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Prevalence of Hypertension among Iranian Hemodialysis Patients and Associated Risk Factors: A Nationwide Multicenter Study

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Abstract: The aim of this study is to document the prevalence of HTN and characterize risk factors associated with HTN in Iranian hemodialysis patients. Three hundred and thirty seven HD patients from 5 university based HD centers around Iran were enrolled in the study. Urea reduction ratio was calculated using formula: 100 * (1-(urea before HD/urea after HD)). Pearson Chi-square test, independent sample t-test and one way ANOVA were used for evaluations, where appropriate. Multivariate logistic regression model was used for defining independent risk factors. Two sided $p<0.05$ were considered significant. Patients with diabetes mellitus and hypertension as causes of ESRD significantly were more likely to have hypertension before and after dialysis ($p<0.05$). Patients with conventional thrice weekly dialysis (compared to twice), hemodialysis duration of more that 6 months, acetate type of dialysate, ESRD cause when diabetes mellitus and hypertension, were significantly associated with having pre-HD hypertension. We also found that hemodialysis center of the capital city had a significant better measures compared to other cities ($p<0.05$). This study revealed a relatively acceptable prevalence of hypertension in our HD population. Nevertheless, because of higher prevalence of HTN in HD centers out of capital city, it seems necessary that we should urgently pay more attention in promotion of these centers toward achieving better outcome with implementing strict guidelines to follow.

Key words: Hypertension, dialysis, hemodialysis, Iran

INTRODUCTION

Hypertension (HTN) is a common and difficult to manage clinical problem in patients undergoing chronic hemodialysis (HD) and exerts a deleterious effect on morbidity and mortality in end-stage renal disease. However, there is scarce data about the prevalence, status and risk factors of high blood pressure among Iranian HD patients.

HTN is a recognized risk factor for ischemic heart disease, cerebrovascular events and mortality both in HD patients and in general population (Burt *et al*., 1995; Sytkowski *et al*., 1996). There is larger frequency of hypertension even in non-dialyzed patients as renal function declines. The reported prevalence of cardiovascular diseases among HD population is nearby in 70-90% (Mittal *et al*., 1999; Salem, 1995; Agarwal *et al*., 2003) and it contributes to the high rate of morbidity and mortality in these patients; Hence, HTN has been implicated as a major cause of poor clinical outcome and high mortality in HD patients and as previously shown, useful management of this problem definitely reduces the incidence of its attributing problems in HD patients (Agarwal, 2005). Systolic hypertension with or without diastolic hypertension is a major problem in hemodialysis (HD) patients; although, isolated diastolic hypertension is uncommon. Expansion of extracellular fluid volume is the major pathophysiologic mechanism for the development of hypertension in these patients; however, Accelerated age-related changes in vascular stiffness, together with factors peculiar to uremia leading to loss of large and small vessel distensibility and profound changes in circulatory function also play significant roles. Diminution of salt intake, lowering dialysate sodium, patient teaching, exercise, ultra filtration and adequate dialysis intensity alongside an effective medication therapy are the most important factors in lowering blood pressure in HD patients (D'Amico and Locatelli, 2002; Vincenti *et al*., 1980; Hagberg *et al*., 1983; Cheigh *et al*., 1992).

The present study aimed to document the prevalence of HTN and characterize risk factors associated with HTN in Iranian hemodialysis patients.

MATERIALS AND METHODS

We enrolled 337 HD consecutively selected patients from 5 university based HD centers around Iran in December 2006. Enrolled HD centers were located in Tehran (Central Iran), Shiraz (Southern Iran), Ahvaz

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Table 1: Causes of ESRD in the studied patient population

Cause of ESRD	Frequency (%)
DM	61 (18.1)
HTN	80 (23.7)
GN	44 (13.1)
Obstructive nephropathy	11 (3.3)
PKD	21 (6.2)
CHF	14 (4.2)
UNKNOWN	106 (31.5)
Total	337 (100.0)

DM = Diabetes Mellitus; HTN = Hypertension; GN = Glomerulonephritis; PKD = Polycystic Kidney Disease; CHF = Chronic Heart Failure

(South Western Iran), Mashhad (North Eastern Iran) and Kermanshah (Western Iran). We extracted the following data from data registries: age, gender, cause of ESRD, previous history for HTN, hypotension and muscle crump through a HD session, previous kidney transplantation, use of erythropoietin, number of weekly dialysis sessions, mean weight gain through dialysis sessions, mean duration of dialysis sessions and dialysate type; the last laboratory measurements including pre- and post-dialysis blood urea values and serum concentrations for potassium (K), phosphorus (P), albumin and creatinine were also retrieved. 192 (57%) of the patient population were male and 145 (43%) were female. 152 (45%) had a positive family history for hypertension. Table 1 shows the causes of ESRD in our patient population; hypertension was documented as the main cause of ESRD in 80 (23.7%) of patients. 56 (17%) of the subjects had a previous transplant history; 297 (88%) of the patients had a history of receiving erythropoietin therapy; history of previous hypertension before starting HD was positive in 280 (83%). Patients were identified as hypertensive if they had pre-dialysis blood pressure more than 140/85 mmHg (Lees *et al*., 2000).

Statistics: Urea reduction ratio was calculated using formula: 100 * (1-(urea before HD/urea after HD)). Pearson Chi-square test, independent sample t-test and one way ANOVA were used for evaluations, where appropriate. Multivariate logistic regression model was used for defining independent risk factors. Two sided $p<0.05$ were considered significant.

