Determining The Probability Of Survival And Its Factors For The Infected Hemodialysis Patients

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Abstract: Hemodialysis patients are highly exposed to infections because the blood has to circulate out of the body through a cleaning machine. Usually an apparatus such as fistula or catheter is used to manipulate the blood access. Grafts and blood factors are thought to be major causes of morbidity and mortality. In this paper, sixty patients are considered, the whole population of the infected hemodialysis patients who came to the infectious service of Hedi Chaker hospital in Sfax Tunisia over 10 years period. The data are not available on all the patients. Statistics on: (1) Clinical factors such as age and gender and (2) Blood factors such as type and resistance of the germs are computed. A univariate analysis for each factor and its effects on the probability of survival are presented. A multivariate analysis is performed in which the probability of survival is found to be related to the non-presence of prosthesis, higher hemoglobin level and stable heart beats per minute. Monte Carlo methodology helped to refine the result by making inferences on the global population of the infected hemodialysis patients.

Index terms: Logistic Regression, haemodialysis, Monte Carlo simulation, Multivariate analysis

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1. INTRODUCTION

Vascular access-related infections are a major cause of morbidity and mortality in chronic Hemodialysis (HD) patients. The vascular access device is primary site of most bacteremic episodes which can cause high mortality rate. Staphylococci, mainly Staphylococcus aureus but also coagulates negative Staphylococci are the predominant organisms causative of these infections [1,2]. [3] discussed the use of mupirocine to protect against the Staphyloccuaureus nasal carriage. [4] gave a deep explanation on the classes of the Staphyloccuaureus carriage and the distribution of the bacteria on the human body. [5] presented the main factors of meticillin resistant S aureus bloodstream infections. Catheter Related Bacteremia (CRB) is an ongoing concern in the Hemodialysis Population [6]. [7] stated that the bacterimea related to catheter is about 23% in 70 hemodialysis patients using 113 catheters. [8] found that the relative risk of infection grows with the presence of arteriovenous grafts and catheter almost 7 folds. [9] insisted on that the prosthetic grafts are a cause of stenose and thrombosis and that catheter are major causes of infections. [10] stated that an arteriovenous fistula must be used and autogenous grafts expose patients to bacterimia and higher risks of endocarditis. [11] suggested coating the catheter with antibiotic to prevent infections. These are not the only viruses to endanger the hemodialysis patient. In fact, there are many indicators of HCV prevalence in HD patients all over the world. [12] studied the viral infections in hemodialysis patients and obtained a prevalence of as high as 76% of HCV. Hepatitis B is common as well as HIV. [13] found that helicobacter pylori infection can be found among the hemodialysis patients and must be eradicated. The cause is mainly mal nutrition.

Cardiovascular problems are the main causes of death in the kidney disease failure [14,15] confirmed the result and stated that it is about 60% and explained that myocardial infarction is the most important cause (22.7 %). They found that the survival of diabetic patients is much worse than the non-diabetic. In this paper, sixty patients are considered, the whole population from 1997 until 2006 inclusive of hemodialysis patients who came to the infectious service of Hedi Chaker hospital in Sfax, Tunisia. Not all the data are available on all patients. In the next section, brief descriptions of the hospital and the infectious department are presented, the data fields are explained. In the following section, clinical factors such as age and length of stay statistics are presented. Percentages of patients suffering from diabetes and thrombopenia are indicated. In section 4, blood factors are presented: the type of germs, the hemoglobin level, the presence of prosthesis' statistics. In section 5, a univariate analysis of important variables is conducted: the dependence of the binary death with each possible causing variable are studied. In section 6, a multivariate model relating the probability of death to possible causing variables is explored. In section 7, results are discussed.

