Gender-based Assessment of Survival in Trauma-hemorrhagic Shock: A Retrospective Analysis of Indian Population

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Abstract

Introduction: Trauma-hemorrhagic shock (THS) is a leading cause of death. Female rats and women experience better outcomes in terms of survival after major trauma as compared to males. There are limited data in Indian population. Authors studied the gender-based outcome of patients with Class IV hemorrhagic shock due to blunt trauma and the distribution of factors among males and females which are known to affect outcome. **Materials and Methods:** It was a retrospective study with data of trauma victims between January 2008 and July 2013. Road traffic crash (RTC), fall, or assault of all ages with Class IV hemorrhagic shock on arrival was included in the study, and data were collected on demographic, clinical, and laboratory parameters. Drowning, burns, penetrating injuries, and septic, neurogenic, and cardiogenic shock were excluded from the study. **Results:** Seven hundred and eighty-one patients were analyzed under three groups: (i) overall group including all patients ($n = 781$), (ii) male group ($n = 609$), and (iii) female group ($n = 172$). After adjusting all variables, mortality was significantly lower in females as compared to males following THS ($P < 0.05$). Age, blood pressure, pulse, male gender, and fall and RTC as mode of injury (MOI) were independent predictors of mortality ($P < 0.05$) in overall group. Among males, age, pulse, and RTC as a MOI were significant ($P < 0.05$), while in females, only systolic blood pressure (SBP) was independent predictor of mortality. **Conclusion:** Females had better survival as compared to males following THS. SBP was an independent predictor of mortality in females with THS.

Keywords: Mode of injury, road traffic crash, systolic blood pressure, trauma-hemorrhagic shock

Introduction

Hemorrhagic shock is a life-threatening condition which continues to claim the lives of patients with major trauma all over the world, especially in middle- and low-income countries. It is the leading cause of potentially preventable death among trauma patients. Early recognition of trauma-hemorrhagic shock (THS) followed by timely and appropriate intervention can save many lives.[1] This shows the importance of comprehensive understanding of THS to improve patient survival.

Much evidence has been accumulated for a sexual dimorphism in host defense after trauma, hemorrhage, and sepsis in experimental animals. Human studies have shown that males have increased risk of infection after major trauma.[2,3] Whereas androgenic hormones seem to have an immunosuppressive effect leading to increased susceptibility to and higher mortality after sepsis, estrogen has been shown to have beneficial effects in different trauma models. Studies suggest that premenopausal women with trauma have a lower incidence of infection, pneumonia, sepsis, and multiple organ failure than men.[4-6]

Various other clinical factors also influence mortality following THS.[7-14] Most of the studies on THS are from Caucasian population. The Indian population may differ from Caucasian population in immunological and constitutional aspects. Because of paucity of data on distribution of factors which are known to affect the outcome of patients with THS in Indian population, authors contemplated to conduct this study.

The main objective of this study was therefore to describe the distribution of factors among males and females which are

Access this article online	
Quick Response Code:	**Website:** www.ijccm.org
	DOI: 10.4103/ijccm.IJCCM_304_16

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How to cite this article: Verma P, Bhoi S, Baitha U, Sinha TP, Mishra PR. Gender-based assessment of survival in trauma-hemorrhagic shock: A retrospective analysis of Indian population. Indian J Crit Care Med 2017;21:218-23.

known to affect the outcome in survivors and nonsurvivors and whether gender affects outcome in Class IV hemorrhagic shock (systolic blood pressure [SBP] <90 mmHg) patients due to blunt trauma.

Materials and Methods

It was an IRB-approved retrospective cohort study conducted at a level 1 trauma center. Data were collected on demographic, clinical, and laboratory parameters using primary information from the "Red Area" patients' registry and computerized patient record system of period between January 2008 and July 2013. "Red area" is the specific area of our emergency department dedicated to manage critically ill patients. Data mining was done, and all patients with Class IV hemorrhagic shock were recruited in the study. Class IV hemorrhage was defined as an estimated blood loss more than 40% (more than 2000 ml for a 70 kg man) of blood volume (as per the Advanced Trauma Life Support (ATLS) guidelines laid by the American College of Surgeons Committee on Trauma) and a SBP <90 mmHg. Patients with this amount of blood loss were recognized clinically with features such as marked tachycardia, a very narrow pulse pressure (or an unobtainable diastolic blood pressure), negligible urinary output, and a depressed mental status.

