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Timing distribution and predictors of mortality following a road traffic injury in northwest Ethiopia: A hospital-based prospective follow-up study

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Abstract

Objective

The objective of this study was to identify timing distribution and predictors of mortality following road traffic injuries among all age groups at Gondar Comprehensive specialized hospital.

Design

A single center follow up study

Setting: The study hospital is a tertiary hospital at North West Ethiopia

Participants

A total of 454 road traffic injury victims who visited the hospital during the data collection period were included in the study. All age group and injury severity were included except those who arrived dead, had no attendant and when the injury time was unknown.

Primary and secondary outcome measures

The primary outcome was time to death measured in hours between road traffic injury and the 30th day of the injury. Secondary outcomes were pre-hospital first aid, length of hospital stay, and hospital arrival time.

Results

A total of 454 victims were followed for 275,534 person-hours. There were 80 deaths with an overall incidence of 2.90 deaths per 10,000 person-hours of observation (95% CI: 2.77, 3.03). The significant predictors of time to death were being a driver (AHR=2.26; 95% CI: 1.09, 4.65, AR=14.8), accident at inter urban roads (AHR=1.98; 95% CI: 1.02, 3.82, AR=21%), hospital arrival time (AHR=0.41; 95% CI: .16, 0.63; AR= 3%), SBP on admission (AHR= 3.66; 95% CI: 2.14, 6.26; AR=57%), GCS of <8 (AHR= 7.39; 95% CI, 3.0819 17.74464;AR=75.7%), head injury with polytrauma (AHR= 2.32 (1.12774 4.79; AR=37%) and interaction of distance from hospital with pre-hospital care.

Conclusion

This study demonstrated that trauma deaths follow the classical tri-modal pattern in low resource settings. Pre-hospital care services and advancing the hospital trauma care system are required.

Further studies on the capability of primary hospitals are essential. The article has been registered with a unique identification number (UIN) of researchregistry6556.

Keywords: Deaths, Predictors, Hazard ratio, attributable risk, population attributable risk, Road traffic injury, timing

Strength and limitation

♠ As to our search, this is the first study of its kind that investigated road traffic injury prospectively using an advanced statistical method (Survival analysis).

♠The study also investigated gaps in pre-hospital services including means of transport to health care facility after injuries.

♠The study didn't include pre-hospital deaths that can underestimate the actual mortality following a road traffic injury.

♠Immediate cause of deaths after discharge from hospital was collected using verbal autopsy by phone, this may lack precision.

Background

Annually, nearly 6 million people die from injury, which is more than deaths caused by a combination of HIV, tuberculosis, and malaria (1). Besides, every fatal injury is responsible for 20–50 non-fatal injuries that influence productivity and consequently affect economic development (2, 3). Road traffic injuries are among the leading causes of injuries, having high economic implications as it mainly affects the economically active segment of the population (4). It impacts more than 3% of gross domestic product for most countries (5). It is roughly estimated that the cost of road crash injuries is about 1% of the gross national product in low-income countries, 1.5% in middle-income countries and 2% in high-income countries (6). Road traffic injury-related mortality continues to increase from time to time globally, but its burden is more than three times higher in low-income countries (7). This discrepancy is mainly due to the poor trauma care system both at the pre-hospital and in-hospital settings (8-10).

Ethiopia is one of the poorest countries with a double burden of communicable and non-communicable diseases (11). The country has one of the highest road traffic injury-related mortality in the sub-Saharan region (12). Despite the efforts made in the training of key emergency personnel, there is no well-established emergency medical system to provide pre-hospital trauma care (13). The only available emergency service is the infrequent Ambulance transportation, which itself lacks health care professionals' support (14). These are the main factors explaining the higher fatality following a traffic injury in Ethiopia (15, 16).

Among many factors affecting mortality following a trauma, time from injury to death has attracted the attention of several scholars for three decades (17-19). The trimodal distribution of mortality was first described by Trunkey in 1983 (17). According to Trunkey, there are three peaks of mortality following trauma. The first peak is observed within minutes of the injury. Most deaths at the scene are from non-survivable injury to the brain and thorax (20). The second peak occurs within the first four hours of injury (21). The most common causes of death during this time are severe cardiovascular, pelvic, and intra-abdominal injuries with the consequence of heavy exsanguinations (22-24). Well-organized pre-hospital care and timely definitive care at hospitals could avoid these deaths (25). The third peak of death following trauma, called "late deaths", occurs after the first week of injury (26). Such deaths are caused by late complications such as sepsis and multiple organ failure (27). The advance in the trauma care system in most developed countries has significantly reduced late deaths. This has changed the classical trimodal pattern of mortality following trauma into a bimodal pattern (19, 25-27). However, studies from low-income countries regarding the timing distribution of mortality showed that mortality following trauma still follows the classical tri-modal pattern (28-27). The advance in the trauma care system in most developed countries has significantly reduced late deaths. This has changed the classical trimodal pattern of mortality following trauma into a bimodal pattern (19, 25-27). However, studies from low-income countries regarding the timing distribution of mortality showed that mortality following trauma still follows the classical tri-modal pattern (28).

Delays in hospital arrival are among various factors that determine the time to death following injury (29). In most areas of low and middle-income countries, Ambulance service is not available to transfer victims from an accident scene, and if at all available, there is poor coordination between ambulance staff and hospital staff. This poor coordination results in delays in trauma care at the health care facility (30). In countries like Ethiopia where there is an absence of a pre-hospital trauma care system and poor road infrastructure, delays in hospital arrival are expected.

There is a paucity of information on the pattern of mortality following traumas in the study area. The few available studies are cross-sectional and document-based which lacks information on important predictors. The previous studies are often institutional-based and only included deaths in the hospital ignoring late deaths at home. There is also a methodological gap in the analysis that ignores the timing component of deaths.

There is also a scarcity of evidence on hospital arrival time, time to death, and predictors of mortality following a road traffic injury in the study area. This study aimed to identify the proportion of victims who got pre-hospital care at the scene of injury. It also describes hospital arrival time, time to death, and its predictors following road traffic injuries. The analysis of trauma mortality and its temporal distribution is crucial for the development and improvement of trauma care systems.

Methods

Study Design

This is a single center prospective hospital-based follow-up study, from May 1, 2019, to February 30, 2020 at north Gondar zone, North West Ethiopia.

Study settings

The study hospital is one of the referral and Teaching Hospitals in the country. With more than 500 bed capacity, it provides basic and advanced services at its different units, including a 24-hour emergency department receiving all emergency cases.

Musculoskeletal and head trauma care is provided by four orthopedic surgeons and one neurosurgeon. General surgeons and specialists in other fields such as thoracic, gastrointestinal, genitourinary, and maxillofacial surgery are also assigned 24hr on-call to manage trauma cases. The emergency department is managed by 29 nurses assigned on 24hr-rotation. Every day, five surgical Residents and one senior orthopedic surgeon are assigned to the emergency department for trauma management. All trauma cases are brought to the emergency department for initial evaluation and resuscitation. The maximum observation period in the emergency department is 24 hours after which the patient is either discharged, admitted to the appropriate unit, or referred.

The hospital provides operative services in two minor surgery facilities, one main theatre complex, an obstetric, fistula, dental, and ophthalmic operative unit. Major emergency operation is provided at the main theatre in three dedicated rooms 24 hours seven days. The hospital has a radiology department staffed with 5 senior radiologists and other supportive technicians. The available imaging services include conventional radiology, ultrasonography, magnetic resonance imaging, and computerized tomography. Based on our pilot study, trauma constituted nearly 30% of emergency-related admissions in the hospital. Concerning to emergency response, the hospital provides 24 hours trauma services but there are no established out-of-hospital emergency care services.

Eligibility criteria

All traffic injury victims regardless of age and sex, who visited the hospital after sustaining a road traffic injury were included except those victims who were dead on arrival, were comatose, and had no attendant. We also excluded Victims when the time of injury was unknown. The enrolled participants were observed on daily basis using a pre-designed checklist.

Study variables

The primary outcome was time to death measured in hours between road traffic injury and the 30th day of injury. Accordingly, those victims who died between injury times to the 30th day of injury were events, and those who were still alive on the 30th day were considered censored. Secondary outcomes were pre-hospital first aid, length of hospital stay, and hospital arrival time. The exposure variable was having any degree of injury by any vehicle. The independent variables were sociodemographic factors (age, sex, educational status, occupation and residence of the victims and the distance between accident location and hospital), accident-related factors (road user category, type of vehicle, time of the accident, day of the week, lighting condition), pre-hospital first aid, means of transport to the hospital, hospital arrival time, anatomic body region injured, vital signs, neurologic status, and injury severity score.

Data sources/ measurement

All road traffic injury victims who visited the hospital after sustaining a road traffic injury during the data collection period were included. Victims who arrived dead and who were comatose and with no attendant and unknown injury time were excluded from the study.

Data were collected by four trained data collectors who were assigned to the emergency department. A predesigned and tested checklist developed by the research team was used to collect data. The information collected includes basic epidemiological variables, crash characteristics, and hospital arrival time. Additionally, information on road user category, availability of pre-hospital first aid, type of transportation used to transfer the victim to the hospital, clinical findings, the outcome in the emergency department, and decision after evaluation at the emergency department were collected. Information regarding the road traffic injury-related events and pre-hospital factors were collected from the victims or the relatives accompanying the victim.

Interviewing a victim was done after securing the initial lifesaving management at an emergency department. For those victims who were seriously ill and unable to communicate, relevant information was collected from the caregivers. Admitted victims were followed up on daily basis for a maximum of one month. Victims discharged before one month or those treated at the outpatient department were.

The cause of in-hospital mortality was collected from the victims' medical records. For late deaths that occurred after hospital discharge, verbal autopsy was collected from family or attendants. Verbal autopsy was collected by phone (33). A checklist was designed for the verbal autopsy that incorporates relevant information including, the clinical condition of the victims during the last days of survival.

Source of bias and minimizing strategy

The severity of the injury is one possible source of bias in this study because including victims with the highest injury severity score will result in overestimation of the outcome (death). To avoid selection bias, participants were enrolled regardless of an injury severity score. To minimize bias due to attrition, an explicit explanation was given for participants on the importance of remaining in the study.

A repeated attempt was made to contact participants after discharge from the hospital to know their status on the 30th day of injury. We also took multiple contact numbers to access the victims or proxy. The data collection tool was also piloted and standardized to avoid interviewer bias. Bias due to instrument error was minimized by checking the reliability of the instruments by comparing the measures with other instruments every day. Bias due to differential selection was minimized by including all degrees of injury (mild and severe cases) at the design stage. At the analysis stage, bias due to confounding was minimized by conducting multivariable analysis and stratified analysis. We used a predefined and prepared data management plan to avoid selective reporting bias.

Sampling and sample size

The sample size was calculated using the sample size calculation formula for survival analysis using STATA 14. Considering the following assumptions, α=0.05, β=0.2, HR=0.643, taken from a study conducted in Turkey indicating hazard of death among victims with low GCS was 0.64% (31), probability of an event from pilot study =0.28, (SD=0.5), and amount of event/probability of an event. Therefore, event=121, n=amount of event/probability of event=121/0.28=432, and considering 5% loss to follow up=454.

Operational definition

Trauma severity was computed using the "Revised Trauma Severity Score" based on three parameters. These parameters are the Glasgow coma scale (GCS), respiratory rate (RR), and systolic blood pressure (SBP) (32). According to the revised trauma score, these three parameters are coded summed up (Table 1).

Table 1: parameters used to measure revised trauma score

GCS	**Code**	**SBP**	**Code**	**RR**	**Code**
13-15	4	›89	4	10-29	4
9-12	3	76-89	3	›29	3
6-8	2	50-75	2	6-9	2
4-5	1	1-49	1	1-5	1
3	0	0	0	0	0

RTS = 0.9368 x GCS_v + 0.7326 x SBP_v + 0.2908 x RR_v, where v is the value (0-4)

Data analysis

Data were analyzed using STATA 14. Tables and graphs were used to summarize descriptive results. A Cox regression model was employed to identify factors that influence mortality. The Cox regression model is the most popular regression technique for survival analysis. This is because it examines the impact of various predictors of the risk of death and also accounts for censoring in the data (34). Variables with a p-value < 0.25 in the univariate Cox regression analysis were included in the multivariate analysis. We estimated hazard ratios and 95% confidence intervals. A cutoff value of p<0.05 was used in the multivariate analysis for statistical significance. Non-parametric tests such as the Kaplan Meir estimate, life table, and log-rank tests were employed. Log-log survival curves were used to assess the proportional hazard assumption based on Schohenfield residuals. Both bivariable and multivariable analyses were performed. The interaction of covariates on the main outcome was examined. Multicollinearity was assessed using variance inflation factor (VIF). The STROBE Checklist was also addressed. Missing data were handled using available case analysis.

Patient and Public Involvement:

At the design stage, the proposed study was discussed with stakeholders, including the traffic office department and zonal health departments. Because of the nature of the study, that it involved emergency cases, we couldn't involve patients at the design stage, but the purpose of the study for the general population was discussed with patients/caregivers during data collection. The policy brief will be prepared in the local language (Amharic) and will be disseminated to decision-makers and program implementers.

Results

Characteristics of the study subjects

Out of 11,960 trauma patients who visited the Emergency Department between May 6, 2019, and February 30, 2020, three thousand eighty-four cases were trauma victims of which road traffic injury constituted (18.2%). Four hundred fifty-four participants were enrolled and studied during the study period and 106 were excluded because of incomplete information. The study participants comprised 327 (72%) men and 127 (28%) women, resulting in a male to female ratio of 2.6:1.

The majority of the participants were in the productive age group. The mean age was 29±15.5 years. The median age was 27 years (IQR: 19, 37 years). The majority of the road traffic injury victims were passengers, (233) followed by pedestrians (167) and drivers (54). As to the educational status, only 130 (28.6%), of the victims completed secondary education while 144 (31.7%), were unable to read and write. The majority of the victims, 116 (25.5%) were farmers by occupation, followed by students (70). Two hundred sixty-four (58.1%) of the victims were urban, while 190 (41.9%) were rural dwellers. Nearly 60% (240) of the victims were reported from the urban areas. The majority of accidents, 402 (88.5%) were sustained during daylight. Tuesday and Friday were found to be the days with the highest frequency of accidents (Table 2).

Table 2: Characteristics of road traffic injury victims, May 2019-February 2020.

Variable	Category	Frequency	Percentage
Age			
	≤5 years	15	3.3%
	6-14	42	9.3%
	15-44	319	70.2%
	≥45	78	17.2%
Sex	Male	127	28%
	Female	327	72%
Road user category	Passengers	168	37%
	Pedestrian	232	51.1%
	Drivers	54	11.9%
Educational status	Can't read and write	144	31.7%
	Can read and write only	44	9%
	Primary education	85	18.7%
	Secondary education	131	29%
	Tertiary education	50	11%
Occupational status	Farmers	116	25.6%
	Gov. employee	53	11.7%
	Merchant	23	5.1%
	Student	70	15.4%
	Self- employee	68	15.0%
	Drivers	60	13.2%
	Others	64	14.0%
Residence	Urban	264	58.1
	Rural	190	41.9
Lighting condition	Daylight	402	88.5%
	Night	52	11.5%
Time of accident	6:00AM-12:59AM	165	36.3%
	1:00PM -6:59 PM	202	44.5%
	7:00PM-11:59PM	44	9%
	12:00PM-5:59AM	43	9%
Day of the week	Monday	63	13.9%
	Tuesday	76	16.7%
	Wednesday	71	15.6%
	Thursday	61	13.4%
	Friday	76	16.7%
	Saturday	66	14.5%
	Sunday	41	9%
Type of vehicle	Heavy truck loaders	59	13%
	Peoples' transport	173	38.1%
	Cars	17	3.7%
	Three wheel vehicles	196	43.2%
	Others	9	2%

Pre-hospital circumstances, hospital arrival time, and means of transportation to the hospital

The median distance from the place of accidents to the hospital was 40km; IQR (10km, 80km). Three hundred twelve, (68.7%) of the accidents were within 60 km distance from the hospital, while the rest 142 (31.3%) were sustained within the distance range of 61 to 500km. Concerning to hospital arrival time, 184 (40.5%) and 176 (38.9%), reported to the hospital within < 1 hour and 1-4 hours respectively. The total pre-hospital time interval in this study was 364 minutes. The mean hospital arrival time was 144 and 537 minutes for accidents sustained in the town and in the rural areas respectively.

