Prevalence of Cardiovascular Risk Factors in Hemodialysis Patients – The CORDIAL Study

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Abstract

Background: **There are scarce epidemiological data on cardiovascular risk profile of chronic hemodialysis patients in Brazil.**

Objective: **The CORDIAL study was designed to evaluate cardiovascular risk factors and follow up a hemodialysis population in a Brazilian metropolitan city.**

Methods: **All patients undergoing regular hemodialysis for chronic renal failure in all fifteen nephrology centers of Porto Alegre were considered for inclusion in the baseline phase of the CORDIAL study. Clinical, laboratory and demographic data were obtained in medical records and in structured individual interviews performed in all patients by trained researchers.**

Results: **A total of 1215 patients were included (97.3% of all hemodialysis patients in the city of Porto Alegre). Their average age was 58.3 years old, 59.5% were male and 62.8% were white. The prevalence of cardiovascular risk factors observed was 87.5% for hypertension, 84.7% for dyslipidemia, 73.1% for sedentary lifestyle, 53.7% for tobacco use, and 35.8% for diabetes. In a multivariate adjusted analysis, we found that sedentary lifestyle (p = 0.032, PR 1.08 – 95%CI: 1.01-1.15), dyslipidemia (p = 0.019, PR 1.08 – 95%CI: 1.01-1.14), and obesity (p < 0.001, PR 1.96 – 95%CI: 1.45-2.63) were more frequent in women; and hypertension (p = 0.018, PR 1.06 – 95%CI: 1.01-1.11) and tobacco use (p = 0.006, PR 2.7 – 95%CI: 1.79-4.17) were more often found among patients under 65 years old. Sedentary lifestyle was independently associated with time in dialysis less than 12 months (p < 0.001, PR 1.23 – 95% CI: 1.14-1.33).**

Conclusion: **Hemodialysis patients in this southern metropolitan Brazilian city have a high prevalence of cardiovascular risk factors resembling many northern countries. (Arq Bras Cardiol. 2014; 102(5):473-480)**

Keywords: **Patients; Renal dialysis; Risk factors; Prevalence.**

Introduction

Cardiovascular diseases (CVD) are the main cause of death in chronic kidney disease (CKD) patients on hemodialysis[1-3]. In these patients, cardiovascular mortality is 10- to 20-fold higher when compared to individuals from the general population of the same sex, age and race[2-5] and can be up to 44 times higher in the presence of diabetes[6]. CVD are present since the early stages of chronic kidney disease and reach around 30 to 44% of those beginning hemodialysis[7-10]. Strikingly, occult ischemic CVD are present in up to 50% of asymptomatic dialysis patients[7,11,12].

This high amount of CVD can be attributed to the high prevalence of cardiovascular risk factors[13]. Although traditional risk factors alone could not entirely explain such a high CVD burden[4,14], they seem to be highly predictive of cardiovascular events[12], especially in the elderly[15]. Likewise, cardiovascular profile seems to allow risk stratification in CKD[16].

A large percentage of patients entering dialysis have a clustering of non-controlled risk factors for CVD[14] leading to an even higher chance of adverse outcomes[17].

This high prevalence of traditional CVD risk factors on chronic hemodialysis patients has been reported in several studies in different world countries[8-10,12,14,18-20]. However, there is a lack of consistent epidemiological data in our country for this population, both for methodological biases and the use of small samples restricted to a single hospital or clinic.

The main objective of this study was to evaluate the prevalence of traditional cardiovascular risk factors in the population of CKD outpatients on chronic hemodialysis in a southern metropolitan city of Brazil.

Methods

Study Design and Research Population

The CORDIAL (Cardiovascular Outcomes Registry in Dialysis Patients) study was designed to collect data on

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cardiovascular risk profile and carry out the follow-up of all CKD patients enrolled in a regular outpatient hemodialysis program in the city of Porto Alegre, Brazil. The present article describes the baseline phase data and reports a cross-sectional analysis of this population.

Eligibility criteria for enrollment included age 18 years or more, being in chronic outpatient dialysis for more than 30 days, and ability to provide informed consent for participation. The study complies with the Declaration of Helsinki and the protocol was approved by the Ethics Committee for Research of Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA) and by the review boards of the clinical centers included.

From August 2010 to March 2011, all CKD patients on hemodialysis in each of the fifteen dialysis centers of the city of Porto Alegre (Appendix 1) were considered for enrollment and 1215 (97.3% of all) matched the inclusion criteria and agreed to provide informed consent.