Summary of patient's inclusion is shown in Figure 1.

Inclusion criteria

Victims with a history of blunt trauma due to road traffic crash (RTC), fall, or assault of all age groups with Class IV shock on arrival as per the ATLS criteria, i.e., SBP at the time of presentation <90 mmHg in adult patients. In pediatric population, Class IV shock was defined using age-adjusted nomogram.

Exclusion criteria

Patients of drowning, burns, penetrating injury, septic shock, neurogenic shock, and cardiogenic shock were excluded from the study.

Statistical analysis

All data were entered into excel sheet and then transferred to Stata version 11 (College station, Texas, USA) for analysis. Data were presented as number (percentage) or mean ± SD as appropriate. Logistic regression analysis was carried out to find the predictors of mortality among patients with THS. The variables (age, sex, SBP, heart rate, pneumothorax, focused assessment by sonography in trauma [FAST] status, mode of injury [MOI], etc.,) that were significant at univariate analysis were considered for multiple logistic regression analyses. The results were reported as odds ratio (OR) (95% confidence interval [CI]). $P < 0.05$ was considered statistically significant. Results were analyzed separately for 3 groups of patients: (i) overall group including all patients (n = 781), (ii) male group (n = 609), and (iii) female group (n = 172).

Results

Out of 781 patients with THS, 609 patients (77.9%) were male and 172 patients (22.1%) were female. In overall group, 510 (65.3%) patients survived and 271 (34.7%) patients died. In male group, out of 609 patients, 383 patients (62.9%) survived and 226 (37.1%) patients died. In female group, 127 (73.8%) patients survived and 45 (26.2%) patients died [Table 1].

Demographic and clinical characteristics of overall, male, and female patients are presented in Table 2. These included age, pulse, SBP, shock index, MOI, FAST, and pneumothorax. The mean age of the overall study group was 31.2 ± 18.2 years (male = 32.4 ± 16.4, female = 28.9 ± 23.1). In the overall and male study group, major MOI that was responsible for the patient presenting with THS was RTC (59.7% and 66.4%), while in female group, "fall" was major MOI (56.4%) [Table 2].

Outcome of patients with THS from emergency department (ED) is shown in Table 3. Out of 781 patients with THS, 338 patients (43.28%) were admitted in Intensive Care Unit and managed either conservatively (fluid and blood transfusion, angio-embolization, and hemodynamic monitoring) or with elective surgery. One hundred and seventy-two patients (22%) were sent to wards (orthopedics, surgery, or

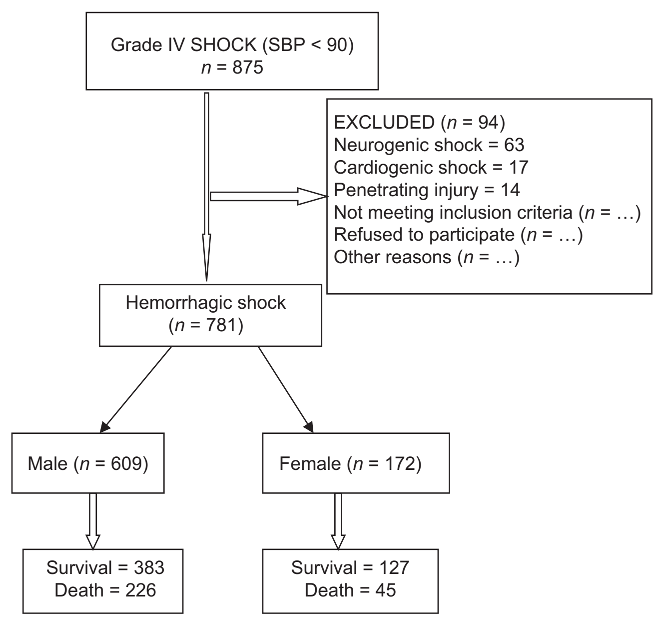

Figure 1: Summary of patients' inclusion. n = Total number, SBP: Systolic blood pressure (mm Hg)

Table 1: Outcome in terms of survival and death in overall, male, and female patients with trauma-hemorrhagic shock

Sex	Survival (%)	Death (%)	Total
Male	383 (62.9)	226 (37.1)	609
Female	127 (73.8)	45 (26.2)	172
Overall	510 (65.3)	271 (34.7)	781

