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Trends and multiple causes of death due to chronic renal failure in a municipality in the Brazilian Amazon

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Abstract *This study examined the mortality trend due to chronic renal failure (CRF) and verified the underlying and associated causes for this trend in the capital of the state of Acre in the Brazilian Amazon. This ecological study used data provided by DATASUS related to mortality due to CRF, which occurred between 1986 and 2012 for male and female residents of the city of Rio Branco, Acre, Brazil. The estimated annual percentage chance (EAPC) was calculated by using Poisson log-linear regression and utilizing the Joinpoint program. The results showed that the adjusted mortality rates due to CRF, with correction, ranged from 15.4 per 100,000 inhabitants in 1986 to 4.0 per 100,000 inhabitants in 2012. The EAPC was -3.5% from 1986- 2012. Deaths by CRF presented associated causes such as respiratory diseases, pneumonia and pulmonary edema, septicemias and poorly defined signs and symptoms. When CRF was analyzed as an associated cause of death, the main primary causes of death were hypertensive diseases and diabetes. Thus, there was a decrease in mortality due to CRF as an underlying cause during the period studied; however, preventive and heath care measures should be maintained.*

Key words *Chronic renal failure, Mortality, Cause of death*

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Introduction

The Brazilian population has been experiencing an epidemiological transition in which mortality due to infectious diseases has declined in the last decade, whereas deaths due to chronic non-communicable diseases have increased; the latter were responsible for 73.9% of deaths in 2010[1]. Changes in morbidity profiles, which are mainly due to unfavorable changes in the diet and level of physical activity of the Brazilian population, have important consequences in the pattern of mortality. These changes have been characterized by an increase in the deaths of adults and the elderly due to non-infectious diseases[2]. Hypertension and diabetes mellitus associated with obesity[3] are some of the main chronic diseases that have increased in Brazil and they are considered to be the principal causes of chronic renal failure (CRF)[4-6].

Renal failure is a serious public health problem with high incidence and prevalence; it results in high costs and a high mortality rate, and it can be either acute or chronic[7]. CRF is defined by the presence of renal damage for a period equal to or greater than three months. It is characterized by structural or functional abnormalities of the kidneys, either with or without changes in the glomerular filtration rate, or if the latter is less than 60 mL/min/1.73/m², independently of the presence of renal damage[8]. The most frequent complications associated with CRF include infections, bleeding and heart failure[9-11].

In addition to the evaluation of mortality due to CRF as an underlying cause of death, it is helpful to analyze CRF as an associated cause of death because the process of death due to chronic disease can coexist with several diseases, including CRF. Thus, analyzing mortality in terms of its underlying and associated causes makes it possible to understand the multiple factors that lead to death, i.e. the diagnoses that are consequences of or complications due to the underlying cause of death, such as cardiac, renal, hepatic and other failures, as well as septicemia[12]. The chronic diseases that are most likely to be reported as associated causes of death include CRF, unspecified renal failure, diabetes mellitus, asthma, chronic obstructive pulmonary disease, and Alzheimer's disease. Thus, when an analysis is performed that only considers the underlying causes of death, this precludes the possibility of the provision of a broader spectrum of information about mortality[13].

Analyzing all the causes of death is a way of generating information about the etiology, clinical evolution and complications of diseases, as well as indirectly influencing the formulation of health actions[14,15]. Furthermore, knowledge about the diagnoses mentioned in a death certificate provides information that is relevant to the planning of health actions[16]. The data contained in the present study is important because it was corrected to take into consideration deaths due to ill-defined and unknown causes. The objective of this study was to evaluate the mortality trend due to CRF and to verify the causes associated with it in the city of Rio Branco, Acre, Brazil.

Methods

This descriptive, ecological study assessed the mortality trend due to CRF from 1986-2012 and the multiple causes of death from 1996-2012. The study included male and female individuals of all ages who were residents of the municipality of Rio Branco in the state of Acre, which is located in the Western Amazon region of Brazil.

