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Original Research Article

Infection in Trauma Patients – Focus on Predisposing Factors, Types of Infection and Antibiotic Usage: A Prospective Study at Emergency Medicine Department of a Tertiary Care Hospital

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Abstract

Background: The India has a high incidence of vehicular accidents (6% of global vehicular accidents). Nosocomial Posttraumatic Infections (NPIs) are one of the most common and fatal complications following trauma and complicate the recovery of significant number of injured patients.

Materials and Methods: This Prospective, observational, single centre, follow-up study was conducted for a duration of 18 months at the Department of Emergency medicine of a Tertiary Care Teaching Hospital, Ahmedabad. Patients meeting inclusion and exclusion criteria were enrolled in the study and patients' demographic details, data related to predisposing factors, antibiotics usage, Culture and sensitivity reports were recorded. Patients who developed infection, their data analysed for; Predisposing factors for developing infection, Types of infection and causative organisms, Antimicrobial resistance pattern and Antibiotics usage. Statistical analysis was carried out with the help of SPSS version 21.0 and Microsoft Excel version 2019. $P<0.001$ was considered as statistically significant.

Results: 105 patients of either gender were enrolled in the study and out of them, 36(34.3%) patients developed infection. Vehicular accidents (22; 61%), Head injury (33, 92%), multiple sites of trauma27(75%), Traumatic brain injury (TBI) (31, 86%), Urinary catheterization (34) followed by Endotracheal tube (25) and 17(47%) had hypotension were the most common predisposing factors in patients with NPIs. Infection rate was 100% in patients having Injury Severity Score (ISS) > 45. Out of 105 patients, 48 (46%) patients had SIRS (Systemic Inflammatory Response Syndrome) score of ≥2 out of which 31(65%) developed infection. Most common type of NPIs was Ventilator Associated Pneumonia (VAP) (78%) and Acinetobacter baumannii (17, 23%) was the most common type of isolate among NPIs. Metronidazole (75, 71%) was most commonly used prophylactic antibiotic and Colistin (23, 64%) was most commonly prescribed antibiotic for NPIs.

Conclusion: Trauma is one of the common causes for nosocomial infections after hospitalization and certain risk factors like brain injury, advanced age, high ISS and SIRS score, invasive

procedures, hypotension also has potential impact on the development of NPIs. Colistin was the most commonly used for NPIs that shows rising trends of antimicrobial resistance.

Keywords: Antibiotics usage, Colistin, Nosocomial Posttraumatic Infections, Predisposing factors, Ventilator Associated Pneumonia.

Introduction

In India trauma registry is not adequately developed. The country has a high incidence of vehicular accidents (6% of global vehicular accidents) [1]. An accident death is reported every 1.9 minutes in India [1].

The rapid industrial growth, coupled with fast moving vehicular traffic in urban areas has contributed to a tremendous increase in trauma populations. Infections are one of the most common and fatal complications following trauma and complicate the recovery of a significant number of injured patients frequently leading to excess morbidity and mortality [1,2]. Trauma-related injuries are the leading cause of death worldwide [2].

The mechanism of traumatic injury itself creates a state of relative immunosuppression by decreasing the responses of both humoral and cell-mediated immunity. The severity of the state of shock at the time of admission to the emergency department is a significant predictor in the trauma patient for the relative risk of infections developing during the hospital stay. Of interest, the study by Cole *et al* found admission shock as measured by base deficit as the sole characteristic associated with subsequent infection present at the time of admission [3].

Haemorrhagic shock induces a host defence response characterized by both local and systemic release of proinflammatory cytokines, complement factors, and other elements involved in the proinflammatory response.

This hyperinflammation leads to the development of SIRS. Bochicchio *et al*. presented findings that suggest serial monitoring of the SIRS score provides an opportunity for early diagnostic intervention for identification and the early pharmacologic management of infection in the trauma population and most predictive of outcomes in trauma patients [3,4].

Predominating infections in traumatized patients are NOSOCOMIAL/Hospital Acquired Infection (HAI). A NPI (also known as hospital-acquired infection) is" a localized or a systemic infection resulting from an adverse reaction to infectious agents or its toxins that develops in 48 hours or more after admission and was not incubating on admission." [5,6].

The most common type of NPIs are urinary tract infections(UTI) (usually catheter associated) (31%) followed by surgical site infections (SSIs) (17%), primary bloodstream infections (BSIs) (usually associated with the use of an intravascular device) (14%), and pneumonia (usually ventilator associated) (13%).

The main bacteria associated with NPIs are S. aureus, coagulase-negative staphylococci, Streptococcus pneumoniae, Escherichia coli, P. aeruginosa, Haemophilus influenzae, Klebsiella pneumoniae, Acinetobacter and Enterococci [6].

Knowledge of proper antimicrobial prescription policy of a particular setting is crucial to optimize the management and reduction of the rate of NPIs; however, the investigation of causative agents and their antimicrobial susceptibility profile are an essential prerequisite [7].

Aims and Objectives

1. Evaluation of Injury severity score and SIRS (Systemic Inflammatory Response Syndrome) score.
2. Evaluation of predisposing factors in patients diagnosed to suffer from infection after trauma.
3. Evaluation of types of infection and antibiotics use and cost burden in patients of trauma.

Materials and Method

This Prospective, observational, single centre, follow-up study began after obtaining approval from institutional review board. It was conducted for a total duration of 18 months at the Department of Emergency medicine and department of pharmacology of a Tertiary Care Teaching Hospital, Ahmedabad.

The sample size for this study was duration based. All the patients confirming the inclusion criteria; those who met trauma and admitted in emergency medicine department, whose age was more than or equal to 18 years and Patients/ their relatives willing to give their written informed consent and were included in the study. Patients who left against medical advice within 1-2 days of admission and patients with burns were excluded from the study.

Patients enrolled in the study were followed twice weekly from admission to discharge or transferred to other wards/ hospital to collect the data. Patients' demographic details, mechanism and site of trauma, organ involvement, Injury severity score (ISS) [8,9] and (Systemic Inflammatory Response Syndrome) SIRS [10] score, interventions (Medical/Surgical), details of prophylactic antibiotics given were recorded in case record form. Culture and sensitivity reports were followed for diagnosis of infection in trauma patients. Patients who developed infection on the basis of microbiological culture, their data analysed for; predisposing factors for developing infection, types of infection and causative organisms, Antimicrobial resistance pattern and Antibiotics usage.

Duration of stay and cost was calculated using admission charges, cost of antibiotics, laboratory charges for all trauma patients. All above data were collected and recorded in a standard case record form.

Data was entered in Microsoft Excel version 2019. Statistical analysis was carried out with the help of Statistical Package for Social Science (SPSS) version 21.0 manufactured by IBM (demo version) and Microsoft Excel 2019. Independent t test and Fischer's exact test were used to compare various parameter among the two group. Assessment of correlation between different factors related to infection in trauma patients done by using Pearson's correlation. P value less than 0.05 was considered as statistically significant.

Results

Total 113 patients presented with trauma, were recruited in the study during the study period. Out of these 8 patients were excluded because they took discharged against medical advice within one day of admission due to the higher cost of admission and treatment. So, our study reported the finding from the 105 patients of either gender.