Table 2: Clinical and derived parameters in overall, male, and female patients with trauma-hemorrhagic shock

Variables	Male (*n*=609)	Female (*n*=172)	Overall (*n*=781)
Age, mean±SD	32.4±16.4	28.9±23.1	31.2±18.2
SBP, mean±SD	79.6±11.6	80.8±11.1	79.9±11.9
Pulse, mean±SD	106.4±23.7	107.5±27.2	106.7±24.5
Shock index, mean±SD	1.43±0.41	1.46±0.50	1.44±0.43
MOI, *n* (%)			
Assault	45 (7.3)	13 (7.6)	58 (7.4)
Fall	160 (26.3)	97 (56.4)	257 (32.9)
RTC	404 (66.4)	62 (36.0)	466 (59.7)
FAST, *n* (%)			
Positive	139 (22.8)	36 (20.9)	175 (22.4)
Negative	470 (77.2)	136 (79.1)	606 (77.6)
Pneumothorax, *n* (%)			
Positive	108 (17.7)	27 (15.7)	135 (17.3)
Negative	501 (82.3)	145 (84.3)	646 (82.7)

SBP: Systolic blood pressure; MOI: Mode of injury; RTC: Road traffic crash; FAST: Focused assessment by sonography in trauma; SD: Standard deviation

Table 3: Outcome from emergency department after admission of patients with trauma-hemorrhagic shock

	Frequency (%)
OT	27 (3.46)
ICU	338 (43.28)
Ward	172 (22.02)
Discharge	244 (31.24)
Total	781 (100)

OT: Operation theater; ICU: Intensive Care Unit

neurosurgery ward) after stabilization in ED. Patients who were nonresponders (27/781 patients, 3.46%) were sent directly to operation theater for definitive management. Patients who were managed effectively in ED were down triaged and then discharged subsequently from ED (244/781, 31.24%).

Univariate analysis in the overall study group revealed age, SBP, pulse, shock index, MOI, namely, "fall and RTC," and "male" sex to have significant value ($P < 0.05$) in determining the mortality. Considering male study group, univariate analysis has shown that age, SBP, pulse, derived parameter such as shock index, RTC as a MOI, and positive FAST examination have a significant value ($P < 0.05$) in determining the mortality. In the female study group, it was only SBP which was found to have significant predictive value ($P < 0.05$) for determining the mortality [Table 4]. Logistic regression analysis of all significant variables (by univariate analysis) was done in the overall study group and revealed age, SBP, pulse, male gender, and "fall and RTC" as MOI were independent predictors of mortality, and in male study group, only age, pulse, and RTC as a MOI were significant ($P < 0.05$) predictors of mortality [Table 5].

Discussion

The study population had 609 (77.9%) males and 172 (22.1%) females, giving a male to female ratio of 3.5:1. Male predominance is consistent with findings of other trauma-related studies.[4-6] Most of the participants were young adults between the age of 18 and 40 years. RTC was the leading cause of injury in overall (59%) and in male (66%) patients while fall (56%) was the most common MOI in females.

Pneumothorax has an adverse effect on outcome in patients with THS. In our study, we found that it has a significant effect on mortality by univariate analysis, but after logistic regression, it has no effect on mortality in patients with THS. Similarly, FAST-positive status also has negative effect on survival by univariate analysis, but after logistic regression, it has no effect on mortality.

Distribution of factors which are known to affect outcome

There were five factors that significantly affected outcome and predict mortality in this study after logistic regression, namely: (i) gender of patient, (ii) age of the patient, (iii) SBP, (iv) pulse rate and (v) MOI (RTC and fall).

In our study, we found better survival in females as compared to males. This gender difference was not related to injury severity and degree of shock as only Class IV shock was taken into consideration. A prospective study conducted in New Jersey in more than 4000 trauma patients demonstrated that hormonally active women tolerate trauma/shock better than men.[4] Various animal and human studies have proven better response and survival in females in trauma-related injury.[2-4] It seems that sex hormones rapidly change in stressed and septic patients with testosterone decreasing in men and estrogen increasing in men and postmenopausal women. The greatest resistance of female animals to organ injury after trauma hemorrhage is during the periods of the estrus cycle in which estradiol levels are the highest.[4]