2. SCOPE

The hospital Hedi Chaker is well known in Tunisia. It is a University hospital since 1927. This hospital is considered to be the field where the doctors, the nurses and the technicians operate and learn. It hospitalizes many patients from all over Tunisia; especially, the south. It consists of many labs: biological, radiographic, and functional. The infectious service is where patients having germs, bacteria, and/or viruses arrive. It has 10 rooms and 30 beds. This study considers only the hemodialysis patients coming with infection to the service. Each patient has the following characteristics, the file number, the entry and the exit dates, the department from which he or she was transferred, the gender, the age, the periods over which he or she has kidney failure, and the dialysis period, the mode of the actual dialysis whether it is with fistula or Catheter, whether he or she has a prostheses, the number of dialysis sessions per week, the artery lowest and highest tensions, the number of heart beats per minute, the physical sign of the fistula or catheter, the examination signs of the abdomen, the blood tests of white globules, hemoglobin, platelets, the

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number of proven type of bacteria in the blood, their names and their classification whether they are sensible or resistant, the secondary localization of the germ, and death.

3. CLINICAL FACTORS AND IMPORTANT STATISTICS

Here are few characteristics of the patients' population. The number of males is not significantly apart from the number of females. See TABLE I

TABLE I, Patients' gender statistics

	Frequency	Percent
Female	30	51.7
Male	28	48.3
Total	58	100.0

The population mean age is 54.72 years. See TABLE II.

TABLE II, Patients' age

	Mean	Std deviation
Age	54.72	14.993

The mean length of stay is 11.32 days but it is skewed to the right. See TABLE III

TABLE III, Length of Stay statistics

	Mean	Median	Minimum	Maximum	Variance	St dev
Length of stay	11.32	9	1	37	333.69	18.26

Almost 29% had diabetes, 25% had trouble with thrombopenia: either a low production or high production of the platelets. 25% had disorder in the number of white globules, 25% had developed a secondary germ in other localization, 48% had trouble with hemostats, 97% had blood oxygenation problems from low production of hemoglobin, 17% had experienced a hypotension (choc) and 17% were dead.

4. BLOOD FACTORS

It was found that 63.8 % have a dialysis entrance with Fistula and the rest of the 38.2% with Catheter. See TABLE IV.

TABLE IV, Dialysis entrance type

	Frequency	Percentage
FAV	37	63.8
catheter	21	36.2
Total	58	100.0

It can be noted from table V that 13% of the population has prosthesis attached to the mean of dialysis, 10% of the patients have a fistula with prosthesis. Only 3% have a catheter with prosthesis. See TABLE V.

TABLE V, Prosthesis presence (G_1:0 is the group of patients with no prosthesis, G_2:1 is the group of patients with prosthesis.)

Prosthesis	FAV	KT	Totals
G_1:0	32	20	52
% Total	53%	34%	87%
G_2:1	6	2	8
% Total	10%	3%	13%
Totals	38	22	60
% Total	63%	37%	

It is inferred that 48.3 percent are found to have an infected means of dialysis. See TABLE VI

TABLE VI, Infection presence in the mean of dialysis

	Frequency	Percentage
Infected	28	48.3
N. infected	30	51.7
Total	58	100.0

In the whole population, 86% of the germs are of type Cocci positive, the rest are of type Bacilli, which means that most of the germs' entry is endovascular. See TABLE VII

TABLE VII, Germs' type

	Frequency	Percent
CG+	50	86.2
BGN	8	13.8
Total	58	100.0

It was found that 63.8% of the germs are metticiline Sensible staphylococci aureus, 10.3% are metticiline resistant staphylococci aureus, and the rest of 25.9% are other type of germs. See TABLE VIII

TABLE VIII, Germs classified by resistance type

	Frequency	Percent
S méti S	37	63.8
S méti R	6	10.3
Other germs	15	25.9
Total	58	100.0

5. UNIVARIATE ANALYSES

It is the objective of this section to find any univariate significance relation between the death and other factors. These factors are often nominal. Logistic regression was used to explain a nominal variable death as a function of the continuous variable age. When logistic regression was fit, no significant relationship between death and age was found (P=0.8.) The variable diabetes is nominal: its value is 0 if the patient does not have diabetes and 1 if the patient has it. A relationship of dependence was explored by the chi square test at 5% level of significance. It was found that there is no noteworthy dependence between death and diabetes status. Other relationship of dependence between the disorders in white globules and death was investigated. No important reliance was found. Similarly, no major dependency was found between death and secondary localization of the germs, the volume of hemoglobin synthesized. The only factor that is associated with death is the choc as a result of hypotension. The death is highly related to this chocking status as indicated by the independence test (see TABLE IX).

