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RESEARCH ARTICLE

The Use of Multiple Imputation Techniques on Short-Term Clinical Complications of Patients Presenting with Traumatic Spinal Cord Injuries

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Abstract:

Background:

With the increase in the use of secondary data in epidemiological studies, the inquiry of how to manage missing data has become more relevant. Our study applied imputation techniques on traumatic spinal cord injuries data; a medical problem where data is generally sporadic. Traumatic spinal cord injuries due to blunt force cause widespread physiological impairments, medical and non-medical problems. The effects of spinal cord injuries are a burden not only to the victims but to their families and to the entire health system of a country. This study also evaluated the causes of traumatic spinal cord injuries in patients admitted to the University Teaching Hospital and factors associated with clinical complications in these patients.

Methods:

The study used data from medical records of patients who were admitted to the University Teaching Hospital in Lusaka, Zambia. Patients presenting with traumatic spinal cord injuries between 1st January 2013 and 31st December 2017 were part of the study. The data was first analysed using complete case analysis, then multiple imputation techniques were applied, to account for the missing data. Thereafter, both descriptive and inferential analyses were performed on the imputed data.

Results:

During the study period of interest, a total of 176 patients were identified as having suffered from spinal cord injuries. Road traffic accidents accounted for 56% (101) of the injuries. Clinical complications suffered by these patients included paralysis, death, bowel and bladder dysfunction and pressure sores among other things. Eighty-eight (50%) patients had paralysis. Patients with cervical spine injuries compared to patients with thoracic spine injuries had 87% reduced odds of suffering from clinical complications (OR=0.13, 95% CI{0.08, 0.22}p<.0001). Being paraplegic at discharge increased the odds of developing a clinical complication by 8.1 times (OR=8.01, 95% CI{2.74, 23.99}, p<.001). Under-going an operation increased the odds of having a clinical complication (OR=3.71, 95% CI{=1.99, 6.88}, p<.0001). A patient who presented with Frankel Grade C or E had a 96% reduction in the odds of having a clinical complication (OR=.04, 95% CI{0.02, 0.09} and {0.02, 0.12} respectively, p<.0001) compared to a patient who presented with Frankel Grade A.

Conclusion:

A comparison of estimates obtained from complete case analysis and from multiple imputations revealed that when there are a lot of missing values, estimates obtained from complete case analysis are unreliable and lack power. Efforts should be made to use ideas to deal with missing values such as multiple imputation techniques.

The most common cause of traumatic spinal cord injuries was road traffic accidents. Findings suggest that paralysis had the greatest negative effect on clinical complications. When the category of Frankel Grade increased from A-E, the less likely a patient was likely to succumb to clinical complications. No evidence of an association was found between age, sex and developing a clinical complication.

Keywords: Missing data, Multiple imputation, Traumatic spinal cord injuries, Clinical complications, Complete case analysis.

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1. INTRODUCTION

Epidemiologic studies continue to be affected by missing data despite great efforts to mitigate this problem at both design and collection stages. Secondary sources of data tend to be more problematic than primary sources of data where missing data is concerned. Despite this shortfall of missing data, secondary data sources including clinical databases have long been recognized as rich data sources for either hypothesis generating or obtaining meaningful inferences. These databases offer many opportunities for research on populations that otherwise would be difficult to enrol in studies [1 - 3]. However, these databases are characterised by the problem of missing data that leads to substantial bias and misleading inference when inadequately handled [4]. Missing data presents two kinds of problems and these are: reduced power and threats to the validity of statistical inference [5]. By potentially reducing the number of available observations for analysis, missing data can reduce the power of a study. To minimise the negative effects of missing data during data analysis, various methods have been formulated. These include list-wise deletion (complete case analysis), last observation carried forward, pairwise deletion, unconditional mean imputation, conditional mean imputation, mean substitution, maximum likelihood, expectation maximization and sensitivity analysis [6] and others. Although such methods are simple and easy to implement, they often lead to biased estimates, overestimated precision, invalid inferences, loss of power, and underestimated uncertainty [7]. To overcome these shortfalls, a Multiple Imputation (MI) procedure, originally proposed by author Little Rubin was designed.

Imputation is a procedure where missing data are generated (imputed) given the available information, replacing each missing value with a set of plausible values that represent the uncertainty about the right value to impute [7]. The objective of MI is not to predict missing values as close as possible to the true ones but to handle missing data in a way resulting in valid statistical inference [8]. It is more flexible than fully-parametric methods, for example, maximum likelihood, purely Bayesian analysis. It accounts for missing-data uncertainty and thus, does not underestimate the variance of estimates like single imputation methods.

