**Research Manuscript: Assessment of the care of acute pain among trauma patients in the largest tertiary hospital in Addis Ababa, Ethiopia: A prospective observational study**

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**Authorship**

Segni Kejela conceptualized and developed the proposal and made the data collection formats for the data collector and participated in writing the discussion

Nebyou Seyoum edited the proposal and the data collection format. As well participated heavily in the manuscript generation.

**Abstract**

**Background**: Trauma and pain are heavily intertwined. It is a link between the event of trauma and chronic pain as well as Posttraumatic stress disorder and in fact, was linked to an increase in morbidity and mortality.

**Methods**: This is an institution based provider and patient blinded observational study on consecutive patients treated at the emergency department with no prior pain management at peripheral hospital presenting within 24 hours of the traumatic event over 3 months.

**Results**: A total of 74 patients were evaluated with pain scoring at 0%. The researcher provided pain scoring showed a severe subjective pain score of 79.7% and a severe functional activity score of 59.5%. Analgesia was provided in 55.4±35.3 minutes and all patients received Diclofenac or Tramadol and all patients who received Diclofenac were in the severe pain group. Satisfactory pain reduction after analgesia for patients initially complaining severe pain, designated as WHO ladder III patients was at 28.8%, for moderate pain as determined with presumed WHO ladder II designation was at 54.6% and for mild at 66.7% when scoring was based on subjective pain score in post-analgesia course with the difference being statistically significant(p-value: 0.05). 40% of patients discharged to the home received no analgesia after the first dose provided upon presentation.

**Conclusion**: Pain scoring was non-existent during the study course.. The poor rate of utilization of combination analgesia and Opioid utilization has led to unsatisfactory pain outcomes in patients evaluated and followed for 24 hours after presentation.

**Keywords:** Acute trauma, Analgesics, Pain scoring, Narcotics

**Background**

Trauma is a global burden with a reported 973 million injuries needing a certain level of medical attention, 4.8 million trauma-related deaths, and DALY of 247.6 million life-years in total in 2013 alone.[1] Furthermore, in 2014 WHO report on the global burden of trauma, it is reported that trauma-related deaths share 9% of the total death toll worldwide [2] Age group predominantly affected are the younger, productive part of the population with median age bein 30 years, mean age of 33+/-11 years and 75% of the victims lie in the age group of 15-45 years of age [3,4]. Ethiopian experience is somewhat similar to the global trend. The age of 30 years being the median with the mean distribution of 35+/-13.5years in one study conducted in the capital of Ethiopia, Addis Ababa [5].

Trauma and pain are heavily intertwined. This can be evidenced by studies on the prevalence of pain upon admission and discharge among trauma patients showing a prevalence of 91% on admission and 86% on discharge [6]. The relationship between trauma and pain goes beyond the emergency rooms and surgical wards to the chronic possibly lifelong complaint. One large scale study done in the USA on over 3000 patients with major trauma reported that one year after trauma, 62.7% of the patients complained pain on the site of injury with pain severity in the moderate range (5.5 in the 10 point pain score scale) [7].

Pain in trauma patients potentiates the stress response which increases tachycardia, oxygen consumption, hypercoagulation, and immunosuppression with alteration of the physiologic response to the likes of ventilation all ending up prolonging and outlasting the recovery time. [8] Consequently, management of pain in trauma patients have had a positive impact on patient outcomes beyond the psychological relief with an overall decrement in morbidity and mortality.[9] Yet, adequate and organized pain management in trauma patients hasn't always been practiced in many trauma centers, and especially so in developing countries [10]

In Ethiopia, a study in trauma and as well in pain is not deep-rooted and quite scarce in the literature. So, this study is aimed at determining the adequacy of pain management among acute trauma patients in the emergency department at a level III hospital and assesses the practice of evaluation for pain, organized pain care and follow-up of patients in pain, and possible changes in the management of pain based on reevaluation by treating team.

**Methods**

**Study design**

The study is a facility-based observational study with data gathered from the patients and their charts over 3 months. The survey design was aimed at providing descriptive data of the acute pain care among trauma patients in the mentioned Hospital with a follow-up period of 24 hours for every patient or until discharge with each observation commencing from the patient presentation. It is a blinded study (both the patient and the treating team were no notified of the study to avoid observational bias).