The data regarding deaths from CRF were collected in a disaggregated form from the Mortality Information System (SIM), which is maintained by the Brazilian Ministry of Health (DATASUS/MS)[17]. The data regarding deaths from 1986-1995 were based on the codification of the 9th revision of the International Statistical Classification on Diseases and Related Health Problems, Injuries and Causes of Death (ICD-9)[18]. The data regarding deaths from 1996-2012 were based on the 10th revision of the International Statistical Classification on Diseases and Related Health Problems (ICD-10)[19]. Thus, CRF corresponds to code 585 in ICD-9 and N18 in ICD-10. Population data were also obtained for the period under analysis; these were obtained from the population database of the Brazilian Institute of Geography and Statistics (IBGE), with populations classified according to age group[20].

The proportion of ill-defined and unknown causes of death, and the under-reporting of deaths in Brazil, remains a key issue, especially in the North of the country. For this reason, in order to guarantee the quality of the data the latter were obtained only from the capital of Acre (Rio Branco) and all the analyses were corrected for ill-defined and unknown causes of death and for unspecified insufficiencies. The proportional redistribution methodology used by the World Health Organization (WHO) was used as a correction factor in the calculation of mortality rates[21,22], with 50% redistribution of deaths

whose underlying cause was classified as " ill-defined and unknown " (Codes 780-799 of ICD-9 and R00-R99 of ICD-10); this criterion was recommended by a previous study[12]. In addition, the data regarding deaths were also corrected by the redistribution of all deaths classified as due to unspecified renal failure (codes 586 of ICD-9 and N19 of ICD-10), maintaining the same proportion of specified deaths[19].

For the analysis of the causes of death, all the deaths in which CRF was mentioned in any line of the death certificate (DC) were studied. Complications in relation to the underlying cause (part I) and contributing causes (part II) of death were considered together as associated causes of death[23]; this information has been available since 1996, and deaths with code N18 were analyzed. The diagnoses mentioned in the death certificate were grouped in accordance with the chapters of ICD-10 in terms of the frequency of diagnoses and the researchers' interest in the relevance of the causes. All duplications of diagnosis were eliminated.

The causes of death were analyzed by means of the respective frequencies, determining the underlying and associated causes. The crude mortality rates were obtained by the ratio between the number of deaths due to chronic renal failure and the estimated population for each year of the series, which was represented by 100,000 inhabitants. These rates were subsequently standardized by age using the direct method and the world population was used as the standard[24,25].

The mortality trend was then analyzed using regression models, utilizing the age-standardized global rate and the age-specific and sex-specific rates of CRF deaths. For the modeling, standardized mortality rates (y) were considered as a dependent variable, and the studied period of years (x) were considered as an independent variable. Poisson log-linear regression was performed, presenting the Estimated Annual Percentage Chance (EAPC), in which points are identified in which the trend is modified. The chosen model was the one with the highest number of points that maintained statistical significance ($p < 0.05$). Trend analysis was also obtained by age and sex. The statistical analyses were performed using the Joinpoint program, version 3.4 (Statistical Research and Applications Branch, National Cancer Institute, USA).

Results

Form 1986-2012 there were 205 deaths with CRF as the underlying cause in the municipality of Rio Branco, of which two were excluded due to lack of information regarding age. The age-adjusted CRF mortality rates, with CRF as underlying cause of death, ranged from 10.8 per 100,000 inhabitants in 1986 to 2.6 per 100,000 inhabitants in 2012. With corrections made based on ill-defined and unknown causes of death and those due to unspecified renal failure the mortality rates were 15.4 per 100,000 inhabitants in 1986 and 4.0 per 100,000 inhabitants in 2012 (Figure 1).

The analysis of the variation in the adjusted mortality rates, between 1986-2012, showed that there was no change in behavior in that period, demonstrating a consistent decrease over the studied period, with the EAPC of CRF being -3.5 (95% CI -5.6, -1.3). The decreasing trend was maintained, both in terms of the division by age group for adults and the elderly, with an EAPC of -4.6 and -2.0, respectively, as well as by gender, with an EAPC for men of -3.3 and -2.6 for women (Figure 1).

The number of deaths in the period from 1996-2012 whose underlying cause was renal failure was 110; in these cases there was an average of 1.9 mentions of causes per death certificate. However, when CRF was analyzed as an associated cause of death it was present in 319 deaths during the same period. The majority of deaths where CRF was cited as a primary or associated cause of death occurred in males aged 60 and over (Table 1). It was also observed that mortality due to renal failure as the underlying cause of death was higher among women up to the age of 59 years compared to men (21.1% versus 7.0% in the age group less than 39 years and 28.9% versus 20.8% in the 40-59 age group, between women and men respectively). However, there was a higher mortality rate for men in all age groups over the age of 60 compared to women (48.6% versus 28.9% between the ages of 60-79, and 23.6% versus 21.1% in the age group of 80 and older, between men and women respectively).