The aim of this investigation was to evaluate the performance of multiple imputation techniques when applied to short term clinical complications of patients presenting with spinal cord injuries at Zambia's largest hospital (University Teaching Hospital). Traumatic spinal cord injury patients are prone to clinical complications due to the nature of their injuries. Traumatic Spinal Cord Injury (TSCI) is often followed by complications, which add to the detrimental effect that loss of motor, sensory and autonomic function have on a person's health, social participation and quality of life [9]. Clinical complications related to spinal cord injuries are said to be medical conditions that occur after a spinal cord injury and their occurrence is higher among patients with spinal cord injuries than in the general population [10]. A patient can experience multiple complications during rehabilitation. Our study looked at some of the common clinical complications which included death, pressure sore, respiratory dysfunction, autonomic dysreflexia, urinary tract infection, paralysis, bowel dysfunction and bladder dysfunction. Autonomic Dysreflexia is a syndrome which occurs in patients with injuries at and above thoracic level six and results into hypertension, bradycardia, tachypnea, tachycardia and varied symptoms such as profuse sweating and headache [11]. Bowel and bladder dysfunction, describes a myriad of lower urinary symptoms, accompanied by bowel complaints, primarily constipation and/or encopresis [12, 13]. Pressure ulcers or pressure sores are localized areas of tissue damage or necrosis that develop because of pressure over a bony prominence [14, 15]. A Urinary Tract Infection (UTI) is an infection in the urinary system. This system includes kidneys, ureters, bladder, and urethra [16]. Learning of what factors increase a patient's risk of succumbing to clinical complications will positively contribute to the treatment of spinal cord injury patients.

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2. MATERIALS AND METHODS

This was a retrospective study that included patients who presented to the University Teaching Hospital between 1st January 2013 and 31st December 2017. Already existing, routinely collected data was used in this study, hence, it was considered an exploratory study. The study only included data from 2013 as this was when the spinal unit at the University Teaching Hospital was established. The hospital receives referral cases from all parts of the country. Hospital death and discharge books were used to identify patients who had presented to the hospital with spinal cord injuries due to blunt force trauma. A total of 176 patients were identified as having suffered from spinal cord injuries due to blunt force trauma from 2013 to 2017. Out of the 176 cases, 106 of the cases were referral cases. However, only 58% (n=101) patient files were available at the hospital during the time of data collection. From the 101 files found, only 31 patients have information on all 28 variables collected.

2.1. Study Variables

Information on the patient's age, sex, date of injury, cause of injury, length of hospital stay and level of injury was collected. Other information collected included the type of paralysis at the time of presentation and discharge as well as Frankel Grade at presentation and discharge. The Frankel Grade is a 5-point severity scale ranging from A to E that is used to assess spinal cord injuries [17]. Grade A is a complete neurological injury. In a complete injury, no motor or sensory function is detected below the level of lesion. Grade B corresponds to preserved sensation only. No motor function is detected below the level of lesion, however, some sensory function below the level of lesion is preserved. A patient with Grade C has preserved motor but non-functional. Some voluntary motor function is preserved below the level of lesion but too weak to serve any useful purpose, sensation may or may not be preserved. A Grade D classification entails functionally useful voluntary motor function below the level of injury. A patient with Grade E has normal motor function and sensory function below the level of lesion, abnormal reflexes may persist [17, 18]. However, the American Spinal Injury Association (ASIA) Impairment Scale which is a modification of the Frankel Grade scale has replaced the Frankel Grade as the gold standard. Despite this change, most patients were assessed using the Frankel grade system [18]. Patients who transferred to another hospital or left the hospital against the doctors advise were excluded from the study. Though only 101 patient files were found, death and discharge books were also used to gather some information about patients whose files were unavailable. Information collected from discharge books were sex, age, length of hospital stay, date of death, cause of injury and in some instances level of injury.

A composite dependent variable indicating whether or not a patient suffered from any clinical complication of interest was created by combining eight variables (Eight medical conditions) into one binary variable. Data from all 176 observations were utilised in the creation of this variable. Note that the composite variable (termed clinical complication) represented eight including; death, pressure sore, respiratory dysfunction, autonomic dysreflexia, urinary tract infection, paralysis, bowel dysfunction and bladder dysfunction. The composite variable had 176 observations and this allowed us to work with a sample size of 176. Out of the 176 patients, 93(52%) had no clinical complications while 85(48%) had developed clinical complications. Independent variables included sex, age of the patient at admission, length of hospital stay, cause of injury, level of injury, Frankel Grade at admission, Frankel Grade at discharge, paralysis at presentation, paralysis at discharge, type of treatment received and lastly whether or not a patient needed implants.