**Study setting**

Tikur Anbessa specialized Hospital is the largest and is the busiest public hospitals in Ethiopia. It serves close to 500,000 patients a year with 24 hours, 7 days a week emergency services provided alongside elective and emergency multidisciplinary surgical services at a level III designation. Data collection lasted for 3 months..

**Study participants**

All patients treated for trauma, alive, dead, admitted, observed, discharged, or referred were evaluated with survey format as long as they present within 24 hours of trauma and no analgesia provided at the referring hospital.

**Inclusion criteria**

All trauma patients presented within 24 hours of trauma and treated at Tikur Anbessa Specialized Hospital, emergency department in the 3 consecutive months of 2020.

**Exclusion criteria**

Patients presented more than 24 hours, post-incident. And those segments of trauma patients who had been treated with analgesic at periphery Hospitals or any health facilities

**Study variables**

**Independent Variables**

Age, sex, occupation, region, time of arrival (day/night), Duration of trauma from the presentation, trauma anatomic site, mechanism of injury, the outcome of trauma, level of training of evaluating physician

**Dependent variables**

Pain scoring documentation, type of analgesic given and dose, delay of analgesic from presentation in hours, pain rescoring after analgesia, interval between analgesia, change in analgesics.

**Ethical consideration**

Before data collection, Ethical clearance will be obtained from the Research Ethics Committee of Faculty of Medicine, AAU at the department of surgery level.

**Operational definition**

Trauma patients: a segment of emergency patients presented with physical injury after inflicted insult to body part from external physical force.

Acute pain: Pain of the subject of study from incident to 24 hours post-trauma.

Pain score: The score determining the severity of experienced pain by the patient.

Functional activity score(FAS): a form of pain scoring using the functional parameters of the extent of activity restricted by the location of the body affected (this includes deep breathing, coughing in the case of chest injury and standing and walking for limb injuries)

In the FAS, there are 3 ranges of injury-related pain:

A – No limitation meaning the patient’s activity is unrestricted by pain

B – Mild/moderate limitation means the patient’s activity is mild to moderately restricted by pain

C - Severe limitation means the patient ability to perform the activity is severely limited by pain

Subjective pain score: it’s a type of pain intensity scoring where the patient is asked to describe his/her pain as mild, moderate or severe based on subjective experience

Analgesics: any pharmacologic agent given with the intent of relieving pain.

Penetrating injury: a type of trauma inflicted on a patient with resulting in a breach in the skin or mucus membrane of the patient

Blunt trauma: a type of trauma inflicted on a patient with resultant damage to soft tissue or internal organs with no injury to the skin or mucus membrane

**Results**

In this study, 74 consecutive patients fulfilling all the strict inclusion criteria were analyzed. 57(77%) of patients were males, 55(74.3%) of the patients were under the age of 45 years and only 3(4.1%) were above the age of 60. More than half, 41(55.4%) of the trauma victims are married, and close to half, 36(48.6%) were from the Addis Ababa and followed by Oromia as the second most common area of patient presentation. Only 13(17.8%) of the patients had a college education and the same amount of participants were uneducated (defined as not attending primary school). Most patients were categorized as private employees 19(26%), students 13(17.8%), and farmers 12(16.4%). The time of presentation after trauma in hours has ranged from 1-24 hours with a mean of 9.19±7.62 hours. The socio-demographic status of the study participants is further elucidated in Table 1.

66(89.2%) of patients were primarily evaluated by interns and 72(97.3) of patients were evaluated by residents either primarily or following interns evaluation. Orthopedic residents were involved in evaluation in 48(64.9%) of the cases, general surgery residents in 13(17.6%), Emergency residents in 8(10.8%), and Neurosurgery residents in 3(4.1%). Regarding residents year on training, 27(36.5%), 23(31.1%), 20(27.8%), and 2(2.8%) patients were evaluated by first, second, third, and fourth-year residents respectively.