TABLE IX, Death as related to Choc.(Death G_1:0 is the group of people who did not die, Death G_2:1 is the group of people who were dead)

Choc	Death G_1:0	Death G_2:1	Totals
G_1:0	45	3	48
% Total	77.59%	5.17%	82.76%
G_2:1	2	8	10
% Total	3.45%	13.79%	17.24%
All Groups	47	11	58
% Total	81.03%	18.97%	

6. MULTIVARIATE ANALYSES

6.1 Sample analysis

As learnt from the previous section, there is independence between death and each of the other variables except the chocking status. We tried to fit a logistic regression to explain death with many variables and many trials. The best we found is a relation between the variable death and cardiovascular frequency at entry, the presence of prosthesis in the mean of hemodialysis, the hemoglobin level, the Glycemia, and the number of localized in the blood. By looking at the correlation matrix between these explicative variables, we did not find any significant correlation (see the following TABLE XI) Here are the variables' definitions. Heart: describes the cardiovascular frequency. For healthy person it is between 50 and 80 per minute at rest. Proth: is a binary variable which has a value of 1 if the mean of dialysis contains prosthesis, 0 otherwise. Hem: the weight of hemoglobin in grams per 100 mL of blood. It is considered to be between 12 g and 18 g for healthy person. Gly: the weight in millimol of glucose per 100 mL of blood. For healthy person it is between 5 to 7 millimol/dl. Loc: the number of germs located in the blood of a patient. It could be 0,1,2,3,…

TABLE XI Correlations (28) Marked correlations are significant at p < .05000 N=28 (Casewise deletion of missing data)

	Means	Std.Dev.	Heart	Proth	Hem	Gly	Loc
Heart	96.64286	21.62340	1.000000	-0.021364	-0.296351	-0.132042	-0.046884
Proth	0.10714	0.31497	-0.021364	1.000000	-0.024633	-0.073803	0.005810
Hem	7.94286	2.04585	-0.296351	-0.024633	1.000000	0.201685	-0.054742
Gly	8.40500	6.31740	-0.132042	-0.073803	0.201685	1.000000	-0.119025
Loc	0.32143	0.72283	-0.046884	0.005810	-0.054742	-0.119025	1.000000

We plotted the variables and we chose the best fit for each continuous variable (see the input module of Arena [18]) For the variable Heart

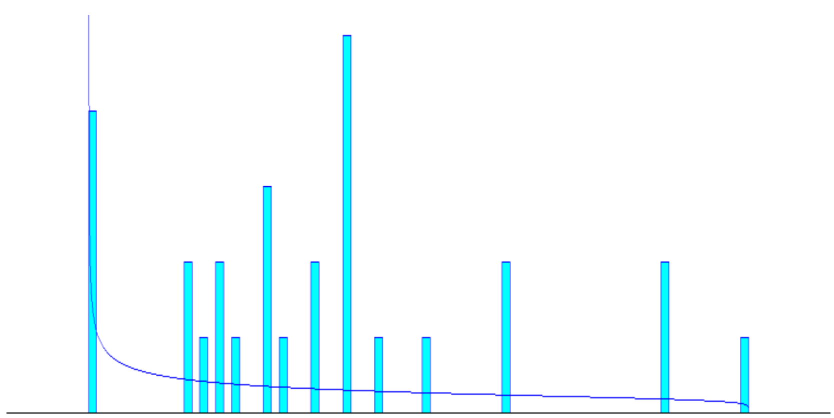

Fig 1 The distribution of the cardiovascular frequency among parents

Distribution Summary
Distribution: Beta
Expression: 67.5 + 83 * BETA(0.66, 1.13)
Square Error: 0.076836
Chi Square Test
Number of intervals = 5
Degrees of freedom = 2

