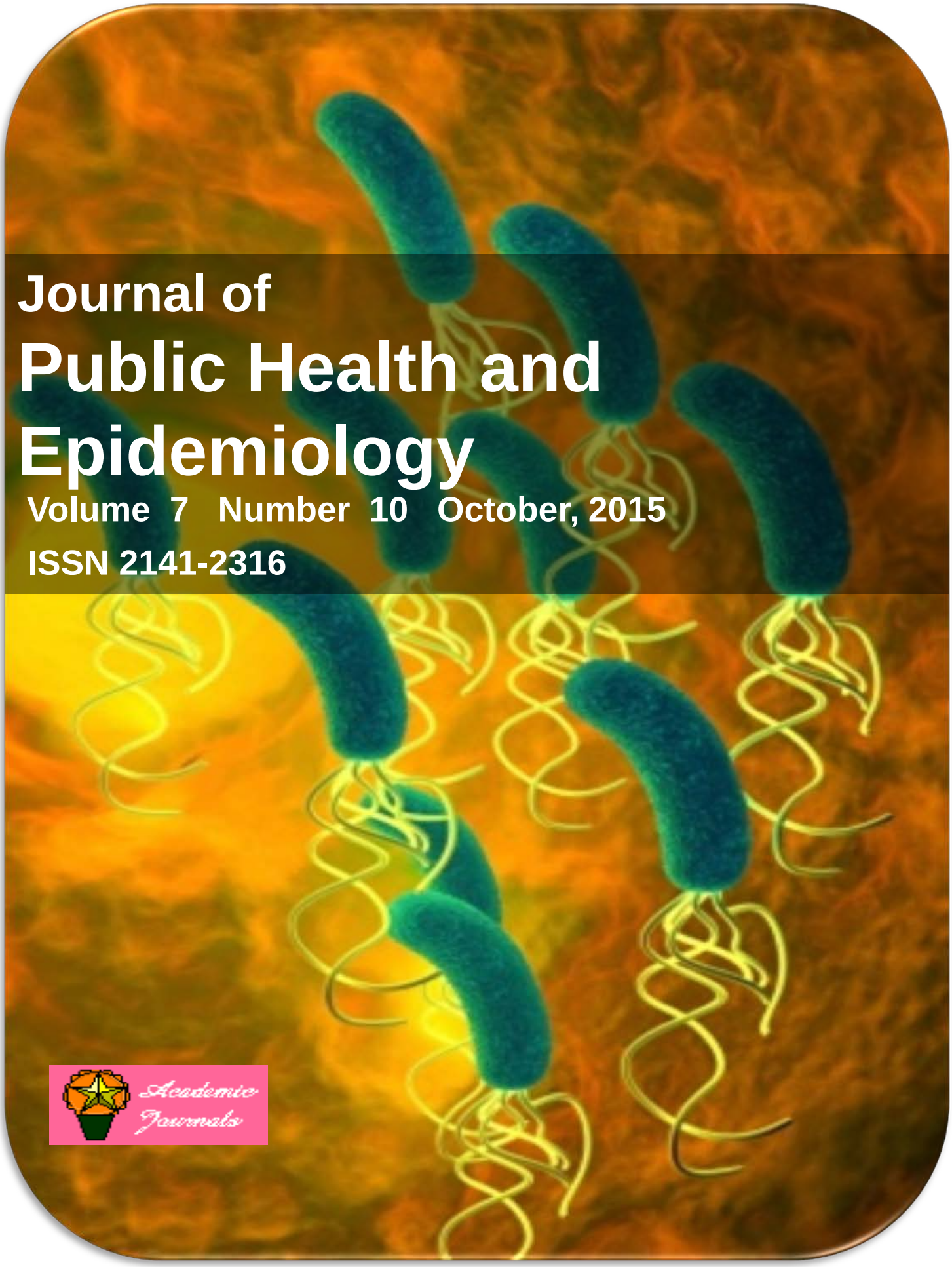

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Pitout JDD, Church DL, Gregson DB, Chow BL, McCracken M, Mulvey M, Laupland KB (2007). Molecular epidemiology of CTXM-producing Escherichia coli in the Calgary Health Region: emergence of CTX-M-15-producing isolates. Antimicrob. Agents Chemother. 51: 1281-1286.

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Full Length Research Paper

Impact of multidisciplinary care in amyotrophic lateral sclerosis hospitalizations in the public health system of Brazil

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There is evidence that multidisciplinary care improves quality of life and there is a growing appreciation of public policies in Brazil that favor home care with a multidisciplinary team in chronic diseases. This study aimed to determine the epidemiological profile of amyotrophic lateral sclerosis in the Federal District and the impact of tertiary reference center creation on patient care. A descriptive, cross-sectional study analyzing secondary data regarding mortality and hospitalizations for amyotrophic lateral sclerosis patients over 10 years and clinical and epidemiological profiles of patients evaluated at the Center of Reference for Neuromuscular Disease over three years was used. An incidence rate of 1.3/100,000 person-years over 20 years and an age at onset of 49.3 ± 15.1 years (Hospital Information System) and 57.2 ± 12.3 years (at the Center admission) was observed. The risk of death was greater in patients older than 75 years (RR = 4.05, p = 0.0018) and in bulbar-onset patients (RR = 2.53, p = 0.0027). Multidisciplinary care reduced 75% of hospitalization frequency and length of stay (p = 0.03) and 80 to 90% of the reimbursement value of hospitalization (p = 0.05). The adoption of multidisciplinary care has improved the efficiency of patient care for amyotrophic lateral sclerosis in the Brazilian public health system.

Key words: Amyotrophic lateral sclerosis, multidisciplinary care, public health.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) has an average worldwide incidence of 2.08/ 100,000 person-years (Chiò et al., 2013) and is a disease of unknown etiology that leads to motor disability, speech disorders, dysphagia and respiratory failure. The median survival time ranges from 24 to 48 months (Turner et al., 2013; Forbes et al., 2004). In the last twenty years, numerous clinical trials with drugs and cell therapies have been conducted, but only Riluzole has shown efficacy in slowing the progression of symptoms (Hardiman et al., 2011). Since

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1989, there is a large body evidence that shows multidisciplinary care improves quality of life, but there is still doubt as to if it increases survival time (Andersen et al., 2012, Miller et al., 1999). In European countries, this is well established; however, there is lack of evidence on the impact of the multidisciplinary treatment of ALS in Latin America, especially in relation to the public health system of Brazil. There is currently a growing appreciation of public policies in Brazil that favor home care with a multidisciplinary team in non-specific chronic diseases (Leopoldina et al., 2015). The objective of this study was to determine the incidence of ALS, the epidemiological and clinical profiles of patients and their survival at three years of follow-up, analyzing the efficiency of a tertiary Reference Center for Neuromuscular Diseases (CRDN) in the Public Health System (SUS) in the Federal District, Brazil.