Regarding the trauma mechanisms and circumstances, blunt trauma was the most common mechanism, 66(89.2%). From the Blunt trauma population, 27(40.9%) were injured by pedestrian versus motor vehicle type accidents. In this study, 4 patients had gunshot injury and no stab injury was reported. On the primary survey, no patient with compromised airway was found to be part of the study but 4(5.5%) patients had either labored or gasping type of breathing with 2 patients presenting with hypotension and 6 patients with GCS of 13 or 12. Patients with tachycardia (HR>100 beats/min) were 29(39.2%) at presentation. The most common site of injury was extremities with fracture or dislocation reported in 59(79.7%) of patients, followed by pelvic injury in 23(31.1%) patients and traumatic brain injury in 16(21.6%) of patients studied. Only 6(8.1%) of patients had an alcohol intake history on presentation and 50(67.9%) of patients presented on day time. Most patients, 51(68.9%) were kept at emergency for observation and investigation, while 15(20.3%) were discharged home after evaluation within 24 hours of presentation. (Table 2)

No patient had any pain score recorded on the chart upon initial evaluation and on follow up evaluation as well. Researcher-provided pre-analgesia score based on subjective pain score showed 59(79.7%) of patients in severe pain range, 13(17.6%) in moderate, and 2(2.7%) in the mild pain range. And based on Functional activity score, severe pain was recorded in 44(59.5%) of the patients while moderate/mild and no pain was recorded in 18(24.3%) and 12(16.2%) patients respectively. (Figure 1 and 2)

The need and type of analgesia needed were determined by the researchers based on the pain score and stratified based on the WHO trauma pain management ladder as I, II, or III. For prediction purposes, both functional activity scores and subjective pain scores were utilized and the more severe score of the two was used for designation of the WHO ladder. Based on this, 60(81.1%) of patients were initially categorized to WHO ladder III, 11(14.9%) to WHO ladder II, and 3(4.1%) to WHO ladder I.

All patients were provided with Analgesia and all were in the WHO ladder I and II. Utilized drugs were Tramadol 50mg IV/IM in 65 patients and Diclofenac 75mg IM in 9(12.2%) patients. No patient had a combination of analgesics. All patients provided with Diclofenac (WHO ladder I medication) had severe pain. Time from presentation to analgesia ranged from 20 minutes to 240 minutes with mean 55.4±35.3 minutes. At 60 minutes after presentation, 3(100%) of patients with predicted WHO ladder I, 10(90.9%) of WHO ladder II and 54(90%) of WHO ladder III have received the first dose of analgesia. No difference between predicted WHO ladder(as a measure of severity of pain) and time of analgesia provision on logistic regression (p-value: 0.639)

Response to analgesia was tried to be retrieved from patients' chart documentation and no patient had pain level scoring after analgesia was provided. The data collector provided pain scoring was done at 114.3±59.7 minutes after the first dose of analgesia. Using subjective pain score parameters 3(4.1%), 57(77%) and 14(18.9%) had severe moderate and mild pain respectively. And considering functional activity scoring 39(52.7%), 21(28.4%) and 14(18.9%) had severe, Mild/Moderate and no pain respectively. Based on satisfaction based stratification (residual moderate or severe pain of subjective pain score and severe pain of functional activity score scored as unsatisfactory), 50(67.6%) of patients had unsatisfactory pain response based on functional activity score and 49(66.2%) of patients had unsatisfactory score based on subjective pain score. (Figure 1 and 2)

Correlation between predicted pre-analgesia WHO ladder and satisfaction based on post-analgesia subjective pain score satisfaction rate showed unsatisfactory pain response in 43 out of 60 (71.2%) of patients stratified to WHO ladder III and 5 of 11 (45.4%) of WHO ladder II patients. The same pre-analgesia WHO ladder prediction correlated with post-analgesia functional activity score based satisfaction, 44 of 60 (73.3%) patients stratified to WHO ladder III had unsatisfactory pain response and 5 of 11 (45.4%) patients stratified to WHO ladder II had unsatisfactory pain outcome. This difference was statistically significant in logistic regression model analysis, with a p-value of 0.05 and 0.04 respectively. (Table 3, Figure 3)