None of the victims received pre-hospital care at the scene of the injury by a trained personnel. From the total injured, 283 (62.3%), were directly transferred from the scene of injury while, 171 (37.7%), were referred from primary hospitals. None of the victims who were transferred from the primary hospitals got surgical intervention at the primary hospitals, except wound dressing, immobilization with local materials, and tetanus prophylaxis.

About means of transportation to the hospital, the majority, 311 (68.5%) were transferred by commercial vehicles. Only 93 (20.5%) were transferred by ambulance, but none received pre-hospital care by trained ambulance crew. Ambulance service was not for free, and the victims had to cover the cost of fuel ranging from 400-800 Ethiopian Birr (40-80 USD) (Table 3).

Table 3: Pre hospital circumstances, hospital arrival time, and means of transportation.

Variables	Category	Frequency	Percentage
Distance from Hospital	≤60km	312	68.7%
	>60km	142	31.3%
Hospital arrival time			
	≤ 1 hour of injury	184	40.5%
	Within 1-4 hours of	176	38.8%
	injury	69	15.2%
	4- 24 hours of injury	25	5.5%
	>24 hours of injury		
Who brought the victims to the hospital	Police man	29	6.8%
	Relative/family	378	82.6%
	Others	47	10.6%

Pre-hospital care	Yes	171	37.7%
	No	283	62.3%
Transport to hospital	Ambulance	93	20.5%
	Commercial vehicles	311	68.5%
	Others	50	11%

Injury patterns and characteristics

Extremities and the head were the most commonly injured body regions accounting for 194 (42.7%) and 113 (24.9%) of cases respectively. Multiple body region injuries accounted for 85 (18.7%), thoraco-abdominal body region accounted for 32 (7%), and other body regions including the face, teeth, and the like accounted for 30(6.6%).

We computed the injury severity score using the revised trauma score. Accordingly, the mean revised trauma score (RTS) was 6.5±2.0. The injury severity score ranges from 0.29 to 7.55. According to our data, RTS of <3 (non-survivable injury score) was observed in 41 (9%) and a score of less than 4 was recorded among 56 (12.3%).

Based on the Glasgow coma scale score, 64 (14.1%) had a severe head injury, 18 (4%) had a moderate head injury and 372 (81.9%) had mild head injuries. Moreover, the rate of mortality was 52 (65%) for severe, 8 (10%) for moderate, and 20 (25%) for mild head injuries. Out of the observed 454 road traffic accidents, a fracture was sustained by 289 (63.7%) of victims. The most frequently involved bone was the lower extremity comprising 42% of all fractures followed by skull fracture (14.8%) (Figure 1).

Management of outcomes of road traffic injury victims

Out of the total 454 victims that visited the hospital, 76 (16.8%) were evaluated and treated at an outpatient department while 378 (83.2%) were admitted to the hospital for further evaluation and treatment. Of the total admitted, surgical intervention was required for 162 (35.7%) cases. The most frequently performed major surgical procedure was craniotomy, 25 (15.4%) followed by intramedullary nailing (IMN) 15 (9%). From the minor procedures, wound debridement was the most frequently performed procedure, 64 (39.5%) followed by immobilization using plaster of Paris (POP) 42 (25.9%). The mean hospital stay was 6.2±10 days, ranging from 1 day to 100 days. Reasons for discharge were on physician advice in 246 (65%) cases followed by death in 71 (18.7%), against medical advice in 38 (10%), and referred for better management to higher centers in 24 (6.3%) cases (Table 4).

Table 4: Management outcome of road traffic injury victims; May 6; 2019 to February 2020.

Variables	Category	Frequency	Percentage
Decision at OPD	Sent home same day	76	16.7%
	Admitted to hospital	378	83.3%
Reason for admission	Requires surgery or resuscitation	256	67.73%
	Requires Close observation	122	32.27%
Commonly performed procedure	Debridement	64	28.9%
	Craniotomy	25	11.3%
	POP	52	23.5%
	Wiring & pin traction	17	7.6%
	Wound repair	22	10%
	Chest tube	12	5.4%
	IMN	18	8%
	Laparotomy	4	1.8%
	Others	7	3.1%
Mean hospital stay	6.6±9.8 days		
Reason for discharge	On medical advise	324	71.4%
	Died	71	15.6%
	Against medical advice	38	8.4%
	Referred	21	4.6%

Survival analysis

Four hundred fifty-four participants were followed for a total of 275,534 person-hours. There were 80 (17.60%) deaths and 15(3.30%) loss to follow up. We used the available case analysis technique as a missing data management option. From the total deaths, 13 (16.25%) occurred within the first hour of injury, 11 (13.75%) between the first and 4 hours of injury, and 18 (22.50%) occurred between 4 and 24 hours of injury. Thirty-two (40%) of the deaths occurred after 24 hours up to the first 7 days while the rest six deaths occurred after a week of injury (Figure 2).

The overall incidence rate of death was 2.90 deaths per 10,000 person-hours of observation (95%CI: 2.77, 3.03). Since more than 75% of participants survived beyond the study time, we couldn't compute the median survival. Instead, we computed the cumulative and mean survival times. The mean survival time was 607 hours or 25.30 days with a standard deviation of 10 days. The cumulative proportion of surviving at the end of the first hour of injury was 97.30% (95% CI: 95.39%, 8.49%). Similarly, it was 94.93% (95% CI: 92.47%, 96.60%), 90.95% (95% CI: 87.92%, 93.23%), 83.89% (95% CI: 80.17, 86.97%) and 82.34% (95% CI: 78.51%, 85.56%) at the end of fourth, 24th, 168th and 720th hours of injury respectively (Table 5).

Table 5: Overall life table of road traffic injury victims; May 2019-February 2020

Time in hours	Number at risk	Loss to follow up	Number of events	Proportion of events	Proportion Surviving	Cumulative Proportion Surviving
1	442	0	12	0.027	0.973	0.973
2	433	0	9	0.02	0.98	0.95
3	432	0	1	0.002	0.99	0.94
4	431	0	1	0.002	0.998	0.938
6	429	0	2	0.004	0.996	0.934
12	428	0	1	0.002	0.998	0.932
24	413	0	15	0.036	0.964	0.89
48	406	0	7	0.0172	0.982	0.87
72	399	0	7	0.0175	0.982	0.85
96	392	0	7	0.0178	0.982	0.83
120	388	0	4	0.010	0.99	0.82
144	386	0	2	0.0052	0.99	0.81
168	381	0	5	0.013	0.98	0.79
288	380	0	1	0.002	0.997	0.77
312	379	0	1	0.002	0.997	0.75
432	378	0	1	0.002	0.997	0.74
480	377	0	1	0.002	0.997	0.73
528	376	0	1	0.002	0.997	0.72
672	375	0	1	0.0026	0.99	0.71
720	359	15	1	0.0027	0.99	0.70

Condition of victims on the 30th day of injury

Assessment on the 30th day of injury revealed that 30 (6.60%) were still in bed with unremarkable improvement, 263 (57.90%) had a better condition, but not completely healed, 45 (9.90%) were healed with some limitation, 21 (4.60%) were completely healed and back to work, 15 (3.30%) were lost to follow-up and 80 (17.6%) died. Apart from those who died, 23 had functional losses (4 (0.88%) had lost teeth, 4 (0.88%), had an amputation of the limb, 3 (0.66%) had hearing loss, 3

(0.66%), had vision loss, 5 (1.10%), had impaired memory and 4 (0.88%) were paraplegic at 30th day of injury).

Immediate causes of deaths at a specific time interval

From the total of 17 deaths in the first hour of admission, 13 (76.5%) were due to non-survivable injury. The leading cause of death in the first four hours of admission to the hospital was hemorrhage (21.3%). Hemorrhage and secondary complications, mainly aspiration pneumonia were the major causes of death between the first 4 and 24 hours. According to our data, late deaths were mainly due to sepsis and multiple organ failure (Figure 3). All deaths were confirmed by the clinician in charge of patient care.

Predictors of mortality following a road traffic injury

The significant predictors of time to death for road traffic injury victims were being a driver (AHR=2.26; 95% CI: 1.09, 4.65, AR=14.8), accident location at the rural residence (AHR=1.98; 95% CI: 1.02, 3.82;AR=21%), hospital arrival time (AHR=0.41; 95% CI: 0.16, 0.63;AR= 3%), systolic blood pressure on admission (AHR= 3.66; 95% CI: 2.14, 6.26; AR=57%), GCS of <8 (AHR= 7.39 ; 95% CI, 3.0819 17.74464; AR=75.5%), GCS between 9-13 (AHR= 8.1565 (3.36 19.82, AR=39%), combined head injury with multiple body site (AHR= 2.33 (1.13, 4.80; AR=37%) and interaction of long distance from hospital (AHR=2.98 (1.46 4.39; AR=5.5%) (Table 6).

Table 6: Predictors of mortality following a road traffic injury, May, 2019 to February 2020

Variables	Categories	Total	RTI deaths	CHR(95%CI)	AHR(95%CI)
Road user category	Pedestrian	168	22	1.00	1.00
	Passengers	234	43	1.47 (.88, 2.46)	1.97 (1.10, 3.52)*
	Drivers	54	15	2.36 (1.22 4.55)	2.61 (1.28 5.30)*
Residence	Urban	264	23	1.00	1.00
	Rural	194	57	3.90 (2.40 6.34)	1.98 (1.02 3.82)*
Hospital arrival time	Within <1 hour	184	32	1.00	1.00
	Within 1-4hours	176	25	.32 (.45 1.30)	.41 (.16 .63)**
	Within 24 hours	69	20	1.74 (.99 3.05)	.42 (.18 .95)
	After 24 hours	25	3	.64 (.19 2.09)	.40 (.10 1.56)
Systolic BP	≤89	53	36	10.07 (6.45 15.71)	3.66 (2.14 6.26)
	>89	401	44	1.00	1.00
GCS	≤8	64	52	32.44 (19.12 55.06)	7.39 (3.08 17.74)**
	9-12	18	8	9.97 (4.39 22.67)	8.15 (3.35 19.82)**

	13-15	372	20	1.00	1.00
Injury site	Non-head injury	262	14	1.00	1.00
	Isolated Head injury	105	33	7.05 (3.77 13.19)	2.28 (1.12 4.65)*
	Combined head injury	87	33	8.50 (4.54 15.89)	2.57 (1.26 5.24)**
Pre-hospital Care # distance	Yes#<60km	93	7	1.00	1.00
	Yes#>60km	79	11	1.74 (.87 3.48)	2.98 (1.46 4.39)*
	No#<60km	217	38	.688 (.25 1.89)	.60 (.28 1.25)
	No#>60km	65	24	3.69 (1.76 7.73)	.81 (.31 2.10)

Key * Significant at P<0.05, **P<0.001

Impact of the study

We have calculated the attributable risk for the predictors of mortality. Our study showed that accidents at inter-urban locations had an increased hazard of death when compared with those accidents in urban locations. The increased death in these locations is due to lack of timely care on-site and delays to hospital arrival, mainly due to poor transport access and long distance from the hospital. This finding implies that the establishment of emergency medical services and improved access to health care facilities could reduce such deaths by 21%.

Those victims who had a systolic blood pressure of less than 90 mmHg on admission had a risk of death by more than 3-fold when compared with their counterparts. This implies that maintaining the hemodynamics of victims as early as possible can reduce deaths following an injury by 57%. With this regard, the role of emergency medical response at the scene of the injury and early transfer of victims to definitive care units will have a vital role in reducing reversible causes of mortality.

The study demonstrated that those victims who had head injury had a higher risk of death when compared with non-head injury cases. Accordingly, victims with an isolated head injury and multiple injuries including head injury had more than twice the risk of death when compared with injury to other body regions. Hence, the use of protective materials such as helmets could potentially reduce mortality following a road traffic injury by 26-32%.

Discussion

The current study demonstrated that deaths following a trauma follow the classical tri-modal pattern in low-resource countries and pre-hospital care is rarely available for victims of road traffic injuries. Free ambulance transportation was in-available for trauma victims resulting in a delay in hospital arrival for accidents sustained on rural roads. Being a driver, accident location in rural areas, low systolic blood pressure, low GCS on admission, injury site, and interaction of providing pre-hospital care and long-distance were found to be predictors of time to death among road traffic injury victims.

The classical tri-modal distribution of trauma deaths was described by Trunkey in 1983 (35). Different previous studies had disproved this traditional distribution of mortalities due to the main reduction in the number of early and late hospital deaths (36). Our study demonstrated that road traffic injury mortality still followed the traditional tri-modal pattern. According to the current study, there were two peaks, one in the first 24 hours and the second at the end of the first week of the injury. Nearly half of the deaths occurred in the hospital after a week of admission. A similar finding was reported by a study conducted in Iran showing two peak times of trauma deaths (28). Poor operative services for severe head injury cases and lack of intensive care unit for severely injured victims could explain the reason for late deaths in our hospital (37). The surgical setup in our case is not optimum to perform surgical intervention for severely injured head injury victims. Besides, there is no well-equipped surgical ICU service to support victims with ventilatory failure. On the other side, the in-availability of pre-hospital basic life support care could have resulted in clinical deterioration of victims that could result in late complications (8).

In this study, none of the victims received pre-hospital care at the scene of injury. This is consistent with previous studies that showed pre-hospital emergency care is under-served or unavailable in most low and middle-income countries (38, 39). The finding is also consistent with a study conducted in Addis Ababa where none of the victims got pre-hospital care (15). The current study also indicated that full package Ambulance service was unavailable for all the victims and only 20% received transportation service without trained personnel accompanying the victims. Our finding is in line with a systematic review indicating Ambulance service was underserved in many low and middle-income countries (40) and a study conducted in Pakistan that reported the majority of participants didn't want to call Ambulance for emergency cases because the Ambulances didn't function properly (41). On top of this, the available ambulance service was not for free, and victims or the family have to cover the cost for fuel and per Diem of drivers. A similar finding was reported from Cambodia (42).

The current study also showed that many trauma victims who were referred from primary hospitals would have been treated at those hospitals. This is in line with a study conducted at Southern India, which showed that trauma care was unnecessarily delayed and liable for unnecessary referrals due to poor resources for trauma case management (30) and another study demonstrated that there are many deficiencies in emergency care services ranging from in-availability of drugs and lack of training to provide the required emergency care (43).

According to our study, the overall incidence of road traffic injury deaths was 29 per 100,000 hours of observation. This finding is higher when compared with a study conducted at Tikur Anbessa Hospital, Addis Ababa, which was 10/100,000 hours of observation (15). The discrepancy could be explained by the fact that the Tikur Anbessa Hospital has a better trauma management setup including an intensive care unit (ICU). Hence the quality of care could explain the lesser death at the Tikur Anbessa Hospital (23). Another explanation could be because follow-up continued after discharge from the hospital in the current study, while the mentioned study didn't follow victims after discharge that ignored deaths at home after discharge.

The study revealed that pedestrians are the most frequently affected road user categories as compared to passengers and drivers. This is in line with the federal police commission report (44) and studies conducted in the capital city, Addis Ababa, (45, 46) all showing pedestrians to be the road user categories most frequently affected by RTI. But severe and fatal injuries were more likely to occur among drivers and passengers in our study. This finding was consistent with a previous study that indicated fatal injuries were more likely among drivers and passengers (47) but in contradiction to findings in a study that showed pedestrians are more likely to die from a vehicle accident (48).

Our study demonstrated that accidents that were sustained in rural areas were more likely to result in a fatal outcome than those at the urban location. Our finding is consistent with a study conducted by Craig Zwerling and colleagues that showed injury severity and fatality was more than three times higher at rural area than urban areas (49). This could be explained by the fact that most areas of the rural residence lack health care facility and transport access to reach the hospital timely resulting in mismanagement and delays of care. This will, in turn, result in bad outcomes (50). The other possible explanation for the increased mortality in rural residence could be the fact that vehicles are very speedy in the rural areas as a result of poor traffic control. Studies showed that accident intensity increases when a crash is caused by a speedy vehicle (51).

Low systolic blood pressure on admission was significantly associated with time to death among road traffic injury victims. This finding is in line with previous studies that showed victims with low blood pressure on admission were more likely to experience death than their counterparts (14, 52-53). This can be explained by the fact that acute blood loss is very likely in trauma patients that had brought the drop in systolic blood pressure (54). Low systolic blood pressure could increase mortality via poor organ perfusion and consequent organ failure (55). Besides, acidosis from poor perfusion and late complications as nosocomial infection and sepsis are also very likely to occur in patients with hemorrhagic shock (56, 57). These are the possible explanations for low systolic blood pressure and increased mortality.