METHODOLOGY

In September, 2011, the CRDN was created; a multidisciplinary unit composed of Medical Neurologists, Pulmonologists, Physical Therapists, Occupational therapists, Psychologists, Nutritionists and Speech Therapists. The goals included: guiding patients and their families; reducing complications of immobility, dysphagia and respiratory failure; implementing the home ventilation program; and giving support to professionals of the home care program (PID). In April, 2013, the Secretariat of Health of Federal District (SES-DF) approved a dehospitalization protocol and started hiring home care, restricting the length of hospitalization of chronic patients in the ICU. A cross-sectional, descriptive study was performed, using three data sources:

1. Mortality data were obtained using the TabWin application from the mortality information system (MIS) of the Federal District, Brazil, between January, 2005 and December, 2014, to estimate the incidence of disease. We used the 2010 Census (IBGE, 2014) for calculating incidence.
2. Admissions data were obtained using the TabWin application from the reduced hospitalar information system (HIS) of the Federal District, between January, 2005 and December, 2014, related to hospital admissions in the SUS.
3. Records from the CRDN at the Secretariat of Health of the Federal District (SES-DF) were analized through the TrakCare software application, with data obtained between September, 2011 and December, 2014. Probable and defined ALS with diagnosis performed by neurologists using El Escorial criteria (Ludolph et al., 2015) after exclusion of other diseases were included. All patients used Riluzole and underwent electromyography.

The following parameters were analyzed: Disease frequency, gender distribution, site of onset, age, diagnostic delay time, duration of disease, electromyography confirming the diagnosis, frequency and length of stay, reimbursements of hospital admission authorizations (AIH), use of the intensive care unit (ICU) in the SUS, and use of domiciliary mechanical ventilation.

The disease duration was defined as the time period between the first symptom and death or tracheostomy (in days). Efficiency measures were frequency, length of stay, reimbursement of AIH and ICU costs. Data were recorded in Excel 2010 and statistical analyses was performed using SAS 9.3 and SPSS 19.0 applications. Chi-square test was used for categorical variables and the two-tailed Student's t-test for quantitative variables, with a 0.05 significance level. Multivariate analyses of survival including all clinical variables was conducted. Initially, Cox regression univariate analysis with $p < 0.25$ was selected for inclusion in the multivariate Cox regression analysis. The final multivariate regression model was built by successive exclusion variable-to-variable from the initial multivariate model, using the likelihood ratio test to determine the importance of each variable excluded (Collett, 2003). The level of significance was 0.05. The survival functions for the patients were estimated using the Kaplan-Meier method and compared using the log-rank test.

This study protocol was approved by the Ethics Committee of the Research and Education Foundation in Health Sciences – (FEPECS/SES, number 820 117/2014 Protocol). The Ethics Committee waived the written consent form because the study consisted of analysis of patient records (many of them were deceased) and public domain databases.

RESULTS

To estimate the regional incidence of ALS in ten years, we used mortality data (MIS). Between 2005 and 2014, the MIS of the Federal District recorded 162 deaths above 20 years of age: 93 men and 69 women with mean ages of 61.5 ± 12.6 years and 65.1 ± 12.2 years, respectively, which was not significantly different ($p = 0.059$). So, the adjusted incidence of the disease above 20 years of age was estimated in 1.3/100,000 person-years and 2.6/100,000 person-years, adjusted above 45 years of age, considering the population of 2,570,160 inhabitants, according to the 2010 Census of the Brazilian Institute of Geography and Statistics – IBGE (IBGE, 2014). It was observed that 97 (59.9%) deaths occurred between 60 and 79 years of age (data not shown). In the same 10-year period, the HIS recorded 172 hospitalar admissions with the same diagnosis: 103 men and 69 women, with a mean age of 49.3 ± 15.1 years. In females, the average age was 45.6 ± 13.9 years, significantly lower than the average male age of 51.7 ± 15.4 years ($p = 0.01$).

Figure 1 compares the ALS incidence mortality-based with the hospitalar admissions and shows that the frequency of ALS hospitalization has fallen by 75% between 2012 and 2014, while the incidence based on mortality was sustained. Between 2005 and 2011, the average annual rate of hospitalizations was 21.6 ± 5.6 hospitalizations/year (range: 15 to 27). Between 2012 and 2014, this average dropped to 7 ± 1.7 admissions per year, with a range of 5 to 8 ($p = 0.03$). The average length for an in-hospitalar stay was 17.1 ± 3.2 days in the first period and 15.0 ± 2.5 days in the second, which was not significant ($p = 0.48$).

Table 1 shows the annual change in frequency, length of stay and reimbursement amounts to the AIH, and amounts transferred by the SUS for ICU spending. It was observed that the higher frequency of hospitalizations occurred in the years 2009, 2007 and 2005 and there was a sharp decline between the years 2012 and 2014. Although the average length of stay did not show significant variation, the total days of hospitalization