Comparing the level of training of residents with the level of satisfactory pain response post analgesia, 34 of 50 patients (68%) treated by junior residents (first and the second year) and 15 of 22 patients (68.2%) treated by senior residents had unsatisfactory pain score post analgesia with the difference between the two not being statistically significant (p-value: 0.98). Comparing fields of residency, the group was classified into orthopedics and all other specialties included in the study (Neurosurgery, Emergency medicine, and General surgery) because of the high numerical proportion of patients evaluated by orthopedics residents, was done. In this regard, patients evaluate by orthopedic residents had unsatisfactory post analgesia pain scores in 31 out of 48 patients (65.6%) and for patients treated by all the other 3 fields of residency, 18 out of 24 (75%) patients had unsatisfactory post analgesia pain outcome. The difference wasn't statistically significant (p-value: 0.374).

Within 24 hours follow up (including those discharged home before 24 hours was reached), 14 (18.9%) patients had a change of analgesics. 5(6.75%) patients initially on Diclofenac and with unsatisfactory pain response had been up-regulated to Tramadol, while one patient with satisfactory pain response with Diclofenac was up-regulated to Tramadol. 4 patients (2 Diclofenac and 2 Tramadol) with unsatisfactory pain response after initial dose were withdrawn while 3 patients initially on Tramadol with satisfactory pain response were withdrawn with a total withdrawal rate of 9.4%. One additional patient initially on Tramadol with unsatisfactory pain response was down-regulated to Diclofenac. All patients kept at ER, admitted to wards, referred, and underwent emergency procedures were continued on Tramadol. 6 of 15 patients (40%) were sent home without analgesics.

**Discussion**

The study's finding of male predominance and a higher proportion of younger age, less than 45 years, is neither surprising nor peculiar as this is commonplace in both national and international studies done elsewhere. [11-14] Socio-demographic factors like lack of higher education is a reflection of the country's status rather than any trauma-related predilection. [15] The vast majority of patients, 1 out of 10, had been primarily evaluated by interns. This in itself may not be a major challenge in trauma patient pain management as almost all of them were also evaluated by residents of different specialties and different levels of training. But the striking finding is the poor involvement of emergency medicine residents in the evaluation of the patients, which might lead one to hypothesize their absence as a potential reason for poor holistic patient care including proper pain management. Regardless, as evidenced by one recent publication addressing knowledge and perception of residents on pain management showed poor medical school curricular structure in teaching proper pain management service, one may suspect this to be the case in most setups as well including countries with low and middle income. [16]

The prevalence of blunt trauma over penetrating and the prevalence of motor vehicle-related injuries are both national and international. [17-19] A more peculiar finding is that pedestrian road traffic accidents are more prevalent than motor vehicle collisions which are particularly more common in national publications. [20] Moderate Traumatic brain injury and alcohol intoxication at presentation was low (8.1% and 10.8% respectively) and had been included in all analysis of pain. Fractures of extremities and pelvis were the most common anatomic site of injury followed by trauma to the head. The predominance of orthopedic and head trauma is fairly familiar both in civilian and combat casualty patients. [21,22] Burn patients were not included in the study because the institution doesn’t provide any burn care.

The time of patient presentation post-trauma was a bit more than 9 hours on average. This is a significant delay in executing life-saving measures and definitive trauma care. Also one must consider that patients with trauma had been in pain for an average of 9 hours before consideration for analgesia was made and this has lasting implications in the long term physical health and psychological outcome of the patients with an increased rate of chronic pain, depression, and PTSD.[23,24,25]