CORDIAL Data Collection

To collect the CORDIAL baseline data we used a standardized case report form adapted and extended to our needs from the REACH registry, a study performed in several countries including Brazil[21]. The form was comprehensively filled after visits to each center where patients, health care staff and electronic clinical records were accessed.

Weight, height and blood pressure measured before and after the dialysis session (mean of the last 3 sessions) were obtained from reviewing the patients' medical records. Prevalence of atherosclerotic cardiovascular disease, diabetes, and hypertension were established by reviewing all history and physical data in the dialysis clinic medical charts and other available medical documents. Furthermore, we considered as hypertensive any patient in use of antihypertensive drugs, or those with mean pre dialysis blood pressure in the stage 1 or up of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) classification[22].

The definition of diabetes included both type 1 and type 2, with or without oral hypoglycemic medication or insulin. Tobacco use was registered as past or present. In accordance with the Kidney Disease Outcomes Quality Initiative of the National Kidney Foundation (K/DOQI-NKF)[23], dyslipidemia was defined as the presence of any of the following – total cholesterol > 200 mg/dL, low-density lipoprotein (LDL)-cholesterol > 100 mg/dL, high-density lipoprotein (HDL)-cholesterol < 40 mg/dL, triglycerides > 150 mg/dL, or the use of statin. Current physical activity was established by an inquiry asking about "any moderate activity (as light walking, bicycling, or gardening) or hard one (running, playing football – soccer, hard swimming) at least 30 min two times per week" and "how many minutes in a week".

Laboratory data were obtained from the medical chart as the most recent result in the six preceding months.

Data about gender were available for all CORDIAL participants, about age for 1213 (99.8%), and race, height and weight for 1206 (99.3%) each.

Information about hypertension status, cardiovascular disease, physical activity, smoking and lipid profile were available respectively for 1210 (99.6%), 1170 (96.3%), 1150 (94.7%), 1147 (94.4%), and 1121 (92.3%) of the individuals in the cohort.

Statistics

Statistical analyses were carried out in STATA 9.0. Descriptive statistics were used to characterize the sample. Unadjusted and adjusted prevalence ratios were calculated separately for each dependent variable (hypertension, diabetes, dyslipidemia, tobacco use, sedentary lifestyle, and obesity) with independent variables (gender, age, race, time in dialysis, and diagnosis of cardiovascular disease). All tests were two-tailed and the significance level used was 0.05.

Results

The present study included 1215 subjects (97.3% population on chronic outpatient hemodialysis) with a mean age of 58.3 years old, being 59.5% males and 62.8 % white.

Table 1 presents demographic and clinical data for all the patients in the CORDIAL study and also stratified by gender.

The prevalence of traditional cardiovascular risk factors displayed in Table 2 reaches almost 90% for hypertension and dyslipidemia, and about 75% of the subjects were sedentary. Diabetes has a prevalence of 35.8 % in the hemodialysis population of Porto Alegre (Table 2).

In a multivariate analysis (Table 3), older patients presented a higher prevalence of diabetes and sedentary lifestyle. Hypertension, tobacco use, and obesity, however, were more prevalent in the younger ones. Tobacco use was more prevalent in males, while obesity, dyslipidemia, and sedentary lifestyle were more common in females. Sedentary lifestyle was more prevalent in those who were on dialysis for less than 12 months (linear tendency). Hypertension, diabetes, dyslipidemia, and low physical activity were more prevalent among those with diagnosis of cardiovascular disease.

Discussion

The 1215 individuals included in our study represent 97.3 % of all outpatients on hemodialysis for chronic renal failure during the collecting data period in Porto Alegre. The demographic characteristics of our study population were similar to other studies in several countries[9,10,12,14,18,19]. The mean age was close to 60 years old (with 35% over 65 years old) and almost 60% of the participants were men. Overall, the baseline cross-sectional phase of the CORDIAL study describes a high prevalence of various traditional cardiovascular risk factors. Prevalence of hypertension (87.5%), dyslipidemia (84.7%), sedentary lifestyle (73.1%), smoking (53.7%) and diabetes (35.8%) were similar to recent studies developed all over the world[9,12,14,18,19,24] and also comparable to findings in pre-dialysis CKD patients[4].

