

ACCIDENTAL TETANUS: PROGNOSIS EVALUATION IN A HISTORICAL SERIES AT A HOSPITAL IN SALVADOR, BAHIA, BRAZIL

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SUMMARY

A total of 868 (84.89%) patients diagnosed with tetanus were studied, out of the 1,024 tetanus patients hospitalized at Couto Maia Hospital (Salvador, Bahia, Brazil), during the period between 1986 and 1997. Of this group (n = 868), 63.5% (n = 551) were discharged, 35.4% (n = 307) died, and 1.1% (n = 10) were transferred. The average age of the deceased patients (38.73 ± 23.31 years) was significantly greater ($p < 0.0001$) than the age of those who survived (29.21 ± 20.05 years). Analyzing the variables of the logistic regression model with statistic significance ($p \leq 0.25$) for univariate analysis, we observed a greater association of risk for worst prognosis (death) in patients aged ≥ 51 years; time of illness < 48 hours; time of incubation < 168 hours; neck rigidity; spasms; opisthotonos; body temperature ≥ 37.7 °C; heart beat ≥ 111 beats/minute; sympathetic hyperactivity and association with pneumonia. Among the group of those who survived, patients with 1 to 5 of those variables (n = 398; 76.8%) were more frequent, while among patients of the group of the deceased, 70.3% (n = 206) presented 6 to 10 of those variables, with a highly significant difference ($p < 10^{-8}$). In conclusion, the indicators described provide early information that may guide the prognosis and medical and nurse care.

KEYWORDS: Tetanus; Clinic; Prognosis indicators.

INTRODUCTION

PATEL⁸, in India, established a clinical classification of tetanus patients based on 5 degrees, according to 5 parameters: trismus; spasms; incubation period of ≤ 7 days; interval between trismus and spasms ≤ 48 hours; rectal temperature ≥ 38 °C at hospital admission or within the first 24 hours of hospitalization. According to this classification⁸, degree I corresponds to the presence of 1 of the parameters, degree II to 2 parameters, and so on. Among other prognosis factors, more intense or frequently recurring spasms have a stronger association with death^{2,10}, as well as dyspnea or crisis of apnea and high body temperature^{2,13,15}.

ANDRADE *et al.*¹ concluded that only generalized hypertonia was associated with the worst prognosis, or death, while the incubation and/or onset periods were not associated with lethality in case studies of 78 patients¹. More recently, MIRANDA-FILHO *et al.*⁵ considered the presence of neck rigidity a factor in the prediction of death risk. However, extreme youth and age were considered by PATEL *et al.*⁷ and TAVARES¹² as an indicator with a stronger association with the worst prognosis.

In the literature, no studies were found that used a scale of prognostic indicators based on demographic and clinical data that could be applied at the time of hospital admission or during the first days of hospitalization of patients with accidental tetanus. During the period between 1960 and 2001³, and encompassing the main databases (e.g. EMBASE, MEDLINE,

Web of Science, LILACS, and Index Medicus), tetanus prognostic studies^{1,2,7,8,10,13,15}, with the exception of MIRANDA-FILHO *et al.*⁵ and OSINUSI & NJINYAM⁶, were based on univariate analyses, which fail to correctly evaluate possible interactions between demographic data and clinical indicators such as the type of hospital exit (dismissal or death). For this reason, this study was planned using patients at Couto Maia Hospital (Salvador, Bahia, Brazil) as its population, because that hospital has been a reference unit in the State of Bahia for 150 years.

MATERIAL AND METHODS

Prior to its execution, the research design³ was approved by the Ethics Commission and the Board of Directors of Couto Maia Hospital. This Hospital, belonging to the Department of Health of the State of Bahia (SESAB), treats most patients diagnosed with infectious/parasitic diseases in the Salvador metropolitan region, and during the period between 1991 and 2001 it was responsible for 71% to 79% of notified cases of tetanus in the State (Epidemiology Division of SESAB, personal communication).