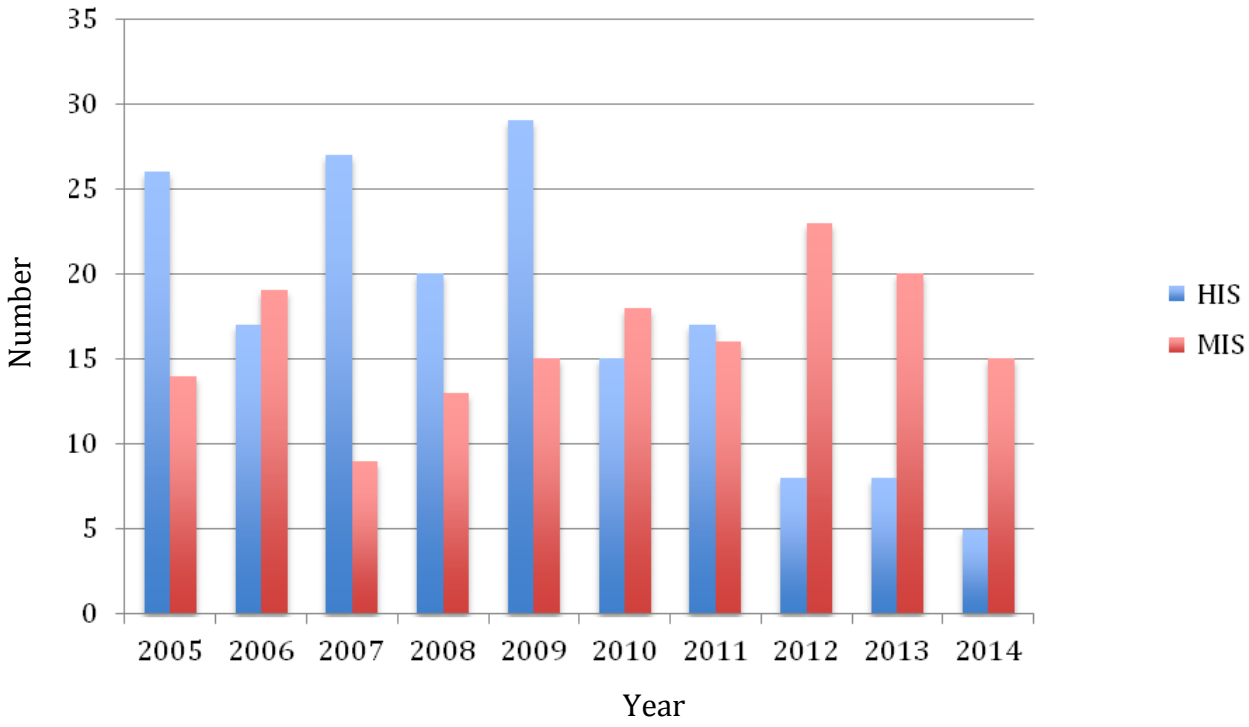

Figure 1. Correlation between mortality (MIS) and frequency of admissions (HIS) in Distrito Federal due to amyotrophic lateral sclerosis. Period: 2005 to 2014.

Table 1. Frequency, length of stay and reimbursement of hospitalization in Motor Neuron Disease in SUS of Distrito Federal, Brazil. Period: 2005 to 2014.

Year	N	length of stay (avg) days	SD	Length of stay (sum)	ICU (ammount R$)	ICU (avg R$)	AIH (avg R$)	AIH (total ammount R$)
2005	26	15.3	18.4	399	10,089	388	1,031	26,826
2006	17	17.8	23.6	303	0	0	602	10,250
2007	27	11.8	11.1	320	0	0	588	15,897
2008	20	15.4	12.8	309	0	0	628	12,571
2009	29	17.4	18.2	504	0	0	562	16,313
2010	15	20	23.2	300	14,361	957	1,645	24,681
2011	17	21.7	28	369	44,042	2,590	3,113	52,921
2012	8	16	10.9	128	0	0	646	5,173
2013	8	12,7	18,7	102	0	0	355	2,841
2014	5	17,8	10,6	89	0	0	447	2,236
Total	172	-	-	2,823	68,492	-	-	169,712

followed the 75% drop observed in frequency (p = 0.03). The total SUS spending on AIH reimbursement also suffered a sharp decline, reaching 80 to 90% of all median and initial totals (Table 1). In 2005, the average cost per patient was R$1,031, and the total sum was R$ 26,826. In 2014, a drop in AIH reimbursement was observed, with an average of R$447 (p = 0.26), and a total of R$2,236. If we compare the period until 2011, the mean total AIH reimbursement was 22,780 ± 14,599 and the mean cost of the second period (2012 to 2014) was 3,416 ± 1,550 (p = 0,05). With regard to gender, there was no significant difference between spending with AIH (p = 0.79) or with ICU use (p = 0.81).

The period between September, 2011 and 2014 was evaluated in the CRDN and included 135 patients with probable or definite diagnosis of the disease. There were 78 (57.8%) men and 57 (42.2%) women, with male-female ratio of 1.4:1. The mean age was 57.2 ± 12.3 years, ranging from 25 to 86 years. The average age was 56.3 ± 12.3 years in males and 58.6 ± 12.3 years in females, with no difference between the sexes (p = 0.179).

Table 2. Patients profile at CRDN (Period: sep 2011 - dec 2014)*El Escorial Classification of ALS patients on admission . NIV: Non-invasive ventilation; IV: invasive ventilation; NV: no ventilation.

Parameter	Onset N (%)			
	Bulbar	Leg	Arm	Total
Possible*	8(24.2)	12(36.4)	12(39.4)	33(24.5)
Definite*	12(15.2)	28(35.4)	39(49.4)	79(58.5)
Probable*	1(7.1)	5(42.9)	7(50)	13(9.6)
Suspect*	5(50)	2(20)	3(30)	10(7.4)
NIV	3(14.3)	8(38.1)	10(47.6)	21(15.5)
IV	3(25)	1(8)	8(67)	12(8.9)
NV	20(19.6)	40(39.2)	42(41.2)	102(75.6)
Total	26(19.1)	48(35.3)	61(45.6)	135(100)

The distribution of patients on admission to the CRDN according to the El Escorial criteria is presented in Table 2. It was observed that 79 patients (58.5%) had a definite form of the disease and in 61 patients (45.6%) the site of onset was in the upper limb. Additionally, according to Table 2, 92 (68.1%) patients had diagnostic confirmation at admission (definite and probable forms), whereas in 43 (31.9%) of them, the diagnosis was confirmed during follow-up. The median time to diagnosis from the first symptoms was 22.7 months in men and 23.5 months in women. Table 2 also shows the frequency of home mechanical ventilation use. It was observed that a majority 102 (75.6%) of the patients did not use mechanical ventilation, while 21 (15.5%) patients used non-invasive ventilation and only 12 (8.9%) used invasive ventilation by tracheostomy. There was no statistically significant difference between the use of ventilation and the form of onset.

Electroneuromyography helped confirm the diagnosis in 119 patients (88.1%), but in cases initially classified as suspected disease, the exam failed in 5 patients (50%). In patients with bulbar-onset, the exam was negative in 4 patients (15.4%) and in those with upper limb-onset, it failed in 10 patients (16.9%). All patients received guidelines from the multidisciplinary team in at least two consultations, with a range of three to four months. Thirty-six patients (26.5%) received between 3 and 6 consultations.

Figure 2 shows the survival curve of patients according to age. In the log-rank test, a survival curve of an age group that differs from the others ($p = 0.0043$) was observed. With the Bonferroni adjustment, it was noted that the survival time for patients aged below 50 years was significantly higher than the survival time for patients over 75 years. For patients younger than 50 years old, approximately 83% were still alive one year after the start of follow-up, while only 22% of patients over 75 years of age were still alive.