Table 1 – Clinical and demographic data for the patients in the CORDIAL study

	All	Male	Female
	(n = 1215)	(n = 723)	(n = 492)
Demographics			
Age (years) – mean(SD)	58.3 (15.0)	59.1 (14.6)	57.1 (15.4)
Race – %			
White	62.8	66.2	57.8
Black	25.9	23.1	30.1
Other	11.3	10.7	12.1
Time in dialysis (months) – median (interquartile range)	34 (12-71)	35 (12-67)	34 (12-72)
Age of beginning dialysis (years-old) – mean (SD)	54.1 (15.9)	54.9 (15.6)	53.0 (16.2)
Clinical data			
Diabetes			
DM 1 – n (%)	27	15 (55.6)	12 (44.4)
DM 2 – n (%)	407	239 (58.7)	168 (41.3)
BMI (kg/m^2) – mean (SD)	**24.7 (4.7)**	**24.3 (4.2)**	**25.2 (5.4)**
< 18.5 (kg/m^2) - %	6.1	5.0	7.8
18.5 to 24.9 (kg/m^2) - %	52.1	56.2	46.2
25 to 29.9 (kg/m^2) - %	29.4	30.0	28.3
≥ 30 (kg/m^2) - %	12.4	8.8	17.7
Pre-dialysis blood pressure			
Systolic (mmHg) – mean (SD)	146.9 (23.4)	147.3 (23.3)	146.4 (23.5)
Diastolic (mmHg) – mean (SD)	82.5 (14.0)	82.8 (13.9)	81.9 (14.1)
Systolic ≥ 140 mmHg – %	70.2	71.6	68.6
Diastolic ≥ 90 mmHg – %	34.7	36.0	32.9
Systolic ≥ 140 mmHg and/or diastolic ≥ 90mmHg – %	72.2	74.7	70.0
Lipid profile			
Cholesterol, total (mg/dL) – mean (SD)	168.2 (48.3)	159.0 (44.1)	183.1 (50.6)
HDL-cholesterol (mg/dL) – mean (SD)	40.1 (14.8)	37.6 (12.6)	43,7 (16.8)
LDL-cholesterol (mg/dL – mean (SD)	94.3 (38.1)	88.6 (35.4)	102.4 (40.4)
Triglycerides (mg/dL) – mean (SD)	171.7 (133.0)	167.8 (145.3)	177.5 (112.6)
Total cholesterol >200 mg/dL – %	22.5	16.3	31.5
HDL-cholesterol <40 mg/dL – %	60.3	64.5	49.5
LDL-cholesterol >100 mg/dL – %	39.4	32.2	49.5
Triglycerides >150 mg/dL - %	45.2	41.6	50.6
Tobacco use			
Ex-smokers - %	40.5	46.8	31.2
Active smokers - %	13.2	15.2	10.2
Years of tobacco use for active smokers – mean (SD)	30.8 (15.0)	31.2 (14.9)	30.0 (15.3)
Number of cig/day for active smokers – mean (SD)	12.5 (10.8)	12.7 (11.2)	12.0 (10.0)
Physical activity			
None - %	73.1	71.1	76.2
Up to 60 minutes/week - %	9.6	10.6	8.0
From 60 to 90 min/week - %	5.6	5.5	5.8
From 90 to 120 min/week - %	4.9	5.2	4.3
Over 120 min/week - %	6.8	7.6	5.6

DM: diabetes mellitus; BMI: body mass index; SD: standard deviation; HDL: high density lipoprotein; LDL: low density lipoprotein.

Hypertension

Hypertension was found in 87.5 % of our patients, a result higher than that found by Portolés et al. (the MAR study) in a multicenter cohort in Spain a decade ago (75.8 %)[19], but similar to others, like 87.1 % in the study by Ohsawa et al. in Japan (KAREN Study, 2005)[18], 86 % in a cohort of 2535 patients in the USA (Agarwal, 2003)[25], and around 86 % in two studies in Spain[9,12]. The CHOICE study found a higher prevalence (96.0 % among 1041 individuals)[14]. Pre dialysis mean blood pressure in our population (about 147/82 mmHg) is similar to other studies (149/79 mmHg in CHOICE, and 147/80 mmHg in DMMS Wave2)[10,14]. Uncontrolled blood pressure in the pre dialysis measurements is 72 % in our cohort (Table 1), similar to the 70 % in the study of Agarwal et al[25] and to the 69 % in the CHOICE study[14]. In CORDIAL, a multivariate adjusted analysis found that patients under 65 years-old presented a higher prevalence of hypertension.

Hypertension has been related to higher mortality in hemodialysis patients[26] and the importance of treating high blood pressure in these individuals was highlighted in two recent meta-analysis suggesting a reduction in cardiovascular events and all-cause mortality in those treated with antihypertensive drugs[27,28].