Medical records of patients hospitalized at Couto Maia Hospital (HCMaia) from 1 January 1986 to 31 December 1997 were reviewed, using a standard form³, and all variables were entered into an Excel[®] spreadsheet. Before beginning a systematic review of patient records, a cross-reference was made with the record number files of HCMaia's

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Epidemiological Vigilance Sector, the nosological files of the Filling and Statistics Sector (SAME), and the registry books of HC Maia's hospitalization units. After building this database (Excel®), the patient records were reviewed by 2 independent observers and, if the third reviewer had a differing opinion, the records and the standard form were analyzed by all three authors³ together. In the standard form were registered demographic and clinical/epidemiological data at hospital admission (including data regarding the possibility of carrying *Clostridium tetani* upon entry), from the first 24 hours through the entire hospitalization period. The type of hospital exit (release or death) was considered a response variable.

As diagnosis criteria for tetanus, patients had to present at least 2 (of) the following signs and/or symptoms: (i) pain in more than one muscular group; (ii) difficulty in locomotion; (iii) trismus; (iv) muscle spasms; (v) spasms on stimulation; (vi) sardonic grin; (vii) opisthotonos; (viii) preserved consciousness, especially in individuals older than 1 year; (ix) signs of sympathetic hyperactivity (heart arrhythmia, variable or instable blood pressure, and excessive or profuse sweating). At the time of hospital admission or during hospitalization, the pneumonia diagnosis was based on clinical and radiological criteria.

The time of illness was considered to be the time span (in hours) between the beginning of symptoms/signs associated to the prodromal period and the date of hospitalization. The period of onset corresponds to the period (in hours) between the beginning of the illness and the first paroxysmal muscle spasm or tonic-clonic spasm.

During the initial clinical evaluation, all symptoms and signs presented by patients at the time of hospital admission were considered, especially those described in the Emergency Service form of the Couto Maia Hospital. It was previously established that, after analyzing the distribution of each clinical variable, only those with a case frequency $\geq 2.0\%$ would be included in the univariate analysis, in order to avoid distortions derived from the small sample "n". This was done even considering that some of the variables (n cases $\geq 2.0\%$) included in the study are not part of the classical clinical case for tetanus, but were maintained in the preliminary analyses because they are usually observed in the clinical history or the physical exam during the initial hospital care.

On the spreadsheet (EXCEL®), based on the dates and times entered, were entered the time of illness, period of incubation, and period of onset. Also, the heart rate was adjusted on the spreadsheet considering the normal values for each age range. In the multivariate analysis (logistical regression), the quantitative variables (continuous or discrete) were transformed into categories, using as the cut-off point the median value or the lowest limit ($p < 0.05$) associated to the dependent variable (death). The data was analyzed using the SPSS program (v. 9.0 for Windows) and, in the statistical analysis, differences with an error probability of type I ($\alpha \leq 5\%$ ($p \leq 0.05$)) were considered significant.

RESULTS

In a 12-year period (from 1986 to 1997), 1,038 patients were hospitalized at HC Maia with tetanus diagnosis. Of these, 14 cases were excluded (1.4%) because they did not meet the defining requirements for tetanus diagnosis. Among the cases studied (n = 1,024), 868 (84.8%) were accidental tetanus and 156 (15.2%) neonatal tetanus. In the cases

of accidental tetanus, age varied from 1 to 96 years (32.7 ± 21.8 years), with a median age of 24 years. In this same group, 63.5% (n = 551) were discharged, 35.4% (n = 307) died, and 1.1% (n = 10) were transferred.

In the analysis of the 858 tetanus cases that were not transferred, the average age of the deceased patients (38.73 ± 23.31 years) was significantly greater ($p < 0.0001$) than the age observed in the cases discharged (29.21 ± 20.05 years). Studying the age in an intervallic scale, the greatest frequency of death was among those with 51 or more years of age, among which 35.7% (109/304) died and 18.6% (102/549) were discharged, this difference being highly significant ($p < 0.00006$). In both patient groups, discharge and death, the proportion of male patients was, respectively, 76.0% (419/551) and 73.9% (227/307), with a statistical difference of ($\chi^2 = 0.47$; $p > 0.49$).

In Table 1, the time of illness, the incubation period and the period of onset of tetanus cases were significantly lower ($p < 0.0001$) in patients that died, when compared with those who were discharged. These periods, when compared with each other in the age groups of 1 to 50 years and 51 to 96 years, showed no difference between patients who were discharged and those who died, except for a lower incubation period ($p < 0.05$) in cases of the death of patients aged 1 to 50 (discharged: 443.37 hours; died: 325.67 hours).