The current study revealed that hospital arrival time is associated with 30 days of mortality following a road traffic injury. Accordingly, victims who arrived at the hospital between one to four hours were more likely to die than those who arrived within one hour of injury and beyond 4 hours of injury. This is contrary to the concept of the "Golden hour" of trauma that depicts the outcome of trauma was better when victims arrive within one hour of injury (58- 59). This could be explained by the fact that victims who are seriously injured and have non-survivable injuries were more likely to be directly transferred to the hospital immediately after injury than less severe injury cases, thus increasing the death rate among victims who arrived within 60 minutes of the injury.

The study showed an interaction between long distance from the hospital and pre-hospital first aid to be significantly associated with 30 days mortality following a road traffic injury. The possible explanation for this finding could be due to delays in definitive care. Though essential trauma care is vital to treat time-sensitive issues such as airway compromise and severe bleeding, delayed patient transfer, and delays in definitive care also endanger the life of trauma victims (60). This is particularly the case in low resource countries like Ethiopia where the majority of primary hospitals are not in a position to provide essential trauma care (61).

Limitation of the study

As our participants were only those victims who visited the hospital during the data collection period, deaths at the scene of the injury and minor cases who didn't come to the hospital were excluded. Such exclusion might underestimate the actual injury and mortality from a road traffic injury. Besides, the exclusion of minor cases might introduce selection bias. The time interval between injury and hospital arrival was determined based on self-report or family report. We expect a recall bias in such a stress full situation. The direct cause of death was assessed using verbal autopsy for those deaths that occurred at home after discharge. This may not be precise without autopsy and physician judgment.

Because many of the drivers escape or were arrested after the accidents, we couldn't assess driver-related risk factors such as speed, presence of drunk driving, age, and experience of driving which could be a source of variability for the outcome of the injury.

Conclusions

This study demonstrated that the classical tri-modal pattern of mortality is still occurring in low resource settings. The study showed that there is a gap in both pre-hospital trauma care and primary trauma care at district hospitals in the study area. Being a driver, accidents at the inter-urban roads, low systolic blood pressure, low GCS on admission, and presence of head injuries were predictors of time to death following road traffic injuries.

The regional and zonal health sectors need to revise the pre-hospital trauma care service implementation including Ambulance access and package. The hospital needs to improve trauma care services, especially surgical and supportive interventions such as mechanical ventilatory support for severely injured victims. Future studies should be conducted to assess the capability of primary hospitals in the area in providing essential trauma care, and barriers to establishing emergency medical service in the country at large and study area in particular.

Generalizability of the study: We tried to use a representative sample based on appropriate power calculation and use a pre-tested and piloted tool to collect data, hence we can generalize the result from this study for all road traffic injury cases in the Amhara region.

Abbreviations

AHR	Adjusted Hazard Ratio

AR	Attributable Risk
BP	Blood Pressure
CI	Confidence Interval
GCS	Glasgow Coma Scale
HIV	Human Immuno Virus
HR	Heart Rate
ICU	Intensive Care Unit
IMN	Intra Medullary Nailing
IQR	Interquartile Range
O_2	Oxygen
POP	Plaster of Paris
PR	Pulse Rate
RTI	Road Traffic Injuries
RTS	Revised Trauma Score
RR	Respiratory Rate
SBP	Systolic Blood Pressure
SD	Standard Deviation

Declarations

Ethics approval and consent to participate

Ethics approval and consent to participate

Ethical clearance was obtained from the University of Gondar Ethical review board (R.N. O/V/P/RCS/051049/2019), and a permission letter was obtained from Gondar University Comprehensive Specialized Hospital. Informed written consent was obtained from participants, caregivers, or proxy as appropriate. The purpose of the study was explained to every victim or an appropriate proxy. On arrival at the emergency department, only hospital arrival time was registered and other information was collected after all the necessary medical care was secured. During our observation, any abnormal finding or complaint such as pain was communicated to the appropriate medical care team for intervention. For those victims who were discharged against medical advice, we continued our follow-up by phone and some of them changed their minds and returned and continued their medical follow-up.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interest

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Authors' contribution

ZD designed the study, analyzed the data, and drafted the manuscript. MY, TA, GB, and KG were involved in the design of the study, analysis, and critically evaluated the manuscript for intellectual content. All authors read and approved the final manuscript.

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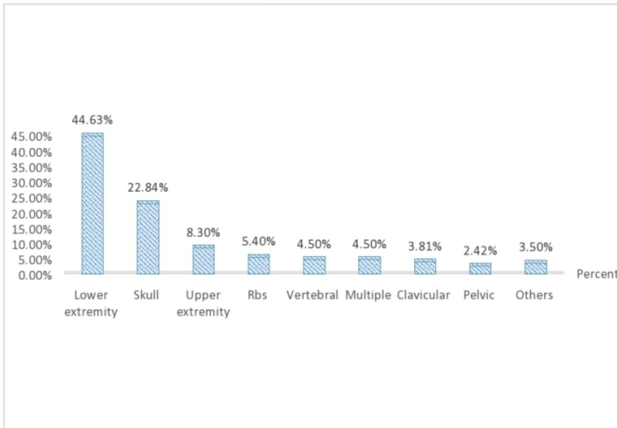

Figure 1: Commonly sustained fractures among RTI victims, Hospital, Ethiopia

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449x582mm (72 x 72 DPI)

Figure 2: Timing distribution of mortality following road traffic injuries, May 6; 2019 to February 30, 2020

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449x582mm (72 x 72 DPI)

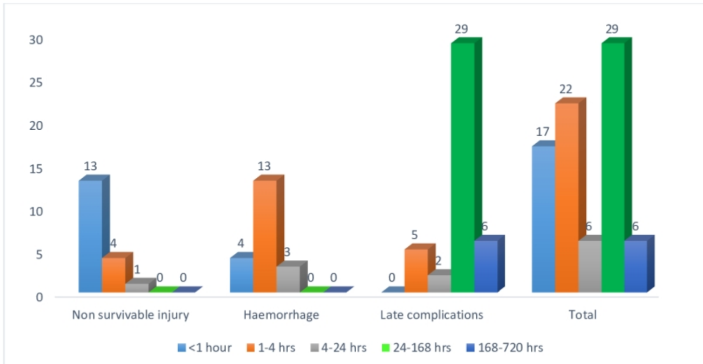

Figure 3: Immediate causes of deaths following a road traffic injury at a specific time interval, May 2019 –February 2020.

Figure 3: Immediate causes of deaths following a road traffic injury at a specific time interval, May 2019 – February 2020.

215x279mm (200 x 200 DPI)

Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title and abstract			Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	Page 1 line 1-2
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	Lines 30-54
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	Lines 70-120

Objectives	#3	State specific objectives, including any prespecified hypotheses	Line 120-124
Methods			
Study design	#4	Present key elements of study design early in the paper	Line 127-128
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Lines 130-149
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	Lines 151-154
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	N/a
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Lines 156-165
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.L	Lines 167-187
Bias	#9	Describe any efforts to address potential sources of bias	Lines 189-202
Study size	#10	Explain how the study size was arrived at	Lines 204-209
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	N/a
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	Lines 217-228
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	Lines 227
Statistical methods	#12c	Explain how missing data were addressed	Lines 228-229
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	Lines 222

Statistical methods	#12e	Describe any sensitivity analyses	n/a
Results			
Participants	#13a	Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed. Give information separately for exposed and unexposed groups if applicable.	Additional file 1
Participants	#13b	Give reasons for non-participation at each stage	Additional file 1
Participants	#13c	Consider use of a flow diagram	Additional file 1
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	Lines 240-253
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	Line 306
Descriptive data	#14c	Summaries follow-up time (e.g., average and total amount)	Lines 214-318
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	Lines 322-328
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Lines 337-344
Main results	#16b	Report category boundaries when continuous variables were categorized	N/a
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Lines 349-365

Other analyses	#17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	#18	Summarise key results with reference to study objectives	Lines 367-454
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	Lines 456-466
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	Lines 468-478
Generalisability	#21	Discuss the generalizability (external validity) of the study results	Lines 479-481
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Lines 505-506

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Do deaths from road traffic injuries follow a classical trimodal pattern in North West Ethiopia? A hospital based follow-up study.

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Abstract

Objective

The objective of this study was to identify timing distribution and predictors of deaths following road traffic injuries among all age groups at Gondar Comprehensive specialized hospital.

Design

A single-center follow-up study.

Setting: The study hospital is a tertiary hospital in North West Ethiopia

Participants

We enrolled 454 participants who sustained road traffic injuries in to the current study. All age groups and injury severity were included except those who arrived dead, had no attendant, and when the injury time was unknown.

Primary and secondary outcome measures

The primary outcome was time to death measured in hours from injury time up to the 30th day of the injuries. Secondary outcomes were pre-hospital first aid, length of hospital stay, and hospital arrival time. The article has been registered, with a unique identification number (UIN) of research registry 6556".

Results

A total of 454 victims were followed for 275,534 person-hours. There were 80 deaths with an overall incidence of 2.90 deaths per 10,000 person-hours of observation (95% CI: 2.77, 3.03). The significant predictors of time to death were being a driver (AHR=2.26; 95% CI: 1.09, 4.65, AR=14.8), accident at inter urban roads (AHR=1.98; 95% CI: 1.02, 3.82, AR=21%), time from injury to hospital arrival (AHR=0.41; 95% CI: .16, 0.63; AR= 3%), SBP on admission of <90mmHG (AHR= 3.66; 95% CI: 2.14, 6.26; AR=57%), GCS of <8 (AHR= 7.39; 95% CI, 3.0819 17.74464;AR=75.7%), head injury with polytrauma (AHR= 2.32 (1.12774 4.79; AR=37%) and interaction of distance from hospital with pre-hospital care.

Conclusion

Though the maturation of trauma centers in many developed countries has changed the temporal pattern of deaths following any trauma, our study demonstrated that trauma deaths follow the traditional tri-modal pattern. That implies that potentially preventable causes of death continued in low-resource countries.

Keywords: Deaths, Predictors, Hazard ratio, attributable risk, population attributable risk, Road traffic injury, timing

Strength and limitation

- As far as our search is concerned, this is the first study of its kind investigating road traffic injury prospectively using an advanced statistical method (Survival analysis).
- Follow-up of victims was extended after discharge from the hospital up to 30 days.
- The dropout rate was minimal.
- Out of hospital deaths were excluded

Background

Annually, nearly 6 million people die from injury, which is more than deaths caused by a combination of HIV, tuberculosis, and malaria (1). Besides, every fatal injury is responsible for 20–50 non-fatal injuries that influence productivity and consequently affect economic development (2, 3). Road traffic injuries are among the leading causes of trauma that affect a country's economies. That is because it mainly affects the economically active segment of the population (4). It impacts more than 3% of gross domestic product for most countries (5). For example, it resulted in 2.1% of economic losses in Ethiopia in 2015 (6). The World Bank estimated that the cost of road crash injuries is about 1% of the gross national product in low-income countries, 1.5% in middle-income countries, and 2% in high-income countries (7). Road traffic injury-related mortality continues to increase from time to time globally, but its burden is more than three times higher in low-income countries (8). This discrepancy is partly due to the immature trauma care system, both in the pre-hospital and in-hospital settings (9-11). Even though Ethiopia has adopted safety legislation that protects vulnerable road users, there is still a considerable gap in practicing traffic laws on drunk driving, seat belt wearing, speed limits, helmets, and child restraints. These are possible explanations for the high prevalence of road traffic injuries and mortalities in Ethiopia (12).

Ethiopia is one of the poorest countries with a double burden of communicable and non-communicable diseases (13). The country has one of the highest road traffic injury-related mortality in the sub-Saharan region (14). Despite the efforts made in the training of key emergency personnel, there is no well-established emergency medical system to provide pre-hospital trauma care (15). The only available emergency service is the infrequent Ambulance transportation, which itself lacks health care professionals' support (16). These are the main factors explaining the higher fatality following a traffic injury in Ethiopia (17, 18).

Among many factors affecting deaths following a trauma, time from injury to death has attracted the attention of several scholars for three decades (19-21). The mortality pattern was described as a trimodal pattern by Trunkey in 1983 (19). According to Trunkey, there are three peaks of deaths following trauma. The first peak of death occurs immediately within minutes of the injury. Most deaths at the scene are from non-survivable injury to the brain and thorax (22).

The second peak occurs within the first four hours of injury (23). The second peak occurs within the first four hours of injury (23). The most common causes of death during the second peak are severe cardiovascular and intra-abdominal injuries. (24-26). Well-organized pre-hospital care and timely definitive care at hospitals could avoid these deaths (27).

The third peak of death following trauma, called "late deaths", occurs after the first week of injury (28). Such deaths have resulted from late complications such as sepsis and multiple organ failure (29). The advance in the trauma care system in most developed countries has significantly reduced late deaths. That has changed the classical trimodal pattern of deaths following trauma into a bimodal pattern (21, 27- 30). However, studies from low-income countries showed that it still follows the classical tri-modal pattern (31).

Delays in hospital arrival are among various factors determining the time to death following injury (32). In most areas of low and middle-income countries, Ambulance service is not available to transfer victims from an accident scene, and if at all available, there is poor coordination between ambulance staff and hospital staff. This poor coordination results in delays in trauma care at the health care facility (33). In countries like Ethiopia, where there is no pre-hospital trauma care system and poor road infrastructure, delays in hospital arrivals are apparent. That could be one reason for the high mortality rate following road traffic injuries. According to a WHO report, the mortality rate from road traffic injuries was 25.3 and 26.7 per 100,000 populations in 2015 and 2018, respectively (7, 8).

There is a paucity of information on the pattern of mortality following traumas in the study area. The few available studies are cross-sectional and document-based which lacks information on important predictors. The previous studies are often institutional-based and only included deaths in the hospital ignoring late deaths at home (17, 18). There was also a methodological gap in the analysis in that it ignores the time component of death.

There is also a scarcity of evidence on hospital arrival time, time to death, and predictors of mortality following a road traffic injury in the study area. This study aimed to identify the proportion of victims who got pre-hospital care at the scene of injury. It also describes hospital arrival time, time to death, and its predictors following road traffic injuries. The analysis of trauma-related death is a crucial step for the development and improvement of trauma care systems.

Methods

Study Design

It is a single-center prospective hospital-based follow-up study, from 01-May 2019 to 30-February 2020, at the north Gondar zone, North West Ethiopia.

Study settings

The study hospital is one of the referral and Teaching Hospitals in the country. With more than 500 bed capacity, it provides basic and advanced services at its different units, including a 24-hour emergency department receiving all emergency cases.

Musculoskeletal and head trauma cases are cared for by four orthopedic surgeons and one neurosurgeon. General surgeons and specialists in other fields such as thoracic, gastrointestinal, genitourinary, and maxillofacial surgery are also assigned 24hr on-call to manage trauma cases. The emergency department is run by 29 nurses assigned on 24hrs-rotation. Every day, five surgical Residents and one senior orthopedic surgeons deliver their expert care in the emergency department. The emergency department provides initial evaluation and resuscitation for trauma victims. The maximum observation time in the emergency department is 24 hours, after which the patient is either discharged, admitted to the appropriate unit, or referred.

The hospital provides general operative services in two minor surgery facilities and one main theatre complex. There are also operative services at obstetric unit, fistula, dental, and ophthalmic operative units.

The hospital has a radiology department staffed with five senior radiologists and other supportive technicians. The available imaging services include conventional radiology, ultrasonography, magnetic resonance imaging, and computerized tomography.

Based on our pilot study, trauma constituted nearly 30% of emergency-related admissions in the hospital. Concerning emergency response, the hospital provides 24 hours trauma services, but there are no established out-of-hospital emergency care services.

Eligibility criteria

All traffic injury victims regardless of age and sex were included except those who were dead on arrival, comatose, and had no attendant. We also excluded Victims when the time of injury was unknown. The enrolled participants were observed on daily basis using a pre-designed checklist.

Study variables

The primary outcome was time to death measured in hours between road traffic injury and the 30th day of injury. Accordingly, those victims who died between injury times to the 30th day of injury were events, and those who were still alive on the 30th day were censored cases. Secondary outcomes were pre-hospital first aid, length of hospital stay, and hospital arrival time. The exposure variable was having any degree of injury by any vehicle. The independent variables were sociodemographic factors (age, sex, educational status, occupation and residence of the victims and the distance between accident location and hospital), accident-related factors (road user category, type of vehicle, time of the accident, day of the week, lighting condition), pre-hospital first aid, means of transport to the hospital, hospital arrival time, anatomic body region injured, vital signs, neurologic status, and injury severity score.