2.2. Statistical Methods

The patients were divided into two groups; patients who suffered from any clinical complication and patients who did not suffer from any clinical complication. The number in these two groups were 80 and 96, respectively. The two groups were described using descriptive statistics such as mean and standard deviation, median and inter-quartile range, frequencies and percentages. Statistical difference between the two groups was also analysed. For categorical variables, the chi-squared test was used if the assumptions of chi-squared test were satisfied otherwise, the Fisher's exact was used. For continuous variables, to explore associations with the outcome, a Wilcoxon rank-sum test was used. Inferential statistics were obtained by first using logistic regression on the complete cases and secondly on the imputed data. Our dependent variable (clinical complication) was binary hence the decision to use logistic regression.

2.3. Imputation Method

The data was non-monotone missing. To assess if the nature of missing was not at random, we inspected the hard copy records to see if there were any characteristics for those with missing values. Using this approach, we had no evidence to suggest that the missing data was Missing Not At Random (MNAR).

From the 176 patients identified, missing values were present in all the variables except sex. Missing values ranged from 1% to 32% with age having the least amount of missing values (one value). Frankel grade at discharge had the highest amount of missing data. Thirty-two percent (57 values) were missing. In general, variables that were collected at the point of discharge had a higher percentage of missing values. This might have been due to the 40 patients (22%) who died during admission. The data for these patients were subsequently classified as missing.

We had both categorical and continuous variables with missing values and the missing pattern was non-monotone. Hence, we decided to use Multivariate Imputation by Chained Equations (MICE). In the Multivariate Imputation by Chained Equations procedure, a series of regression models were performed and each variable with missing data was modelled conditional upon the other variables in the data. This also meant that each variable was modelled according to its distribution. For example, binary variables were modelled using logistic regression and continuous variables were modelled using linear regression [19 - 21]. To ensure appropriate imputation, continuous variables (age and length of hospital stay) were checked for normality. Non-normally distributed variables that are imputed by assuming normality produce imputed values that do not resemble that of the observed values [22, 23]. This is the reason why one of the continuous variables (length of hospital stay) which was not normally distributed was transformed using a square root transformation before imputation and was later transformed back to the original state before analysis. Twenty sets of imputations were created [7, 23 - 25].

3. RESULTS

The results of the descriptive and inferential statistics are presented below. Table **1** below shows descriptive statistics of the two groups of the patients, that is, patients with clinical complications and patients with no clinical complications before imputation.

Table 1. Demographic and clinical characteristics at presentation and discharge.

Variable (% of Non-Missing Values)	No Clinical Complications	Clinical Complications	p-value
Sex-complete cases: 176(100%) Female Male	12(14,8) 68(85.2)	19(19.6.0) 77(80.4)	0.403[c]
Age (in years)-complete cases: 175(99%)	36(13.6)[d]	34(14.4)[d]	0.4393[a]
Length of hospital stay (in days)-complete cases:155(88%)	20(8,35)[e]	47(12,79)[e]	<0.0001[a]

(Table 1) contd.....

Variable (% of Non-Missing Values)	No Clinical Complications	Clinical Complications	p-value
Aetiology-complete cases: 151(86%) Fall Falling object Road traffic accident Other	21(27.6) 1(1.3) 51(67.1) 3(4.0)	18(23.7) 9(11.8) 39(51.3) 10(13.2)	0.007[c]
Level of injury-complete cases: 102(58%) Thoracic Cervical Lumbar	7(21.9) 15(46.9) 10(31.3)	26(37.1) 39(55.7) 5(7.1)	0.007[b]
Frankel grade at presentation-complete cases: 82(47%) A B C D E	0(0,0) 0(0.0) 0(0.0) 3(12.5) 21(87.5)	36(62.1) 8(13.8) 5(8.6) 7(12.1) 2(3.5)	<0.0001[b]
Frankel grade at discharge-complete cases:57(32%) A B C D E	0(0.0) 0(0.0) 0(0.0) 2(10.0) 18(90.0)	14(37.8) 6(16.2) 5(13.5) 11(29.7) 1(2.7)	<0.0001[b]
Paralysis at presentation-complete cases: 93(53%) Monoplegia Hemiplegia Paraplegia Tetraplegia No paralysis	0(0.0) 0(0.0) 1(4.0) 0(0.0) 24(96.0)	3(4.4) 3(4.4) 29(42.7) 28(30.4) 5(7.4)	<0.0001[b]
Paralysis at discharge-complete cases:74(42%) Monoplegia Hemiplegia Paraplegia Tetraplegia No paralysis	0(0.0) 0(0.0) 1(4.0) 0(0.0) 24(96.0)	1(2.0) 2(4.1) 25(51.0.9) 15(30.6) 6(12.2)	<0.0001[b]
Patient needed implants/screws-complete cases:87(49%) No Yes	17(65.4) 9(34.6)	23(37.7) 38(62.3)	0.018[c]
Type of treatment received-complete cases:92(52%) Non-operative Operative	20(74.1) 7(25.9)	40(61.5) 25(38.5)	0.250[c]