In the analysis of mortality due to CRF as an underlying cause of death, diseases of the respiratory tract were the main indications of causes of death, especially pneumonia (39.7%) and pulmonary edema (17.5%), followed by poorly defined signs and symptoms, as well as unspecified septicemia (Table 2).

When CRF was an associated cause of death, the main underlying causes of death were circu-

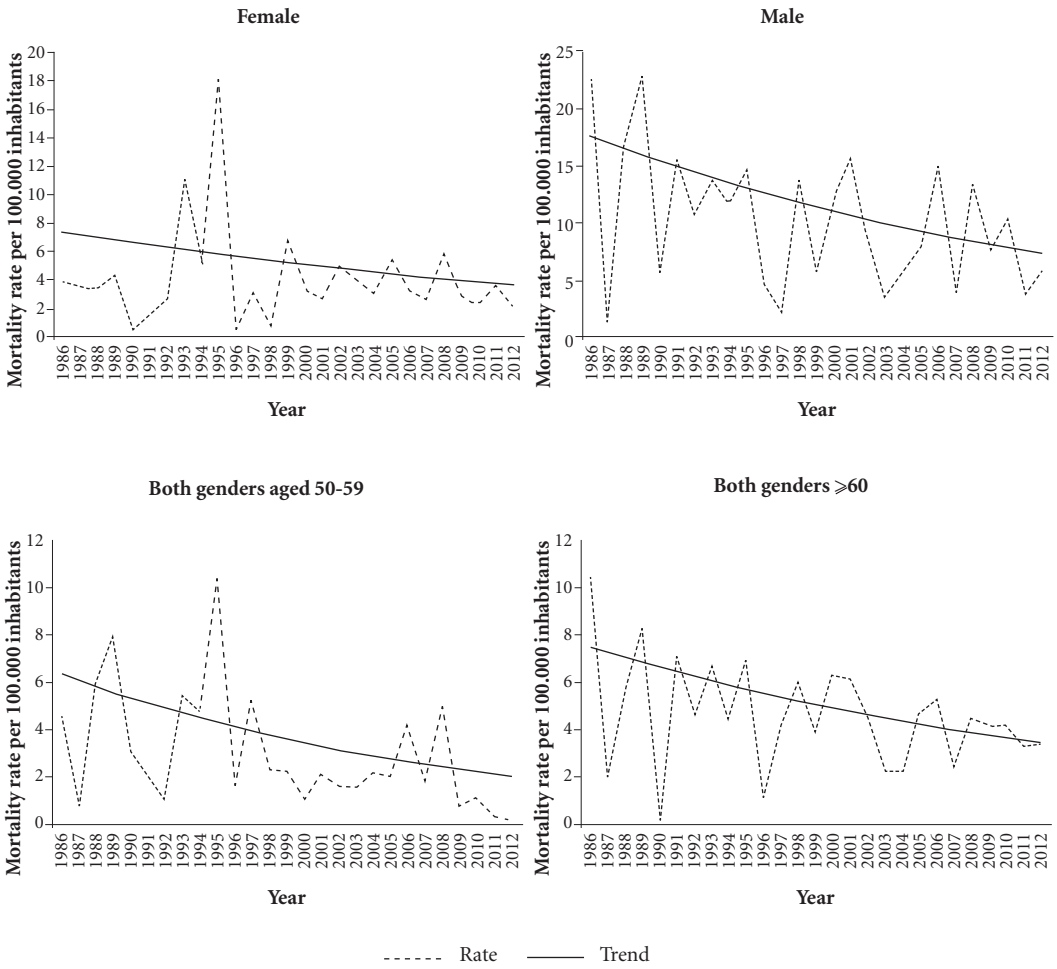

Figure 1. General trend, by age and gender, of adjusted mortality rates (with correction) of chronic renal failure as the underlying cause of death per 100,000 inhabitants in Rio Branco, Acre, Brazil, 1986-2012.

latory diseases, followed by endocrine, nutritional and metabolic diseases, as well as respiratory diseases (Table 3). Of the endocrine, nutritional and metabolic diseases, diabetes mellitus accounted for 22.3% of all deaths.