Data sources/ measurement

We included all road traffic injury victims who visited the hospital during the data collection period. We excluded Victims who arrived dead, were comatose, and with no attendant and unknown injury time.

Four trained data collectors collect the data using a structured and tested checklist. The information collected includes epidemiological variables, crash characteristics, and hospital arrival time. Additionally, we collected data on road user category, availability of pre-hospital first aid, type of transportation used to transfer the victim, clinical findings, the outcome in the emergency department, and decision after evaluation at the emergency department. We collected data regarding road traffic injury-related events and pre-hospital factors from the victims or the relatives accompanying the victim.

Interviewing a victim was done after securing the initial lifesaving management at an emergency department. For seriously sick victims unable to communicate, we collect data from the caregivers. The maximum follow-up time was one month. Victims discharged before one month and sent home the same day were contacted by phone on the 30th day of injury to know their status.

We collected the immediate cause of in-hospital mortality from the victims' medical records. For late deaths that occurred after hospital discharge, we collected verbal autopsies from family or attendants. Verbal autopsy was collected by phone (34). A checklist was developed for the verbal autopsy that incorporates relevant information. The verbal autopsy checklist comprised the clinical condition of the victims during the last days of survival.

Source of bias and minimizing strategy

The severity of the injury is one possible source of bias in this study. Thus we enrolled participants regardless of an injury severity score. To minimize bias due to attrition, we explained the value of remaining in the study for participants.

We made a repeated attempt to contact participants after discharge from the hospital to know their status on the 30th day of injury. We also took multiple contact numbers to access the victims or proxy. The data collection tool was also piloted and standardized to avoid interviewer bias. Bias due to instrument error was minimized, by taking measurements repeatedly. Bias due to differential selection was minimized by including all degrees of injury (mild and severe cases) at the design stage. At the analysis stage, bias due to confounding was minimized, by conducting multivariable analysis and stratified analysis. We used a predefined and prepared data management plan to avoid selective reporting bias.

Sampling and sample size

The sample size was calculated using the sample size calculation formula for survival analysis using STATA 14. Considering the following assumptions, α=0.05, β=0.2, HR=0.643, taken from a study conducted in Turkey indicating hazard of death among victims with low GCS was 0.64% (35), probability of an event from pilot study =0.28, (SD=0.5), and amount of event/probability of an event. Therefore, event=121, n=amount of event/probability of event=121/0.28=432, and considering 5% loss to follow up=454.

Operational definition

The trauma severity score was computed using the "Revised Trauma Severity Score" based on three parameters. These parameters are the Glasgow coma scale (GCS), respiratory rate (RR), and systolic blood pressure (SBP) (36). According to the revised trauma score, these three parameters are coded and summed up (Table 1).

Table 1: Parameters used to measure revised trauma score

GCS	**Code**	**SBP**	**Code**	**RR**	**Code**
13-15	4	›89	4	10-29	4
9-12	3	76-89	3	›29	3
6-8	2	50-75	2	6-9	2
4-5	1	1-49	1	1-5	1
3	0	0	0	0	0

RTS = 0.9368 x GCS_v + 0.7326 x SBP_v + 0.2908 x RR_v, where v is the value (0-4)

Data analysis

We used STATA 14 software for analysis. Tables and graphs were used to summarize descriptive results. A Cox regression model was employed to identify factors that influence mortality. The Cox regression model is the most popular regression technique for survival analysis. Cox regression model examines the impact of various predictors of the risk of death and also accounts for censoring in the data (37). Variables with a p-value < 0.25 in the univariate Cox regression model, were included in the multivariate analysis. We estimated hazard ratios and 95% confidence intervals.

A cutoff value of $p<0.05$ was used for statistical significance. Non-parametric tests such as the Kaplan Meir estimate, life table, and log-rank tests were employed. Log-log survival curves were used to assess the proportional hazard assumption based on Schohenfield residuals. Both bivariable and multivariable analyses were employed. Interaction of covariates on the main outcome was examined as necessary. Multicollinearity was assessed using variance inflation factor (VIF). We used the STROBE Checklist for reporting. Missing data were handled using available case analysis.

Patient and Public Involvement:

At the design stage, the proposed study was discussed with stakeholders, including the traffic office and zonal health departments. Because of the nature of the study, which involved emergency cases, we couldn't involve patients at the design stage. We informed the participants during data collection about the importance of the study to the community in the future. The policy brief will be prepared in the local language (Amharic) and will be disseminated to decision-makers and program implementers.

Results

Characteristics of the study subjects

Out of 11,960 trauma patients who visited the Emergency Department between 6- May 2019 and 30- February 2020, three thousand eighty-four cases were trauma victims of which road traffic injury constituted (18.2%). Four hundred fifty-four participants were enrolled and studied during the study period, and we excluded 106 from analysis because of incomplete information (Supplementary file). The study participants comprised 327 (72%) men and 127 (28%) women, resulting in a male to female ratio of 2.6:1.

The majority of the participants were in the productive age group. The mean age was 29±15.5 years. The median age was 27 years (IQR: 19, 37 years). The majority of the road traffic injury victims were passengers (232), followed by pedestrians (168) and drivers (54). As to the educational status, only 130 (28.6%) of the victims completed secondary education, while 144 (31.7%), were unable to read and write. The majority of the victims, 116 (25.5%), were farmers by occupation, followed by students (70). Two hundred sixty-four (58.1%) of the victims were urban, while 190 (41.9%) were rural dwellers. Nearly 60% (240) of the victims were from urban areas. The majority of accidents, 402 (88.5%), were sustained during daylight. Tuesday and Friday were found to be, the days with the highest frequency of accidents (Table 2).

Table 2: Characteristics of road traffic injury victims, May 2019-February 2020.

Variable	**Category**	**Frequency**	**Percentage**
Age			
	≤5 years	15	3.3%
	6-14	42	9.3%
	15-44	319	70.2%
	≥45	78	17.2%
Sex	Male	127	28%
	Female	327	72%
Road user category	Passengers	168	37%
	Pedestrian	232	51.1%
	Drivers	54	11.9%
Educational status	Can't read and write	144	31.7%
	Can read and write only	44	9%
	Primary education	85	18.7%
	Secondary education	131	29%
	Tertiary education	50	11%
Occupational status	Farmers	116	25.6%
	Gov. employee	53	11.7%
	Merchant	23	5.1%
	Student	70	15.4%
	Self- employee	68	15.0%
	Drivers	60	13.2%
	Others	64	14.0%
Residence	Urban	264	58.1
	Rural	190	41.9
Lighting condition	Daylight	402	88.5%
	Night	52	11.5%
Time of accident	6:00 AM-12:59AM	165	36.3%
	1:00 PM -6:59 PM	202	44.5%
	7:00 PM-11:59 PM	44	9%
	12:00 PM-5:59AM	43	9%
Day of the week	Monday	63	13.9%
	Tuesday	76	16.7%
	Wednesday	71	15.6%
	Thursday	61	13.4%
	Friday	76	16.7%
	Saturday	66	14.5%
	Sunday	41	9%

Type of vehicle	Heavy truck loaders	59	13%
	Peoples' transport	173	38.1%
	Cars	17	3.7%
	Three wheel vehicles	196	43.2%
	Others	9	2%

Pre-hospital circumstances, hospital arrival time, and means of transportation to the hospital

The median distance from the scene to the hospital was 40km; IQR (10km, 80km). Three hundred twelve (68.7%) of the accidents were within 60 km from the hospital, while the rest 142 (31.3%), were sustained within the distance range of 61 to 500km. Concerning hospital arrival time, 184 (40.5%) and 176 (38.9%), reported to the hospital within < 1 hour and 1-4 hours, respectively. The total pre-hospital time interval in this study was 364 minutes. The mean hospital arrival time was 144 and 537 minutes for accidents sustained in the town and the rural areas respectively.

None of the victims received pre-hospital care at the scene of the injury by trained personnel. Of the total injured, 283 (62.3%), were directly transferred from the scene, while 171 (37.7%) were referred from primary hospitals. None of the victims transferred from the primary hospitals got surgical intervention at the primary hospitals, except wound dressing, immobilization with local materials, and tetanus prophylaxis.

About means of transportation to the hospital, the majority, 311 (68.5%), were transferred by commercial vehicles. Only 93 (20.5%) were transferred by Ambulance, but none received pre-hospital care by a trained ambulance crew. Ambulance service was not for free, and the victims had to cover the cost of fuel ranging from 400-800 Ethiopian Birr (40-80 USD) (Table 3).

Table 3: Pre-hospital circumstances, hospital arrival time, and means of transportation.

Variables	**Category**	**Frequency**	**Percentage**
Distance from Hospital	≤60km	312	68.7%
	>60km	142	31.3%
Hospital arrival time			
	≤ 1 hour of injury	184	40.5%
	Within 1-4 hours of	176	38.8%
	injury	69	15.2%
	4- 24 hours of injury	25	5.5%
	>24 hours of injury		

Who brought the victims to the hospital?	Policeman	29	6.8%
	Relative/family	378	82.6%
	Others	47	10.6%
Transferred from	Primary hospitals	171	37.7%
	From the scene of an injury	283	62.3%
Transport to hospital	Ambulance	93	20.5%
	Commercial vehicles	311	68.5%
	Others	50	11%

Injury patterns and characteristics

Extremities and the heads were the most commonly injured body regions, accounting for 194 (42.7%) and 113 (24.9%) of cases, respectively. Multiple body region injuries accounted for 85 (18.7%), thoraco-abdominal body region accounted for 32 (7%), and other body regions including the face, teeth, and the like accounted for 30(6.6%).

We computed the injury severity score using the revised trauma score. Accordingly, the mean revised trauma score (RTS) was 6.5±2.0. The injury severity score ranges from 0.29 to 7.55. According to our data, 41 (9%) had RTS of <3 (non-survivable injury score) and 56 (12.3%) had RTS of <4.

Based on the Glasgow coma scale score, 64 (14.1%) had a severe head injury, 18 (4%) had moderate head injuries and 372 (81.9%) had no head injuries. Moreover, the rate of mortality was 52 (65%) for severe, 8 (10%) for moderate, and 20 (25%) for mild head injuries. Out of the observed 454 road traffic accidents, a fracture was sustained by 289 (63.7%) of victims. The most frequently involved bone was the lower extremity comprising 42% of all fractures followed by skull fracture (14.8%) (Figure 1).

Management of outcomes of road traffic injury victims

Out of the total 454 victims, 76 (16.8%) were evaluated and treated at an outpatient department, while 378 (83.2%) were admitted to the hospital for further evaluation and treatment. Of the total admitted, surgical intervention was required, for 162 (35.7%) cases. The most frequently performed major surgical procedure was craniotomy, 25 (15.4%) followed by intramedullary nailing (IMN) 15 (9%). From the minor procedures, wound debridement was the most frequently performed procedure, 64 (39.5%) followed by immobilization using plaster of Paris (POP) 42 (25.9%). The mean hospital stay was 6.2±10 days, ranging from 1 day to 100 days. Reasons for discharge were on physician advice in 246 (65%) cases followed by death in 71 (18.7%), against medical advice in 38 (10%), and referred for better management to higher centers in 24 (6.3%) cases (Table 4).

Table 4: Management outcome of road traffic injury victims; May 6; 2019 to February 2020.

Variables	Category	Frequency	Percentage
Decision at OPD	Sent home same day	76	16.7%
	Admitted to hospital	378	83.3%
Reason for admission	Requires surgery or resuscitation	256	67.73%
	Requires Close observation	122	32.27%
Commonly performed procedure	Debridement	64	28.9%
	Craniotomy	25	11.3%
	POP	52	23.5%
	Wiring & pin traction	17	7.6%
	Wound repair	22	10%
	Chest tube	12	5.4%
	IMN	18	8%
	Laparotomy	4	1.8%
	Others	7	3.1%
Mean hospital stay	6.6±9.8 days		
Reason for discharge	On medical advise	324	71.4%
	Died	71	15.6%
	Against medical advice	38	8.4%
	Referred	21	4.6%

Survival analysis

Four hundred fifty-four participants were followed, for a total of 275,534 person-hours. There were 80 (17.60%) deaths and 15(3.30%) losses to follow up. We used the available case analysis technique as a missing data management option. From the total deaths, 13 (16.25%) deaths occurred within the first hour of injury, 11 (13.75%) between the first and 4 hours of injuries, and 18 (22.50%) occurred between 4 and 24 hours of injury. Thirty-two (40%) of the deaths occurred after 24 hours up to the first seven days, while the rest six deaths occurred after a week of injury (Figure 2).

The overall incidence rate of death was 2.90 deaths per 10,000 person-hours of observation (95%CI: 2.77, 3.03). Since more than 75% of participants survived beyond the study time, we couldn't compute the median survival. Instead, we computed the cumulative and mean survival times. The mean survival time was 607 hours or 25.30 days with a standard deviation of 10 days. The cumulative proportion of surviving at the end of the first hour of injury was 97.30% (95% CI: 95.39%, 8.49%). Similarly, it was 94.93% (95% CI: 92.47%, 96.60%), 90.95% (95% CI: 87.92%, 93.23%), 83.89% (95% CI: 80.17, 86.97%) and 82.34% (95% CI: 78.51%, 85.56%) at the end of fourth, 24th, 168th and 720th hours of injury respectively (Table 5).

Table 5: Overall life table of road traffic injury victims; May 2019-February 2020

Time in hours	Number at risk	Loss to follow up	Number of events	Proportion of events	Proportion Surviving	Cumulative Proportion Surviving
1	442	0	12	0.027	0.973	0.973
2	433	0	9	0.02	0.98	0.95
3	432	0	1	0.002	0.99	0.94
4	431	0	1	0.002	0.998	0.938
6	429	0	2	0.004	0.996	0.934
12	428	0	1	0.002	0.998	0.932
24	413	0	15	0.036	0.964	0.89
48	406	0	7	0.0172	0.982	0.87
72	399	0	7	0.0175	0.982	0.85
96	392	0	7	0.0178	0.982	0.83
120	388	0	4	0.010	0.99	0.82
144	386	0	2	0.0052	0.99	0.81
168	381	0	5	0.013	0.98	0.79
288	380	0	1	0.002	0.997	0.77
312	379	0	1	0.002	0.997	0.75
432	378	0	1	0.002	0.997	0.74
480	377	0	1	0.002	0.997	0.73
528	376	0	1	0.002	0.997	0.72
672	375	0	1	0.0026	0.99	0.71

720	359	15	1	0.0027	0.99	0.70

Condition of victims on the 30th day of injury

Assessment on the 30th day of injury revealed that 30 (6.60%) were still in bed with unremarkable improvement, 263 (57.90%) had a better condition but not completely healed, 45 (9.90%) were healed with some limitation, 21 (4.60%), were completely healed, and back to work, 15 (3.30%) were lost to follow-up, while 80 (17.6%) died. Apart from those who died, 23 had functional losses (4 (0.88%) had lost teeth, 4 (0.88%), had an amputation of the limb, 3 (0.66%) had hearing loss, 3 (0.66%), had vision loss, 5 (1.10%), had impaired memory and 4 (0.88%) were paraplegic at 30th day of injury).

Immediate causes of deaths at a specific time interval

From the total of 17 deaths in the first hour of admission, 13 (76.5%) were due to non-survivable injury. The leading cause of death in the first four hours of admission to the hospital was hemorrhage (21.3%). Hemorrhage and secondary complications, mainly aspiration pneumonia were the major causes of death between the first 4 and 24 hours. According to our data, late deaths have resulted from sepsis and multiple organ failure (Figure 3). All deaths were confirmed by the clinician in charge of patient care.

Predictors of mortality following a road traffic injury

The significant predictors of time to death for road traffic injury victims were being a driver (AHR=2.26; 95% CI: 1.09, 4.65, AR=14.8), accident location at the rural residence (AHR=1.98; 95% CI: 1.02, 3.82;AR=21%), time from injury to hospital arrival (AHR=0.41; 95% CI: 0.16, 0.63;AR= 3%), systolic blood pressure on admission of <90mmHG(AHR= 3.66; 95% CI: 2.14, 6.26; AR=57%), GCS of <8 (AHR= 7.39 ; 95% CI, 3.0819 17.74464; AR=75.5%), GCS between 9-13 (AHR= 8.1565 (3.36 19.82, AR=39%), combined head injury with multiple body site (AHR= 2.33 (1.13, 4.80; AR=37%) and interaction of long distance from hospital (AHR=2.98 (1.46 4.39; AR=5.5%) (Table 6).