[a]Two-sample Wilcoxon rank-sum test, [b]Fisher's exact, [c]chi-sqaure test, [d]Mean(SD), [e]Median(IQR)
Frankel A: lesion was found to be complete, both motor and sensory, below the segmental level marked.
Frankel B: some sensation present below the level of lesion but the motor paralysis was complete below that level
Frankel C: motor power present below the lesion but it was of no practical use to the patient
Frankel D: useful motor power below the level of the lesion.
Frankel E: patient was free of neurological symptoms

3.1. Patient Characteristics

From the 176 observations in our dataset, 83%(145) of these were males. The mean age for individuals who did not suffer from any clinical complications was 36 years (SD=13.6) while it was approximately 34 years (SD=14.4) for those who had suffered from clinical complications. Median length of hospital stay in days was longer for individuals who had suffered from clinical complications by 27 days in comparison to individuals who did not suffer from any clinical complications. This finding was statistically significant (p<.0001).

Causes of injury included, falling, falling object, sports, assault with a blunt object, road traffic accidents and being thrown from a moving ox-cart (a trailer pulled by a cow). Road traffic accidents were the most common cause of injuries in both groups, accounting for 67% (51) and 51% (39) of the injuries in the patients with no clinical complications and patients without clinical complication respectively. A chi square test for association showed a statistically significant association between the cause of injury (aetiology) and a patient developing a clinical complication (p=.007).

Most spinal cord injuries occurred in the most mobile part of the spine, and as such 54 out of 102 patients (53%) presented with cervical injuries. Thirty-nine of these patients had clinical complications. Only 15 (15%) patients had injuries involving the lumbar nerves. The majority of the patients 36 (44%) patients presented with Frankel Grade A injuries and all of these patients had clinical complications as would be expected. Three of the patients who had Frankel Grade D injuries did not suffer from clinical complication while 21 (91%) out of 23 patients with Frankel Grade E injuries did not suffer from clinical complications.

3.2. Clinical Complications

Injuries to the spine translate into impairment of bodily functions and the extent of this impairment is greatly dependant on the level of the injury and degree on neurology dysfunction. This is the reason why clinical complications are common among patients of traumatic spinal cord injuries. It is also common for a patient to experience multiple clinical complications at the same time. Our study considered seven common complications suffered by these patients. One of the visible signs of traumatic spinal cord injury is paralysis which is cause by damage to the nervous system. Paralysis was the most common complication and was suffered by 68%(62) of the patients. 34 (44%) of the patients with paralysis were diagnosed with Frankel Grade A neurology at presentation (Results not shown). Bowel and bladder dysfunction was suffered by 54 (59%) and 47 (50%) patients respectively. Forty-six patients (49%) suffered from both bowel and bladder dysfunction. Out of the 176 patients, 40 (23%) died during admission. Respiratory complications and urinary tract infections were the least common and affected 6%(5) and 4%(4) of the patients respectively. Twenty-six (29%) of the patients suffered from pressure sores during admission (Table **2**).

3.3. Associated Factors of Clinical Complications in patients with Traumatic Spinal Cord Injuries (Using Complete Case Analysis)

With reference to Table **3**, using complete case analysis to conduct univariable analysis proved to be inefficient and results for most variables were not generated. No results were obtained for two variables, that is, paralysis at presentation and paralysis at discharge, while for other variables such as Frankel grade at presentation and Frankel grade at discharge, results were only generated for one category (level D). The inefficiency of the use of complete case analysis in this data is made evident by the wide confidence intervals as shown in Table **3**. Extremely wide confidence intervals ranging from 8 to 1224 is observed for Frankel grade at discharge and a range of 3 to 178 with a corresponding odds ratio of 99 for Frankel grade at presentation. It is almost impossible to make meaningful presentation and interpretation of such results.

Table 2. Patients clinical complications.