Out of 105 patients of trauma, 36(34.3%) patients developed infection during the course of treatment. Demographic variables mentioned in Table 1.

Cause of Trauma

As shown in Figure 1, Out of 105 patients of trauma, RTA (Road Traffic Accidents); (86, 82%) was the most common cause followed by fall (17, 16%). Among 86 patients of RTA, 73(85%) were vehicular accidents and 13(15%) were pedestrian injury and out of 17 patients of fall, 9(53%) were low energy fall and 8(47%) were fall from height. Among all above cause of trauma, vehicular accidents (70%) was the most common cause of trauma.

Site of Trauma

Head (85%) was the most common site of trauma followed by extremity (33%) and thorax (25%). Out of 105 patients, 61(58%) patients had multiple sites (≥2) of trauma whereas 44(42%) patients had ≤1 site of trauma.

Predisposing factors for infection in trauma patients(n=36)

RTA; Vehicular accidents (22, 61%) was most common mechanism of trauma among infection. Head injury (33, 92%) was the most common in trauma patients with infection followed by extremity (15;42%) followed by thorax (10;28%), abdomen (3;8%), spine (3;8%) and other. Out of 36 patients of trauma with infection, 27(75%) patients had multiple sites of trauma. TBI (31, 86%) was the most common in trauma patients developing infection followed by lung (12) and urinary bladder (1). Out of 36 patients, 10 (28%) patients had multiple organ involvement.

Infection rate was 48% in patients having ISS between 31-45 and 100% in patients having ISS >46. Infection was most common (61%) in patients having ISS ≥ 31(n=28). (Table 2) It suggests that as the ISS score increased, % of development of infection among the trauma patients increases.

Out of 105 patients, 48(46%) patients had SIRS score of ≥2 among which 31(65%) patients developed infection (NPIs). (Figure 2) Out of 36 patients of infection, 31(86%) patients had SIRS score ≥ 2 and 5 patients had SIRS score ≤ 1.

Among 105 trauma patients most commonly used invasive procedure were urinary catheterization (80, 76%) followed by endotracheal tube insertion (53, 50%) followed by central line insertion (23,22%) followed by tracheostomy tube (13, 12%) followed by surgeries (10,10%). (Figure 3)

Out of 105 patients of trauma, 79 patients had multiple invasive procedures, among which 25(32%) patients developed one or more type of infection (NPIs). Among 36 patients of infection, most common invasive procedure was Urinary catheteriztion (34) followed by Endotracheal tube (25), ryle's tube (23), central line (19) insertion, tracheal tube insertion (8).

Out of 36 patients, 17(47%) had hypotension, 10(28%) had diabetes and 9(25%) patients had Hypertension.

Type of infection in trauma patients

Out of 36 patients, 18(50%) patients had multiple NPIs and other 18(50%) had only one type of infection. Most common type of NPI in trauma patients admitted to emergency medicine was VAP (78%) followed by CA - UTI (47%) followed by septicaemia (39%) followed by SSIs (6%).

A total of 75 isolates were identified (n=36), most common being Acinetobacter baumannii (17, 23%) and Klebsiella pneumoniae (16, 21%). Others were Candida species (10, 13%), Pseudomonas aeruginosa (9, 12%), Staphylococcus epidermidis (7;9.3%), Serratia marcescens (4;5.3%), Staph. Haemolyticus (3,4%), E. Coli (3,4%), Myroides species (2,3%), Proteus Mirabilis (2,3%), Enterococcus faecalis (1, 1.3%) and Providencia stuartii (1,1.3%).

Among 28 patients of VAP, 9(32%) patients had multiple organism. Acinetobacter baumannii complex (15, 54%) was the most common cause of VAP in trauma patients. Among 17 patients of UTI, only one patient had multiple organism (Pseudomonas aeruginosa and E. coli).

Candida species (10, 59%) was the most common cause of UTI in trauma patients. Among 14 patients of septicaemia, 3 patients had multiple organism. Staphylococcus epidermidis (7, 50%) was the most common cause of septicaemia in trauma patients.

Antibiotics resistance pattern

Antimicrobial resistance rates were investigated for the 3 most frequent isolates. Resistance rates <20% were only seen with Colistin (0%) and Tigecycline (18%). Resistance rate exceeded >50% for all other antibiotics. (Table 3) Among 7 patients with staphylococcus epidermidis isolate, <20% resistance rate only seen with Linezolid (0%) and Tigecycline (14.2%).

Antibiotics usage

Average number of antibiotics prescribed per patient(n=105): 2.7 ± 1.4

Pattern of prescribing prophylactic antibiotics in all trauma patients (n=105)

Total 196 formulations of prophylactic antibiotics were prescribed in trauma patients. Average number of prophylactic antibiotics per patient was 1.8 ± 0.63. Most commonly used dosage form was injection (193, 98%) and only 3(2%) antibiotics given as a tablet form. All injection given by intravenous (IV) route. In most of the patients (68, 65%) two prophylactic antibiotics were given for the prevention of infection in trauma. Metronidazole (75, 71%), Cefoperazone and Sulbactam combination (66, 63%) and Ceftriaxone (22, 21%) were most commonly used antibiotics as prophylaxis in patients with trauma**.** (Figure 4)

Pattern of antibiotics usage in NPIs according to culture and sensitivity (n=36)

Total 82 formulations of antibiotics were prescribed for the treatment of infection in trauma patients. Average number of antibiotics per patient was 2.3 ± 0.82. Most commonly used dosage form was injection (82) and all injection given by Intravenous route of drug administration. In most of the patients (22, 61%) two antibiotics were given for the treatment of infection in trauma. Colistin (23, 64%) was most commonly prescribed antibiotic for the treatment of infection in trauma, it shows that most of the patients were resistant to multiple antibiotics. (Figure 5)

Duration of stay and cost analysis

Average duration of stay of trauma patients without NPIs(n=69) and patients with NPIs(n=36) are 8.7 ± 5.4 days and 27.08 ± 13 days respectively. Total average cost per day were 2824.35 ± 2606.06 INR and 7251. 19 ± 3351.94 INR among patients without NPIs(n=69) and patients with NPIs(n=36) respectively.

Caspofungin (7980 INR), Colistin (4,575.37 INR), Meropenem (3330 INR), Tigecycline (2850 INR) and Cefoperazone + Sulbactam (Zostum) (531. 90 INR) were the costliest antibiotics used in this study.

As shown in Table 4, there is statistically significant difference found for various parameters like ISS, average number of antibiotics per patient, Duration of Stay, average cost in INR per day among two groups of patients.

Correlation between different factors associated with infection in trauma patients are summarized in Table 5. There was significant correlation found between infection and various factors like age, ISS, SIRS score, Hypotension, Multiple trauma, number of interventions, duration of stay and cost.