Analyzing the deaths due to diseases of the circulatory system, with CRF as an associated cause, hypertensive diseases were the main cause of death, followed by cerebrovascular diseases (Table 4).

Discussion

This study found that there was a decrease in mortality due to CRF over the analyzed period and that this decrease was higher among the elderly and women. It was also found that among the deaths due to CRF the mentions of causes of death were predominantly related to the respiratory system. When diseases of the circulatory system were evaluated as an associated cause of death they were the main underlying causes of death.

Comparatively, the mortality rates observed in Rio Branco in 2009 were higher when compared to the rates observed in Brazil as a whole. Brazil was ranked eighth in terms of deaths due to CRF in 2009 among the countries of the Americas, with a mortality rate of 3.8 per 100,000 male inhabitants and 4.8 per 100.000 female inhabitants[26]. The estimated prevalence of CRF in

Table 1. Underlying and associated causes of death due to chronic renal failure according to gender and age in Rio Branco, Acre, Brazil, 1996-2012.

Variable	Underlying cause		Associated cause	
	N	%	N	%
Gender				
Male	72	65.5	214	67.1
Female	38	34.5	105	32.9
Married status [a]				
Single	40	41.2	91	34.5
Married	33	34.0	110	41.7
Widow(er)	19	19.6	45	17.0
Legally separated	05	5.2	18	6.8
Age (years)				
< 39	13	11.9	34	10.6
40 - 59	26	23.6	81	25.4
60 - 79	46	41.8	153	48.0
80 and above	25	22.7	51	16.0
Total	110	100.0	319	100.0

[a] underlying cause N = 97; associated cause N = 264.

Source: Department of Information Technology of SUS (Mortality Information System). http://www.datasus.gov.br, accessed 7 March 2014.

Table 2. Mention of causes referred to as an underlying cause of death in deaths due to chronic renal failure (N = 110)a in Rio Branco, Acre, Brazil, 1996-2012.

Associated causes of death (ICD-10)	N	%
Unspecified septicemia (A41.9)	30	27.3
Endocrine, nutritional and metabolic diseases (E00-E90)	15	13.6
Diseases of the nervous system (G00-G99)	06	5.4
Diseases of the circulatory system (I00-I99)	24	21.8
Diseases of the respiratory tract (J00-J99)	63	57.3
Symptoms, signs, and abnormal findings from clinical and laboratory tests not classified elsewhere (R00-R99)	45	40.9
Other associated causes	28	25.6

[a] Percentages calculated in relation to the number of deaths due to renal failure.

Source: Department of Information Technology of SUS (Mortality Information System). http://www.datasus.gov.br, accessed 7 March 2014.

Table 3. Underlying causes of death when chronic renal failure was referred to as an associated cause in the death certificate in Rio Branco, Acre, Brazil, 1996-2012.

Underlying causes of death (ICD-10)	N	%
Infectious and parasitic diseases (A00-B99)	20	6.3
Neoplasms (C00-D48)	32	10
Endocrine, nutritional and metabolic diseases (E00-E90)	88	27.6
Diseases of the circulatory system (I00-I99)	113	35.4
Diseases of the respiratory system (J00-J99)	29	9.1
Diseases of the digestive system (K00-K93)	15	4.7
Diseases of the genitourinary system (N00-N99) [a]	10	3.1
Other underlying causes	12	3.8
Total	319	100.0

[a] Excluding diagnosis N18 (ICD-10).

Source: Department of Information Technology of SUS (Mortality Information System). http://www.datasus.gov.br, accessed 7 March 2014.

Table 4. Deaths related to renal failure as an associated cause according to the underlying cause of death due to diseases of the circulatory system in Rio Branco, Acre, Brazil, 1996-2012.

Diseases of the circulatory system (I00-I99)	N	%
Hypertensive diseases (I10-I15)	66	58.4
Ischemic heart diseases (I20-I25)	10	8.9
Other forms of heart disease (I30-I52)	17	15.0
Cerebrovascular diseases (I60-I69)	18	15.9
Other diseases of the circulatory system	02	1.8
Total	113	100.0

Source: Department of Information Technology of SUS (Mortality Information System). http://www.datasus.gov.br, accessed 7 March 2014.