Table 3 shows the clinical features associated with lower survival in the group over 75 years of age. When analyzing the unadjusted hazard ratio, the following variables were not statistically significant and were excluded: sex, pyramidal syndrome, dementia, smoking, alcohol consumption, use of pesticides, heavy metals, clinical and diagnosis of ALS (data not shown). The multivariate Cox regression model showed that only the age of onset and shape were significant risk factors for survival time. The risk of death among patients older than 75 years was approximately four times higher ($RR = 4.05$, $p = 0.0018$) than among patients younger than 50 years. However, the risk of death in patients in the age groups 51 to 60 and 61 to 75 years did not differ significantly compared to patients younger than 50 years. The risk of death for patients with the early bulbar form of ALS was approximately two and a half times ($RR = 2.53$, $p = 0.0027$) that of patients with the early spinal form of ALS.

DISCUSSION

Estimating disease incidence is important for determining the size of public health services. Prospective epidemiological studies based on case records associated with the use of secondary databases, such as mortality, using capture-recapture techniques are the ideal approach (Bresch et al., 2014; Chiò et al., 2013). However, the record of incident cases requires the existence of reference centers with the formation of a registration basis. In the absence of such, mortality data was used, which produced an incidence rate of the disease at 1.3/100,000 person-years over 20 years of age and 2.6/100,000 person-years over 45 years of age, which were similar to other studies (Chiò et al., 2013). The use of adjusted rates by age is necessary because the incidence of ALS is more common over 45 years of age and because approximately 38% of the inhabitants of the Federal District are under 20 years of age (IBGE, 2014). Mean age at hospitalization (49.3 ± 15.1 years), at death by disease (61.5 ± 12.6) and at admission to the Reference Center (57.2 ± 12.3 years) were significantly lower than the average age of onset of the disease observed in European countries, which is between 61 and 66.2 years (Chiò et al., 2009). These findings are corroborated by other studies in Latin American

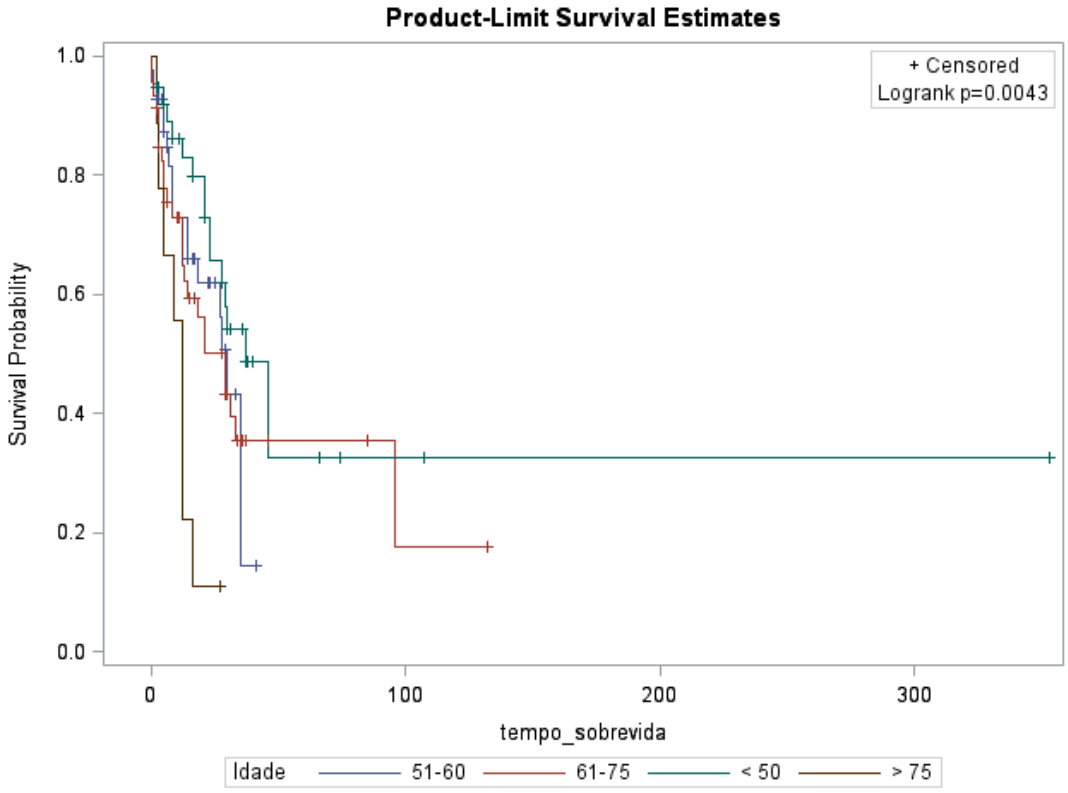

Figure 2. Survival Kaplan Meier Analysis of 135 ALS patients evaluated in CRDN according to age of onset. Period: September, 2011 to December, 2014.

Table 3. Crude and adjusted Risk Ratio for survival in Amyotrophic Lateral Sclerosis, by clinical selected variables in patients under multidisciplinar care and Riluzole. Period: set 2011 - dez 2014 [a] Adjusted for age and site of onset.

Parameter	Risk ratio - RR (CI 95 %)			
	Crude (CI)	p-value	Adjusted[a] (CI)	p-value
Age (years)		0.0212		0.0135
≤ 50	1	-	1	-
51 - 60	1.54(0.78 – 3.02)	0.2129	1.21(0.60 – 2.44)	0.4854
61 – 75	1.60(0.86 – 2.96)	0.1383	1.54(0.81 – 2.91)	0.188
> 75	4.48(1.88 – 10.72)	0.0007	4.05(1.69 – 9.75)	0.0018
Onset	-	0.0052	-	0.0027
Spinal	1	-	1	-
Leg	1	-	1	-
Arm	1.08(0.62 – 1.87)	0.7935	1.25(0.69 – 2.27)	0.4615
Bulbar	2.43(1.36 – 4.33)	0.0052	2.53(1.38– 5.62)	0.0027
Diagnostic delay time (months)	-	0.0334	-	-
≤ 12	2.11(1.12 – 3.96)	0.0205	-	-
13 - 24	1.96(1.05 – 3.66)	0.034	-	-
> 24	1	-	-	-

populations (Valenzuela et al., 2015; Vázquez et al., 2008; Zaldivar et al., 2009).

The frequency of hospitalizations from disease has fallen by 75% between 2012 and 2014, after the creation of CRDN, despite the increased incidence-based mortality rate from the disease. There are studies showing improved quality of life (Andersen et al., 2012; Miller et al., 1999; Traynor et al., 2003) from over the past decade, but it is still uncertain whether there is increased survival (Aridegbe et al., 2013; de Rivera et al., 2011) of

ALS patients with the multidisciplinary care. This includes physical and occupational therapy to preserve patient autonomy, respiratory therapy for elimination of airway secretions and strengthening cough, nutritional support and speech therapy associated with assistive technologies (Andersen et al., 2012; Miller et al., 1999; Venkova-Hristova et al., 2012).