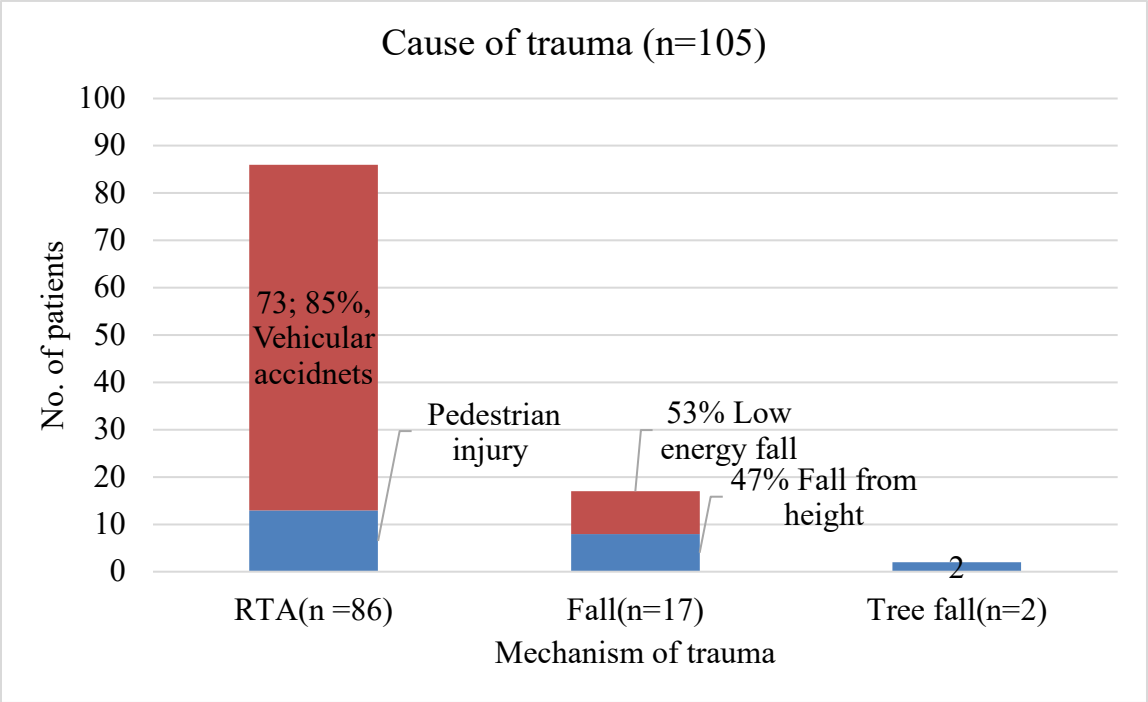

Figure 1: causes of trauma (n=105)

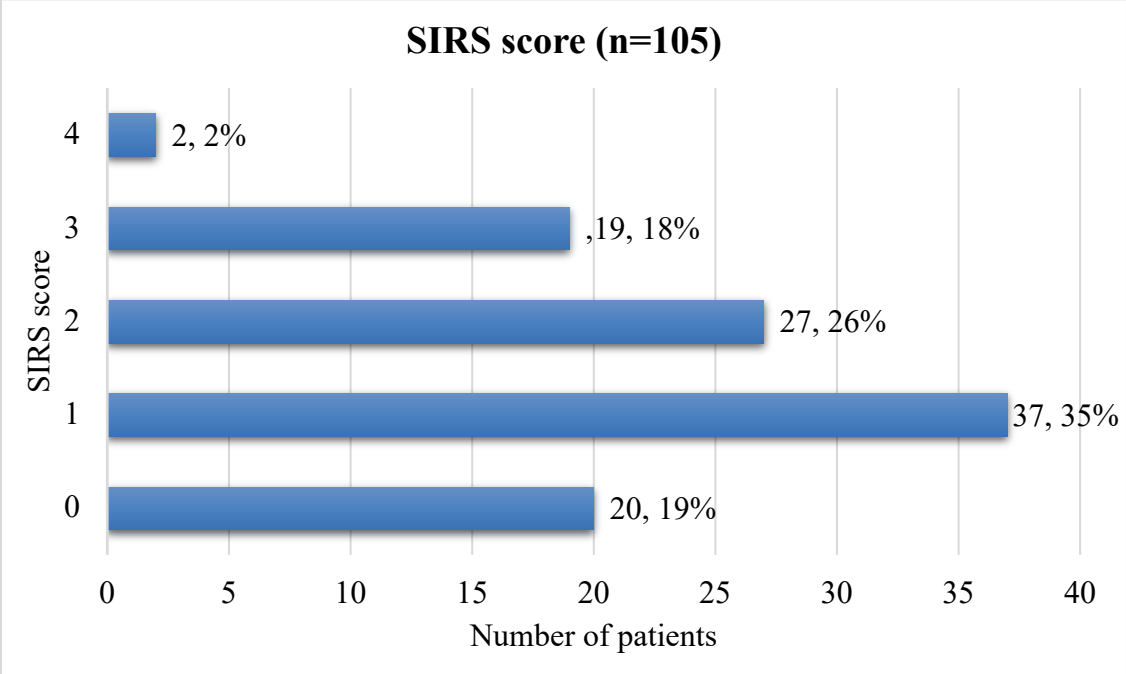

Figure 2: SIRS score and as a predictor of NPIs (n=105)