Table 6: Predictors of mortality following a road traffic injury, May 2019 to February 2020

Variables	Categories	Total	RTI deaths	CHR(95%CI)	AHR(95%CI)
Road user category	Pedestrian	168	22	1.00	1.00
	Passengers	234	43	1.47 (.88, 2.46)	1.97 (1.10, 3.52)*
	Drivers	54	15	2.36 (1.22 4.55)	2.61 (1.28 5.30)*
Residence	Urban	264	23	1.00	1.00
	Rural	194	57	3.90 (2.40 6.34)	1.98 (1.02 3.82)*
Hospital arrival time	Within <1 hour	184	32	1.00	1.00
	Within 1-4hours	176	25	.32 (.45 1.30)	.41 (.16 .63)**
	Within 24 hours	69	20	1.74 (.99 3.05)	.42 (.18 .95)
	After 24 hours	25	3	.64 (.19 2.09)	.40 (.10 1.56)
Systolic BP	≤89	53	36	10.07 (6.45 15.71)	3.66 (2.14 6.26)
	>89	401	44	1.00	1.00
GCS	≤8	64	52	32.44 (19.12 55.06)	7.39 (3.08 17.74)**
	9-12	18	8	9.97 (4.39 22.67)	8.15 (3.35 19.82)**
	13-15	372	20	1.00	1.00
Injury site	Non-head injury	262	14	1.00	1.00
	Isolated Head injury	105	33	7.05 (3.77 13.19)	2.28 (1.12 4.65)*
	Combined head injury	87	33	8.50 (4.54 15.89)	2.57 (1.26 5.24)**
Pre-hospital Care # distance	Yes#<60km	93	7	1.00	1.00
	Yes#>60km	79	11	1.74 (.87 3.48)	2.98 (1.46 4.39)*
	No#<60km	217	38	.688 (.25 1.89)	.60 (.28 1.25)
	No#>60km	65	24	3.69 (1.76 7.73)	.81 (.31 2.10)

Key * Significant at P<0.05, **P<0.001

Impact of the study

We have calculated the attributable risk for the predictors of mortality. Our study showed that accidents at inter-urban locations had an increased hazard of death when compared with those accidents in urban areas. The high mortality in these locations was partly due to lack of timely care on-site and delays to hospital arrival, mainly due to poor transport access and long distance from the hospital. This finding implies that the establishment of emergency medical services and improved access to health care facilities could reduce such deaths by 21%.

Those victims who had a systolic blood pressure of less than 90 mmHg on admission had a risk of death by more than 3. That implies restoring the hemodynamics of victims as early as possible can reduce deaths following an injury by 57%. With this regard, the role of emergency medical response at the scene of the injuries and early transfer of victims to definitive care units will have a vital role in reducing reversible causes of mortality.

The study demonstrated that those victims who had head injuries had a higher risk of death when compared with non-head injury cases. Accordingly, victims with an isolated head injury and multiple injuries had more than twice the risk of death when compared with other body regions. Hence, the use of protective materials such as helmets could potentially reduce mortality following a road traffic injury by 26-32%.

Discussion

The current study demonstrated that deaths following a trauma follow the classical tri-modal pattern in low-resource countries, and pre-hospital care is rarely available for victims of road traffic injuries. Free ambulance transportation was in-available for trauma victims resulting in a delay in hospital arrival for accidents sustained on rural roads. Driver, accident location in rural areas, low systolic blood pressure, low GCS on admission, injury site, and interaction of providing pre-hospital care and long-distance were significantly associated with time to death among road traffic injury victims.

The current study demonstrated that deaths following a trauma follow the classical tri-modal pattern in low-resource countries, and pre-hospital care is rarely available for victims of road traffic injuries. Free ambulance transportation was in-available for trauma victims resulting in a delay in hospital arrival for accidents sustained on rural roads. Being a driver, accident location in rural areas, low systolic blood pressure, low GCS on admission, injury site, and interaction of providing pre-hospital care and long-distance was found to be, predictors of time to death among road traffic injury victims.

The classical tri-modal distribution of trauma deaths was described by Trunkey, in 1983 (38). Different previous studies had disproved this traditional distribution of mortalities due to a reduction in the number of early and late hospital deaths (39). Our study demonstrated that road traffic injury mortality still followed the traditional tri-modal pattern. According to the current study, there were two peaks. One peak was in the first 24 hours and the second at the end of the first week of the injury. Nearly half of the deaths occurred in the hospital after a week of admission. A similar finding was reported by a study conducted in Iran showing two peak times. (31). Poor operative services for severe head injury cases and lack of intensive care unit for severely injured victims could explain the reason for late deaths in our hospital (40). The surgical setup in our case is not optimum to perform surgical intervention for severely injured head injury victims. Besides, there is no well-equipped surgical ICU service to support victims with ventilatory failure. On the other side, the in-availability of pre-hospital basic life support care could have resulted in clinical deterioration of victims that could result in late complications (10).

In this study, none of the victims received pre-hospital care at the scene of injury. This is consistent with previous studies that showed pre-hospital emergency care is under-served or unavailable in most low and middle-income countries (41, 42). The finding is also consistent with a study conducted in Addis Ababa, where none of the victims got pre-hospital care (17). The current study also indicated that full package Ambulance service was unavailable for all the victims, and only 20% received transportation service without trained personnel accompanying the victims. Our finding is in line with a systematic review, indicating Ambulance service was underserved in many low and middle-income countries (43) and a study conducted in Pakistan that reported the majority of participants didn't want to call Ambulance for emergency cases because the Ambulances didn't function properly (44). On top of this, the available ambulance service was not for free. The victims or the family have to cover the cost of fuel and per Diem of drivers. A similar finding was reported in Cambodia (45).

The current study also showed that many trauma victims who were referred from primary hospitals would have been treated, at those hospitals. This is in line with a study conducted at Southern India, which showed that trauma care was unnecessarily delayed and liable for unnecessary referrals due to poor resources for trauma case management (31) and another study demonstrated that there are many deficiencies in emergency care services ranging from in-availability of drugs and lack of training to provide the required emergency care (46).

According to our study, the overall incidence of road traffic injury deaths was 29 per 100,000 hours of observation. This finding is higher when compared with a study conducted at Tikur Anbessa Hospital, Addis Ababa, which was 10/100,000 hours of observation (17). The discrepancy could be explained by the fact that the Tikur Anbessa Hospital has a better trauma management setup including an intensive care unit (ICU). Hence the quality of care could explain the lesser death at the Tikur Anbessa Hospital (17). Another explanation could be because follow-up continued after discharge from the hospital in the current study, while the mentioned study didn't follow victims after discharge that ignored deaths at home after discharge.

The study revealed that pedestrians are the most frequently affected road user categories when compared with passengers and drivers. This is in line with the federal police commission report (47) and studies conducted in the capital city, Addis Ababa. (48) Both studies showed pedestrians to be the road user categories most frequently affected by RTI. But severe and fatal injuries were more likely to occur among drivers and passengers in our study. Though the number of injured drivers was less in number when compared with both passengers and pedestrians, the proportion of fatality was higher among drivers. This could be explained by the fact that the majority of drivers in Ethiopia are reluctant in using seat belts and they are more likely to have crashes resulting in a fatality. From a previous study, it was found that 57.5% of drivers unfasten their seat belts while driving (49). This finding was consistent with a previous study that indicated fatal injuries were more likely among drivers and passengers (50). But another study reported a contradictory finding, showing pedestrians are more likely to die from a vehicle accident (51).

Our study demonstrated that accidents sustained in rural areas were more likely to result in a fatal outcome than in urban locations. Our finding is consistent with a study conducted by Craig Zwerling and colleagues that showed injury severity and fatality was more than three times higher in the rural area than urban areas (52). Lack of appropriate health care facilities and limitation of transportation access could explain the finding. That will, in turn, result in bad outcomes (53). Risky driving behavior such as over speeding is more common in rural areas due to poor traffic control. That could explain the high mortality in rural areas.

Previous evidence showed that accident intensity increases when a crash is caused by a speedy vehicle (54).

Low systolic blood pressure on admission was significantly associated with time to death among road traffic injury victims. This finding is in line with previous studies that showed, victims with low blood pressure on admission were more likely to experience death than their counterparts (16, 55-56). Exsanguination from severe injury explains the drop in blood pressure (57). Low systolic blood pressure could increase mortality via poor organ perfusion and consequent organ failure (58). Nosocomial infections and sepsis are likely in hemorrhagic shock resulting in acidosis and poor perfusion (59, 60). These are the possible explanations for low systolic blood pressure and increased mortality.

The current study revealed that hospital arrival time is associated with 30 days of mortality following a road traffic injury. Accordingly, victims who arrived at the hospital between one to four hours were more likely to die than those who arrived within one hour of injury and beyond 4 hours of injury. The finding is contrary to the concept of the "Golden hour" of trauma that depicts the outcome of trauma, which is better when victims arrive within one hour of injury (61- 62). That could be because victims who are seriously injured and have non-survivable injuries were more likely to be directly transferred to the hospital immediately after injury, while less severe injury cases took their time.

The study showed an interaction between long distances from the hospital and pre-hospital first aid to be significantly associated with 30 days mortality following a road traffic injury. The possible explanation for this finding could be due to delays in definitive care. Though essential trauma care is vital to treat time-sensitive issues, delayed expert-requiring procedures could result in poor outcomes (63). This is particularly the case in low-resource countries like Ethiopia where the majority of primary hospitals are not in a position to provide essential trauma care (64).

Limitation of the study

As our participants were only those victims who visited the hospital during the data collection period, we excluded deaths at the scene of the injury and minor cases who didn't come to the hospital. Such exclusion might underestimate the actual injuries and mortalities from a road traffic injury. Besides, the exclusion of minor cases might introduce selection bias. Besides, the exclusion of minor cases might introduce selection bias. The time interval between injury and hospital arrival was determined based on self-report or family report. We expect a recall bias in such a stress full situation. The direct cause of death was assessed using verbal autopsy for those deaths that occurred at home after discharge. This may not be precise without autopsy and physician judgment.

Because many of the drivers escape or were arrested after the accidents, we couldn't assess driver-related risk factors such as speed, presence of drunk driving, age, and experience of driving which could be a source of variability for the outcome of the injury.

Conclusions

This study demonstrated that the classical tri-modal pattern of mortality is still occurring in low-resource settings. The study showed that there is a gap in both pre-hospital trauma care and primary trauma care at district hospitals in the study area. Being a driver, accidents at the inter-urban roads, low systolic blood pressure, low GCS on admission, and presence of head injuries were predictors of time to death following road traffic injuries.

The regional and zonal health sectors need to revise the pre-hospital trauma care service implementation including Ambulance access and package. The hospital needs to improve trauma care services, especially surgical and supportive interventions such as mechanical ventilatory support for severely injured victims. Future studies should be conducted to assess the capability of primary hospitals in the area in providing essential trauma care, and barriers to establishing emergency medical service in the country at large, and the study area in particular.

Generalizability of the study: We tried to use a representative sample based on appropriate power calculation and use a pre-tested and piloted tool to collect data, hence we can generalize the result from this study for all road traffic injury cases in the Amhara region.

Figure legend

Figure 1: Commonly sustained fractures among RTI victims, Hospital, Ethiopia

Figure 2: Timing distribution of mortality following road traffic injuries, May 6; 2019 to February 30, 2020

Figure 3: Immediate causes of deaths following a road traffic injury at a specific time interval, May 2019 –February 2020.

Abbreviations

AHR	Adjusted Hazard Ratio
AR	Attributable Risk
BP	Blood Pressure
CI	Confidence Interval
GCS	Glasgow Coma Scale
HIV	Human Immuno Virus
HR	Heart Rate

ICU	Intensive Care Unit
IMN	Intra Medullary Nailing
IQR	Interquartile Range
O_2	Oxygen
POP	Plaster of Paris
PR	Pulse Rate
RTI	Road Traffic Injuries
RTS	Revised Trauma Score
RR	Respiratory Rate
SBP	Systolic Blood Pressure
SD	Standard Deviation

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from the University of Gondar Ethical review board (R.N. O/V/P/RCS/051049/2019), and a permission letter was obtained from Gondar University Comprehensive Specialized Hospital. Informed written consent was obtained from participants, caregivers, or proxy as appropriate. The purpose of the study was explained to every victim or an appropriate proxy. On arrival at the emergency department, only hospital arrival time was registered and other information was collected after all the necessary medical care was secured. During our observation, any abnormal finding or complaint such as pain was communicated to the appropriate medical care team for intervention. For those victims who were discharged against medical advice, we continued our follow-up by phone and some of them changed their minds and returned and continued their medical follow-up.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interest

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Authors' contribution

ZD designed the study, analyzed the data, and drafted the manuscript. MY, TA, GB, and KG were involved in the design of the study, analysis, and critically evaluated the manuscript for intellectual content. All authors read and approved the final manuscript.

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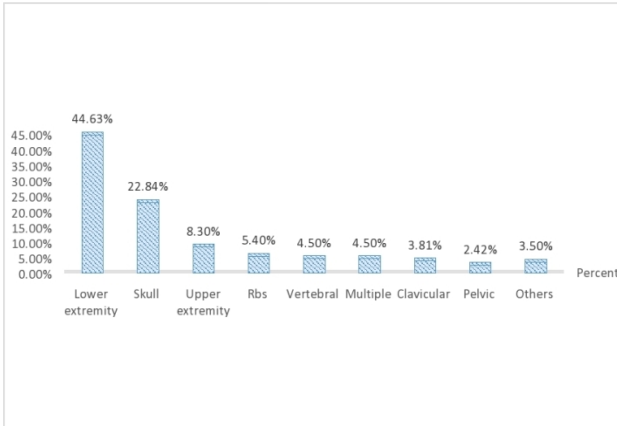

Figure 1: Commonly sustained fractures among RTI victims, Hospital, Ethiopia

449x582mm (72 x 72 DPI)

Figure 2: Timing distribution of mortality following road traffic injuries, May 6; 2019 to February 30, 2020

Figure 2: Timing distribution of mortality following road traffic injuries, May 6; 2019 to February 30, 2020

449x582mm (72 x 72 DPI)

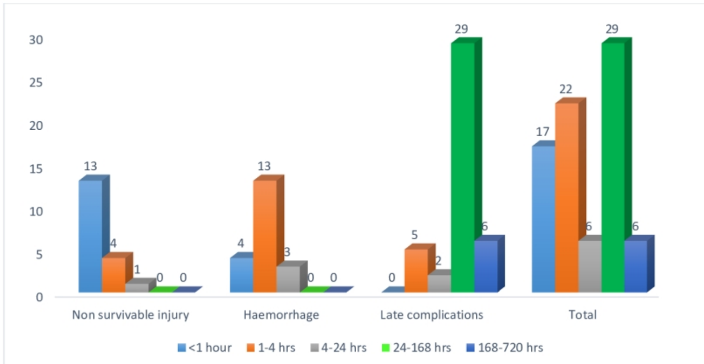

Figure 3: Immediate causes of deaths following a road traffic injury at a specific time interval, May 2019 –February 2020.

Figure 3: Immediate causes of deaths following a road traffic injury at a specific time interval, May 2019 – February 2020.