Pre-analgesia pain scoring was not performed for any consecutive trauma patients evaluated in this study by the treating team. This is staggeringly low compared to study from developed countries as evidenced by Silka et al, which reported a pain scoring rate of 73%. [26] Using data collectors pain pre-analgesia pain scoring showed severe pain in close to 60% and 80% with SPS and FAS scoring systems respectively. It is expected to attain a higher proportion of patients with severe acute pain in the trauma population. [27] WHO ladder was predicted based on both SPS and FAS scores, with a more severe score used to predict the type of analgesia needed. The WHO ladder predicted for more than 80% of the patients was ladder III (strong Opioid) based on the WHO trauma pain management ladder. [28] Every patient was provided with analgesia with a mean time of the door to needle of 55 minutes. This value is not a disappointing one compared to studies from low-income countries, as in the case of Ouagadougou which showed analgesia time from time of presentation of 75 minutes. [10] All analgesia provided were from the WHO ladder I, Diclofenac, and WHO ladder II, Tramadol. These were provided regardless of the level of pain reported by the patients as evidenced by the fact that all patients provided with Diclofenac were in the severe pain group and were predicted to receive WHO ladder III analgesics. With the failure in treating team to perform reevaluation and scoring of pain level, researcher-performed pain rescoring showed more than close to three-quarters of patients in predicted WHO ladder III during pre-analgesia evaluation had unsatisfactory improvement in pain status compared to close to half in predicted WHO ladder II and only a third in WHO ladder I group based on both FAS and SPS with the difference being statistically significant. This depicted the need for pain scoring before analgesia and adherence to the regimens in the respective groups for the assigned ladder category to achieve proper analgesia for every individual patient contrary to an arbitrary assignment of different analgesics as per the discretion of the treating physician.

In this study, no difference in the level of training in residency was found regarding the primary outcome of satisfactory pain control in acute trauma patients evaluated in this study with both groups having two-third unsatisfactory post analgesia pain scores. This may imply that the delivery of comprehensive management of acute pain in trauma patients has not been addressed in any level of the training of the residents and curricular deficit of this subject matter may have played a pivotal role. Similarly, orthopedic surgery residents (the specialty with the highest number of patients evaluated) had a 65.6 percent rate of unsatisfactory SPS outcome compared to other specialties with a 75% unsatisfactory SPS score but the difference is not statistically significant meaning a lack of proper acute pain management transcends departmental boundary.

Regarding ongoing pain management beyond the first dose of analgesia, within 24 hours 14 of 74 patients had a change in the regimen. 4(5.4%) patients requiring up-regulation were withdrawn from the medications instead while 3 patients requiring maintenance with initial satisfactory response were also withdrawn. And one patient with Diclofenac with satisfactory response requiring maintenance with the same class regimen was up-regulated to Tramadol. This outcome evidenced that pain management wasn’t dependent on patient response to analgesia, but rather the discretion of the physician and even probably, the specific environment of the day. A more worrying outcome is the fact that 40% of patients discharged to home were sent home with no analgesia. As one study from the Netherlands showed, two-thirds of patients discharged from the emergency department with musculoskeletal origin pain had moderate to severe pain. This has shown the need for maintained analgesia for patients being discharged after acute trauma.

**Conclusion**

The concept of acute pain management is certainly not new but the practice seems quite variable across centers and countries. The institution of interest, in one of the low-income countries studied here, showed non-existent pain scoring practice, disorganized analgesia provision, and poor pain care for discharged patients. In addition, in groups managed with some sort of analgesia, no combination of any sort was provided, no strong opioid was prescribed and as a result, more than two-thirds of patients with severe pain weren't treated to the level the pain was satisfactorily manageable for the patients to handle. Based on all these findings, one must recommend curricular inclusion of both acute and chronic pain management, guideline-based pain management protocols, and provision of proper analgesia with monitoring of their proper and controlled utilization in addition to utilization and availability of pain management experts and teams.

**Abbreviations**

DALY: Disability Adjusted Life Years

FAS: Functional Activity Score

GCS: Glasgow Coma Scale

PTSD: Post-traumatic Stress Disorder

SPS: Subjective Pain Score

USA: United States of America

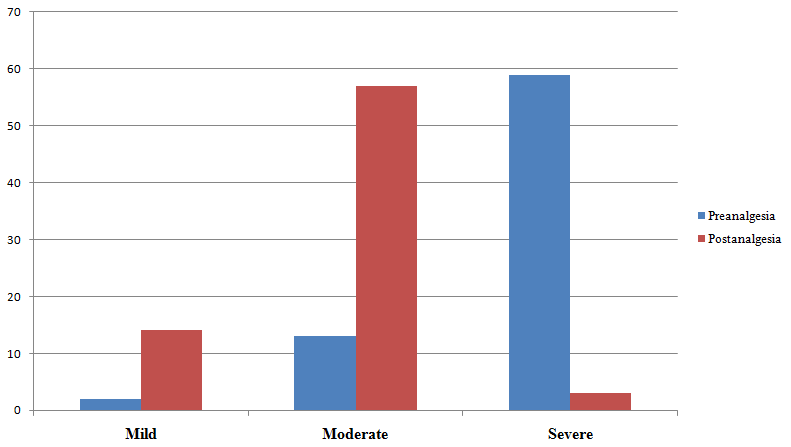
WHO: World Health Organization**Acknowledgments**