Clinical Complication	Yes n(%)	No n(%)
Death	40 (23%)	136 (77%)
Pressure sores	26 (29%)	65 (71%)
Autonomic Dysreflexia	11 (88)	80 (12)
Bowel dysfunction	54 (59%)	41(41%)
Bladder dysfunction	47 (50%)	47 (50%)
Respiratory dysfunction	5 (6%)	84 (94%)
Urinary tract infection	4 (4%)	87 (96%)
Paralysis=91	62 (68%)	29 (32%)

Table 3. Univariate analysis of factors affecting clinical complications in patients with traumatic spinal cord injuries using complete case analysis.

Factor (% of Non-Missing Values)	Odds Ratio (CI)	Standard Error	p-value
Age (In years)-complete case=175(99%)	0.99 (0.971, 1.014)	0.0109	0.463
Sex-complete cases=176(100%) *Female* *Male*	0.715 (0.324, 1.581)	0.2893	0.407
Length of hospital stay (in days)-complete cases=155(88)	1.027 (1.014, 1.040)	0.0065	<0.0001
Aetiology-complete cases=151(55%) *Fall* *Falling object* *Road traffic accident* *Other*	10 (1.151, 86.876) 0.850 (0.397, 1.819) 3.70 (0.879, 15.613)	11.030 0.330 2.719	0.037 0.675 0.074
Level of injury-complete cases=102(58%) *Thoracic* *Cervical* *Lumbar*	0.7 (0.251, 1.951) 0.135 (0.035, 0.524)	0.3662 0.0933	0.495 0.004
Frankel grade at presentation-complete cases=33(18%) *A* *B* *C* *D* *E*	1 (NA) 1 (NA) 1 (NA) 24.5 (3.372,178.009) 1 (NA)	24.789	NA NA NA 0.002 NA

(Table 3) contd.....

Factor (% of Non-Missing Values)	Odds Ratio (CI)	Standard Error	p-value
Paralysis at presentation-complete cases=59(34%) *Monoplegia* *Hemiplegia* *Paraplegia* *Tetraplegia*	1 (NA) 1 (NA) 139.2 (15.21,1274.13) 1 (NA)	157.25	NA NA <0.0001 NA
Paralysis at discharge-complete cases=45(26%) *Monoplegia* *Hemiplegia* *Paraplegia* *Tetraplegia*	1 (NA) 1 (NA) 1 (NA) 1 (NA)	Na Na Na Na	NA NA NA NA
Patient needed implants/screws-complete cases=87(49%) *No* *Yes*	3.121 (1.195, 8.148)	Ref 1.5280	0.020
Treatment received-complete cases=92(52%) *Non-operative* *Operative*	1.78 (0.66, 4.831)	Ref 0.9068	0.254

NA=No results obtained because the software did not converge due to missing values.
Frankel A: lesion was found to be complete, both motor and sensory, below the segmental level marked.
Frankel B: some sensation present below the level of lesion but the motor paralysis was complete below that level
Frankel C: motor power present below the lesion but it was of no practical use to the patient
Frankel D: useful motor power below the level of the lesion.
Frankel E: the patient was free of neurological symptoms

Table 4. univariate logistic regression of factors affecting clinical complications in patients with traumatic spinal cord injuries using complete case analysis (Variables with more than 50 non missing values).

Factor (% of Non-Missing Values)	Odds Ratio (CI)	Standard Errors	p-value
Age (in years)-complete case=175(99%)	0.99 (0.971,1.014)	0.0109	0.463
Sex-complete cases=176(100%) *Female* *Male*	0.715 (0.324, 1.580)	0.2893	0.407
Length of hospital stay (in days)-complete cases=155(88)	1.027 (1.014, 1.040)	0.0065	<0.0001
Aetiology-complete cases=151(55%) *Fall* *Falling object* *Road traffic accident* *Other*	10 (1.151, 86.876) 0.850 (0.397, 1.819) 3.70 (0.879, 15.613)	11.030 0.330 2.719	0.037 0.675 0.074
Level of injury-complete cases=102(58%) *Thoracic* *Cervical* *Lumbar*	0.7 (0.251,1.951) 0.135 (0.035, 0.524)	Ref 0.3662 0.0933	0.495 0.004
Patient needed implants/screws-complete cases=87(49%) *No* *Yes*	3.121 (1.195, 8.148)	Ref 1.5280	0.020
Treatment received-complete cases=92(52%) *non-operative* *operative*	1.78 (.66, 4.831)	Ref 0.9068	0.254

Simple logistic regression revealed that the higher the percentage of missing data, the more inefficient our results were as demonstrated by the large confidence intervals obtained. Variables with less than 50 percent of the values missing performed better than variables with more than 50% values missing. Table **4** was obtained by only including variables with less than 50% of the observations missing at univariate analysis.