Regarding the length of stay, the global average length of stay was 16.4 ± 18.4 days, with no significant change during the study period. Hospitalizations should be avoided whenever possible because both higher frequency and longer durations predispose the patient to increased risk of infections and greater immobility, contributing to increased risk of respiratory complications (Miller et al., 1999). It was also observed that there were reduced financial expenses with hospitalizations as a decline in AIH reimbursements, which were reduced in their average sum, reaching approximately 10 to 20% of the initial average and total value, according to Table 2. Evaluating the AIH reimbursement may be useful and has been used as an indirect measure of cost in Brazilian public health system, although it does not take into account the total direct and indirect costs of a health system (Bertó and Beulke, 2012), only the monetary reimbursement made by SUS.

The risk of death among patients older than 75 years was approximately four times higher (RR = 4.05, p = 0.0018) than among patients younger than 50 years. The risk of death for patients with the early bulbar form was approximately two and a half times (RR = 2.53, p = 0.0027) that of patients with early spinal form (Table 4). These findings are consistent with other studies (Aridegbe et al., 2013; Turner et al., 2010). The ALS practice parameter of the American Academy of Neurology (AAN) recommended that, at an early stage of the disease, patients be sent to a multidisciplinary specialized center to assess their individual needs and to focus on their quality of life (Miller et al., 1999). The time from diagnosis to referral for the CRDN was long (22.7 months in men and 23.5 months in women), surpassing the time described in European studies, where the average time to diagnosis was approximately 10 months (Chiò et al., 2009). There is great discussion about the adoption of the criteria El Escorial and Awaji in electroneuromyography for the diagnosis of ALS (Carvalho and Swash, 2009; Ludolph et al., 2015). In cases initially classified as suspect and bulbar-onset, the exam did not help the diagnosis in 50 and 15.4% of cases, respectively, despite incorporating the Awaji criteria. This is confirmed by other studies showing, primarily in the bulbar form, that the procedure has a sensitivity of 16 to 19.5% (Bresch et al., 2014; Okita et al., 2011). In patients without diagnostic confirmation, follow-up in a specialized center has the objective of assisting with further diagnostic confirmation, based on clinical evolution, without delaying the introduction of multidisciplinary care.

A study conducted in England in 2012 with Cox regression in 437 patients with ALS showed that follow-up in specialized reference centers in relation to general outpatient care is an independent positive predictive factor for improved survival (HR 1.93, 95% CI 1.37 to 2.72, p = 0.001) (Aridebge et al., 2012). Another study conducted in Madrid claims that the specialized centers increase survival even in the bulbar-onset form because the treatment is provided early. Other recent European studies corroborate these findings (Chiò et al., 2006, Miller et al., 2009, Pouget, 2013; de Rivera et al., 2011; Traynor et al., 2003). In Barcelona, the program for the treatment of ALS adds multidisciplinary teams to home care teams, considering the evolution of the disease, because of increased difficulties in walking to specialized centers (Guell et al., 2013). In recent years, there has been significant growth in the scope of home care teams in the Federal District, which enabled this joint action (Leopoldina et al., 2015).

Despite several clinical trials of drugs and cell therapy, ALS remains an incurable disease (Hardiman et al., 2011). Respiratory failure is the natural course of the disease and advocates for the use of Non-Invasive Ventilation (NIV) (Andersen et al., 2012; Miller et al., 1999). In July, 2008, the Ordinance of the Brazilian Ministry of Health (Brasil, 2008), recognizing the need for deinstitutionalization of patients, established the Program of Noninvasive Ventilator Assistance to Neuromuscular Disease Carriers, but did not create sources of funding for it.

Invasive ventilation by tracheostomy is always a second choice and must be requested by the patient, except for young patients with the early bulbar form of disease and inability to use NIV (Heritier et al., 2013). A study conducted in Italy (Volanti et al., 2011) with 44 patients with ALS showed that there are difficulties in the acceptance and adaptation of NIV equipment, which make its use difficult, but it can be overcome by intensive training in multidisciplinary centers.

It was observed that there was a low frequency of use of home mechanical ventilation in this study, with 15.5% of patients using NIV and 8.9% using invasive ventilation by tracheostomy. In 2009, an extensive study conducted with ALS CARE database involving 5,600 patients in North America between 1997 and 2004 found that only 21% of patients used NIV (Miller et al., 1999). More recent studies from multidisciplinary and well-established centers showed greater adherence to the use of NIV, reaching 64.28% in early bulbar forms and 35.71 to 79% in the early spinal forms (Heritier et al., 2013; de Rivera et al., 2011; Volanti et al., 2011).

Conclusion

The incidence rates of ALS in the Federal District population was 1.3/100,000 person-years, adjusted for

the population aged over 20 and 2.6/100,000 person-years for the population over 45. Treatment by a multidisciplinary team showed increased efficiency with reduced hospitalization rates, length of stay and AIH reimbursement. Thus, under the public health systems, the adoption of a comprehensive national public care policy for patients with ALS is suggested along with the creation of multidisciplinary reference centers combined with a deinstitutionalization policy of the Home Care Program (PID) and Non-Invasive Ventilation Program Homecare.

Conflict of interest

The authors declare no conflicts of interest and use of Sources of Funding Statement. There were no sponsors in study design, collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

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Full Length Research Paper

Risk factors, electrolyte disturbances and lipid profiles in sudanese patients with stroke

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Stroke is a growing public health concern in low- and middle- income countries, however no systematic study has been conducted to elucidate possible causes of stroke among most low- and middle- income countries. The aim of the study was to determine the prevalence of stroke, associated risk factors, electrolyte disturbances and lipid profiles in Sudanese stroke patients. A retrospective hospital-based study was conducted for 188 stroke patients. A 59.6% of patients are males and 40.4% are females, 42.55% of their age ranged between 41 to 60 years, with mortality rate 17.02%. A 78.2% of patients had ischemic infarction and 21.8% had hemorrhage. Predisposing factors for the development of stroke was hypertension 43.6%, diabetes mellitus16.5%, heart disease 4.3%, smoking 3.7% and alcohol consumption 3.7%. Stroke patients had strong family history of hypertension 12.23%, diabetes mellitus 10.11%, stroke 3.72% and heart diseases 1.10%. The electrolyte disturbances and lipid profiles showed a significant different (P<0.05) between males and females in hemoglobin (HB), hematocrit (HCT), cholesterol and low density lipoprotein (LDL) levels, and a significant different (P<0.05) between ischemic and hemorrhage stroke in platelets (PLTs), potassium and HDL levels. Our results confirm a high prevalence of risk factors for stroke, and a better understanding of stroke risk factors and outcome may help guide efforts at reducing the community burden of stroke in Sudan.