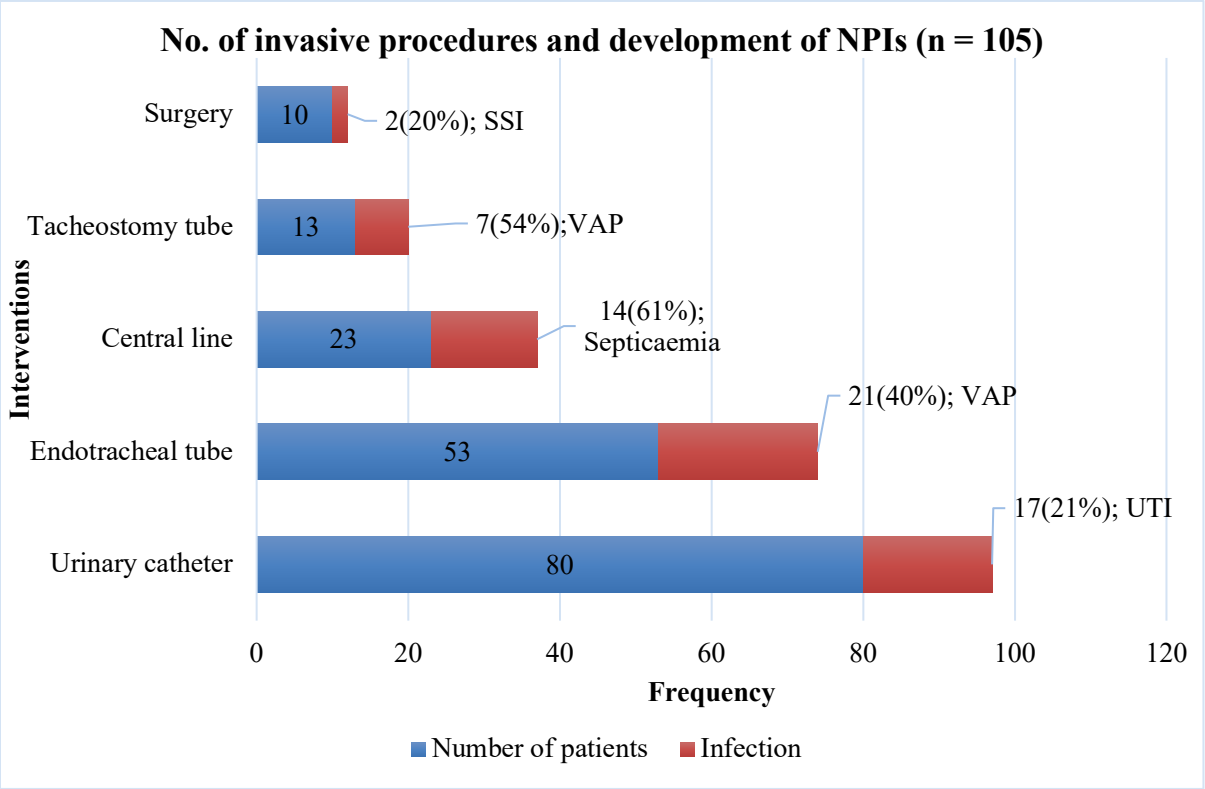

Figure 3: Number of invasive procedures and development of infection(n=105)

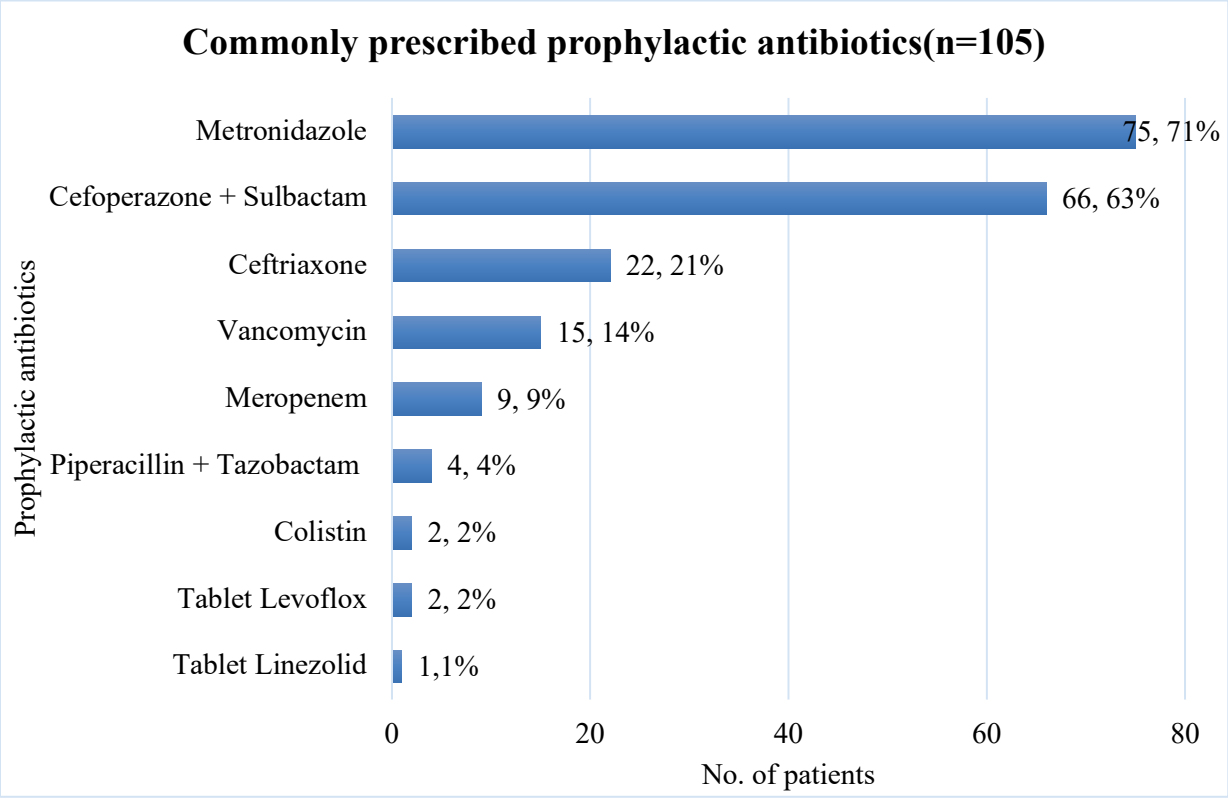

Figure 4: Commonly prescribed prophylactic antibiotics in all trauma patients(n=105)

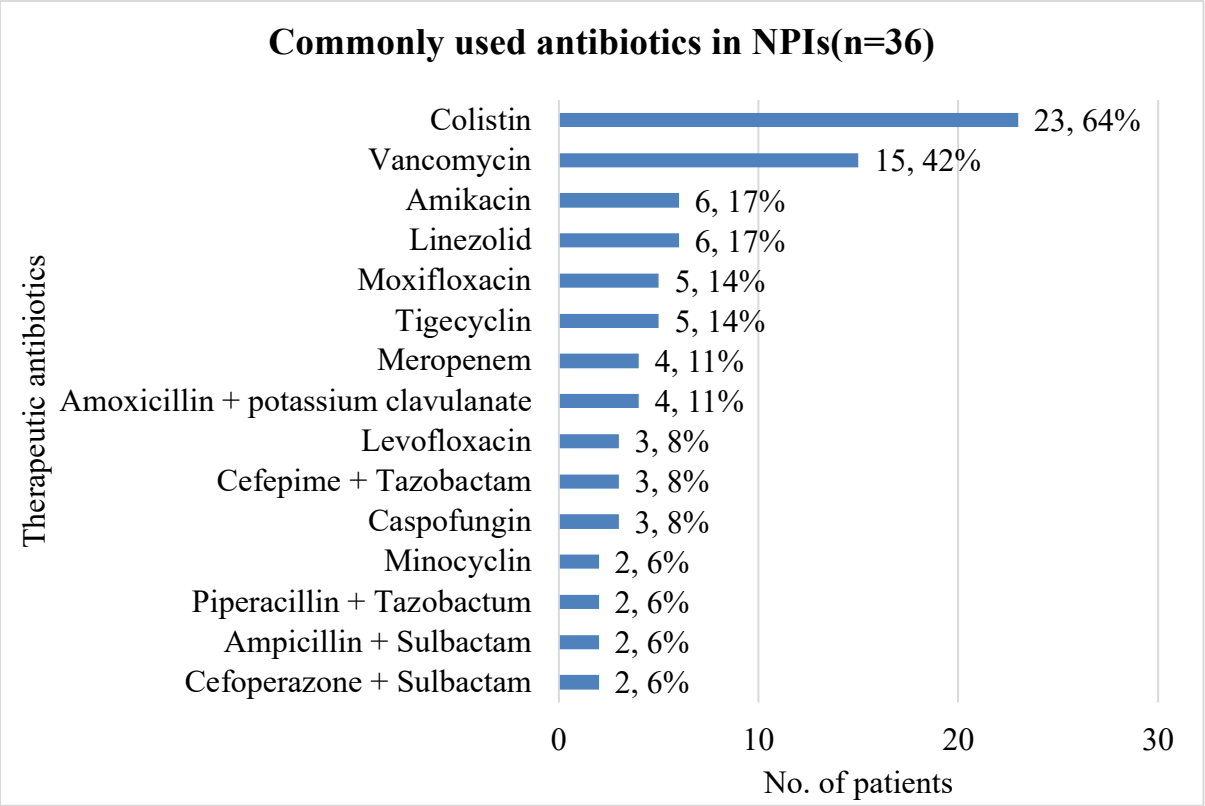

Figure 5: Commonly used antibiotics in patients with NPIs (n =36)

