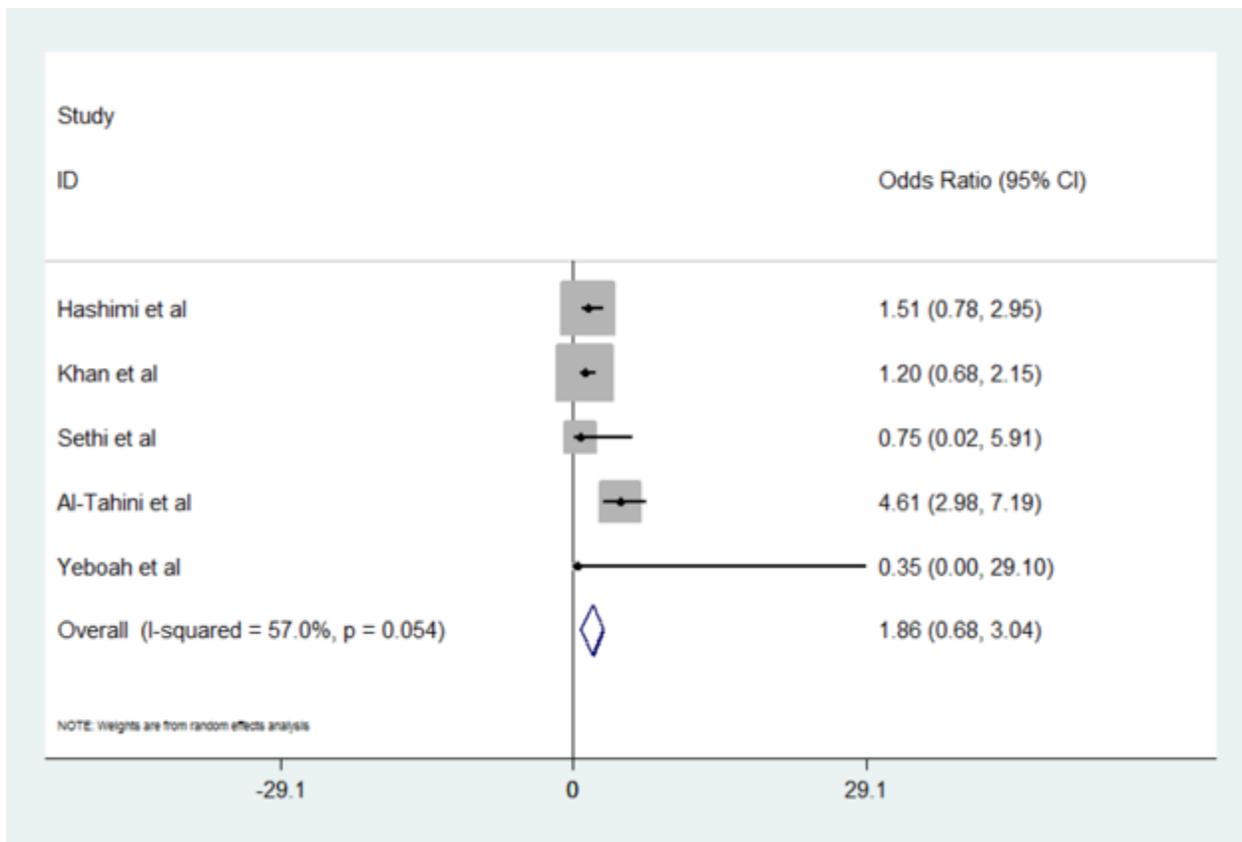
Figure 9: Location of death

Figure 10: Meta-analysis

<u>Prehospital care</u>

Three studies included data on prehospital care, however only one study had appropriate data to calculate an odds ratio for the likelihood of mortality between people who did not experience adequate prehospital care versus those who did. In Joosse et al[10] the OR was 2.21 with a 95% CI of (0.82, 6.13).

In the Arreola-Risa et al[9] and Mock et al[7] studies prehospital interventions data had no corresponding mortality data thus we were unable to calculate odds ratio.

<u>Intubation</u>

Three studies included data on prehospital intubation. In the Mock et al[7] study, the Kumasi population had no treatment performed en route to the hospital. In Monterrey, only 5% of hypotensive (systolic blood pressure <or=to 80) patients had undergone prehospital endotracheal intubation.

In the Al-Thani et al[9] study univariate analysis demonstrated an OR of 0.20 with a 95% CI of 0.13, 0.31.

The Arreola-Risa et al[8] study looked at the rates of EMS interventions before, during, and after EMT certification course. In all trauma patients, the percentage of patients receiving endotracheal intubation decreased from 0.5% to 0.3% to 0.2% in the before, during, and after groups. In the population of trauma patients in respiratory distress, the percentage of patients receiving endotracheal intubation decreased from 4.4% to 4.7% to 2.7% in the before, during, and after groups.