Animal studies document that proestrus female rats, in which estradiol levels are high, are largely protected from the deleterious effects of trauma hemorrhage on cardiac and hepatic function as well as gut and lung injury.[2] Studies

Table 4: Univariate analysis for male, female, and overall patients with hemorrhagic shock

Variable	Male				Female				Overall			
	Survival	Death	OR (CI)	P	Survival	Death	OR (CI)	P	Survival	Death	OR (CI)	P
Age	31.4±16.2	34.1±16.7	1.0 (0.9-1-0)	0.05	28.1±23.5	31.2±22.0	1.0 (0.9-1.0)	0.43	30.6±18.3	33.6±17.7	1.0 (1.0-1.0)	0.02
SBP	80.1±11.3	78.8±11.9	0.99 (0.9-1.0)	0.17	82.2±9.7	76.9±13.7	0.96 (0.9-1.0)	0.01	80.6±10.9	78.4±12.2	0.98 (0.9-1.0)	0.01
Pulse	105.0±22.7	108.8±25.1	1.0 (0.9-1.0)	0.06	106.5±26.3	110.4±29.7	1.0 (0.9-1.0)	0.40	105.4±23.6	109.1±25.9	1.0 (1.0-1.0)	0.04
Shock index	1.39±0.4	1.49±0.5	1.7 (1.1-2.5)	0.01	1.43±0.5	1.54±0.5	1.5 (0.8-2.9)	0.21	1.41±0.4	1.49±0.5	1.6 (1.1-2.25)	0.01
MOI												
Assault	35 (77.8)	10 (22.2)	1.0		10 (76.9)	3 (23.1)	1.0		45 (78.9)	13 (21.1)	1.0	
Fall	104 (65)	56 (35)	1.9 (0.9-4.1)	0.10	70	27	1.28 (0.33-5.03)	0.36	174 (67.7)	83 (32.2)	2.0 (1.0-3.9)	0.14
RTC	244 (60.4)	160 (39.6)	2.3 (1.1-4.8)	0.03	47	15	1.06 (0.26-4.38)	0.09	291	175	2.0 (1.1-3.9)	0.03
Pneumothorax												
Negative	327	174	1.0		110	35	1.0		437	209	1.0	
Positive	56	52	1.8 (0.8-4.4)	0.01	17	10	1.85 (0.77-4.40)	0.17	73	62	1.4 (0.8-2.6)	0.00
FAST												
Negative	309	161	1.0		102	34	1.0		411	195	1.0	
Positive	161	65	1.7 (1.1-2.6)	0.01	25	11	1.32 (0.6-2.96)	0.50	99	76	1.2 (0.7-2.1)	0.01
Sex												
Female									127	45	1.0	
Male									383	226	1.7 (1.1-2.4)	0.01

OR: Odds ratio; CI: Confidence interval; SBP: Systolic blood pressure; MOI: Mode of injury; RTC: Road traffic crash; FAST: Focused assessment by sonography in trauma

on shock and sepsis have shown that administration of the testosterone receptor blocker flutamide also significantly improved cardiac performance, hepatic microvascular blood flow, and hepatocellular function in male rats after trauma and hemorrhagic shock.[5]

Trentzsch *et al*. studied 7560 males and 2774 females to analyze sex differences in trauma-hemorrhage patient.[7] They found higher rates of multiple organ failure (24.4 vs. 21.3%, OR 1.19 (95% CI 1.07–1.33, P = 0.001) and sepsis (16.5 vs. 11.3%, OR 1.55 (95% CI 1.35–1.77), $P < 0.001$) in males when compared to females. Organ function of lung, cardiocirculatory system, liver, and kidney was better in females; however, there was no difference in mortality. Females in particular age group of 16–44 years had improved organ function which may indicate effects of sex hormones in females at reproductive age. Increased rates of sepsis in males were observed throughout virtually all age groups starting at 16 years of age, except in age group of 54–64 years. This may suggest a suppressive effect of testosterone on immune function.

Sperry *et al*. studied the gender dimorphism in trauma victims and found that female gender was independently associated with a 43% and 23% lower risk of multiple organ failure and nosocomial infection, respectively (men [n = 680] and women [n = 356]).[8] Gender remained an independent risk factor in young and old subgroup analysis, with the protection afforded by female gender remaining unchanged. The independent protective effect of female gender on multiple organ failure and nosocomial infection rates remains significant in both premenopausal and postmenopausal women when compared with similarly aged men. This is contrary to previous experimental studies, and the known physiologic sex hormone changes that occur after menopause in women. These results suggest that factors other than sex hormones may be responsible for gender-based differences after injury.