Table 1: Demographic variables

Variables	n = 105 (all trauma patients)	n=36 (trauma patients with infection)
Mean age	43.4 ±17 years	48.72 ± 17.28
Most common age group	21 – 40 years	41-60 years
Male to female ratio	8.54(90% male, 10% female)	(86% male, 14% female)

Table 2: ISS and % of development of NPIs

Severity score	Severity category	No. of patients	No. of patients developing infection	% of infection
1 -15	1	43	8	19
16 – 30	2	34	11	32
31 – 45	3	21	10	48
46 – 60	4	4	4	100
61 - 75	5	3	3	100

Table 3: antibiotics resistance pattern(n=36)

	Acinetobacter baumannii (n=17)		Klebsiella pneumoniae (n=16)		Pseudomonas aeruginosa (n=9)	
	R/S	% of resistance	R/S	% of resistance	R/S	% of resistance
Amikacin	16/1	94	12/4	75	6/3	67
Cefepime	14/3	82	12/4	75	6/3	67
Cefoperazone /Sulbactam	17/0	100	13/3	81	6/3	67
Ciprofloxacin	17/0	100	12/4	75	6/3	67
Colistin	0/17	0	0/16	0	0/9	0
Gentamicin	12/5	71	12/4	75	6/3	67
Imipenem	17/0	100	12/4	75	7/2	78
Levofloxacin	17/0	100	12/4	75	7/2	78
Meropenem	17/0	100	12/4	75	7/2	78
Piperacillin /Tazobactam	17/0	100	11/5	69	6/3	67
Tigecycline	3/14	18	10/6	63	5/4	56
Minocycline	12/5	71	11/5	69	6/3	67
Ampicillin	17/0	100	14/2	88	6/3	67
Ceftriaxone	17/0	100	15/1	94	6/3	67
Ertapenem	17/0	100	12/4	75	6/3	67
Nalidixic acid	17/0	100	13/3	81	6/3	67
Ofloxacin	17/0	100	13/3	81	6/3	67
Trimethoprim-sulfamethoxazole	15/2	88	14/2	88	6/3	67
Amoxicillin Clavulanic acid	17/0	100	11/5	69	6/3	67
Cefuroxime	17/0	100	14/2	88	6/3	67

R = Resistance and S = Sensitive

Table 4: Comparison between various parameters among two groups

Parameter	Trauma patients without infection (n= 69)	Trauma with NPIs* (n=36)	P value
Age	40.51 ±16 years	48.72 ± 17.28	0.995[a]
Gender			
Male	63	31	0.5053[b]
Female	6	5	
ISS*	18.6 ± 11.27	33 ± 17.8	0.0002[a]
Average number of antibiotics per patient	1.8 ±0.6	4.2 ± 1.05	0.00037[a]
DOS*	8.7 ± 5.4 days	27.08 ± 13 days	0.0000[a]
Avg. cost in INR/day	2824. 35 ± 2606.06	7251. 19 ± 3351.94	0.008[a]

*ISS = Injury Severity Score, NPIs = Nosocomial posttraumatic infections, DOS = Duration of stay, a= Unpaired t test; b = Fischer' s exact test; P value less than 0.05 was considered as statistically significant.

Table 5: Correlation between factors related to infection

	Infection (NPIs)	ISS	Comorbidities	DOS	Cost
Age	0.041*	0.454	0.0000**	0.501	0.148
ISS	0.000004**	1	0.006**	0.0001**	0.056
SIRS score	0.000002	0.006**	0.172	0.000002**	0.000006**
Hypotension	0.000002**	0.122	0.40	0.000053**	0.00038**
Multiple trauma	0.01*	0.0005**	0.890	0.038*	0.07*
Number of interventions	0.0000**	0.000001**	0.001**	0.000009**	0.002**
DOS	0.0000**	0.0001**	0.74	1	0.0002**
Cost	0.0000**	0.056	0.28	0.0002**	1

Pearson's correlation; **Correlation is significant at the 0.01 level (2- tailed) *Correlation is significant at the 0.05 level(2-tailed). ISS – Injury Severity Score. DOS – Duration of Stay. SIRS score – Systemic Inflammatory Response Syndrome score

Discussion

Rising population, urbanization, industrialization, and a drastic rise in vehicular transport have contributed to an annual increase in RTAs. As young adults, with no underlying illness are more commonly involved in RTA, there is a greater need to save them. ICU admission in emergency department after traumatic injury in adults is common. Trauma itself and hospital admission, both have a greater risk for infection. Our study conducted in emergency medicine and evaluated trauma patients with and without infection in terms of potential risk factors for developing infection, types NPIs in trauma, pattern of prescribing prophylactics antibiotics and antibiotics for the treatment of infection, duration of stay and cost burden among trauma patients only vs trauma patients with infection.

In our study, total 105 number of trauma patients admitted to emergency medicine department were included with mean age of 43.4 ±16.96 years, most common age group being a 21-40 years. Mandal R. reported the mean age at 35.17 years [11]. In our study male outnumbered the female, which was similar to previous study related to trauma by Jamulitrat Silom *et al* [12].

During follow up, among 105 patients of trauma, 36(34.28%) patients developed at least 1 hospital acquired infection during the course of management in emergency department. Rabin Mandal and Harrison M *et al* found that out of 101 major trauma patients 49, (48.51%) and out of 5537 trauma patients 9.1 % patients developed HAI that was higher as compared to our study [11,13]. Mean age of trauma patients without infection and infected trauma patients was 40. 51 ±16 years and 48.72 ± 17.28 years respectively which is almost similar to study conducted by Harrison M *et al* [13].

Our study found positive correlation between age and development of infection($p<0.001$). It suggests that as the age increases chances of development of infection increases. In advanced age poor functional status like deranged cardiopulmonary function, poor nutritional status at the baseline in trauma patient may easily result in a longer hospital stay and increase the risk of developing NPIs [14]. Bochicchio *et al*. demonstrated that

elderly had a higher probability to develop a NPIs as compared to the younger counterparts [15]. In our study a greater number of male patients (86%) were found to be affected with NPIs which was similar to findings in study by Gannon *et al* [16].

The most frequent cause of injury was vehicular accidents (61%) followed by pedestrian injury (14%). Previously Pories SE *et al* found falls (41.5%) as most common mechanism of trauma.17

Head injury(33, 92%) was the most common in trauma patients with infection followed by extremity(15, 42%) followed by thorax(10, 28%) followed by abdomen and spine which was almost similar to findings in the study by Pories *et al* [17]. Head injury is most frequently associated with VAP in trauma patients because of change in respiratory mechanism, which leads to prolonged mechanical ventilation with continuous enteric feeding and associated craniotomy have been shown to be risk factors for nosocomial pneumonia [18].