215x279mm (200 x 200 DPI)

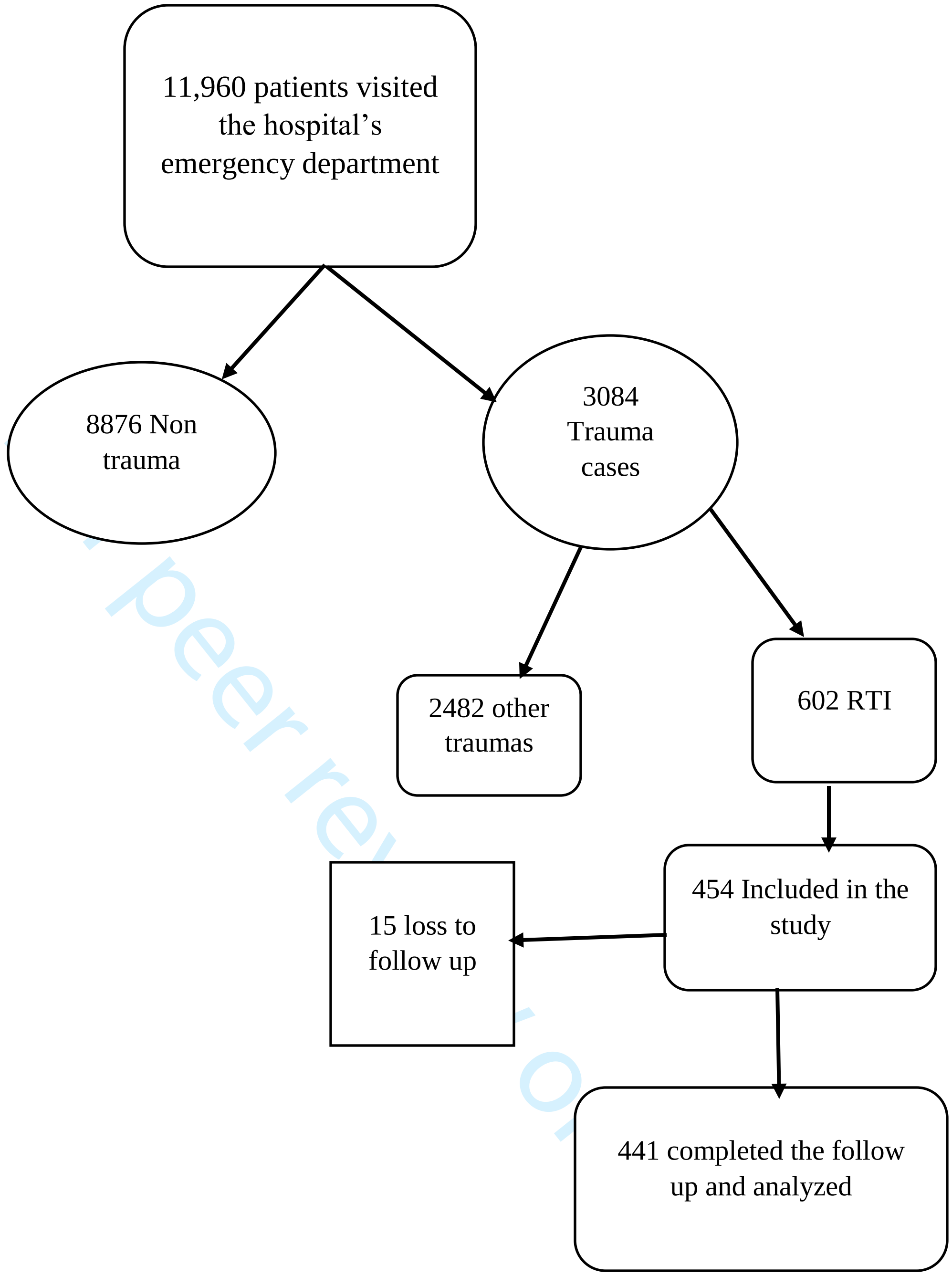

Figure 1: Schematic presentation of participants' selection

Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	Page 1 line 1-2
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	Lines 30-58
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	Lines 68-121
Objectives	#3	State specific objectives, including any prespecified hypotheses	Line 122-126
Methods			
Study design	#4	Present key elements of study design early in the paper	Line 129-130
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Lines 132-151
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	Lines 153-155
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	N/a
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Lines 157-166
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for exposed and	Lines 168-186

		unexposed groups if applicable.	
Bias	#9	Describe any efforts to address potential sources of bias	Lines 188-199
Study size	#10	Explain how the study size was arrived at	Lines 201-206
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	N/a
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	Lines 214-227
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	Lines 224-225
Statistical methods	#12c	Explain how missing data were addressed	Lines 226
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	Lines 226
Statistical methods	#12e	Describe any sensitivity analyses	n/a
Results			
Participants	#13a	Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed. Give information separately for exposed and unexposed groups if applicable.	Additional file 1
Participants	#13b	Give reasons for non-participation at each stage	Additional file 1
Participants	#13c	Consider use of a flow diagram	Additional file 1
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	Lines 237-251
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	Line 302-304
Descriptive data	#14c	Summaries follow-up time (e.g., average and total amount)	Lines 302-304
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	Lines 320-326
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Lines 335-343
Main results	#16b	Report category boundaries when continuous variables were categorized	N/a
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Lines 348-363
Other analyses	#17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	#18	Summarize key results with reference to study objectives	Lines 365-460
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	Lines 462-473
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	Lines 467-480

Generalisability	#21	Discuss the generalizability (external validity) of the study results	Lines 487-489
Other Information		Ethical approval	Lines 500-509
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Lines 519-520

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Do deaths from road traffic injuries follow a classical trimodal pattern in North West Ethiopia? A hospital based prospective cohort study.

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Abstract

Objective

The objective of this study was to identify timing distribution and predictors of deaths following road traffic injuries among all age groups at Gondar Comprehensive specialized hospital.

Design

A single-center prospective cohort study.

Setting: The study hospital is a tertiary hospital in North West Ethiopia

Participants

We enrolled 454 participants who sustained road traffic injuries in to the current study. All age groups and injury severity were included except those who arrived dead, had no attendant, and when the injury time was unknown.

Primary and secondary outcome measures

The primary outcome was time to death measured in hours from injury time up to the 30th day of the injuries. Secondary outcomes were pre-hospital first aid, length of hospital stay, and hospital arrival time. The article has been registered, with a unique identification number (UIN) of research registry 6556".

Results

A total of 454 victims were followed for 275,534 person-hours. There were 80 deaths with an overall incidence of 2.90 deaths per 10,000 person-hours of observation (95% CI: 2.77, 3.03). The significant predictors of time to death were being a driver (AHR=2.26; 95% CI: 1.09, 4.65, AR=14.8), accident at inter urban roads (AHR=1.98; 95% CI: 1.02, 3.82, AR=21%), time from injury to hospital arrival (AHR=0.41; 95% CI: .16, 0.63; AR= 3%), SBP on admission of <90mmHG (AHR= 3.66; 95% CI: 2.14, 6.26; AR=57%), GCS of <8 (AHR= 7.39; 95% CI, 3.0819 17.74464;AR=75.7%), head injury with polytrauma (AHR= 2.32 (1.12774 4.79; AR=37%) and interaction of distance from hospital with pre-hospital care.

Conclusion

Though the maturation of trauma centers in many developed countries has changed the temporal pattern of deaths following any trauma, our study demonstrated that trauma deaths follow the traditional tri-modal pattern. That implies that potentially preventable causes of death continued in low-resource countries.

Keywords: Deaths, Predictors, Hazard ratio, attributable risk, population attributable risk, Road traffic injury, timing

Strength and limitation

- As far as our search is concerned, this is the first study of its kind investigating road traffic injury prospectively using an advanced statistical method (Survival analysis).
- Follow-up of victims was extended after discharge from the hospital up to 30 days.
- The dropout rate was minimal.
- Out of hospital deaths were excluded

Background

Annually, nearly 6 million people die from injury, which is more than deaths caused by a combination of HIV, tuberculosis, and malaria (1). Besides, every fatal injury is responsible for 20–50 non-fatal injuries that influence productivity and consequently affect economic development (2, 3). Road traffic injuries are among the leading causes of trauma that affect a country's economies. That is because it mainly affects the economically active segment of the population (4). It impacts more than 3% of gross domestic product for most countries (5). For example, it resulted in 2.1% of economic losses in Ethiopia in 2015 (6). The World Bank estimated that the cost of road crash injuries is about 1% of the gross national product in low-income countries, 1.5% in middle-income countries, and 2% in high-income countries (7). Road traffic injury-related mortality continues to increase from time to time globally, but its burden is more than three times higher in low-income countries (8). This discrepancy is partly due to the immature trauma care system, both in the pre-hospital and in-hospital settings (9-11). Even though Ethiopia has adopted safety legislation that protects vulnerable road users, there is still a considerable gap in practicing traffic laws on drunk driving, seat belt wearing, speed limits, helmets, and child restraints. These are possible explanations for the high prevalence of road traffic injuries and mortalities in Ethiopia (12).

Ethiopia is one of the poorest countries with a double burden of communicable and non-communicable diseases (13). The country has one of the highest road traffic injury-related mortality in the sub-Saharan region (14). Despite the efforts made in the training of key emergency personnel, there is no well-established emergency medical system to provide pre-hospital trauma care (15). The only available emergency service is the infrequent Ambulance transportation, which itself lacks health care professionals' support (16). These are the main factors explaining the higher fatality following a traffic injury in Ethiopia (17, 18).

Among many factors affecting deaths following a trauma, time from injury to death has attracted the attention of several scholars for three decades (19-21). The mortality pattern was described as a trimodal pattern by Trunkey in 1983 (19). According to Trunkey, there are three peaks of deaths following trauma. The first peak of death occurs immediately within minutes of the injury. Most deaths at the scene are from non-survivable injury to the brain and thorax (22).
The second peak occurs within the first four hours of injury (23). The second peak occurs within the first four hours of injury (23). The most common causes of death during the second peak are severe cardiovascular and intra-abdominal injuries. (24-26). Well-organized pre-hospital care and timely definitive care at hospitals could avoid these deaths (27).

The third peak of death following trauma, called "late deaths", occurs after the first week of injury (28). Such deaths have resulted from late complications such as sepsis and multiple organ failure (29). The advance in the trauma care system in most developed countries has significantly reduced late deaths. That has changed the classical trimodal pattern of deaths following trauma into a bimodal pattern (21, 27- 30). However, studies from low-income countries showed that it still follows the classical tri-modal pattern (31).

Delays in hospital arrival are among various factors determining the time to death following injury (32). In most areas of low and middle-income countries, Ambulance service is not available to transfer victims from an accident scene, and if at all available, there is poor coordination between ambulance staff and hospital staff. This poor coordination results in delays in trauma care at the health care facility (33).   In countries like Ethiopia, where there is no pre-hospital trauma care system and poor road infrastructure, delays in hospital arrivals are apparent. That could be one reason for the high mortality rate following road traffic injuries. According to a WHO report, the mortality rate from road traffic injuries was 25.3 and 26.7 per 100,000 populations in 2015 and 2018, respectively (7, 8).

There is a paucity of information on the pattern of mortality following traumas in the study area. The few available studies are cross-sectional and document-based which lacks information on important predictors. The previous studies are often institutional-based and only included deaths in the hospital ignoring late deaths at home (17, 18). There was also a methodological gap in the analysis in that it ignores the time component of death.

There is also a scarcity of evidence on hospital arrival time, time to death, and predictors of mortality following a road traffic injury in the study area. This study aimed to identify the proportion of victims who got pre-hospital care at the scene of injury. It also describes hospital arrival time, time to death, and its predictors following road traffic injuries. The analysis of trauma-related death is a crucial step for the development and improvement of trauma care systems.

Methods

Study Design

It is a single-center prospective hospital-based follow-up study, from 01-May 2019 to 30-February 2020, at the north Gondar zone, North West Ethiopia.

Study settings

The study hospital is one of the referral and Teaching Hospitals in the country. With more than 500 bed capacity, it provides basic and advanced services at its different units, including a 24-hour emergency department receiving all emergency cases.

Musculoskeletal and head trauma cases are cared for by four orthopedic surgeons and one neurosurgeon. General surgeons and specialists in other fields such as thoracic, gastrointestinal, genitourinary, and maxillofacial surgery are also assigned 24hr on-call to manage trauma cases. The emergency department is run by 29 nurses assigned on 24hrs-rotation. Every day, five surgical Residents and one senior orthopedic surgeons deliver their expert care in the emergency department. The emergency department provides initial evaluation and resuscitation for trauma victims. The maximum observation time in the emergency department is 24 hours, after which the patient is either discharged, admitted to the appropriate unit, or referred.

The hospital provides general operative services in two minor surgery facilities and one main theatre complex. There are also operative services at obstetric unit, fistula, dental, and ophthalmic operative units.

The hospital has a radiology department staffed with five senior radiologists and other supportive technicians. The available imaging services include conventional radiology, ultrasonography, magnetic resonance imaging, and computerized tomography.

Based on our pilot study, trauma constituted nearly 30% of emergency-related admissions in the hospital. Concerning emergency response, the hospital provides 24 hours trauma services, but there are no established out-of-hospital emergency care services.

Eligibility criteria

All traffic injury victims regardless of age and sex were included except those who were dead on arrival, comatose, and had no attendant. We also excluded Victims when the time of injury was unknown. The enrolled participants were observed on daily basis using a pre-designed checklist.

Study variables

The primary outcome was time to death measured in hours between road traffic injury and the 30th day of injury. Accordingly, those victims who died between injury times to the 30th day of injury were events, and those who were still alive on the 30th day were censored cases. Secondary outcomes were pre-hospital first aid, length of hospital stay, and hospital arrival time. The exposure variable was having any degree of injury by any vehicle. The independent variables were sociodemographic factors (age, sex, educational status, occupation and residence of the victims and the distance between accident location and hospital), accident-related factors (road user category, type of vehicle, time of the accident, day of the week, lighting condition), pre-hospital first aid, means of transport to the hospital, hospital arrival time, anatomic body region injured, vital signs, neurologic status, and injury severity score.

Data sources/ measurement

We included all road traffic injury victims who visited the hospital during the data collection period. We excluded Victims who arrived dead, were comatose, and with no attendant and unknown injury time.

Four trained data collectors collect the data using a structured and tested checklist. The information collected includes epidemiological variables, crash characteristics, and hospital arrival time. Additionally, we collected data on road user category, availability of pre-hospital first aid, type of transportation used to transfer the victim, clinical findings, the outcome in the emergency department, and decision after evaluation at the emergency department. We collected data regarding road traffic injury-related events and pre-hospital factors from the victims or the relatives accompanying the victim.

Interviewing a victim was done after securing the initial lifesaving management at an emergency department. For seriously sick victims unable to communicate, we collect data from the caregivers. The maximum follow-up time was one month. Victims discharged before one month and sent home the same day were contacted by phone on the 30th day of injury to know their status.

We collected the immediate cause of in-hospital mortality from the victims' medical records. For late deaths that occurred after hospital discharge, we collected verbal autopsies from family or attendants. Verbal autopsy was collected by phone (34). A checklist was developed for the verbal autopsy that incorporates relevant information. The verbal autopsy checklist comprised the clinical condition of the victims during the last days of survival.

Source of bias and minimizing strategy

The severity of the injury is one possible source of bias in this study. Thus we enrolled participants regardless of an injury severity score. To minimize bias due to attrition, we explained the value of remaining in the study for participants.

We made a repeated attempt to contact participants after discharge from the hospital to know their status on the 30th day of injury. We also took multiple contact numbers to access the victims or proxy. The data collection tool was also piloted and standardized to avoid interviewer bias. Bias due to instrument error was minimized, by taking measurements repeatedly. Bias due to differential selection was minimized by including all degrees of injury (mild and severe cases) at the design stage. At the analysis stage, bias due to confounding was minimized, by conducting multivariable analysis and stratified analysis. We used a predefined and prepared data management plan to avoid selective reporting bias.

Sampling and sample size

The sample size was calculated using the sample size calculation formula for survival analysis using STATA 14. Considering the following assumptions, α=0.05, β=0.2, HR=0.643, taken from a study conducted in Turkey indicating hazard of death among victims with low GCS was 0.64% (35), probability of an event from pilot study =0.28, (SD=0.5), and amount of event/probability of an event. Therefore, event=121, n=amount of event/probability of event=121/0.28=432, and considering 5% loss to follow up=454.

Operational definition

The trauma severity score was computed using the "Revised Trauma Severity Score" based on three parameters. These parameters are the Glasgow coma scale (GCS), respiratory rate (RR), and systolic blood pressure (SBP) (36). According to the revised trauma score, these three parameters are coded and summed up (Table 1).

Table 1: Parameters used to measure revised trauma score

GCS	**Code**	**SBP**	**Code**	**RR**	**Code**
13-15	4	›89	4	10-29	4
9-12	3	76-89	3	›29	3
6-8	2	50-75	2	6-9	2
4-5	1	1-49	1	1-5	1
3	0	0	0	0	0

RTS = $0.9368 \times GCS_v + 0.7326 \times SBP_v + 0.2908 \times RR_v$, where v is the value (0-4)

Data analysis

We used STATA 14 software for analysis. Tables and graphs were used to summarize descriptive results. A Cox regression model was employed to identify factors that influence mortality. The Cox regression model is the most popular regression technique for survival analysis. Cox regression model examines the impact of various predictors of the risk of death and also accounts for censoring in the data (37). Variables with a p-value < 0.25 in the univariate Cox regression model, were included in the multivariate analysis. We estimated hazard ratios and 95% confidence intervals.

A cutoff value of p<0.05 was used for statistical significance. Non-parametric tests such as the Kaplan Meir estimate, life table, and log-rank tests were employed. Log-log survival curves were used to assess the proportional hazard assumption based on Schohenfield residuals. Both bivariable and multivariable analyses were employed. Interaction of covariates on the main outcome was examined as necessary. Multicollinearity was assessed using variance inflation factor (VIF). We used the STROBE Checklist for reporting. Missing data were handled using available case analysis.