Discussion

Summary of Evidence

In this study, we aimed to identify and categorize the contributing prehospital factors that lead to increased mortality and morbidity in trauma patients in developing countries. In this systematic review, we were able to analyze data from eight studies. Only prehospital delay had enough papers with data and thus was the only factor we were able to perform a meta-analysis. Our analysis found that patients who experienced a prehospital delay had an 86% increase in mortality. While univariate analysis demonstrated that prolonged scene time was associated with increased mortality, this was not statistically significant. It is important to note that when calculating the odds ratio from Yeboah et al[2] study, there was only data on patients who did or did not experience a barrier and died. Mortality occurred in 100% of the study population as this paper looked at trauma deaths and retrospectively analyzed them as either preventable, potentially preventable, or not preventable. Prehospital delays were the barrier that accounted for 22 out of 50 definitely and potentially preventable deaths. In Khan et al[6], they also reported the average time of injury to emergency room as 4.7 hours. Furthermore, non-surviving patients had an average transport time of 6.2 hours while surviving patients had an average of 4.6 hours. In the study by Sethi et al, data on transport time was missing for 122 cases, making interpretation of the importance of this variable difficult.

In Joosse et al[10] the OR was 2.21 with a 95% CI of (0.82, 6.13) thus, patients who did not experience adequate prehospital care had a 2.2x increased likelihood of mortality. This data, however is not statistically significant. In this study, adequate prehospital care was defined as the presence of one or two intravenous fluid lines, a cervical collar, and splinting of fractures in the extremity if needed. There was no change in the rates of either cervical or thoracic spinal immobilization. Considering all patients, the use of any intravenous (IV) fluid declined slightly, from 4.7% to 3.0%. Considering only patients who were viable enough to receive some treatment, whether at the scene or en route to the hospital, the mortality rate declined from 1.8% in the before period to 0.5% in the after period (p < 0.002). Such deaths included those who died at the scene after receiving treatment, those who died during transport, and those

who died on arrival to the emergency department while the prehospital personnel were still present to note the death. Mock et al[7] found that in the Monterrey population, 70% of hypotensive patients had intravenous fluid administration en route, the remaining 30% did not. In the Kumasi population, no treatment was rendered en route to the hospital.

In the Al-Thani et al[9] study, univariate analysis demonstrated that prehospital intubation was associated with increased mortality. The OR was 0.20 with a 95% CI of 0.13, 0.31 thus, patients who were intubated in the emergency department were 80% less likely to die compared those that were intubated in the prehospital setting. It is important to note that the study population was based off total trauma patients that were intubated, comparing a group of patients that were intubated in the field vs being intubated in the emergency room. Thus, the barrier in the data that was calculated in the analysis is not receiving prehospital intubation. The other two studies showed that prehospital intubation is associated with increased mortality but improved education and training leads to improved outcomes of mortality.

Limitations

Limitations may have influenced the outcome of this study and need to be addressed. While low- and middle-income countries carry the heaviest global burden of injuries, a scarcity of trauma and injury data exists. Consequently, there is an apparent lack of quality research conducted and there are limited number of epidemiologists and other trained researchers, and there is little funding support[11]. In a systematic review by O'Reilly et al[12], they found that from developing countries, there have been less than 100 trauma registry publications in the medical literature covering less than 50 registries across just 21 countries. Most of these registries do not use ISS-based inclusion criteria, collect data from across all variable groups, including pre-hospital information, ED vital signs and survival, and focus only upon questions of epidemiology. This is directly apparent in this study as we were only able to gather 8 primary research articles out of a pool of 944 search results to be used in a systematic review.

Additionally, even though these papers included prehospital data, not all of these had extensive data points correlating a wide range of prehospital variables to mortality. In regard to prehospital care, which was not a well-defined factor across all three papers, one paper found that patients who did not experience adequate prehospital care had a 226% increase in mortality while the other papers only included frequency rates of interventions and corresponding data on mortality. In regard to intubation, one study showed that prehospital intubation was associated with increased mortality compared to emergency department intubation. The other two papers only included frequency rates of interventions and corresponding data on mortality. These data support the need of basic trauma infrastructure, which is often lacking or underdeveloped in developing countries in order to reduce the morbidity and mortality of trauma patients.

Conclusions

Even though this paper was trying to examine a wide range of prehospital factors in order to identify which ones may lead to increased mortality, we were unable to do so given the limited number of papers and data. Additionally, even though we were able to calculate the OR for prehospital delay, the results were not statistically significant. It is important to consider the aforementioned lack of studies and data that may have impacted this result. Moving forward, it should be a goal for countries and their governments to establish a central clearinghouse of health information, especially trauma registries. Additionally, more research in developing countries should be conducted to begin to ameliorate the paucity of literature that can then start driving evidence-based improvements and initiatives in healthcare. In conclusion, this study adds to the scarce literature how a lack of prehospital infrastructure is associated with an increased likelihood of mortality. It also highlights the importance and necessity of an increase in quality primary research conducted in developing countries.