Out of 36 patients of trauma with infection, 75% of patients had multiple trauma. Multiple trauma was significantly associated with infection in trauma patients. ($p<0.05$). Jordi Rello *et al* in their study on multiple trauma patients concluded that nosocomial respiratory tract infections are a frequent problem in multiple trauma patients [19].

TBI (86%) was the most common in trauma patients developing infection. Out of 36 patients, 10 patients had multiple organ involvement. Because of compromised airway protection capability after TBI due to head trauma and the requirement of robust tissue oxygenation, mechanical ventilation is frequently recommended in patients with TBI, and therefore VAP is often encountered after TBI [20].

Injury severity can be related to sepsis risk because a greater lesion can cause major immunologic dysfunction. Mean ISS of trauma patients with infection was 33 ± 17. 8 as compared to 18.6 ± 11.27 in trauma patients without infection which was highly significant. (<0.001) and also there was a highly significant correlation between ISS and infection. Incidence of infection in trauma patients with ISS > 45 was 100%. Jamulitrat *et al*. also investigated about a potential relationship between a scoring system for trauma patients and the incidence of NPIs and they found significant relationship was observed between the ISS and the incidence of NPIs.12 The main limitation of ISS: it only considered three of the patient's most severe injuries. This limitation would result in ISS disregarding more severe injuries that happen to be in the same body region as the most severe injury, in favor of another injury in another body region which may not be of comparative severity. In situations where, multiple injuries are confined to a single body region, ISS would underestimate the severity of the patient's condition Despite its limitations, the ISS has proved very robust in use in trauma centers around the world [21].

SIRS score is a significant independent risk factors for infection in trauma patients. Persistent SIRS in trauma may be related to a continued inflammatory reaction to the traumatic injury versus the onset of a newly acquired infection after injury. Out of 36 patients of infection, 31(86%) patients had SIRS score ≥ 2 and also there was a significant correlation between SIRS score and infection($p<0.05$) which suggests that the high (≥2) SIRS score on 2nd day of ICU admission was associated with development of infection. In our study SIRS score was positively correlated with infection($p<0.001$). These findings are similar to findings of the studies by Talmor *et al* and Napolitano *et al* [22,23].

Insertion of devices, which traverse the sterile spaces, as part of diagnostic/ therapeutic work up, acting as foreign bodies and increasing the chances of nosocomial infections. In order to

save the patient's life, emergency procedures often neglect the precautions to reduce infections like gentle tissue handling, device handling, careful surgical preparation and obliteration of dead space [24]. However, plastic devices are easily colonized with bacteria and fungi, able to be colonized by microorganisms at a rate of up to 0.5 cm per hour. The most significant hospital-acquired infections, based on frequency and potential severity, are those related to procedures e.g. surgical site infections and medical devices, including urinary tract infection in catheterized patients, pneumonia in patients intubated on a ventilator and bacteraemia related to intravascular catheter use [25]. Among 80 patients with urinary catheterization, 17(21%) patients developed UTI, among 53 patients with endotracheal tube insertion 21(40%) patients developed VAP and among 13 patients with tracheostomy tube insertion 54% developed VAP, among 23 patients with central line inserted 14(61%) patients developed septicaemia and among 10 patients with surgeries 2(20%) patients developed SSI. We also found positive correlation between number of invasive procedures and infection in trauma patients($p<0.001$). Despotovic A *et al* found invasive procedures during hospitalization as most significant risk factor for HAI acquisition [26].

Hypotension at the time of admission was significantly associated with development of infection($p<0.001$). Also, there was a positive correlation between hypotension and infection($p<0.001$). Claridge *et al* found that patients who were hypotensive at admission were more likely to develop infection than those who were not in shock on admission ($P<.0001$) [27]. Regional hypoxia due to reduced blood flow following hemorrhage due to trauma appears to be a primary mediator that initiates the cascade of events leading to immunodepression and increased susceptibility to infection.

In our study, 28% of patient had diabetes and 25% had hypertension and there was positive correlation between the infection and comorbidities. Morris et al. identified diabetes mellitus and hypertension as pre-existing conditions with a worse prognosis following trauma [28]. The greater frequency of infections in diabetic patients is due to hyperglycemic environment in them which favors immune dysfunction, decrease in the antibacterial activity of urine and greater number of medical interventions in these patients [29].

Because traumatised patients have simultaneous injuries at multiple sites, infections at different foci with different organisms are common. Infections in trauma patients can be acquired either exogenously from the environment at the time of trauma or nosocomially [30]. They may also be acquired from the patient's endogenous flora because of the breakdown of patients own host barriers like skin and abdominal infections subsequent to hollow viscous injury. However, the predominant infections in traumatised patients are nosocomial [31]. Out of 36 patients of nosocomial infections, VAP (n=28, 78%) was the most common followed by UTI(n=17) followed by septicaemia(n=14) followed by SSIs. Rabin Mandal *et al* and Giamberardino, H. I. G. *et al* also found the VAP as the common HAI in trauma patients [11,32].

Total 75 number of isolates causing infection were identified among them Acinetobacter baumanii (17, 23%) was the commonest followed by klebsiella pneumoniae (16, 21%) followed by candida spp. followed by pseudomonas aeruginosa. Giamberardino, H. I. G. *et al* found coagulase-negative *staphylococci* (21%) as the most common organism whereas *Acinetobacter baumanii* (19.7%) was the 2nd most common organism involved in HAI [32]. Among the 28 patients of VAP, Acinetobacter baumanni(15, 54%) was the commonest followed by Klebsiella

pneumoniae(12, 43%). Wyeth showed that S. aureus was the most common pathogen causing VAP but P. aeruginosa and Acinetobacter isolates were significantly more prevalent among patients with VAP.33 Candida species (10, 59%) was the most common in Catheter associated UTI. Staphylococcus epidermidis (7,50%) was the most common cause of septicaemia in trauma patients followed by staphylococcus epidermidis.

Antimicrobial resistance rates were investigated for the 3 most frequent isolates found in our study like Acinetobacter baumannii, Klebsiella pneumoniae and pseudomonas aeruginosa. Resistance rates < 20% were only seen for tigecycline (18%), colistin (0%), and linezolid (0%). Resistance rates exceeded 50% for all other antimicrobials and antimicrobial groups. All except 2 isolate of Acinetobacter baumanii exhibited MDR patterns (15, 88%). Equally high rates of MDR Klebsiella (16, 94 %) and Pseudomonas aeruginosa (9, 89%) were identified. Among 7 staphylococcus epidermidis isolate, <20% resistance rate only seen with Linezolid (0%) and Tigecycline (14.2%). Our findings were almost similar to antimicrobial resistance pattern showed by Despotovic A *et al* [26].