Key words: Stroke subtypes, risk factors, lipid profiles, Sudan.

INTRODUCTION

Stroke is the second killer in the world, with 6.2 million deaths representing 11.4% of the 54.6 deaths that occurred in 2011 (Boutayeb et al., 2014). Worldwide, stroke incidence showed a divergent trend rates during the last four decades (Boutayeb et al., 2014). While stroke incidence decreased by 42% in high-income countries, it increased by more than 100% in low to middle income countries (Feigin et al., 2009). Differences in burden due to stroke were existing within countries where the incidence and mortality rates vary across

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socioeconomic groups. Studies in Western countries have demonstrated a significant positive association between socioeconomic disadvantage and the incidence and mortality due to stroke (Kaplan and Keil, 1993; Cox et al., 2006). Few studies available in developing countries show various patterns, as the social gradient for risk factors leading to stroke may change over time (Engels et al., 2014). In UK, the costs of stroke are estimated to be nearly twice those of coronary heart disease (Rothwell, 2001), accounting 6% of total National Health Service (NHS) and Social Services expenditure (Rothwell, 2001). Among the Asians, the number who died from stroke was more than three times that for coronary heart disease (CHD) (WHO, 1994). In India, stroke represented 1.2% of the total deaths, when all ages were included (Anand et al., 2001).

The epidemiology of stroke in the Middle East and North Africa reported an extensive variation of incidence between different countries (Boutayeb et al., 2014). In African region, more than 1.1 million deaths were caused by cardiovascular diseases and more than half of these were due to ischaemic heart disease and stroke (Laurence et al., 2011). During the period, 1980 to 2007, the age standardized incidence rate of stroke (per 100000) in Saudi Arabia, Iran, Palestine, Kuwait, Bahrain, Libya and Qatar was 38.5, 61.5, 62.7, 92.2, 96.2, 114.2 and 123.7, respectively (Tran et al., 2010). Some developed countries such as the United States, Canada, France, Switzerland, and Australia have experienced declines in mortality, which may be associated with the increased use of preventative treatment, better control of vascular risk factors, and the advances in acute stroke care (Sun et al., 2013).

There are racial and social differences in susceptibility to stroke and in the incidence of the various stroke subtypes. Some of these racial differences are partly caused by differences in risk factor prevalence (Forouhi and Sattar, 2006). In some developed countries, up to 67.3 to 80.5% of stroke cases are attributed to ischemic stroke, whereas only 6.5 to 19.6% are attributed to intracerebral hemorrhage; approximately 0.8 to 7.0% to subarachnoid hemorrhage; and 2.0 to 4.5%, to undetermined types (Feigin et al., 2003). The international prospective epidemiological studies identified the major atherogenic risk factors for stroke as hypertension, diabetes mellitus, hyperlipidemia, and smoking (Wolf, 2004). Fuster and Kelly (2010) indicated that the risk of coronary heart disease and ischaemic stroke increases steadily with overweight/obesity and there is a continuous relationship between blood pressure and the risk of developing heart attacks and stroke. In China, the risk from major stroke factors, including obesity and hypercholesterolemia, has substantially increased (Sun et al., 2013). The rural Japanese prospective studies showed that low total serum cholesterol was related to increased incidence of cerebral hemorrhage (Yano et al., 1989). In Morocco, there was a significant association between household socioeconomic status and the prevalence of stroke (Engels et al., 2014). Electrolyte disturbances are also commonly found in stroke cases and may contribute to mortality of these patients. Kusuda et al. (1989) noted that disorders of sodium and potassium concentration are the commonest electrolyte abnormalities found in stroke patients. Thus, early diagnosis of electrolyte disturbances is essential to prevent morbidity and mortality of Cerebral Vascular Accident (CVA) patients to a large extent (Roy et al., 2014). Studies describing these electrolyte disturbances in stroke patients are rare in Sudan. Therefore, the aim of the present study was to determine the frequency of stroke sub types, associated risk factors, electrolyte disturbances and lipid profiles in Sudanese stroke patients.

MATERIALS AND METHODS

Study design and data collection

A retrospective study of 188 stroke patients admitted to the Soba University Hospital, Sudan was conducted using medical history records during the period of January, 2012 through December, 2013. The diagnosis of stroke was established if patients were already treated with stroke drugs or were diagnosed during their hospital stay. We selected only treated stroke patients who had a record of continued medication in their medical records since being diagnosed with stroke, any other diseases subsequent to stroke onset was included. The data taken from each patient records included demographic data, clinical characteristics of stroke (ischemic or hemorrhagic), occurrence of in-hospital death and stroke risk factors that is, hypertension, diabetes mellitus, dyslipidemia, cardiac disease, smoking status, and previous history of stroke. Biochemical variables presented with stroke including electrolyte disturbances, plasma glucose, serum urea and creatinine, total cholesterol (TC), triglycerides (TG), and high density lipoprotein-cholesterol (HDL-C). Low density lipoprotein cholesterol (LDL-C) was calculated by Friedewald's equation. Ethical approval was received from the local ethics committee prior to the start of the study.

Statistical analysis

Results are given as means ± standard error for continuous variables and number, and percentage for categorical variables. The chi-square test or Fisher's exact test was used for categorical variables and the Students t-test for continuous variables. Statistical analyses were performed using SPSS v.18 (SPSS, Chicago, Illinois, USA) and a p value less than 0.05 was considered significant.

RESULTS

Risk factors of stroke

A total of 188 patients admitted to the Soba University

Table 1. Distribution of Stroke Subtypes and associated risk factors.