References

1. Hashmi ZG, Haider AH, Zafar SN, et al. Hospital-based trauma quality improvement initiatives: First step toward improving trauma outcomes in the developing world. J Trauma Acute Care Surg. 2013;75(1):60-8; discussion 68.

2. Yeboah D, Mock C, Karikari P, Agyei-Baffour P, Donkor P, Ebel B. Minimizing preventable trauma deaths in a limited-resource setting: A test-case of a multidisciplinary panel review approach at the komfo anokye teaching hospital in ghana. World J Surg. 2014;38(7):1707-1712.

3. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380:2095–128. doi: 10.1016/S0140-6736(12)61728-0.

4. Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study 2010. Lancet. 2012;380:2197–223. doi: 10.1016/S0140-6736(12)61689-4.

5. Henry JA, Reingold AL. Prehospital trauma systems reduce mortality in developing countries: A systematic review and meta-analysis. J Trauma Acute Care Surg. 2012;73(1):261-268.

6. Khan A, Zafar H, Naeem SN, Raza SA. Transfer delay and in-hospital mortality of trauma patients in pakistan. Int J Surg. 2010;8(2):155-158.

7. Mock CN, Jurkovich GJ, nii-Amon-Kotei D, Arreola-Risa C, Maier RV. Trauma mortality patterns in three nations at different economic levels: Implications for global trauma system development. J Trauma. 1998;44(5):804-12

8. Arreola-Risa C, Vargas J, Contreras I, Mock C. Effect of Emergency Medical Technician Certification for All Prehospital Personnel in a Latin American City. The Journal of Trauma: Injury, Infection, and Critical Care. 2007;63(4):914-919.

9. Al-Tahani H, El-Menyar A, Latifi R. Prehospital versus Emergency Room Intubation of Trauma Patients in Qatar: A-2-year Observational Study. North American Journal of Medical Sciences. 2014;6(1):12. doi:10.4103/1947-2714.125855.

10. Joosse P, Soedarmo S, Luitse JS, Ponsen KJ. Trauma outcome analysis of a jakarta university hospital using the TRISS method: Validation and limitation in comparison with the major trauma outcome study. trauma and injury severity score. J Trauma. 2001;51(1):134-140.

11. Hofman K, Primack A, Keusch G, Hrynkow S. Addressing the Growing Burden of Trauma and Injury in Low- and Middle-Income Countries. American Journal of Public Health. 2005;95(1):13-17. doi:10.2105/AJPH.2004.039354.

12. O'Reilly GM, Joshipura M, Cameron PA, Gruen R. Trauma registries in developing countries: A review of the published experience. Injury. 2013;44(6):713-721. doi:10.1016/j.injury.2013.02.003.

13. Arreola-Risa C, Mock CN, Padilla D, Cavazos L, Maier RV, Jurkovich GJ. Trauma care systems in urban latin america: The priorities should be prehospital and emergency room management. J Trauma. 1995;39(3):457-462.

14. Masella CA, Pinho VF, Costa Passos AD, Spencer Netto FA, Rizoli S, Scarpelini S. Temporal distribution of trauma deaths: Quality of trauma care in a developing country. J Trauma. 2008;65(3):653-658.

15. Mock C, Joshipura M, Arreola-Risa C, Quansah R. An estimate of the number of lives that could be saved through improvements in trauma care globally. World J Surg. 2012;36(5):959-963.

16. Mock CN, Adzotor KE, Conklin E, Denno DM, Jurkovich GJ. Trauma outcomes in the rural developing world: Comparison with an urban level I trauma center. J Trauma. 1993;35(4):518-523.

17. Roudsari BS, Nathens AB, Arreola-Risa C, et al. Emergency medical service (EMS) systems in developed and developing countries. Injury. 2007;38(9):1001-1013.

18. Sakran JV, Greer SE, Werlin E, McCunn M. Care of the injured worldwide: Trauma still the neglected disease of modern society. Scand J Trauma Resusc Emerg Med. 2012;20:64-7241-20-64.

19. Sethi D, Aljunid S, Saperi SB, et al. Comparison of the effectiveness of major trauma services provided by tertiary and secondary hospitals in malaysia. J Trauma. 2002;53(3):508-516.

20. Solagberu BA, Ofoegbu CK, Abdur-Rahman LO, Adekanye AO, Udoffa US, Taiwo J. Pre-hospital care in nigeria: A country without emergency medical services. Niger J Clin Pract. 2009;12(1):29-33.

21. Whitfield CG, Shiwani MH. Optimal trauma care requires personnel and infrastructure to deliver optimal care. J Pak Med Assoc. 2009;59(6):423-424.

22. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews and Meta-Analyses:* The PRISMA Statement. BMJ 2009;339:b2535.