3.4. Multivariable Analysis

The combined effects of missing values in each variable was made more pronounced during multiple regression. This was made evident by the lack of meaningful output in STATA when all variables were used. Including only variables with more than 50 non missing values undercuts the combined effect of missing values as demonstrated in Table **5** below. Though this approach produces relatively useful results, it renders other variables collected redundant. Therefore, information contained in these explanatory variables cannot be used to explain variations observed in the odds of experiencing a clinical complication. Table **5** shows the results obtained when variables with more than 50 non missing values are used in a multiple logistic model. With the use of this approach, only 72 observations are included in the analysis and the remaining 104 are dropped because the covariates contained missing data.

Table 5. Multivariable analysis of factors affecting clinical complications in patients with traumatic spinal cord injuries using complete case analysis (Variables with more than 50 non missing values).

Factor (% of Non-Missing Values)	Odds Ratio	Standard Errors	p-value
Age (in years)	0.991 (0.940, 1.045)	0.2670	0.733
Sex *Female* *Male*	Ref 1.59 (0.263, 9.723)	Ref 1.4723	Ref 0.611
Length of hospital stay (in days)	1.044 (1.012, 1.076)	.0162	.006
Aetiology Fall *Falling object* *Road traffic accident* *Other*	Ref 3.32 (.222, 49.70) 1.14 (.187, 6.918) 0.951 (0.085, 10.602)	Ref 4.587 1.048 1.170	Ref 0.384 0.888 0.967
Level of injury *Thoracic* *Cervical* *Lumbar*	Ref 1.349 (0.243, 7.500) .177 0(.019, 1.612)	Ref 1.181 1.994	Ref 0.723 0.124
Patient needed implants/screws *No* *Yes*	Ref 3.26 (0.358, 29.62)	Ref 3.669	Ref 0.294
Treatment cases *Non-operative* *Operative*	Ref 0.553 (0.052, 5.89)	Ref 0.6681	Ref 0.634

Table 6. Factors affecting clinical complications of patients with traumatic spinal cord injuries after multiple imputations.

Factor	Odds Ratio (CI)	Standard Error	p-value
Sex *Female* *Male*	Ref 1.46 (.76, 2.80)	Ref 0.486	Ref 0.260
Age	1.03 (1.01, 1.05)	0.009	0.003
Length of hospital stay	1.03 (1.02, 1.04)	0.004	<0.0001
Cause of injury *Fall* *Falling object* *Road traffic accident* *Other*	Ref 216.14 (73.82, 632.88) 2.65 (1.53, 4.57) 6.69 (2.19, 20.39)	Ref 118.477 0.737 3.804	Ref <0.0001 <0.0001 0.001
Level of injury *Thoracic* *Cervical* *Lumbar*	Ref 0.33(0.18, 0.61) 0.31 (0.16, 0.62)	Ref .103 .109	Ref <0.0001 0.001
Type of treatment *Non-operative* *Operative*	Ref 3.88 (1.96, 7.62)	Ref 1.338	Ref <0.0001
Patient needed implants *No* *Yes*	Ref 0.446 (0.25, 0.79)	Ref 0.129	Ref 0.005
Paralysis at presentation *No paralysis* *Monoplegia/Hemiplegia* *Paraplegia* *Tetraplegia*	Ref 2.92(1.46, 5.86) 5.66(1.70, 18.85) 1(NA)	Ref 1.037 3.474 NA	Ref 0.003 0.005 NA
Paralysis at discharge *No paralysis* *Monoplegia/Hemiplegia* *Paraplegia* *Tetraplegia*	Ref 4.86 (2.33, 10.12) 22.69 (6.60, 78.00) 1 (NA)	Ref 1.819 14.296	Ref <0.0001 <0.0001
Frankel Grade at presentation *A* *B* *C* *D* *E*	Ref 0.28 (0.11, 0.72) 0.07 (0.03, 0.19) 0.14 (0.05, 0.39) 0.05 (0.12, 0.16)	Ref 0.135 0.036 0.072 0.030	Ref 0.008 <0.0001 <0.0001 <0.0001

(Table 6) contd.....

Factor	Odds Ratio (CI)	Standard Error	p-value
Frankel Grade at discharge			
A	Ref	Ref	Ref
B	0.44 (.16, 1.23)	0.232	0.119
C	0.31 (.11, .84)	0.157	0.021
D	0.44 (.16, 1.20)	0.225	0.109
E	0.04 (.01, .11)	0.022	<0.0001

Table 7. Effect of explanatory variables on clinical complications after multiple imputations.