Factors	Frequency	Percent (%)
Sex		
Male	112	59.6
Female	76	40.4
Stroke type		
Ischemic	147	78.2
Hemorrhage	41	21.8
Side weakness		
Right	109	58
Left	79	42
Risk factors		
Hypertension	82	43.6
Heart disease	8	4.3
Diabetes Mellitus	31	16.5
Smoking	7	3.7
Alcohol	7	3.7
Family history		
Hypertension	23	12.23
Diabetes mellitus	19	10.11
Stroke	7	3.72
Heart disease	2	1.10

Hospital were studied, 59.6% are males and 40.4% are females. Approximately 78.2% of the patients had ischemic infarction and 21.8% of the patients had hemorrhage, representing 58% right side weakness and 42% left side weakness, while 17.02% of patients were dead. Age, hypertension, diabetes mellitus, hyperlpidemia, obesity and heart disease are known predisposing factors for the development of stroke. In the present study, 43.6% of stroke patients had hypertension, 16.5% had diabetes mellitus and 4.3% had heart disease. Smoking and alcohol consumption are very low among patients represented by 3.7 and 3.7%, respectively. The patients had strong family history of the factors for the development of stroke, 12.23% had hypertension, 10.11% had diabetes mellitus, 3.72% had stroke and 1.10% had heart diseases (Table 1). The common affected age group was between 41 and 60 years (42.55%), followed by age group 61 and 80 (40.96%) (Figure 1).

Hematological, serum urea, ceartinine and electrolyte levels in stroke patients

Serum electrolyte analysis should be a part of initial evaluation in all stroke patients, there were significant difference ($P < 0.05$) between males and females in HB and HCT levels, whereas there was a significant difference ($P < 0.05$) between ischemic and hemorrhage stroke in PLTs level (Table 2). Sex has no significant effect on serum urea, creatinine, sodium and potassium levels in patients with stroke. However, there was a significant difference ($P < 0.05$) on potassium levels in patients with ischemic and hemorrhage stroke (Table 3).

Lipid profiles in stroke patients

Cholesterol and LDL level were significantly ($P < 0.05$) different between males and females, while HDL level was significantly ($P < 0.05$) different between patient with ischemic and hemorrhage stroke (Table 4).

DISCUSSION

Cardiovascular diseases caused 17.3 million deaths in 2008 and this number is expected to reach 23.3 million by 2030 (Boutayeb et al., 2014). The incidence of stroke has reached an epidemic level in low to middle income countries (Feigin et al., 2009). Engels et al. (2014) indicate the increase in mortality due to stroke is expected to be faster in low income and middle-income countries than in high-income countries, as a result of the

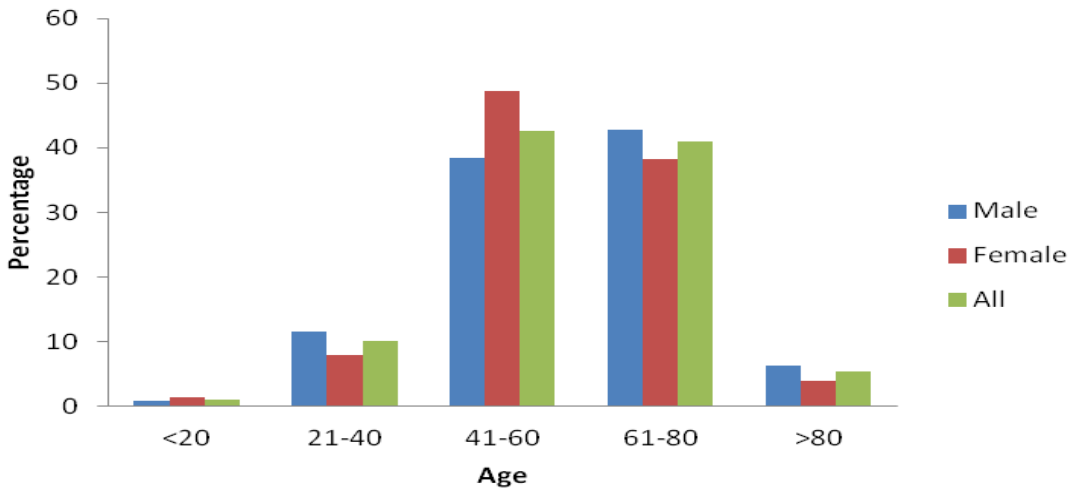

Figure 1. Age distribution of the patients with stroke.

Table 2. Hematological parameters in the patients with stroke.

Items	Over all	Sex			Stroke type		
		Male (n=64)	Female (n=51)	P value	Ischemic (n=87)	Hemorrhage (n=28)	P value
TWBCs	8.51±0.39	7.88±0.49	9.15±0.62	0.110	8.96±0.38	8.07±0.69	0.258
HB	12.51±0.29	13.10±0.36	11.92±0.45	0.043	12.36±0.28	12.66±0.51	0.604
HCT	37.98±0.84	39.96±1.04	36.00±1.32	0.020	37.43±0.80	38.53±1.47	0.510
MCV	84.66±1.01	83.36±1.26	85.95±1.59	0.205	83.78±0.97	85.53±1.78	0.390
MCH	27.74±0.35	27.71±0.44	27.77±0.55	0.919	27.69±0.34	27.78±0.62	0.894
MCHC	32.56±0.25	32.86±0.31	32.26±0.39	0.228	32.50±0.24	32.62±0.43	0.807
PLTs	242.43±13.55	230.59±16.77	254.27±21.28	0.384	275.28±12.96	209.58±23.79	0.017

Total white blood cells (TWBCs); Haemoglobin (HB); Mean Corpuscular Volume or Cell (MCV); Mean Corpuscular Haemoglobin (MCH); Mean Corpuscular Haemoglobin Concentration (MCHC); Platelets (PLTs)

Table 3. Serum urea, creatinine and electrolyte levels in the patients with stroke.

Items	Over all	Sex			Stroke type		
		Male (n=68)	Female (n=53)	P value	Ischemic (n=91)	Hemorrhage (n=30)	P value
Urea	50.15±5.91	49.93±7.14	50.37±9.42	0.970	53.14±5.63	47.16±10.39	0.613
Creatinine	1.51±0.28	1.51±0.33	1.51±0.44	0.999	1.81±0.26	1.21±0.48	0.275
Serum Na	138.04±0.87	136.72±1.05	139.37±1.38	0.130	138.37±0.83	137.72±1.53	0.711
Serum K	3.56±0.09	3.62±0.12	3.50±0.14	0.517	3.74±0.08	3.38±0.15	0.040

Urea mg/dl; creatinine mg/dl; Serum Na and K meq/l

increasing prevalence of risk factors (due to both an ageing population and changes in lifestyle) and lesser availability of primary prevention and acute care programs (Paul et al., 2007; Strong et al., 2007; Addo et al., 2012). A systematic review of population-based studies carried out from 1970 to 2008 showed a 42% decrease in incidence of stroke in high-income countries, as compared to a more than 100% increase in incidence in low and middle-income countries (Johnston et al., 2009).

Table 4. Lipid profiles in the patients with stroke.