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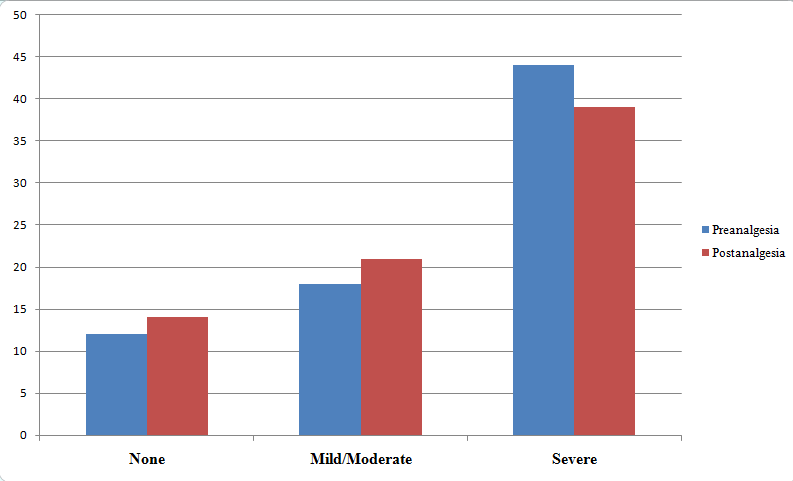
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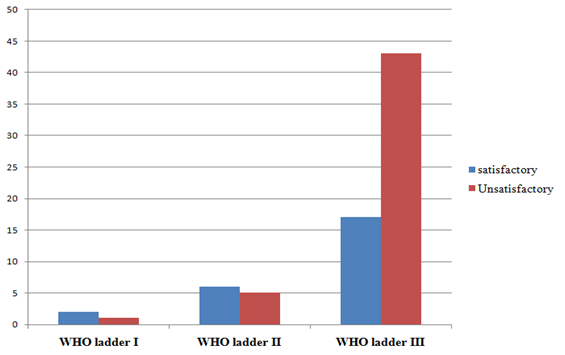
**Figure 1: Subjective pain score before and after analgesia**

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**Figure 2: Functional activity score before and after analgesia**

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**Figure 3: Correlation between predicted analgesia level expressed based on WHO ladder and post analgesia SPS and FAS score**

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**Table 1: Socio-demographic factors of the study subjects**

| **No.** | **Category** | **Number** | **Percentage (%)** |
| --- | --- | --- | --- |
| 1 | Sex |  |  |
|  | Male | 57 | 77.0 |
|  | Female | 17 | 23.0 |
|  |  |  |  |
| 2 | Age(years) |  |  |
|  | 13-18 | 9 | 12.2 |
|  | 19-30 | 29 | 39.2 |
|  | 31-45 | 17 | 23.0 |
|  | 46-60 | 16 | 21.6 |
|  | >60 | 3 | 4.1 |
|  |  |  |  |
| 3 | Marital status |  |  |
|  | Single | 33 | 44.6 |
|  | Married | 41 | 55.4 |
|  |  |  |  |
| 4 | Region |  |  |
|  | Oromia | 23 | 31.1 |
|  | Addis Ababa | 36 | 48.6 |
|  | Amhara | 5 | 6.8 |
|  | Afar | 4 | 5.4 |
|  | Gambella | 1 | 1.4 |
|  |  |  |  |
| 5 | Educational status |  |  |
|  | Uneducated | 13 | 17.8 |
|  | Completed primary school | 23 | 31.5 |
|  | Completed 10th grade | 13 | 17.8 |
|  | Completed 12th grade | 11 | 15.1 |
|  | Completed college | 13 | 17.8 |
|  |  |  |  |
| 6 | Occupation |  |  |
|  | Farmer | 12 | 16.4 |
|  | Civil servant | 8 | 11.0 |
|  | Private employee | 19 | 26.0 |
|  | House wife | 9 | 12.3 |
|  | Student | 13 | 17.8 |
|  | Construction worker | 2 | 2.7 |
|  | Unemployed | 10 | 13.7 |