Factor	Odds Ratio (CI)	Standard Error	p-value
Sex			
Female	Ref	Ref	Ref
Male	1.20 (0.70, 2.08)	0.335	0.507
Age	1.01 (0.99, 1.03)	0.008	0.260
Length of hospital stay	1.03 (1.02, 1.04)	0.004	<0.0001
Level of injury			
Thoracic	Ref	Ref	Ref
Cervical	0.13 (0.08, .22)	0.035	<0.0001
Lumbar	0.09 (0.05, .17)	0.028	<0.0001
Type of treatment			
Non-operative	Ref	Ref	Ref
Operative	3.71 (1.99, 6.88)	1.170	<0.0001
Patient needed implants			
No	Ref	Ref	Red
Yes	0.54 (0.32, 0.93)	0.149	0.026
Paralysis at presentation			
No paralysis	Ref	Ref	Ref
Monoplegia/Hemiplegia	2.28 (1.23, 4.23)	0.718	0.009
Paraplegia	6.71 (2.19, 20.59)	3.839	0.001
Tetraplegia	1 (NA)	NA	NA
Paralysis at discharge			
No paralysis	Ref	Ref	Ref
Monoplegia/Hemiplegia	2.88 (1.52, 5.47)	.943	0.001
Paraplegia	8.10 (2.74, 23.99)	4.488	<0.0001
Tetraplegia	1 (NA)	NA	NA
Frankel Grade at presentation			
A	Ref	Ref	Ref
B	0.20 (0.08, 0.49)	0.090	<0.0001
C	0.04 (0.02, 0.09)	0.016	<0.0001
D	0.07 (0.03, 0.19)	0.035	<0.0001
E	0.04 (0.02, 0.12)	0.022	<0.0001
Frankel Grade at discharge			
A	Ref	Ref	Ref
B	0.83 (0.33, 2.10)	0.394	0.692
C	0.56 (0.22, 1.39)	0.260	0.211
D	1.18 (0.48, 1.89)	0.539	0.721
E	0.17 (0.07, 0.45)	0.084	<0.0001

3.5. Factors Affecting Clinical Complications in Patients with Traumatic Spinal Cord Injuries (After Imputation)

In this section, we present results obtained from performing multiple regression on imputed data. The following are our findings (Table **6**): a unit increase in age was associated with a 3% (OR=1.03, 95% CI {1.01, 1.05}, p-value = 0.009) increased odds in a patient succumbing to a clinical complication. Similarly, a unit increase in hospital stay measured in days' was associated with an increase in the odds of a patient suffering from a clinical complication by 3% (OR=1.03, 95% CI {1.02, 1.04}). Cause of injury (aetiology) estimates were questionable with large odds ratios and corresponding standard errors. This variable had 151 not missing values out of 176 observations. Twenty-seven observations were imputed using a multinomial model. However, the estimates obtained are indicative of problems in the convergence of this variable.

Table **7** above shows the model obtained after dropping aetiology from the analysis due to the suspiciously high odds. We still draw similar conclusions about the effect of each factor on clinical complications. Patients with cervical spine injuries as compared to patients with thoracic spine injuries had 87% reduced odds to suffer from clinical complications as compared to patients with thoracic injuries (OR=0.13, 95%CI {0.08, 0.22}, p<.0001). Similarly, patients with lumbar spine injuries had 91% (OR=0.09, 95%CI {0.05, 0.17}, p<.0001) reduced odds of having clinical complications when compared to patients with thoracic injuries. Being paraplegic at discharge had the highest negative effect on a clinical complication. This effect was to increase the odds of a patient developing a clinical complication by 8.1 times (OR=8.01, 95%CI {2.74, 23.99}, p<.001). Under-going an operation increased the odds of having a clinical complication (OR=3.71, 95%C I {1.99, 6.88}, p<.0001). Conservative treatment still showed reduced odds of having a clinical complication (OR=0.23, 95% CI {0.12, 0.45}, p-value<0.001). A patient who presented with Frankel Grade C or E had a 96% reduction in the odds of having a clinical complication (OR=0.04, 95%CI {0.02, 0.09) (OR= 0.04, 95%CI {0.03, 0.19}) respectively.

3.6. Comparison of Standard Errors

Table **8** below shows a naïve comparison of standard errors from the complete case multivariable analysis of variables with more than 50 non missing values and from the multivariable analysis of the final model using imputed variables. Comparison of the two shows that as expected, standard errors of the analysis using imputed data were smaller. Reductions of up to 96% were observed for a nominal variable (Level of injury). The lowest improvement was observed for sex which only had 1 missing value.