Patient and Public Involvement:

At the design stage, the proposed study was discussed with stakeholders, including the traffic office and zonal health departments. Because of the nature of the study, which involved emergency cases, we couldn't involve patients at the design stage. We informed the participants during data collection about the importance of the study to the community in the future. The policy brief will be prepared in the local language (Amharic) and will be disseminated to decision-makers and program implementers.

Results

Characteristics of the study subjects

Out of 11,960 trauma patients who visited the Emergency Department between 6- May 2019 and 30- February 2020, three thousand eighty-four cases were trauma victims of which road traffic injury constituted (18.2%). Four hundred fifty-four participants were enrolled and studied during the study period, and we excluded 106 from analysis because of incomplete information (Supplementary file). The study participants comprised 327 (72%) men and 127 (28%) women, resulting in a male to female ratio of 2.6:1.

The majority of the participants were in the productive age group. The mean age was 29±15.5 years. The median age was 27 years (IQR: 19, 37 years). The majority of the road traffic injury victims were pedestrians (232), followed by passengers (168) and drivers (54). As to the educational status, only 130 (28.6%) of the victims completed secondary education, while 144 (31.7%), were unable to read and write. The majority of the victims, 116 (25.5%), were farmers by occupation, followed by students (70). Two hundred sixty-four (58.1%) of the victims were urban, while 190 (41.9%) were rural dwellers. Nearly 60% (240) of the victims were from urban areas. The majority of accidents, 402 (88.5%), were sustained during daylight. Tuesday and Friday were found to be, the days with the highest frequency of accidents (Table 2).

Table 2: Characteristics of road traffic injury victims, May 2019-February 2020.

Variable	Category	Frequency	Percentage
Age			
	≤5 years	15	3.3%
	6-14	42	9.3%
	15-44	319	70.2%
	≥45	78	17.2%
Sex	Male	327	72%
	Female	127	28%
Road user category	Passengers	168	37%
	Pedestrian	232	51.1%
	Drivers	54	11.9%
Educational status	Can't read and write	144	31.7%
	Can read and write only	44	9%
	Primary education	85	18.7%
	Secondary education	131	29%
	Tertiary education	50	11%
Occupational status	Farmers	116	25.6%
	Gov. employee	53	11.7%
	Merchant	23	5.1%
	Student	70	15.4%
	Self- employee	68	15.0%
	Drivers	60	13.2%
	Others	64	14.0%
Residence	Urban	264	58.1
	Rural	190	41.9
Lighting condition	Daylight	402	88.5%
	Night	52	11.5%
Time of accident	6:00 AM-12:59AM	165	36.3%
	1:00 PM -6:59 PM	202	44.5%
	7:00 PM-11:59 PM	44	9%
	12:00 PM-5:59AM	43	9%

Day of the week	Monday	63	13.9%
	Tuesday	76	16.7%
	Wednesday	71	15.6%
	Thursday	61	13.4%
	Friday	76	16.7%
	Saturday	66	14.5%
	Sunday	41	9%
Type of vehicle	Heavy truck loaders	59	13%
	Peoples' transport	173	38.1%
	Cars	17	3.7%
	Three wheel vehicles	196	43.2%
	Others	9	2%

Pre-hospital circumstances, hospital arrival time, and means of transportation to the hospital

The median distance from the scene to the hospital was 40km; IQR (10km, 80km). Three hundred twelve (68.7%) of the accidents were within 60 km from the hospital, while the rest 142 (31.3%), were sustained within the distance range of 61 to 500km. Concerning hospital arrival time, 184 (40.5%) and 176 (38.9%), reported to the hospital within < 1 hour and 1-4 hours, respectively. The total pre-hospital time interval in this study was 364 minutes. The mean hospital arrival time was 144 and 537 minutes for accidents sustained in the town and the rural areas respectively.

None of the victims received pre-hospital care at the scene of the injury by trained personnel. Of the total injured, 283 (62.3%), were directly transferred from the scene, while 171 (37.7%) were referred from primary hospitals. None of the victims transferred from the primary hospitals got surgical intervention at the primary hospitals, except wound dressing, immobilization with local materials, and tetanus prophylaxis.

About means of transportation to the hospital, the majority, 311 (68.5%), were transferred by commercial vehicles. Only 93 (20.5%) were transferred by Ambulance, but none received pre-hospital care by a trained ambulance crew. Ambulance service was not for free, and the victims had to cover the cost of fuel ranging from 400-800 Ethiopian Birr (40-80 USD) (Table 3).

Table 3: Pre-hospital circumstances, hospital arrival time, and means of transportation

Variables	Category	Frequency	Percentage
Distance from Hospital	≤60km	312	68.7%
	>60km	142	31.3%
Hospital arrival time			
	≤ 1 hour of injury	184	40.5%
	Within 1-4 hours of	176	38.8%
	injury	69	15.2%
	4- 24 hours of injury	25	5.5%
	>24 hours of injury		
Who brought the victims to the hospital?	Policeman	29	6.8%
	Relative/family	378	82.6%
	Others	47	10.6%
Transferred from	Primary hospitals	171	37.7%
	From the scene of an injury	283	62.3%
Transport to hospital	Ambulance	93	20.5%
	Commercial vehicles	311	68.5%
	Others	50	11%

Injury patterns and characteristics

Extremities and the heads were the most commonly injured body regions, accounting for 194 (42.7%) and 113 (24.9%) of cases, respectively. Multiple body region injuries accounted for 85 (18.7%), thoraco-abdominal body region accounted for 32 (7%), and other body regions including the face, teeth, and the like accounted for 30(6.6%).

We computed the injury severity score using the revised trauma score. Accordingly, the mean revised trauma score (RTS) was 6.5±2.0. The injury severity score ranges from 0.29 to 7.55. According to our data, 41 (9%) had RTS of <3 (non-survivable injury score) and 56 (12.3%) had RTS of <4.

Based on the Glasgow coma scale score, 64 (14.1%) had a severe head injury, 18 (4%) had moderate head injuries and 372 (81.9%) had no head injuries. Moreover, the rate of mortality was 52 (65%) for severe, 8 (10%) for moderate, and 20 (25%) for mild head injuries. Out of the observed 454 road traffic accidents, a fracture was sustained by 289 (63.7%) of victims. The most frequently involved bone was the lower extremity comprising 42% of all fractures followed by skull fracture (14.8%) (Figure 1).

Management of outcomes of road traffic injury victims

Out of the total 454 victims, 76 (16.8%) were evaluated and treated at an outpatient department, while 378 (83.2%) were admitted to the hospital for further evaluation and treatment. Of the total admitted, surgical intervention was required, for 162 (35.7%) cases. The most frequently performed major surgical procedure was craniotomy, 25 (15.4%) followed by intramedullary nailing (IMN) 15 (9%). From the minor procedures, wound debridement was the most frequently performed procedure, 64 (39.5%) followed by immobilization using plaster of Paris (POP) 42 (25.9%). The mean hospital stay was 6.2±10 days, ranging from 1 day to 100 days. Reasons for discharge were on physician advice in 246 (65%) cases followed by death in 71 (18.7%), against medical advice in 38 (10%), and referred for better management to higher centers in 24 (6.3%) cases (Table 4).

Table 4: Management outcome of road traffic injury victims; May 6; 2019 to February 2020.

Variables	Category	Frequency	Percentage
Decision at OPD	Sent home same day	76	16.7%
	Admitted to hospital	378	83.3%
Reason for admission	Requires surgery or resuscitation	256	67.73%
	Requires Close observation	122	32.27%
Commonly performed procedure	Debridement	64	28.9%
	Craniotomy	25	11.3%
	POP	52	23.5%
	Wiring & pin traction	17	7.6%
	Wound repair	22	10%
	Chest tube	12	5.4%
	IMN	18	8%
	Laparotomy	4	1.8%
	Others	7	3.1%
Mean hospital stay	6.6±9.8 days		
Reason for discharge	On medical advise	324	71.4%
	Died	71	15.6%
	Against medical advice	38	8.4%
	Referred	21	4.6%

Survival analysis

Four hundred fifty-four participants were followed, for a total of 275,534 person-hours. There were 80 (17.60%) deaths and 15(3.30%) losses to follow up. We used the available case analysis technique as a missing data management option. From the total deaths, 13 (16.25%) deaths occurred within the first hour of injury, 11 (13.75%) between the first and 4 hours of injuries, and 18 (22.50%) occurred between 4 and 24 hours of injury. Thirty-two (40%) of the deaths occurred after 24 hours up to the first seven days, while the rest six deaths occurred after a week of injury (Figure 2).

The overall incidence rate of death was 2.90 deaths per 10,000 person-hours of observation (95%CI: 2.77, 3.03). Since more than 75% of participants survived beyond the study time, we couldn't compute the median survival. Instead, we computed the cumulative and mean survival times. The mean survival time was 607 hours or 25.30 days with a standard deviation of 10 days. The cumulative proportion of surviving at the end of the first hour of injury was 97.30% (95% CI: 95.39%, 8.49%). Similarly, it was 94.93% (95% CI: 92.47%, 96.60%), 90.95% (95% CI: 87.92%, 93.23%), 83.89% (95% CI: 80.17, 86.97%) and 82.34% (95% CI: 78.51%, 85.56%) at the end of fourth, 24th, 168th and 720th hours of injury respectively (Table 5).

Table 5: Overall life table of road traffic injury victims; May 2019-February 2020

Time in hours	Number at risk	Loss to follow up	Number of events	Proportion of events	Proportion Surviving	Cumulative Proportion Surviving
1	442	0	12	0.027	0.973	0.973
2	433	0	9	0.02	0.98	0.95
3	432	0	1	0.002	0.99	0.94
4	431	0	1	0.002	0.998	0.938
6	429	0	2	0.004	0.996	0.934
12	428	0	1	0.002	0.998	0.932
24	413	0	15	0.036	0.964	0.89
48	406	0	7	0.0172	0.982	0.87
72	399	0	7	0.0175	0.982	0.85
96	392	0	7	0.0178	0.982	0.83

120	388	0	4	0.010	0.99	0.82
144	386	0	2	0.0052	0.99	0.81
168	381	0	5	0.013	0.98	0.79
288	380	0	1	0.002	0.997	0.77
312	379	0	1	0.002	0.997	0.75
432	378	0	1	0.002	0.997	0.74
480	377	0	1	0.002	0.997	0.73
528	376	0	1	0.002	0.997	0.72
672	375	0	1	0.0026	0.99	0.71
720	359	15	1	0.0027	0.99	0.70

Condition of victims on the 30th day of injury

Assessment on the 30th day of injury revealed that 30 (6.60%) were still in bed with unremarkable improvement, 263 (57.90%) had a better condition but not completely healed, 45 (9.90%) were healed with some limitation, 21 (4.60%), were completely healed, and back to work, 15 (3.30%) were lost to follow-up, while 80 (17.6%) died. Apart from those who died, 23 had functional losses (4 (0.88%) had lost teeth, 4 (0.88%), had an amputation of the limb, 3 (0.66%) had hearing loss, 3 (0.66%), had vision loss, 5 (1.10%), had impaired memory and 4 (0.88%) were paraplegic at 30th day of injury).

Immediate causes of deaths at a specific time interval

From the total of 17 deaths in the first hour of admission, 13 (76.5%) were due to non-survivable injury. The leading cause of death in the first four hours of admission to the hospital was hemorrhage (21.3%). Hemorrhage and secondary complications, mainly aspiration pneumonia were the major causes of death between the first 4 and 24 hours. According to our data, late deaths have resulted from sepsis and multiple organ failure (Figure 3). All deaths were confirmed by the clinician in charge of patient care.

Predictors of mortality following a road traffic injury

The significant predictors of time to death for road traffic injury victims were being a driver (AHR=2.26; 95% CI: 1.09, 4.65, AR=14.8), accident location at the rural residence (AHR=1.98; 95% CI: 1.02, 3.82;AR=21%), time from injury to hospital arrival (AHR=0.41; 95% CI: 0.16, 0.63;AR= 3%), systolic blood pressure on admission of <90mmHG(AHR= 3.66; 95% CI: 2.14, 6.26; AR=57%), GCS of <8 (AHR= 7.39 ; 95% CI, 3.0819 17.74464; AR=75.5%), GCS between 9-13 (AHR= 8.1565 (3.36 19.82, AR=39%), combined head injury with multiple body site (AHR= 2.33 (1.13, 4.80; AR=37%) and interaction of long distance from hospital (AHR=2.98 (1.46 4.39; AR=5.5%) (Table 6).

Table 6: Predictors of mortality following a road traffic injury, May 2019 to February 2020

Variables	Categories	Total	RTI deaths	CHR(95%CI)	AHR(95%CI)
Road user category	Pedestrian	232	43	1.00	1.00
	Passengers	168	22	1.47 (.88, 2.46)	1.97 (1.10, 3.52)*
	Drivers	54	15	2.36 (1.22 4.55)	2.61 (1.28 5.30)*
Residence	Urban	264	23	1.00	1.00
	Rural	194	57	3.90 (2.40 6.34)	1.98 (1.02 3.82)*
Hospital arrival time	Within <1 hour	184	32	1.00	1.00
	Within 1-4hours	176	25	.32 (.45 1.30)	.41 (.16 .63)**
	Within 24 hours	69	20	1.74 (.99 3.05)	.42 (.18 .95)
	After 24 hours	25	3	.64 (.19 2.09)	.40 (.10 1.56)
Systolic BP	≤89	53	36	10.07 (6.45 15.71)	3.66 (2.14 6.26)
	>89	401	44	1.00	1.00
GCS	≤8	64	52	32.44 (19.12 55.06)	7.39 (3.08 17.74)**
	9-12	18	8	9.97 (4.39 22.67)	8.15 (3.35 19.82)**
	13-15	372	20	1.00	1.00
Injury site	Non-head injury	262	14	1.00	1.00
	Isolated Head injury	105	33	7.05 (3.77 13.19)	2.28 (1.12 4.65)*
	Combined head injury	87	33	8.50 (4.54 15.89)	2.57 (1.26 5.24)**
Pre-hospital Care # distance	Yes#<60km	93	7	1.00	1.00
	Yes#>60km	79	11	1.74 (.87 3.48)	2.98 (1.46 4.39)*
	No#<60km	217	38	.688 (.25 1.89)	.60 (.28 1.25)
	No#>60km	65	24	3.69 (1.76 7.73)	.81 (.31 2.10)

Key * Significant at P<0.05, **P<0.001

Impact of the study

We have calculated the attributable risk for the predictors of mortality. Our study showed that accidents at inter-urban locations had an increased hazard of death when compared with those accidents in urban areas. The high mortality in these locations was partly due to lack of timely care on-site and delays to hospital arrival, mainly due to poor transport access and long distance from the hospital. This finding implies that the establishment of emergency medical services and improved access to health care facilities could reduce such deaths by 21%.

Those victims who had a systolic blood pressure of less than 90 mmHg on admission had a risk of death by more than 3. That implies restoring the hemodynamics of victims as early as possible can reduce deaths following an injury by 57%. With this regard, the role of emergency medical response at the scene of the injuries and early transfer of victims to definitive care units will have a vital role in reducing reversible causes of mortality.

The study demonstrated that those victims who had head injuries had a higher risk of death when compared with non-head injury cases. Accordingly, victims with an isolated head injury and multiple injuries had more than twice the risk of death when compared with other body regions. Hence, the use of protective materials such as helmets could potentially reduce mortality following a road traffic injury by 26-32%.

Discussion

The current study demonstrated that deaths following a trauma follow the classical tri-modal pattern in low-resource countries, and pre-hospital care is rarely available for victims of road traffic injuries. Free ambulance transportation was in-available for trauma victims resulting in a delay in hospital arrival for accidents sustained on rural roads. Driver, accident location in rural areas, low systolic blood pressure, low GCS on admission, injury site, and interaction of providing pre-hospital care and long-distance were significantly associated with time to death among road traffic injury victims.

The current study demonstrated that deaths following a trauma follow the classical tri-modal pattern in low-resource countries, and pre-hospital care is rarely available for victims of road traffic injuries. Free ambulance transportation was in-available for trauma victims resulting in a delay in hospital arrival for accidents sustained on rural roads. Being a driver, accident location in rural areas, low systolic blood pressure, low GCS on admission, injury site, and interaction of providing pre-hospital care and long-distance was found to be, predictors of time to death among road traffic injury victims.