Initial aim of prescribing antibiotics is to prevent the trauma induced infection in patients admitted to emergency medicine department. Esnault *et al*., Sanabria *et al*. and Bosman *et al*. reported that antibiotic prophylaxis exerts protective effects against development of NPIs [34-36]. In present study, total 196 formulations of prophylactic antibiotics prescribed in trauma patients; average. Intravenous route (193) was the most commonly used formulation. Metronidazole (75, 71%) was the most commonly used prophylactic antibiotic followed by Cefoperazone + sulbactam combination (66, 63%) followed by Ceftriaxone (22, 21%). In most of the patients (68) two prophylactic antibiotics were given for the prevention of infection in trauma among them Metronidazole and Cefoperazone + Sulbactam combination (53, 78%) was most commonly prescribed followed by Ceftriaxone and metronidazole combination. In few patients Colistin (2%), Linezolid (1%), and Vancomycin (14%) were also prescribed as prophylaxis that was not an ideal prescribing in our study. We must realize that these antimicrobials are reserved drugs for MDR pathogens.

Total 82 intravenous formulations of antibiotics were prescribed for the treatment of infection, with average 2.3 ± 0.82 antibiotics per patient. In most of the patients (22, 61%) out of 36, two prophylactic antibiotics were given. Colistin (23, 64%) was most commonly prescribed antibiotic for the treatment which showed that increasing resistance to multiple antibiotics of causative pathogen. Vancomycin (15, 42%) was the 2nd most commonly prescribed antibiotic followed by Amikacin (6, 17%), Linezolid (6, 17%) and Tigecycline (5, 14%). Other antibiotics like Moxifloxacin (14%), Meropenem (11%), Amoxicillin Clavulanate (11%), Levofloxacin (8%), Cefepime and Tazobactam combination (8%), Caspofungin (8%), Minocycline (6%), Piperacillin + Tazobactam (6%), Ampicillin + Sulbactam (6%), Cefoperazone + Sulbactam (6%) were also used for treatment of NPIs. We found statistically significant difference in average number of antibiotics prescribed per patient among 2 groups ($p<0.001$). Once a pathogen is isolated, therapy is streamlined to a narrow-targeted antibiotic. Proper antimicrobial doses and schedules are crucial to maximizing efficacy and minimizing toxicity. Duration of therapy should be as short as is necessary and timely escalation and de-escalation of antibiotic is must according to sensitivity report because prolonged therapies lead to emergence of resistance.

The infection group had a duration of stay 3-fold longer than the non-infected patient

group (27.08 *versus* 8.7 days) which was similar to findings of study by Giamberardino *et al*.32 We found highly statistical significant difference between duration of stay among only trauma patients and trauma patients with infection($p<0.001$) and also there was positive correlation between infection and increased duration of stay. It showed that duration of stay was more among the patients with infection as compared to trauma without infection which was similar to the findings of Glance *et al*. and Amanda J *et al* [37,38].

Trauma patients often require expensive hospital-based treatment like multiple scans, head injury patients require mechanical ventilation, catheterization, central line for resuscitation in hypotensive patients which increases risk for NPIs. Patients with NPIs required sensitivity report based antimicrobial therapy and prolonged hospitalization which increases cost burden among trauma patients with NPIs than trauma patients without NPIs.39 In our study we found statistical significant difference between average cost per patient per day among trauma patients and trauma patients with infection. ($p<0.05$) which was similar to findings of Glance *et al* and Robert Haley [39,40]. Also there was positive correlation between infection, duration of stay and cost per patient per day. ($p<0.001$) There are numerous estimates of cost per hospital day and unit type. Colistin, commonly used for the treatment of infection in trauma, which is of rupees 4575. 37 INR.

On basis of observation that Colistin was most commonly prescribed for treatment of infection in trauma patients, we conclude that antimicrobial resistance is increasing; and antimicrobial drug development is slowing. To reduce the antimicrobial resistance antibiotic stewardship programme should be launched in all institutes. Antimicrobial stewardship is defined as "the optimal selection, dosage and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance" [41]. To reduce the error in prophylactic antibiotics prescribing repeated regular sensitization program for physician should be conducted in all the institute and use of antibiotics like Tigecycline, Colistin should be very judicious as they are toxic drugs.

Conclusion

Here we conclude that trauma was one of the causes for nosocomial infections after hospitalization. Head injury, multiple trauma, traumatic brain injury (TBI), advanced age, male gender, higher ISS, SIRS score ≥ 2 on 2nd day of admission, invasive procedures like catheter insertion/surgeries, hypotension, comorbidities like diabetes; hypertension were the predisposing factors for NPIs. Ventilator Associate Pneumonia (VAP) was the most common NPI, followed by Urinary Tract Infection (UTI) followed by septicaemia followed by SSIs. Acinetobacter baumannii, Klebsiella pneumoniae, candida, pseudomonas aeruginosa were the common isolates among patients with NPIs which suggest that rising trend of gram-negative infection. Antibiotics resistance rates < 20% were only seen for Tigecycline (18%), Colistin (0%), and Linezolid (0%). Resistance rates exceeded 50% for all other antimicrobials and antimicrobial groups. Increasing resistance rate is due to the incorrect prescribing of prophylactic antibiotics in terms of optimal selection, dosage and duration. In our study, Colistin was most commonly prescribed antibiotic among patients with NPIs which also give idea about rising trends of antimicrobial resistance. To reduce and monitor the antimicrobial resistance, a robust Antibiotic Stewardship program should be in place. Duration of stay in hospital and cost of treatment were more among the patients with NPIs than trauma patients without NPIs which affects financial status of the patients

immensely. In light of the preventability of many NPIs and the magnitude of the clinical and economic burden associated with NPIs, policies aiming to decrease the incidence of NPIs may have a potentially large impact on outcomes in injured patients.

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References

1. Saini S, Saini R. Hospital infection control: clinical guidelines. 1st edition. Paras medical publisher new Delhi ,2012
2. Tribble DR, Conger NG, Fraser S, *et al*. Infection-associated clinical outcomes in hospitalized medical evacuees after traumatic injury: trauma infectious disease outcome study. *J Trauma*. 2011;71(1 Suppl): S33–S42.
3. (Cole, E., Davenport, R., Willett, K., & Brohi, K. (2014). The burden of infection in severely injured trauma patients and the relationship with admission shock severity. Journal of Trauma and Acute Care Surgery, 76(3), 730–735.)
4. Moore K. (2015). Infections in Trauma Patients: Prevention Begins in the Emergency Department. Journal of Emergency Nursing, 41(2), 170–171.
5. Razine R, Azzouzi A, Barkat A. Prevalence of hospitalacquired infections in the university medical center, Rabat, Morocco, International Archives of Medicine, 2012; 5(1):26.
6. Kouchak F, Askarian M. Nosocomial infections: the definition criteria, Iranian Journal of Medical Sciences, 2012; 37(2): 72-73.
7. Tolera M, Abate D, Dheresa M, Marami D. Bacterial Nosocomial Infections and Antimicrobial Susceptibility Pattern among Patients Admitted at Hiwot Fana Specialized University Hospital, Eastern Ethiopia. *Adv Med*. 2018; 2018:2127814. Published 2018 Dec 4.
8. Copes WS, Sacco WJ, Champion HR, Bain LW, Progress in Characterising Anatomic Injury, In Proceedings of the 33rd Annual Meeting of the Association for the Advancement of Automotive Medicine, Baltimore, MA, USA 205-218
9. Whitaker IY, Gennari TD, Whitaker AL. The difference between ISS and NISS in a series of trauma patients in Brazil. Annu Proc Assoc Adv Automot Med. 2003; 47:301-309.
10. Napolitano, L. M., Ferrer, T., McCarter, R. J., & Scalea, T. M. Systemic Inflammatory Response Syndrome Score at Admission Independently Predicts Mortality and Length of Stay in Trauma Patients. The Journal of Trauma: Injury, Infection, and Critical Care, 2000; 49(4): 647–653.
11. Mandal R, Hossain A. Hospital-Acquired Infections in Patients with Major Trauma – Outcome Evaluation in a Tertiary Care Hospital. Int J Sci Stud 2021;8(11):82-86
12. Jamulitrat S, Narong MN, Thongpiyapoom S. Trauma severity scoring systems as predictors of nosocomial infection. Infect Control Hosp Epidemiol. 2002;23(5):268–73
13. Lazarus HM, Fox J, Burke JP, Lloyd JF, Snow GL, Mehta RR, Evans RS, Abouzelof R, Taylor C, Stevens MH. Trauma patient hospital-associated infections: risks and outcomes. J Trauma. 2005 Jul; 59(1):188-94.
14. Hashmi A, Ibrahim-Zada I, Rhee P, Aziz H, Fain MJ, Friese RS, *et al*. Predictors of mortality in geriatric trauma patients: a systematic review and meta-analysis. J Trauma Acute Care Surg. 2014; 76(3): 894–901.
15. Bochicchio GV, Joshi M, Knorr KM, Scalea TM. Impact of nosocomial infections in trauma: does age make a difference? J Trauma. 2001;50(4):612–7.