Table 1

Time of illness, incubation period, and period of onset of cases of tetanus hospitalized at Couto Maia Hospital (Salvador, Bahia, Brazil), from 1986 to 1997

PERIOD (in hours)	Release	Death	P value
OF ILLNESS			
n	551	302	
Limits	3 — 408	3 — 410	
Median	72.0	24.0	
Average	77.73	48.75	< 0.0001 ^(a)
D.P. (±)	62.04	44.26	
OF INCUBATION			
n	528	303	
Limits	24 — 980	12 — 984	
Median	192.0	168.0	
Average	236.70	180.58	< 0.0001 ^(a)
D.P. (±)	124.13	99.91	
OF ONSET			
n	524	300	
Limits	1 — 288	1 — 168	
Median	20.0	12.0	
Average	28.94	17.04	< 0.0001 ^(a)
D.P. (±)	50.61	17.05	

(a) Student-t test

Table 2 lists the symptoms, signs, and other clinical findings observed at the time of patient hospitalization, distributed according to the type of exit. In the group of deceased patients, the cases with neck rigidity were significantly more frequent ($p < 0.002$). At the time of hospital admission, body temperature with a value $\geq 37.7^\circ\text{C}$ was more frequent in the group of deceased patients (22.8; 70/307) in a highly significant way ($p <$

Table 2

Symptoms, signs, and other clinical findings described at the time of hospitalization at Couto Maia Hospital of patients with tetanus, distributed according to type of hospital exit

Clinical condition at the time of hospitalization	Exit (n, yes) %		Total (n = 858)	p value ^a
	Release (n = 551)	Death (n = 307)		
Myalgia	(332) 60.3	(179) 58.3	(511) 59.6	>0.57
Back pain	(275) 49.9	(156) 50.8	(431) 50.2	>0.79
Neck rigidity	(268) 48.6	(183) 59.6	(451) 52.6	<0.002 ^b
MMII pain	(230) 41.7	(115) 37.5	(345) 40.2	>0.22
Abdominal pain	(245) 44.5	(117) 38.1	(362) 42.2	>0.07
Difficulty in locomotion	(342) 62.1	(185) 60.3	(527) 61.4	> 0.60
Dyspnea	(59) 10.7	(44) 14.3	(103) 12.0	>0.11
°Paresthesia	(5.329)	5.9 (18)	5.5 (47)	0.71<
Fever	(150) 27.2	(107) 34.8	(257) 30.0	<0.02 ^b
Pain while chewing	(222) 40.3	(120) 39.1	(342) 39.9	>0.73
Dysphagia	(351) 63.7	(186) 60.6	(537) 62.6	>0.36
Trismus	(521) 94.6	(297) 96.7	(818) 95.3	>0.14
Generalized Hypertonia	(528) 95.8	(296) 96.4	(824) 96.0	>0.67
Spasms	(368) 66.8	(269) 87.6	(637) 74.2	<0.000001 ^b
Spasms after stimulus	(310) 56.3	(232) 75.6	(542) 63.2	<0.000001 ^b
Sardonic grin	(184) 33.4	(158) 51.5	(342) 39.9	<0.000001 ^b
Opisthotonos	(56) 10.2	(76) 24.8	(132) 15.4	<0.000001 ^b
Pale mucosae	(441) 80.0	(196) 63.8	(637) 74.2	<0.000001 ^b
Precarious general state	(216) 39.2	(217) 70.7	(433) 50.5	<0.000001 ^b
Alteration of consciousness	(22) 4.0	(27) 8.8	(49) 5.7	<0.004 ^b
Arrhythmia	(14) 2.5	(15) 4.9	(29) 3.4	>0.06
Extrasystoles	(38) 6.9	(34) 11.1	(72) 8.4	<0.04 ^b
Excessive sweating	(128) 23.2	(136) 44.3	(264) 30.8	<0.000001 ^b
Pneumonia	(44) 8.0	(60) 19.5	(104) 12.1	<0.000001 ^b

(a) chi square; (b) significant; (c) in the region of the affected area.

0.02) than in the group of discharged patients (14.7%; 81/551). Also at the time of admission, heart rate of ≥ 111 beats/minute, was significantly ($p < 0.00005$) more frequent (28.3%) in the group of deceased patients (87/307) than in the group of discharged patients (18.7%; 103/551). However, both diastolic and systolic pressures were similar at the time of admission in both groups.