Sex hormones can regulate immunity by alteration of the T-helper (Th-1 and Th-2) profile of cell-mediated immune function. A number of clinical and experimental studies have shown the suppressive effects of androgens on immunity. Specifically, the peripheral B-cell fraction as well as the production of interleukin-2 and interferon-γ by peripheral T-cells is enhanced in androgen-deficient mice.[12] The study presented herein will add to the human data supporting beneficial effect of female sex hormones on outcome preventing mortality in blunt trauma patients with Class IV hemorrhagic shock in Indian population.

There was a significant difference in mean age between survivors and nonsurvivors as overall (P = 0.01) and male (P = 0.02) group. Age is an important factor known to affect the outcome of patients with traumatic hemorrhagic shock.[15] Numerous studies have shown that the elderly trauma population tolerates injury poorly compared with younger patients. Lehmann *et al*. found that elderly trauma victims are less likely to undergo rapid trauma evaluation as they require multispecialty consultation due to comorbidities and have significantly worse outcomes compared with younger patients.[15] The present study includes all the age groups, and subcategorization was not done among young and elderly group; however, despite lesser difference in mean age among survivor and nonsurvivors, it was noted that increasing trend in age has a worse outcome.

Table 5: Predictors of mortality in males and overall patients with hemorrhagic shock by multivariate logistic regression analysis

Variable	Logistic regression	
	OR (95% CI)	*P*
Overall	1.01 (1.0-1.0)	0.01
Age	0.98 (0.9-1.0)	0.02
SBP	1.0 (1.0-1.00	0.02
Pulse	1.6 (1.1-2.4)	0.02
Male gender		
MOI		
Assault	1.0	
Fall	2.0 (1.0-3.9)	0.04
RTC	2.0 (1.1-3.9)	0.03
Pneumothorax		
Negative	1.0	
Positive	1.4 (0.8-2.6)	0.26
FAST		
Negative	1.0	
Positive	1.2 (0.7-2.1)	0.51
Male		
Age	1.01 (0.9-1.0)	0.02
Pulse	1.01 (1.0-1.0)	0.03
MOI		
Assault	1.0	
Fall	2.1 (0.9-4.5)	0.06
RTC	2.3 (1.1-4.7)	0.03
Pneumothorax		
Negative	1.0	
Positive	1.3 (0.7-2.6)	0.41
FAST	1.0	
Negative	1.37 (0.75-2.52)	0.30
Positive		

SBP: Systolic blood pressure; MOI: Mode of injury; RTC: Road traffic crash; FAST: Focused assessment by sonography in trauma

In our study, we found SBP as an independent and only predictor of mortality in female group but not in male patients. In contrast to other studies, in our study in male group, factors other than blood pressure such as age, heart rate, and MOI had more significant effect on outcome.

In our study, RTC emerged as an independent predictor of mortality in patients with blunt trauma induced hemorrhagic shock in overall and male patients. RTC is a major cause of death and disability globally, with a disproportionate number occurring in developing countries. Chalya *et al*. from Tanzania showed that RTC constitutes a major public health problem involving their young adult male in their economically productive age group.[11]

In contrast to the western world studies, we have found that MOI as fall has a significant effect on outcome and predicts mortality in patients with THS. Fall as such is a broad category that includes various mechanisms of injury encompassing fall from roof, construction buildings, fall from stairs, fall from bed, fall on level ground, etc., Male construction workers working in hazardous environment without any protective and safety measure are at very high risk of fall from height and suffer from various injuries, especially head injury and long bone fractures. Females, on the other hand, working at homes at risk of fall on level ground and fall from stairs due to working on wet floors and stairs.

Limitations

The injury severity score was not calculated as the study included patients of Class IV hemorrhagic shock. Since this was a retrospective study, among those patients with THS having pneumothorax, the shock cannot be totally attributable to hemorrhage. Critical care-related complications were not considered while analyzing outcome of patients with THS as we mainly focused on demographic profile and initial clinical presentation.

Conclusion

The study revealed a significant effect of gender on outcome of patients with THS, with better survival among female patients as compared to males. SBP was an independent predictor of mortality in females with THS.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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