Brazil is approximately 503 patients per million inhabitants and the mortality rate tended to fall in 2012[27].

This study found that there was a decreasing trend in CRF mortality rates in the city of Rio Branco. There is a worldwide variation in the mortality behavior of this disease. For example, in the city of Michigan in the USA the mortality rate due to CRF increased from 14.8 per 100,000 inhabitants in 1999 to 15.4 per 100,000 inhabitants in 2005; it was highest among elderly people, reaching 173.6 per 100.000 inhabitants for those aged over 75[28]. In the present study, the highest mortality rates were also found among the elderly.

In a cohort study conducted in the USA (NHANES II) over 16 years of follow-up, it was observed that individuals with CRF had a higher risk of death from all causes of death, with a predominance of cardiovascular diseases[29]. In a study carried out in the Brazilian state of Paraná other causes of death included septicemia, neoplasias and malnutrition[30].

A Brazilian study, which included nationwide data from patients who started renal replacement therapy in 2002 and 2003, and was followed up until 2004, revealed that 42% of patients on peritoneal dialysis and 33% of those on hemodialysis died; these deaths were particularly related to diabetes mellitus and cardiovascular diseases[31]. A further study of mortality due to CRF, which was performed from 2000-2004, found that diabetes and cardiovascular diseases were the main underlying causes of death due to CRF; in the analysis of associated causes of death it was found that 48% of deaths resulted from complications related to treatment, especially infections[32].

In the present study, the main causes of death due to CRF listed in death certificates were diseases of the respiratory tract, followed by poorly defined signs and symptoms, and septicemia. The predisposition of patients with CRF to infections is associated with age, comorbidities, hypoalbuminemia, immunosuppressive therapy, nephrotic syndrome, uremia, anemia and malnutrition. Many of these conditions may be present even before the start of dialysis. Added to these factors are vascular access and the dialysis procedure itself[33].

The main underlying causes of death with CRF as an associated cause were circulatory, endocrine, nutritional and metabolic diseases, with an emphasis on hypertensive diseases and diabetes, which corroborates the findings of other studies[34-39]. In data from 2011, which related to mortality in Australia, CRF accounted for 10% of the multiple causes of death, 39% of which were associated with cardiovascular diseases[40].

CRF promotes the progression of cardiovascular disease through volume expansion, disorders of the calcium-phosphate metabolism, dyslipidemia, and hypertension. On the other hand, cardiovascular disease can promote the decline of renal function due to heart failure and atherosclerosis[41]. In this context, studies on multiple causes of mortality foreground the understanding of CRF, with a view to preventing factors related to death[13]. It should be mentioned that the data presented in the present study refers to individuals with CRF who were, therefore, at a higher risk of death.

The limitations of the present study were the use of a secondary database, which is subject to inaccuracies. To minimize this issue, the rates were calculated to take into account correction for ill-defined and unknown causes of death and for unspecified renal failure. Another possible limitation of this study was the quality of the information that was used, because this depends on the complete and correct completion of death certificates[42]. However, the positive aspects of this study are that it includes an analysis of the

causes of death due to CRF (as an underlying and associated cause), and the possibility of suggesting designs for actions to minimize related complications that result in death in the city of Rio Branco. This contributes to the accumulation of knowledge that supports the adoption of more comprehensive measures that are appropriate to local conditions.

The focus on underlying causes of death, as well as associated causes of death, makes it possible to identify the diseases that participate in the morbid process of death due to CRF. Consequently, understanding the temporal evolution and the causes involved in the death process makes it possible to assess the public health problem constituted by chronic renal failure.

It was concluded that there was a reduction in mortality due to CRF in Rio Branco in the studied period, with the greatest decrease found to be among those aged over 50 and among women. The deaths caused by the CRF presented respiratory diseases, including pneumonia and pulmonary edema, as well as abnormal findings and septicemia as causes of death. When CRF was analyzed as an associated cause of death the most frequent main causes of death were hypertensive diseases and diabetes.

Collaborations

TLM Amaral, CA Amaral and AL Miranda Filho contributed to the design of the research project, collecting, processing, analyzing, interpreting data and writing the manuscript; GTR Monteiro, participated in the analysis and interpretation of the data, critical review and approval of the final version of the manuscript.

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