Table 3 shows the frequencies of pneumonia and sympathetic hyperactivity diagnosis at the time of hospitalization, among cases of releases and deaths. Cases of both pneumonia and sympathetic hyperactivity diagnosis were more frequent in the group of deceased patients ($p < 0.000001$).

Then, a model of logistical regression analysis was built, where the dependent variable was the type of hospital exit (1 – death; 0 – release). Individuals without information regarding age ($n = 3$), incubation period ($n = 27$) or time of illness ($n = 5$) were excluded from this analysis. As a result, 825 patients remained (297 deaths and 528 releases). This multivariate analysis was divided in three stages. In the first, the independent variables that participated in the regression analysis were those associated ($p \leq 0.25$, cited in Tables 1, 2, and 3) to the dependent variable (type of exit) in the univariate analyses. In this first stage, the variables associated to the dependent variables were included one by

Table 3

Frequencies, throughout hospitalization, of diagnoses of lung infection and sympathetic hyperactivity among cases of tetanus *versus* the type of hospital exit

	Type of Hospital Exit n(%)		p value*
	Release (n = 551)	Death (n = 307)	
Pneumonia			
No	482 (87.5)	184 (59.9)	
Yes	69 (12.5)	123 (40.1)	< 0.000001
Sympathetic hyperactivity			
No	505 (91.6)	185 (60.3)	
Yes	46 (8.4)	122 (39.7)	< 0.0000001

(*) chi square

one in the binary logistic regression; for the second stage, variables without significant association ($p > 0.05$) were excluded (MMII pain, abdominal pain, dyspnea, trismus and alteration of consciousness). In the second stage, with the exception of the age variable, all other variables

were maintained in the regression model and analyzed as a whole, without observing a significant association with the dependent variable ($p > 0.05$) of pale mucosae and precarious general state. Also in the second stage, the “period of onset” variable was excluded from the logistical model because there was no significant difference ($p > 0.11$) between discharged and deceased individuals relative to age, because statistical significance ($p < 0.008$) was only observed when the incubation period was excluded from the analysis. In the third stage of the logistic regression, age was initially included as a continuous variable (in years) and later in an interval scale (with 5-year classes), but only when it was categorized (< 51 or ≥ 51 years of age) there was a significant association with the dependent variable. Table 4 shows the variables with statistic significance ($p < 0.05$) in the regression model: patients with an age equal to or greater than 51 years have a risk 3.6 times greater of presenting the worst prognosis; a risk 2.8 times greater if the time of illness is less than 48 hours; and a risk 3.2 times greater if the incubation period is less than 168 hours. Similar risks were observed for neck rigidity (1.7x), spasms (2.0x), opisthotonos (1.9x), body temperature greater than ≥ 37.7 °C (2.1x), heart rate ≥ 111 beats/min. (1.3x), excessive sweating (2.1x), and associated pneumonia diagnosis (2.1x). The other variables (history of fever, spasms after stimulus, sardonic grin, extrasystoles and arrhythmia) also included (Table 4) in the third stage of the logistical regression did not present a significant association ($p > 0.21$).

Table 4

Logistical model of the clinical variables studied in patients with tetanus, where the response (or dependent) variable is the type of hospital exit (death)

Variable	p value	Odds Ratio [IC 95%]
Age	<0.00001	3.6646 [2.4473 — 5.4874]
Time of illness	<0.00001	2.8003 [1.9349 — 4.0528]
Incubation period	<0.00001	3.1747 [2.2122 — 4.5558]
Neck rigidity	0.0041	1.6762 [1.1775 — 2.3860]
History of fever	0.5359	1.1422 [0.7497 — 1.7402]
Spasms	0.0120	2.0183 [1.1671 — 3.4901]
Spasms after stimulus	0.2809	1.3008 [0.8065 — 2.0980]
Sardonic grin	0.6855	1.0788 [0.7474 — 1.5570]
Opisthotonos	0.0077	1.8951 [1.1841 — 3.0330]
Body temperature	0.0009	2.0563 [1.3428 — 3.1491]
Heart rate	0.0297	1.2828 [1.0248 — 1.6057]
Extrasystoles	0.2123	1.5143 [0.7889 — 2.9067]
Arrhythmia	0.5929	0.7648 [0.2862 — 2.0435]
Excessive sweating	0.0001	2.1071 [1.4425 — 3.0781]
Lung infection	0.0058	2.0773 [1.2354 — 3.4931]