16. Gannon CJ, Pasquale M, Tracy JK, McCarter RJ, Napolitano LM. Male gender is associated with increased risk for postinjury pneumonia. Shock. 2004; 21(5): 410–4.
17. Pories, S. E. The Epidemiologic Features of Nosocomial Infections in Patients with Trauma. Archives of Surgery, 1991; 126(1): 97.
18. Sirgo G, Bodí M, Díaz E, Rello J. Pneumonia in head-injured and severe trauma patients. Semin Respir Crit Care Med 2002; 23:435-41.
19. Meisner, M., Adina, H. & Schmidt, J. Correlation of procalcitonin and C-reactive protein to inflammation, complications, and outcome during the intensive care unit course of multiple-trauma patients. Crit Care. 2005;10:R1.
20. Yuan, KC., Huang, HC. Antimicrobial Prophylaxis in Patients with Major Trauma. Curr Trauma Rep. 2017; 3: 292–299.
21. Samin OA, Civil ID. The New Injury Severity Score Versus the Injury Severity Score in Predicting Patient Outcome: A Comparative Evaluation on Trauma Service Patients of the Auckland Hospital. Annu Proc Assoc Adv Automot Med. 1999; 43:1-15.
22. Talmor M, Hydo L, Barie PS. Relationship of systemic inflammatory response syndrome to organ dysfunction, length of stay, and mortality in critical surgical illness: effect of intensive care unit resuscitation. Arch Surg. 1999 Jan;134(1):81-7.
23. Napolitano L, Ferrer T, McCarter R, Scalea T. Systemic inflammatory response syndrome score at admission independently predicts mortality and length of stay in trauma patients. J Trauma. 2000; 49:647– 652.
24. Caplan ES, Hoyt NJ. Identification and treatment of infections in multiply traumatized patients. Am J Med 1985; 79:68-76.)
25. Guggenbichler JP, Assadian O, Boeswald M, Kramer A. Incidence and clinical implication of nosocomial infections associated with implantable biomaterials - catheters, ventilator-associated pneumonia, urinary tract infections. GMS Krankenhhyg Interdiszip. 2011;6(1): Doc18.
26. Despotovic A, Milosevic B, Milosevic I, Mitrovic N, Cirkovic A, Jovanovic S, Stevanovic G. Hospital-acquired infections in the adult intensive care unit-Epidemiology, antimicrobial resistance patterns, and risk factors for acquisition and mortality. Am J Infect Control. 2020 Oct;48(10):1211-1215.
27. Claridge JA, Crabtree TD, Pelletier SJ, Butler K, Sawyer RG, Young JS. Persistent occult hypoperfusion is associated with a significant increase in infection rate and mortality in major trauma patients. J Trauma. 2000;48(1):8–14.
28. Morris JA, MacKenzie EJ, Edelstein S. The effect of pre-existing conditions on mortality in trauma patients. JAMA 1990; 236:1942-46.
29. Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: A review of pathogenesis. Indian J Endocrinol Metab. 2012;16 Suppl 1(Suppl1):S27-S36.
30. Caplan ES, Hoyt N, Cowley RA. Changing patterns of nosocomial infections in severely traumatized patients. Am Surg 1979; 45:204-10.
31. Patel JC, Mollitt DL, Tepas JJ. Infectious complications in critically injured children. J Pediatr Surg 2000; 35:1174-8
32. Giamberardino, H. I. G., Cesário, E. P., Carmes, E. R., & Mulinari, R. A. Risk factors for nosocomial infection in trauma patients. Brazilian Journal of Infectious Diseases, 2007; 11(2): 285–289.
33. Bradford PA, Petersen PJ, Tuckman M, Jones CH. In vitro activity of tigecycline and occurrence of tetracycline resistance

determinants in isolates from patients enrolled in phase 3 clinical trials for communityacquired pneumonia. Clin Microbiol Infect 2008; 14:882–886
34. Esnault P, Nguyen C, Bordes J, D'Aranda E, Montcriol A, Contargyris C, *et al*. Early-onset ventilator-associated pneumonia in patients with severe traumatic brain injury: incidence, risk factors, and consequences in cerebral oxygenation and outcome. Neurocrit Care. 2017.
35. Sanabria A, Valdivieso E, Gomez G, Echeverry G. Prophylactic antibiotics in chest trauma: a meta-analysis of high-quality studies. World J Surg. 2006 Oct;30(10):1843-7.
36. Bosman, A & Jong, M & Debeij, Jan & Broek, Pieter & Schipper, Inger. Systematic review and meta-analysis of antibiotic prophylaxis to prevent infections from chest drains in blunt and penetrating thoracic injuries. The British journal of surgery. 2012; 99: 506-13.
37. Glance LG, Dick AW, Osler TM, *et al*. The association between nurse staffing and hospital outcomes in injured patients. BMC Health Serv Res 2012; 12:247.
38. Hessels AJ, Kuo YH, Ahmed N. Epidemiology and Impact of Healthcare-Associated Infections in Trauma Patients: A National Data Analysis. Surg Infect (Larchmt). 2020 Dec;21(10):871-876.
39. Glance LG, Stone PW, Mukamel DB, Dick AW. Increases in mortality, length of stay, and cost associated with hospital-acquired infections in trauma patients. Arch Surg. 2011 Jul;146(7):794-801.
40. Haley R. Managing Hospital Infection Control for Cost Effectiveness. Chicago, Ill: American Hospital Publishing; 1997.
41. Gerding DN. The search for good antimicrobial stewardship**.** Jt Comm J Qual Improv**.** 2001;27(8):403-404