Table 2 – Prevalence of cardiovascular risk factors in CORDIAL (%)

Hypertension	87.5
Diabetes	35.8
Dyslipidemia	84.7
Tobacco use	53.7
Sedentary lifestyle	73.1
Elderly (≥ 65 years)	34.9
Male	59.5
Obesity (BMI ≥ 30)	12.4

Dyslipidemia

Among our patients, the prevalence of dyslipidemia was 84.7 %, a higher rate comparing to other studies like 50% in CHOICE[14]. The different criteria in each study preclude a more accurate comparison. Our mean LDL-cholesterol (94.3 mg/L) was similar to others[9,12,14,18,19], with Kronnnenberg reporting a higher value (115 mg/dL)[24].

Table 3 – Adjusted prevalence rates (PR) of each cardiovascular risk factor in CORDIAL study

	Hypertension		Diabetes		Dyslipidemia		Tobacco		Sedentary lifestyle		Obesity	
	PR (95%CI)	p	PR (95%CI)	p	PR (95%CI)	p	PR (95%CI)	p	PR (95%CI)	p	PR (95%CI)	p
Gender		0.883		0.453		0.019		0.006		0.032		< 0.001
Female	1.00		1.00		1.00		1.00		1.00		1.00	
Male	1.00 (0.96-1.05)		0.94 (0.81-1.10)		0.93 (0.88-0.99)		1.57 (1.14-2.15)		0.93 (0.87-0.99)		0.51 (0.38-0.69)	
Age – years-old		0.018		< 0.001		0.645		< 0.001		< 0.001		< 0.001
< 65	1.00		1.00		1.00		1.00		1.00		1.00	
≥ 65	0.94 (0.90-0.99)		1.46 (1.26-1.69)		1.01 (0.95-1.08)		0.37 (0.24-0.56)		1.16 (1.09-1.24)		0.53 (0.37-0.77)	
Race		0.232		0.753		0.534		0.057		0.884		0.840
White	1.00		1.00		1.00		1.00		1.00		1.00	
Other	0.97 (0.93-1.02)		0.97 (0.83-1.14)		1.02 (0.96-1.08)		1.33 (0.99-1.78)		1.01 (0.94-1.08)		0.97 (0.71-1.31)	
Time in dialysis – months		0.384		0.334		0.442		0.091		< 0.001		0.936
1 – 12	1.00		1.00		1.00		1.00		1.00		1.00	
13 – 24	1.01 (0.95-1.07)		1.09 (0.89-1.34)		1.04 (0.95-1.15)		1.23 (0.75-2.03)		0.86 (0.77-0.95)		0.98 (0.61-1.58)	
25 – 36	0.98 (0.91-1.06)		1.05 (0.83-1.33)		1.06 (0.96-1.18)		1.60 (0.96-2.66)		0.90 (0.81-1.00)		0.72 (0.39-1.35)	
> 36	0.98 (0.93-1.03)		0.92 (0.76-1.12)		1.03 (0.96-1.11)		1.39 (0.94-2.06)		0.81 (0.75-0.88)		1.03 (0.70-1.51)	
Diagnosis of cardiovascular disease		< 0.001		< 0.001		0.009		0.564		0.049		0.230
No	1.00		1.00		1.00		1.00		1.00		1.00	
Yes	1.14 (1.09-1.18)		1.42 (1.22-1.66)		1.08 (1.02-1.15)		0.91 (0.67-1.25)		1.07 (1.00-1.15)		1.21 (0.89-1.65)	

The prevalence of elevated triglycerides was 45.2 % in our cohort, higher than the study by Collado et al[12] and the CHOICE study (36.9 % over 200mg/dL)[14]. Mean values were 171.7 mg/dL in CORDIAL, higher than in KAREN and ANSWER, similar to the MAR study and Kronenberg et al[24], and lower than CHOICE (199mg/dL)[9,14,18,19,24]. HDL-cholesterol under 40 mg/dL was more prevalent in our cohort (60.3 %) than in others[9,14,18,19]. An exception was the 66 % reported by Kronenberg et al[24].

In CORDIAL, there was a higher adjusted prevalence of dyslipidemia in female patients, while Ohsawa et al. reported an opposite finding[18]. Although there is not a proven association between serum lipids and the development CVD outcomes in dialysis patients[29], lipid measurements and treatment remains a cornerstone approach to prevent CVD even in CKD patients[24].

Smoking

Tobacco use is associated with a markedly increased risk of heart disease in dialysis patients[8,16]. Smoking (past or present) was described in 53.7 % of our patients, in accordance to others studies[9,10,12,14,19]. Thirteen percent of our patients were current smokers, similar to other authors[9,14,19], except for the KAREN study, with 28.2%[18]. In CORDIAL, the adjusted prevalence of tobacco use was higher in males and in those with less than 65 years.