As in the multivariate analysis (Table 4), the variables were dichotomized and codified based on previous analyses, giving a score of 1 (one) to the answer associated with the worst prognosis result (from a clinical perspective), such as: age (≥ 51 years = 1); time of illness (< 48 hours = 1); incubation period (< 168 hours = 1); neck rigidity present (present = 1); opisthotonos (present = 1); axillary body temperature or body temperature (≥ 37.7 °C = 1); heart rate (≥ 111 beats/min = 1); excessive sweating (yes = 1); and pneumonia or lung infection (yes = 1). The scores of the 10 variables were added and distributed according to the type of hospital exit in Table 5, therefore resulting in possible limits of 0 to 10 points for this new variable. In the group of

discharged patients, most (76.8%; $n = 398$) had 1 to 5 points, while in the group of deceased patients, most (70.3%; $n = 206$) had from 6 to 10 points, with a highly significant difference ($\chi^2 = 156.06$; $p < 10^{-8}$).

Table 5

Sum (Σ) of independent variables*, distributed according to the type of hospital exit

Σ [scores]	Hospital exit, n (%)	
	Release (n = 518)	Death (n = 293)
1	14 (2.7)	0
2	68 (13.1)	3 (1.0)
3	98 (18.9)	9 (3.1)
4	112 (21.6)	32 (10.9)
5	106 (20.5)	43 (14.7)
6	67 (12.9)	63 (21.5)
7	32 (6.2)	60 (20.5)
8	18 (3.5)	48 (16.4)
9	2 (0.4)	27 (9.2)
10	1 (0.2)	8 (2.7)

(*) age (≥ 51 years = 1); time of illness (< 48 hours = 1); incubation period (< 168 hours = 1); neck rigidity (present = 1); spasms (present = 1); opisthotonos (present = 1); body temperature (≥ 37.7 °C = 1); heart rate (≥ 111 beats./min = 1); excessive sweating (yes = 1) and lung infection (yes = 1).

DISCUSSION

This study evaluated the clinical data that are usually part of the admission exam records of the Hospital Couto Maia (HCMaia) Emergency Center, not only because they contain more homogeneous information than the first clinical history of the hospitalization unit, but also because the time periods associated to tetanus (e.g. time of illness, period of incubation, and period of onset) are better described and more easily associated to the time of the first medical care. For the same reason, in the statistical analyses, these time periods were counted in hours instead of days in order to achieve a greater accuracy in their estimation, avoiding gross approximations and/or the inclusion in the records of cases with times of zero days, especially in the case of time of illness and period of onset. On the other hand, the statistical software permits automatic calculation of each time period, registering the date and time of the first medical care at HCMaia and the date and (estimated) time of occurrence of the clinical event or accident associated to exposure to *C. tetani*.

Some clinical data included in the study (Table 2) are not part of the prognostic indicators described in the literature^{1,2,5-8,10,13,15}, but of the more common clinical investigation performed in many emergency centers. On the other hand, these clinical data are not only frequent ($> 2\%$) in the cases studied, but some of them are variables that can confuse or modify effects, and were for that reason maintained in the univariate analysis.

In the case analysis, the average age of cases of tetanus was 24 years, which is in agreement with the literature^{4,9,14}. The average number of cases resulting in death was significantly higher than that of those discharged, and, when divided into age groups, the highest occurrence was among people aged 51 or more, which agrees with the results observed by PATEL *et al.*⁷, TAVARES¹⁰ and VICENT & VENTURINO¹⁶.

The time of illness, incubation period, and period of onset were significantly lower in patients who died when compared to those who were discharged, results that are similar to those observed by TAVARES^{10,12} and MIRANDA-FILHO *et al.*⁵ but dissimilar with the findings by ANDRADE *et al.*¹ Those periods in both age groups studied (1 to 50 years and 51 to 96 years) were similar for patients who were discharged and died, except for the incubation period among the deceased aged from 1 to 50, similarly to what was observed by TAVARES¹². Associated lung infection and sympathetic hyperactivity, when present, predominated significantly among the group of deceased patients, as was also observed by BEZERRA² and TAVARES¹².

These results reinforce the need to accurately record the clinical history of patients hospitalized with a suspicion of tetanus, because it may suggest, at the time of admission, the cases with the worst prognosis, therefore deserving faster and more intensive medical and nursing care.