Test Statistic = 2.35
Corresponding p-value = 0.327

Data Summary
Number of Data Points = 28
Min Data Value = 68
Max Data Value = 150
Sample Mean = 96.6
Sample Std Dev = 21.6

Histogram Summary
Histogram Range = 67.5 to 151
Number of Intervals = 83

For the variable Hem see the figure below

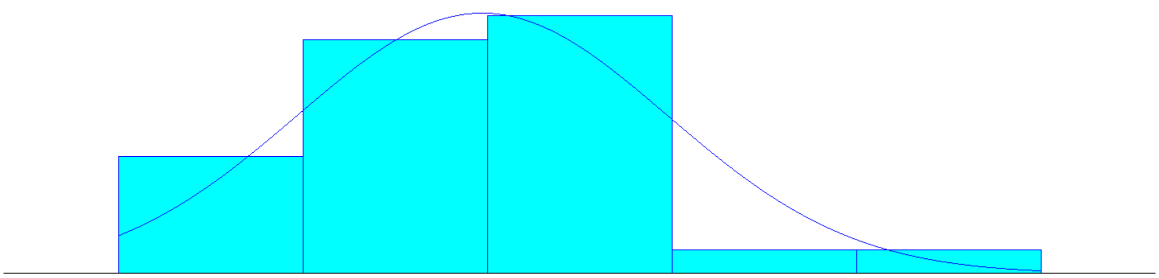

Fig 2 The distribution of the Hemoglobin level among patients

Distribution: Normal
Expression: NORM(7.94, 2.01)
Square Error: 0.014107

Kolmogorov-Smirnov Test
Test Statistic = 0.143
Corresponding p-value > 0.15
Data Summary

Number of Data Points = 28
Min Data Value = 4.9
Max Data Value = 14
Sample Mean = 7.94
Sample Std Dev = 2.05

Histogram Summary
Histogram Range = 4 to 14
Number of Intervals = 5
For the variable Gly

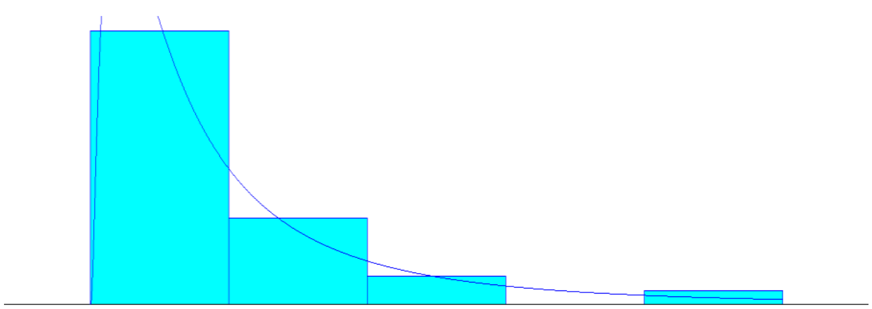

Fig 3 The distribution of the Glycemia level among patients

Distribution Summary

Distribution: Lognormal
Expression: 2 + LOGN(7.69, 11.8)
Square Error: 0.002579
Kolmogorov-Smirnov Test
Test Statistic = 0.189
Corresponding p-value > 0.15

Data Summary

Number of Data Points = 28
Min Data Value = 2.07
Max Data Value = 33.2
Sample Mean = 8.4
Sample Std Dev = 6.32

Histogram Summary
Histogram Range = 2 to 34
Number of Intervals = 5

6.2 Monte Carlo Simulation

The size of this sample is 28 and is considered to be small to conclude anything. So I developed my own scheme to simulate from the population. Monte Carlo simulation is highly utilized in medical applications [16,17]. For each of the continuous variables, I fit a distribution and I generated 5000 vectors of observations having the characteristics of the original population. For each dichotomous variable, I used discrete distributions with a probability corresponding to zero in the sample. Since there is no correlation between explicative variables, each variable was generated by itself.