The classical tri-modal distribution of trauma deaths was described by Trunkey, in 1983 (38). Different previous studies had disproved this traditional distribution of mortalities due to a reduction in the number of early and late hospital deaths (39). Our study demonstrated that road traffic injury mortality still followed the traditional tri-modal pattern. According to the current study, there were two peaks. One peak was in the first 24 hours and the second at the end of the first week of the injury. Nearly half of the deaths occurred in the hospital after a week of admission. A similar finding was reported by a study conducted in Iran showing two peak times. (31). Poor operative services for severe head injury cases and lack of intensive care unit for severely injured victims could explain the reason for late deaths in our hospital (40). The surgical setup in our case is not optimum to perform surgical intervention for severely injured head injury victims. Besides, there is no well-equipped surgical ICU service to support victims with ventilatory failure. On the other side, the in-availability of pre-hospital basic life support care could have resulted in clinical deterioration of victims that could result in late complications (10).

In this study, none of the victims received pre-hospital care at the scene of injury. This is consistent with previous studies that showed pre-hospital emergency care is under-served or unavailable in most low and middle-income countries (41, 42). The finding is also consistent with a study conducted in Addis Ababa, where none of the victims got pre-hospital care (17). The current study also indicated that full package Ambulance service was unavailable for all the victims, and only 20% received transportation service without trained personnel accompanying the victims. Our finding is in line with a systematic review, indicating Ambulance service was underserved in many low and middle-income countries (43) and a study conducted in Pakistan that reported the majority of participants didn't want to call Ambulance for emergency cases because the Ambulances didn't function properly (44). On top of this, the available ambulance service was not for free. The victims or the family have to cover the cost of fuel and per Diem of drivers. A similar finding was reported in Cambodia (45).

The current study also showed that many trauma victims who were referred from primary hospitals would have been treated, at those hospitals. This is in line with a study conducted at Southern India, which showed that trauma care was unnecessarily delayed and liable for unnecessary referrals due to poor resources for trauma case management (31) and another study demonstrated that there are many deficiencies in emergency care services ranging from in-availability of drugs and lack of training to provide the required emergency care (46).

According to our study, the overall incidence of road traffic injury deaths was 29 per 100,000 hours of observation. This finding is higher when compared with a study conducted at Tikur Anbessa Hospital, Addis Ababa, which was 10/100,000 hours of observation (17). The discrepancy could be explained by the fact that the Tikur Anbessa Hospital has a better trauma management setup including an intensive care unit (ICU). Hence the quality of care could explain the lesser death at the Tikur Anbessa Hospital (17). Another explanation could be because follow-up continued after discharge from the hospital in the current study, while the mentioned study didn't follow victims after discharge that ignored deaths at home after discharge.

The study revealed that pedestrians are the most frequently affected road user categories when compared with passengers and drivers. This is in line with the federal police commission report (47) and studies conducted in the capital city, Addis Ababa. (48) Both studies showed pedestrians to be the road user categories most frequently affected by RTI. But severe and fatal injuries were more likely to occur among drivers and passengers in our study. Though the number of injured drivers was less in number when compared with both passengers and pedestrians, the proportion of fatality was higher among drivers. This could be explained by the fact that the majority of drivers in Ethiopia are reluctant in using seat belts and they are more likely to have crashes resulting in a fatality. From a previous study, it was found that 57.5% of drivers unfasten their seat belts while driving (49). This finding was consistent with a previous study that indicated fatal injuries were more likely among drivers and passengers (50). But another study reported a contradictory finding, showing pedestrians are more likely to die from a vehicle accident (51).

Our study demonstrated that accidents sustained in rural areas were more likely to result in a fatal outcome than in urban locations. Our finding is consistent with a study conducted by Craig Zwerling and colleagues that showed injury severity and fatality was more than three times higher in the rural area than urban areas (52). Lack of appropriate health care facilities and limitation of transportation access could explain the finding. That will, in turn, result in bad outcomes (53). Risky driving behavior such as over speeding is more common in rural areas due to poor traffic control. That could explain the high mortality in rural areas.

Previous evidence showed that accident intensity increases when a crash is caused by a speedy vehicle (54).

Low systolic blood pressure on admission was significantly associated with time to death among road traffic injury victims. This finding is in line with previous studies that showed, victims with low blood pressure on admission were more likely to experience death than their counterparts (16, 55-56). Exsanguination from severe injury explains the drop in blood pressure (57). Low systolic blood pressure could increase mortality via poor organ perfusion and consequent organ failure (58). Nosocomial infections and sepsis are likely in hemorrhagic shock resulting in acidosis and poor perfusion (59, 60). These are the possible explanations for low systolic blood pressure and increased mortality.

The current study revealed that hospital arrival time is associated with 30 days of mortality following a road traffic injury. Accordingly, victims who arrived at the hospital between one to four hours were more likely to die than those who arrived within one hour of injury and beyond 4 hours of injury. The finding is contrary to the concept of the "Golden hour" of trauma that depicts the outcome of trauma, which is better when victims arrive within one hour of injury (61-62). That could be because victims who are seriously injured and have non-survivable injuries were more likely to be directly transferred to the hospital immediately after injury, while less severe injury cases took their time.

The study showed an interaction between long distances from the hospital and pre-hospital first aid to be significantly associated with 30 days mortality following a road traffic injury. The possible explanation for this finding could be due to delays in definitive care. Though essential trauma care is vital to treat time-sensitive issues, delayed expert-requiring procedures could result in poor outcomes (63). This is particularly the case in low-resource countries like Ethiopia where the majority of primary hospitals are not in a position to provide essential trauma care (64).

Limitation of the study

As our participants were only those victims who visited the hospital during the data collection period, we excluded deaths at the scene of the injury and minor cases who didn't come to the hospital. Such exclusion might underestimate the actual injuries and mortalities from a road traffic injury. Besides, the exclusion of minor cases might introduce selection bias. Besides, the exclusion of minor cases might introduce selection bias. The time interval between injury and hospital arrival was determined based on self-report or family report. We expect a recall bias in such a stress full situation. The direct cause of death was assessed using verbal autopsy for those deaths that occurred at home after discharge. This may not be precise without autopsy and physician judgment.

Because many of the drivers escape or were arrested after the accidents, we couldn't assess driver-related risk factors such as speed, presence of drunk driving, age, and experience of driving which could be a source of variability for the outcome of the injury.

Conclusions

This study demonstrated that the classical tri-modal pattern of mortality is still occurring in low-resource settings. The study showed that there is a gap in both pre-hospital trauma care and primary trauma care at district hospitals in the study area. Being a driver, accidents at the inter-urban roads, low systolic blood pressure, low GCS on admission, and presence of head injuries were predictors of time to death following road traffic injuries.

The regional and zonal health sectors need to revise the pre-hospital trauma care service implementation including Ambulance access and package. The hospital needs to improve trauma care services, especially surgical and supportive interventions such as mechanical ventilatory support for severely injured victims. Future studies should be conducted to assess the capability of primary hospitals in the area in providing essential trauma care, and barriers to establishing emergency medical service in the country at large, and the study area in particular.

Generalizability of the study: We tried to use a representative sample based on appropriate power calculation and use a pre-tested and piloted tool to collect data, hence we can generalize the result from this study for all road traffic injury cases in the Amhara region.

Figure legend

Figure 1: Commonly sustained fractures among RTI victims, Hospital, Ethiopia

Figure 2: Timing distribution of mortality following road traffic injuries, May 6; 2019 to February 30, 2020

Figure 3: Immediate causes of deaths following a road traffic injury at a specific time interval, May 2019 –February 2020.

Abbreviations

AHR	Adjusted Hazard Ratio
AR	Attributable Risk
BP	Blood Pressure
CI	Confidence Interval
GCS	Glasgow Coma Scale
HIV	Human Immuno Virus
HR	Heart Rate
ICU	Intensive Care Unit
IMN	Intra Medullary Nailing
IQR	Interquartile Range
O_2	Oxygen
POP	Plaster of Paris
PR	Pulse Rate
RTI	Road Traffic Injuries
RTS	Revised Trauma Score
RR	Respiratory Rate
SBP	Systolic Blood Pressure
SD	Standard Deviation

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from the University of Gondar Ethical review board (R.N. O/V/P/RCS/051049/2019), and a permission letter was obtained from Gondar University Comprehensive Specialized Hospital. Informed written consent was obtained from participants, caregivers, or proxy as appropriate. The purpose of the study was explained to every victim or an appropriate proxy. On arrival at the emergency department, only hospital arrival time was registered and other information was collected after all the necessary medical care was secured. During our observation, any abnormal finding or complaint such as pain was communicated to the appropriate medical care team for intervention. For those victims who were discharged against medical advice, we continued our follow-up by phone and some of them changed their minds and returned and continued their medical follow-up.

Consent for publication

Not applicable

Availability of data and materials

Extra data can be accessed via the Dryad data repository at http://datadryad.org/ with the doi:10.5061/dryad.s4mw6m979

Competing interests

The authors declare no competing interest

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Authors' contribution

ZD designed the study, analyzed the data, and drafted the manuscript. MY, TA, GB, and KG were involved in the design of the study, analysis, and critically evaluated the manuscript for intellectual content. All authors read and approved the final manuscript.

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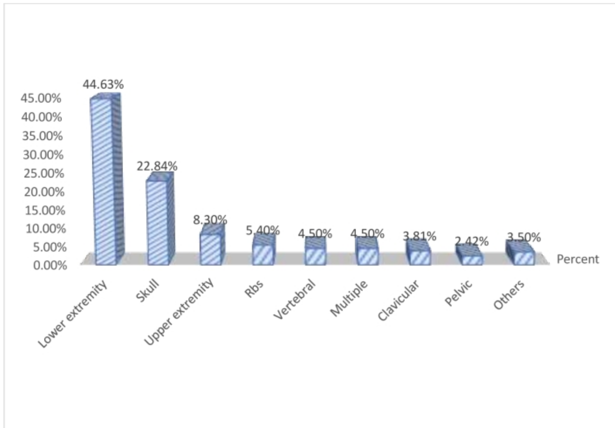

Figure 1: Commonly sustained fractures among RTI victims, Hospital, Ethiopia

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215x279mm (300 x 300 DPI)

Figure 2: Timing distribution of mortality following road traffic injuries, May 6; 2019 to February 30, 2020

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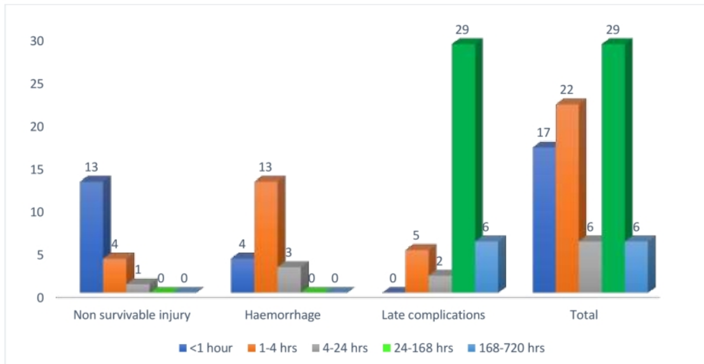

Figure 3: Immediate causes of deaths following a road traffic injury at a specific time interval, May 2019 –February 2020.

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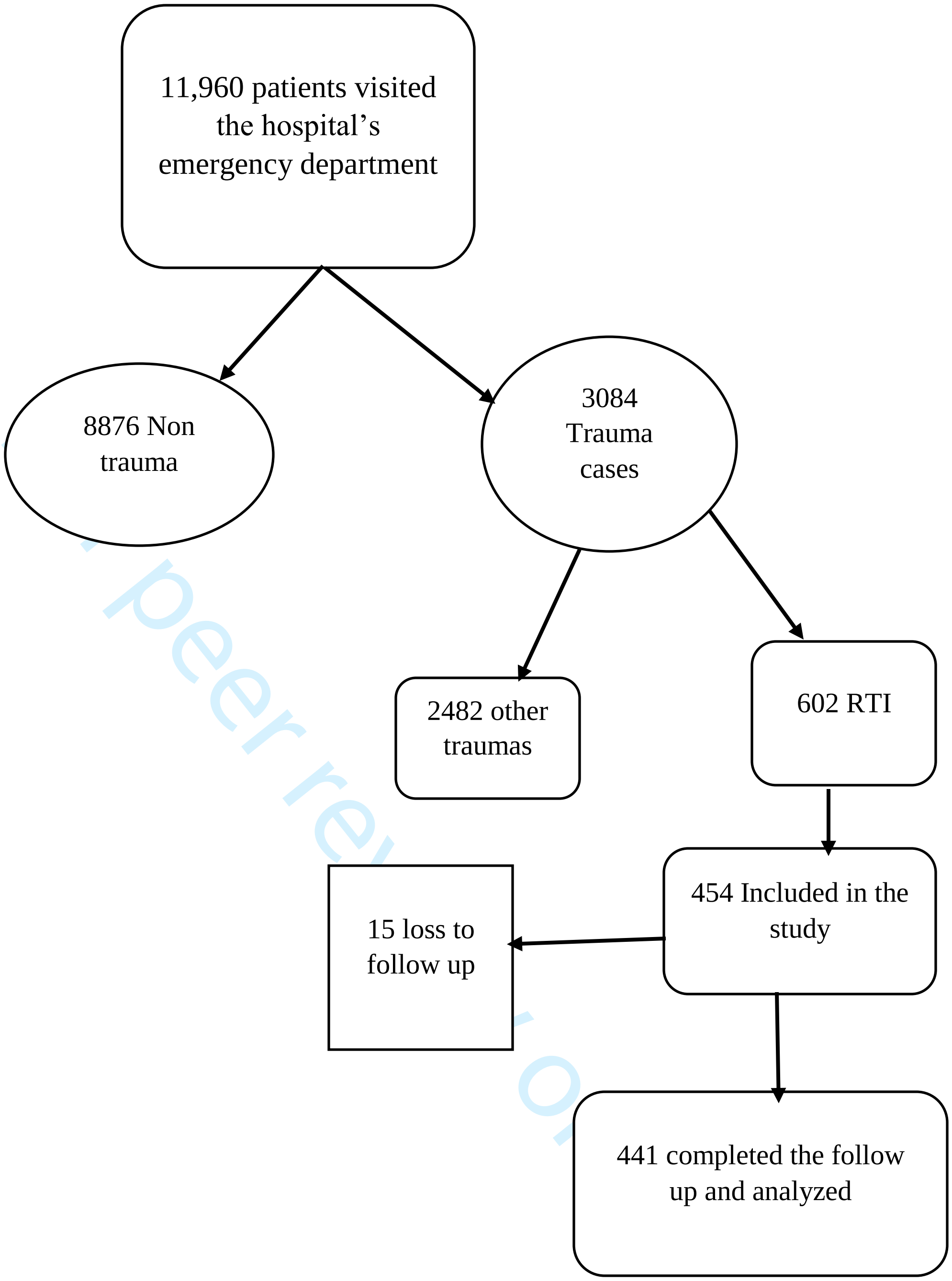

Figure 1: Schematic presentation of participants' selection

Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	Page 1 line 1-2
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	Lines 30-58
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	Lines 68-121
Objectives	#3	State specific objectives, including any prespecified hypotheses	Line 122-126
Methods			
Study design	#4	Present key elements of study design early in the paper	Line 129-130
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Lines 132-151
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	Lines 153-155
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	N/a
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Lines 157-166
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for exposed and	Lines 168-186

		unexposed groups if applicable.	
Bias	#9	Describe any efforts to address potential sources of bias	Lines 188-199
Study size	#10	Explain how the study size was arrived at	Lines 201-206
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	N/a
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	Lines 214-227
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	Lines 224-225
Statistical methods	#12c	Explain how missing data were addressed	Lines 226
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	Lines 226
Statistical methods	#12e	Describe any sensitivity analyses	n/a
Results			
Participants	#13a	Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed. Give information separately for exposed and unexposed groups if applicable.	Additional file 1
Participants	#13b	Give reasons for non-participation at each stage	Additional file 1
Participants	#13c	Consider use of a flow diagram	Additional file 1
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	Lines 237-251
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	Line 302-304
Descriptive data	#14c	Summaries follow-up time (e.g., average and total amount)	Lines 302-304
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	Lines 320-326
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Lines 335-343
Main results	#16b	Report category boundaries when continuous variables were categorized	N/a
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Lines 348-363
Other analyses	#17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	#18	Summarize key results with reference to study objectives	Lines 365-460
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	Lines 462-473
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	Lines 467-480

Generalisability	#21	Discuss the generalizability (external validity) of the study results	Lines 487-489
Other Information		Ethical approval	Lines 500-509
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Lines 519-520