However, a prognostic evaluation in cases of tetanus, as proposed, was not observed in the literature^{1,2,5,7,8,13,15}. Except for cases of neonatal tetanus, as described by OSINUSI & NJINYAM⁶, who showed that the occurrence of death in newborns was strongly associated with the concomitance of pneumonia, episodes of recurrent apnea, and the presence of opisthotonos and cyanosis.

More recently, MIRANDA-FILHO *et al.*⁵ performed a control case study and observed that the 152 tetanus cases (death) differed from the 152 control cases (dismissed) in that they presented a shorter time of illness, period of incubation and of onset, as well as respiratory complaints, respiratory deficiency, neck rigidity, and spasms. However, contrary to MIRANDA-FILHO *et al.*⁵, a strong association between the periods of incubation and of onset was observed in the present study. For this reason, the period of onset was excluded from the final model of the multivariate analysis.

For this reason too, the accuracy of the indicators used to estimate the prognosis must be evaluated in other case studies and, if confirmed, it would be advisable to adopt them in registration forms and patient records of specialized or emergency hospitals and in routine manuals, in order to speed up the introduction of early support measures or actions, especially for patients evaluated as having the worst prognosis.

Within the model studied, the scale for estimating the prognosis may suffer distortions resulting from the heterogeneity of the 10 clinical data included in it, because they have equal weights and different natures, such as body temperature and patient age. However, these indicators, taken in isolation, are described in the literature as being strongly associated to the worst prognosis of tetanus^{2,8,12}. Nonetheless, in spite of this limitation of the proposed scale, similar investigations are needed using other case studies, in order to verify the applicability and reproducibility of the model, as well as to use different weights according to the indicator's group, depending on its greater, medium or lower association to the worst prognosis. However, the introduction of a more complex evaluation model may substantially reduce its applicability in emergency centers.

For this very reason, on the other hand, this prognosis evaluation is more accurate after the first 24 hours of hospitalization, when it is possible to better evaluate the 10 criteria or variables (age \geq 51 years; time of

illness $<$ 48 hours; incubation period $<$ 168 hours; neck rigidity; spasms; opisthotonos; body temperature \geq 37.7 °C; heart rate \geq 111 beats/min.; sympathetic hyperactivity; and associated pulmonary infection). Still, the presence of 6 to 10 of these criteria was strongly associated with patient death. In sum, these prognosis indicators may also serve as an auxiliary instrument in the initial evaluation of patients with tetanus, as well as in subsequent evaluations, allowing the healthcare team to offer more intensive care to patients presenting more than 5 of those indicators.

RESUMO

Tétano acidental: avaliação do prognóstico em uma série histórica de hospital de Salvador, Bahia, Brasil

Foram estudados 868 (84,8%) pacientes com diagnóstico de tétano acidental, entre aqueles 1.024 com diagnóstico de tétano internados no Hospital Couto Maia (Salvador, Bahia, Brasil), do período de 1986 a 1997. Neste grupo, saíram de alta 63,5% (n = 551) pessoas, outras 35,4% (n = 307) foram a óbito e 1,1% (n = 10) transferidas. A média da idade dos casos de óbito (38,73 \pm 23,31 anos) foi maior (p < 0,0001), quando comparada a dos saídos-vivos (29,21 \pm 20,05 anos). Analisadas as variáveis no modelo de regressão logística, entre aquelas com significado estatístico na análise univariada (p \leq 0,25), foi observado maior risco de pior prognóstico (óbito) com: idade \geq 51 anos; tempo de doença $<$ 48 horas; período de incubação $<$ 168 horas; rigidez de nuca; espasmos; opistótono; temperatura corporal \geq 37,7 °C; frequência cardíaca \geq 111 bat./minuto; hiperatividade simpática e a associação com pneumonia. No grupo de saídos-vivos, foram mais frequentes os pacientes com até 5 daquelas variáveis (398/518; 76,8%), enquanto os pacientes do grupo óbito, 70,3% (n = 206) tiveram a presença de 6 a 10 daquelas variáveis, sendo a diferença estatisticamente significativa (p < 10⁻⁸). Em conclusão, os indicadores descritos oferecem, mais precocemente, informações que podem orientar o prognóstico e os cuidados médicos e de enfermagem.

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