**Table 2: Trauma mechanisms of the study subjects**

| **No.** | **Category** | **Number** | **Percentage (%)** |
| --- | --- | --- | --- |
| 1 | Trauma mechanism |  |  |
|  | Blunt | 66 | 89.2 |
|  | Penetrating | 8 | 10.8 |
|  |  |  |  |
| 2 | Blunt trauma mechanisms |  |  |
|  | Motor vehicle collision | 14 | 21.2 |
|  | Pedestrian versus motor vehicle | 27 | 40.9 |
|  | Assault | 11 | 16.7 |
|  | Falling down accident | 12 | 18.2 |
|  | Other | 2 | 3.0 |
|  |  |  |  |
| 3 | Penetrating trauma mechanisms |  |  |
|  | Gunshot wound | 4 | 57.1 |
|  | Other | 3 | 42.9 |
|  | Stab | 0 | 0 |
|  |  |  |  |
| 4 | Primary assessment and vital signs |  |  |
|  | Intact airway | 74 | 100 |
|  | Labored/gasping | 4 | 5.5 |
|  | Hypotension | 2 | 2.7 |
|  | GCS 12 or 13 | 6 | 8.1 |
|  | HR>100/min | 29 | 39.2 |
|  |  |  |  |
| 5 | Anatomic site of trauma |  |  |
|  | Head injury | 16 | 21.6 |
|  | Face/Neck injury | 10 | 13.5 |
|  | Chest injury | 3 | 4.1 |
|  | Abdominal injury | 1 | 1.4 |
|  | Pelvic injury | 23 | 31.1 |
|  | Extremity fracture/dislocation | 59 | 79.7 |
|  | Penetrating extremity injury | 3 | 4.1 |
|  |  |  |  |
| 6 | Alcohol and medication history |  |  |
|  | Alcohol intoxication | 6 | 8.1 |
|  | Medication prior to trauma | 2 | 2.7 |
|  |  |  |  |
| 7 | 24 hours disposition |  |  |
|  | Kept at Emergency for observation | 51 | 68.9 |
|  | Discharge | 15 | 20.3 |
|  | Emergency surgery | 4 | 5.1 |
|  | Admitted to wards | 3 | 4.1 |
|  | Referred | 1 | 1.4 |

**Table 3: Correlation between Predicted WHO analgesia ladder and Type of analgesia provided, SPS based satisfaction and FAS based satisfaction of patients**

|  |  | **Predicted WHO ladder analgesia based on pain score** | | | P value |
| --- | --- | --- | --- | --- | --- |
| **No** | **Categories** | WHO ladder I(%) | WHO ladder II(%) | WHO ladder III (%) |
| 1 | Analgesia provided |  |  |  |  |
|  | Diclofenac | 0(0) | 0(0) | 9(15.0) |  |
|  | Tramadol | 3(100) | 11(100) | 51(85.0) |  |
|  | Total | 3(100) | 11(100) | 60(100) | 0.998 |
|  |  |  |  |  |  |
| 2 | SPS based satisfaction |  |  |  |  |
|  | Unsatisfactory(moderate/severe pain) | 1(33.3) | 5(45.4) | 43(71.2) |  |
|  | Satisfactory(mild/none) | 2(66.7) | 6(54.6) | 17(28.8) |  |
|  | Total | 3(100) | 11(100) | 60(100) | 0.05 |
|  |  |  |  |  |  |
| 3 | FAS based satisfaction |  |  |  |  |
|  | Unsatisfactory(severe pain) | 1(33.3) | 5(45.4) | 44(73.3) |  |
|  | Satisfactory(mild/none) | 2(66.7) | 6(54.6) | 16(26.7) | 0.04 |