6.3 Logistic Regression

The logistic regression was run to explain the variable death with the candidate variables using STATISTICA software [19]. It is found that death could be explained by the presence of prosthesis, the hemoglobin level and the number of germs in the blood. (See TABLE XII for the coefficients and the odd ratios)

TABLE XII Model: Logistic regression (logit) N of 0's: 4471 1's: 529 (5000) Dep. var: Death Loss: Max likelihood Final loss: 1684.0525227 Chi²(3)=8.3260 p=.03975

	Const.B0	Heart	Proth	Hem
Estimate	-2.82084	0.002396	-0.115061	0.057105
Odds ratio (unit ch)	0.05956	1.002399	0.891312	1.058767
Odds ratio (range)		1.216967	0.891312	2.322525

7. RESULTS AND DISCUSSIONS

This section is dedicated to provide inferences about the population of the infected hemodialysis patients coming to the infectious department and not limited to the 60 patients. At no more than 5% risk (p=.03975), the significant variables are the presence of prosthesis; the hemoglobin level, and the cardiovascular frequency. These variables can predict the odd ratio of survival. The probability p of survival is given by the equation

$$\log\left(\frac{p}{1-p}\right) = -2.82084 + 0.002396\text{Heart} - 0.115061\text{Proth} + 0.057105\text{Hem}$$

the presence of prosthesis tends to increase the risk of death by 11% holding everything equal. For the hemoglobin, an increase by one unit tends to increase the probability of survival by 5.8% and p is highly increased it if the reading of hemoglobin is increased. These could be explained by the fact the prosthesis presents a high risk proxy to germs and the hemoglobin level is precarious on the breathing status of a patient. The cardiovascular frequency should be kept stable.

8. CONCLUSION

In this Study, factors affecting the death of infected hemodialysis patients inside Hedi Chaker Hospital were explored. The population of 60 patients was considered but inferences about the whole population are given. Not all the data are available on patients. The univariate analysis gave that hypotension is a major cause of death. All other factors are not cause of death when considered on single basis. A logistic regression model that explains the binary variable death with the influencing factors: systolic scores, Glycemia, the hemoglobin level, and presence of prosthesis was developed. Since there are only 28 data available and in order to make inferences on the whole population, a large sample was constructed on the basis of independence between factors. 5000 records were obtained from simulation. It can be inferred for the population of the infected hemodialysis patients that for the surviving patients are characterized by a non-presence of prosthesis and higher hemoglobin level and moderate cardiovascular frequency. To the best of our knowledge, [20] are one of the few people who published work on the morbidity and mortality of the infected hemodialysis patients. They came up with the conclusion that morbidity and mortality are related to age, serum albumin level, and the type of infection. Their work was conducted on more than 740 people. Our medical contribution consists of coming up with other factors explaining mortality and our statistical contribution consists of making inferences on the whole population of the infected hemodialysis patients; small size sample does not prevent us from doing so. Monte carlo simulation provided the way.

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APPENDIX

Death	Loc	Gly	Hem	Proth	Heart
0	0	9	8.2	1	80
0	0	5.5	7.5	0	140
0	0	16.75	6.2	0	96
0	0	6.39	14	0	68
0	0	4.3	8.2	0	84
0	1	5.5	7.5	0	82
0	0	7.5	8.5	0	84
0	0	4.5	6.5	0	120
0	0	5.9	5.2	0	90
0	1	7.3	12	0	90
0	0	6.4	6.6	0	68
0	0	5.5	7.7	0	68
0	3	5.3	4.9	0	104
0	0	4	7	0	100
0	1	9.32	9.5	0	80
0	0	33.24	9.4	0	100
0	0	2.07	5.6	0	110
0	0	4.9	6	0	100
0	0	8.5	8.6	0	90
0	0	12.25	7.1	0	96
0	0	6.5	8.2	0	92
0	0	14	10	0	68
0	0	5	10	0	150
0	2	6.6	9.1	0	100
1	0	19.87	8.7	0	100
1	0	2.5	7.8	1	120
1	1	9.75	7.4	1	86
1	0	7	5	0	140