Sedentary lifestyle

Sedentary lifestyle was identified in 73.1% of our patients. In the CHOICE study[14], only 14 % reported physical activity to perspiration at least 3 times a week. Tentori et al. (2010)[30] described results of 20,920 patients in the DOPPS study with a self-reported regular physical activity of 47.4 %. Comorbidities and physical limitations could explain the low adherence of haemodialysis patients to exercise programs[31]. Besides, older age could represent another limitation to physical activity – among our patients, adjusted prevalence of physical inactivity was higher in those over 65 years than in younger patients (Table 3).

Diabetes

Diabetes prevalence among dialysis patients is already high and increasing[32]. The 5-year survival rate among diabetic patients on hemodialysis is worse than in non-diabetics. A recent study in Brazil found 41.1 *versus* 62.7 %, respectively[33]. According to the 2009 United States Renal Data System (USRDS) database, only 30 % of the diabetic patients survived five years after beginning hemodialysis[1].

In CORDIAL, diabetics were 35.8 % of the population, a lower rate than the one presented in CHOICE (54%)[14], but similar to the 38.5% in the 2012 USRDS Annual Report[34], with others ranging from 26 to 43 %[9,10,18-20].

Obesity

Obesity estimated by body mass index (BMI) was present in 12.4% of individuals in CORDIAL. The MAR study[19] reported obesity in 14% of their patients, while in ANSWER and CHOICE the prevalence was higher (20 and 26%, respectively)[9,14]. Unlike the general population, overweight dialysis patients have better prognosis, supposedly due to a better nutritional status[35]. Recently, BMI has been considered a non-efficient tool in the assessment of excess body fat content and thereafter obesity[36]. Reverse epidemiology and inadequate assessment of fat accumulation could explain the "obesity paradox" in CKD[37].

Age

In CKD patients on hemodialysis, older age confers a cardiovascular risk that parallels the relationship described in the general population[38]. There is a growing prevalence of elderly in the hemodialysis population all-over the world[9,10,19]. In the Brazilian dialysis census of 2000, those with age 60 or more were 26 %[39], while in 2011 there were 31.5 % with age 65 or more[40]. In CORDIAL, also in 2011, we found a rate of 34.9 %.

Limitations

Our data presents the usual drawbacks of cross-sectional studies limiting causal inferences. We had to rely on clinical laboratory measurements of 15 dialysis centers instead of using a core lab. We described similar rates observed in other studies, but our data cannot be generalized to other cities in our country. Our data, however, has the strength of having been acquired from a large population with few dropouts and double-checking structured individual interviews and clinical charts.

Conclusion

The population in chronic hemodialysis in this large metropolitan south-American city described in the CORDIAL study presents a high prevalence of cardiovascular risk factors. These findings confirm in Brazil what has been previously verified in northern hemisphere countries, the high-risk cardiovascular profile of hemodialysis patients. Prospective studies and clinical trials are needed to further clarify interventions that can be transformed in public health strategies to prevent cardiovascular death in hemodialysis patients.

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Appendix 1 – Dialysis clinical centers of Porto Alegre, Brazil

Centro de Dialise e Transplante, CliniRim, Clinica Nefron, Clinica Vita Rim, Hospital das Clinicas de Porto Alegre, Hospital Divina Providência, Hospital Ernesto Dornelles, Hospital Mãe de Deus, Hospital Moinhos de Vento, Hospital N. Sra. da Conceição, Hospital Parque Belém, Hospital Santa Casa Porto Alegre, Hospital São Lucas, Hospital Vila Nova, Mãe de Deus Center.

Appendix 2 – Associated researchers to the CORDIAL study

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Author contributions

Conception and design of the research: Burmeister JE, Rosito GA; Acquisition of data: Burmeister JE, Mosmann CB, Costa VB, Saraiva RT, Grandi RR, Bastos JP; Analysis and interpretation of the data: Burmeister JE, Mosmann CB, Costa VB, Bastos JP, Gonçalves LF, Rosito GA; Statistical analysis: Burmeister JE, Bastos JP, Gonçalves LF, Rosito GA; Writing of the manuscript: Burmeister JE, Mosmann CB, Costa VB, Saraiva RT, Grandi RR, Bastos JP, Rosito GA; Critical revision of the manuscript for intellectual content: Burmeister JE, Mosmann CB, Costa VB, Bastos JP, Gonçalves LF, Rosito GA; Coordination work of collecting and recording data: Burmeister JE; General Coordinator of the Project: Rosito GA.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

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