Table 8. Naive comparison of standard errors and confidence intervals.

Variable (% Missing)	SE (Complete Case Analysis)	SE (Multiple Imputation)	% Change
Sex (0%) *Female* *Male*	Ref 1.4723	Ref 0.3422	Ref -76%
Age (1%)	0.0267	0.0090	-66%
Length of hospital stay (12%)	0.0162	0.0036	-78%
Level of injury (42%) *Thoracic* *Cervical* *Lumbar*	Ref 1.181 0.1994	ref. 0.0446 0.0363	Ref 96% 82%
Patient Need implants/screws (51%) *No* *Yes*	Ref 3.669	Ref 0.1817	Ref -95%
Type of treatment (48%) *Operative* *Non-operative*	Ref 0.6681	Ref 1.170	Ref 75%

4. DISCUSSION

Multiple imputation was used to impute missing covariates for the factors of clinical complications in patients with traumatic spinal cord injuries. Results at both univariate and multivariable analysis using complete case analysis provided estimates that lacked precision as captured by the large standard errors and confidence intervals. In the presence of high missing data, statisticians have suggested increasing the number of imputations. According to Hippel, in order to achieve reliable estimates and standard errors, it is recommended that in the presence of a lot of missing data, the number of imputations should be increased [24, 26]. In our study, relatively smaller standard errors and stable estimates were obtained with 20 imputations.

With regards to gender, males are more prone to experiencing traumatic spinal cord injuries than females as reported in different studies [27 - 29]. Approximately, 80% of our study participants were male with a mean age of 35 years. Violence and alcohol have been cited as potential reasons for the high traumatic spinal cord injury incidence in males than in females [30]. Other studies have shown that men are more likely than women to be driving or walking on the road under the influence of alcohol and thereby increase their chances of being in a road traffic accident [31]. Road traffic accidents were a major cause of spinal cord injuries. According to a report by the National Spinal Cord Injury Statistical Center, motor vehicles are the leading cause of injury, and are becoming an increasingly common cause in developing nations [19]. Road traffic accidents have been on the increase in resource strained countries in Africa were proper road infrastructure is lacking, motor vehicles which are not road worthy are used, less regulation and poor enforcement and poor safety culture exist [32].

Clinical complications were observed in 85(48%) of the patients. This high rate may be due to forces involved in trauma or due to the neurological status of the patients [33]. In our study, clinical complications included pressure sore, paralysis, urinary tract infection, bowel and bladder dysfunction, autonomic dysreflexia and respiratory complications. Other studies also found similar clinical complications [34 - 37]. No evidence of an association was observed between age, sex and a patient developing a clinical complication. These findings are similar to findings in Brazil [34]. However, a strong association was observed between clinical complications and ASIA Grade. Patients with ASIA A or B had a 2.3-fold greater relative risk of developing clinical complications [34]. From the descriptive statistics we presented earlier, all patients who presented with Frankel Grade A, B, C succumbed to clinical complication during admission. Factors that were associated with increased odds of experiencing a clinical complication included age, increase in length of hospital stay, paralysis and operative treatment. Paraplegia and tetraplegia had the largest negative effect on clinical complication. Patients who underwent operative treatment had an increased chance of having clinical complication. McKinley *et al.,* attributed this to the inherent risk of surgical intervention and immediate postoperative immobility [38].

CONCLUSION

Different conclusions on factors that are associated with clinical complications were drawn from the two types of analyses (complete case analysis and multiple imputation). The large confidence intervals and larger standard errors obtained under complete case analysis were indicative of lack of power and possible biases in the inferences. Multiple imputation techniques provide a way to make health data more useful especially in low income countries like Zambia were data entry and data management systems are poor resulting in missing data. Findings from the imputed data suggest that there is no evidence of an association between age, sex and developing a clinical complication. However, more attention should be given to paraplegic and tetraplegic patients as they are the most at risk of suffering from complications. Similarly, patients who undergo operative treatment need better clinical management post-operation in order to reduce their odds of succumbing to clinical complications.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Approval to conduct the research was obtained from the University of Zambia Biomedical Research and Ethics committee (Reference number 027-06-17). Permission to use data from patient records was sought from the hospital administration (Hospital superintendent) and Head of Department of the surgery department.

HUMAN AND ANIMAL RIGHTS

No animals/humans were used for studies that are the basis of this research.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest, financial or otherwise.

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