Items (mg/dl)	Over all	Sex			Stroke type		
		Male (n=17)	Female (n=5)	P value	Ischemic (n=18)	Hemorrhage (n=4)	P value
Cholesterol	171.867±9.61	151.82±12.22	191.92±14.82	0.051	161.73±10.27	182.00±16.24	0.305
Triglyceride	86.275±12.93	76.22±16.46	96.33±19.96	0.447	97.80±13.83	74.75±21.86	0.385
HDL	56.928±3.70	60.86±4.71	53.00±5.71	0.303	43.61±3.96	70.25±6.26	0.002
LDL	77.550±7.51	52.27±9.56	102.83±11.59	0.003	82.10±8.03	73.00±12.69	0.552

HDL, high density lipoprotein; LDL, low density lipoprotein.

In the present study, 59.6% of stroke patients are males and 40.4% are females, and 78.2% of the patients had ischemic infarction and 21.8% had hemorrhage. Similarly, Boutayeb et al. (2014) indicated that stroke is more prevalent among men than women with ratios varying from 1.3:1 to 2:1. In the previous studies, stroke caused by infarction was found in 58.3% while stroke caused by hemorrhage was found in 41.6% in Sudanese population (Sokrab et al., 2002). In Congo, haemorrhagic and ischemic strokes were present in 52 and 48% of the study population, respectively (Longo-Mbenza et al., 2008). Stroke subtype identification was often not possible in early studies because of a lack of brain and vascular imaging and it remains problematic today because of the frequent difficulty in ascribing a cause for a given stroke even when imaging is available.

Although hypertension, obesity, diabetes mellitus, and atrial fibrillation were important stroke risk factors, in many patients, these were detected only after a stroke. In the present study 43.6% of stroke patients had hypertension, 16.5% had diabetes mellitus and 4.3% had heart disease. Smoking and alcohol consumption are very low among patients represented by 3.7 and 3.7%, respectively. Hypertension was the most common associated risk factor constituting 46.9%, cardiac disease was found in 16%, diabetes mellitus in 14.6%, syphilis in 4.1%, and previous transient ischemic attack in 2.1% (Sokrab et al., 2002). In Congo, the rates of hypertension and diabetes mellitus among the stroke patients were 81 and 14.6%, respectively (Longo-Mbenza et al., 2008). The population of the Eastern Mediterranean region is known to suffer from high rates of diabetes and hypertension and the problem is accentuated by the late diagnosis and the high proportions of people who are unaware of their disease (Boutayeb et al., 2014). The relationship between smoking and cerebral infarction has been confirmed in case control studies from the U.S., Australia, U.K., Scandinavia, and Russia (Donnan et al., 1989).

In a study among more than 400 patients in Australia, Donnan and colleagues found that the risk of cerebral infarction due to smoking was substantially higher than in the previous meta-analysis (Donnan et al., 1989). Another review on global variation in stroke burden and mortality indicated raised mean systolic blood pressure and greater prevalence of smoking as predictors of stroke mortality but the national per capita income was the strongest predictor of mortality (Johnston et al., 2009). Sudanese patients had strong family history of the factors for the development of stroke such as hypertension, diabetes mellitus, stroke and heart diseases.

The most effected age group was between 41 and 60 years 42.55% and the mortality rate was 17.02%. The proportion of stroke death was increased with age, and in the oldest group (> 70 years of age) stroke contributed to 2.4% of all deaths (Anand et al., 2001; Gaziano, 2008). A 44% of all stroke type patients, 29% of haemorrhagic stroke and 31% of ischaemic stroke patients were dead (Longo-Mbenza et al., 2008). Compared to the survivors, deceased patients were significantly (p < 0.001) older with higher leukocyte counts and haematocrit, haemoglobin and fibrinogen levels, but lower glycaemic levels (Longo-Mbenza et al., 2008). Cerebrovascular accident represents a major cause of death and disability among women. In Sudan, the common age group affected was between 70 and 79 years (27.2%) (Shadia et al., 2011). The age-standardized death rate attributed to stroke varies six-fold between developed countries while very little is known about the developing world (Connor et al., 2007). Approximately 25% of men and 20% of women can expect to suffer a stroke if they live to be 85 years old (Bonita, 1992).

The definition of the available independent correlates of serum biomarkers with cerebral lesions and sites could further help in the clinical practice for the acute ischemic stroke management reducing complications following acute treatment (Meng and Ji, 2011). Sex and stroke subtypes have a significant effect on hematological, serum urea, creatinine and electrolytes levels. Blood glucose and urea levels and leukocyte counts were higher in patients who died than in survivors, and altered awareness of risks for stroke was the major independent predictor of fatality rates (M'Buyamba-Kabangu et al., 1995). Serum urea and bicarbonate can be helpful in estimation of fluid deficit independently from serum sodium (Gurubacharya et al., 2006).

The relationship between plasma lipid abnormalities and ischemic stroke remains controversial, in the present study cholesterol and LDL level were significantly ($P < 0.05$) different between males and females, while HDL level was significantly ($P < 0.05$) different between patient with ischemic and hemorrhage stroke. A meta-analysis of 45 prospective cohorts, including 450,000 subjects and 13,000 strokes, found no association between total cholesterol and stroke (Prospective Studies Collaboration, 1995). Hypertriglyceridemia is commonly found in patients with ischemic cerebrovascular disease whatever the etiologic subtype, whereas hypercholesterolemia is more related to large vessel disease and small vessel disease (Boutayeb et al., 2014; Laloux et al., 2004). However, they are not as well established as risk factors for first or recurrent stroke in contrast to what is seen in cardiac disease (The American Stroke Association, 2006). Therefore, epidemiological studies can help identify groups of individuals or regions at higher risk of stroke. They can also help better understand the natural history of certain associated conditions and therefore push the direction of prevention and therapeutic investigations (Sun et al., 2013). Health decision makers should pay a particular attention to the high burden of stroke due to ageing and risk factors like hypertension, diabetes, smoking, dyslipidemia, overweight/obesity and physical inactivity (Boutayeb et al., 2014).

CONCLUSION AND RECOMMENDATION

The study concludes that there was a high prevalence of risk factors of stroke (hypertension, diabetes mellitus, heart disease). The family history of the factors for the development of stroke hypertension, diabetes mellitus, stroke and heart diseases, electrolyte disturbances and lipid profiles were strongly associated with the prevalence of stroke. Electrolyte abnormalities may adversely affect outcome of the stroke patients. Serum electrolytes level should be determined in every patient with stroke. Further studies with larger samples are needed. Therefore a better understanding of stroke risk factors and outcome may help guide efforts at reducing the community burden of stroke in Sudan.

Conflicts of interest

The authors declare that they have no conflict of interest

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