RESULTS AND DISCUSSION

A total of 337 HD patients from 5 university based HD centers were entered in the study. 171 (51%) of patients were older than 50 years. Mean±SD weight before dialysis session was 62±14 (range: 11-96) kg. Mean±SD (range) laboratory findings before dialysis session were: hemoglobin 9.8±2.2 (2-19) mg dL^{-1}; serum creatinine 9±3 (2-19) mg dL^{-1}; serum calcium 8.6±1.2 (5-13) mg dL^{-1}; serum phosphorus 5.9±1.7 (2-14) mg dL^{-1}; serum potassium 5.4±1.0 (2-10) mmol L^{-1}; serum albumin 5.2±2.6 (2-19) mg mL^{-1}. Mean blood urea values before and after dialysis session were 66±41 (range: 2-227) and 31±21 (range: 3-96) mg dL^{-1}, respectively. Patients with different causes of ESRD, significantly differ in having hypertension before and after dialysis (Table 2). Previous history for hypertension ($p<0.001$), cause of ESRD when diabetes mellitus, hypertension and glomeulonephritis ($p = 0.002$), not having previous transplantation history ($p = 0.007$), hypotension during a dialysis session ($p<0.001$), dialysis duration >6 months ($p = 0.05$), using hypertonic sodium ($p<0.001$), acetate type of dialysate ($p = 0.001$) and blood urea after dialysis ($p = 0.01$, $F = 5.68$) were significantly associated with pre-HD hypertension among our HD patients.

Multivariate analysis using logistic regression after adjusting for other risk factors revealed that patients with conventional thrice weekly dialysis (compared to twice), hemodialysis duration of more that 6 months, acetate type of dialysate, ESRD cause when diabetes mellitus and hypertension, were significantly associated with having pre-HD hypertension (Table 3). Differences in patients of 5 studied HD centers with regard to their pre- and post-HD session hypertension are shown in Table 4.

Hypertension (HTN) is found frequently in patients with renal disease including HD patients (Cheigh *et al*., 1992) and its prevalence is influenced by a variety of factors such as salt intake, volume overload, elevated sympathetic tone and uremic toxins (Flamigan, 2004); the most important of them is the degree of renal failure, given that as renal function deteriorates the frequency of HTN increases significantly to such an extent that virtually all patients starting HD may be hypertensive (Zucchelli and Santoro, 1988; Ridao *et al*., 2001).

In our patient population who were collected from cities around the country (Tehran, Central; Shiraz, Southern; Kermanshah, Western; Mashhad, Eastern and Ahvaz, South Western Iran), the prevalence of hypertension before and after HD sessions were 58 and 29%, respectively, which are lower than previous reports worldwide (Raine *et al*., 1992; Salem, 1995; Al-Hilali *et al*., 2006). Nonetheless, the existing proportion of hypertensive HD patients is not such low to make us feel free from considering the problem seriously. Between Iranian HD centers took part in this study, we found a significant difference in prevalence of hypertensive patients ($p<0.001$, Table 4); where the capital city (Tehran) HD center has significantly better condition compared to other centers around the country, both in pre and post-HD blood pressure. This may partly be due to lower economic level of the local population and also lower

Table 2: Blood pressure before and after HD sessions and their relationship with causes of ESRD

	ESRD cause								
Count	DM	HTN	GN	Obstructive nephropathy	PKD	CHF	Unknown	Total	p-value
Blood pressure before HD session									0.002
HTN	38	43	19	6	9	3	44	162	
norm	11	22	16	4	11	10	44	118	
Total	49	65	35	10	20	13	88	280	
Blood pressure after HD session									0.003
HTN	18	29	4	2	2	1	22	78	
norm	31	34	28	8	18	10	62	191	
Total	49	63	32	10	20	11	84	269	

Table 3: Multivariate logistic regression for potential risk factors for hypertension before HD sessions

				95% Confidence interval for odds ratio (OR)	
Blood pressure before an HD session		Sig.	Odds ratio (OR)	Lower bound	Upper bound
Age	<50 y/o	0.791	1.111	0.512	2.411
	>50 y/o	-	-	-	-
Gender	Male	0.534	0.800	0.396	1.617
	Female	-	-	-	-
Mean weight gain	>2 kg	0.957	1.021	0.484	2.151
	<2 kg				
Family history for HTN	Positive	0.898	1.052	0.482	2.297
	Negative	-	-	-	-
Cause of ESRD	DM	0.022	0.280	0.094	0.832
	HTN	0.024	0.287	0.097	0.850
	GN	0.263	0.537	0.180	1.596
	Obstructive nephropathy	0.749	0.759	0.139	4.129
	PKD	0.874	1.124	0.266	4.755
	CHF	0.462	2.033	0.307	13.437
	Unknown	-	-	-	-
Transplantation history	Positive	0.061	2.284	0.961	5.425
	Negative	-	-	-	-
Hypotension during HD session	Positive	0.053	2.126	0.989	4.573
	Negative	-	-	-	-
Muscle crump	Positive	0.452	0.709	0.289	1.739
	Negative	-	-	-	-
Hypertonic sodium administration	Positive	0.279	0.589	0.226	1.535
	Negative	-	-	-	-
Erythropoietin administration	Positive	0.130	3.141	0.714	13.820
	Negative	-	-	-	-
ASA administration	Yes	0.989	1.006	0.450	2.246
	No	-	-	-	-
System buffer	Bicarbonate	0.025	2.819	1.141	6.963
	Acetate	-	-	-	-
Dialysis duration	< 6 mo	0.003	4.399	1.665	11.624
	> 6 mo	-	-	-	-
HD sessions per week	Twice	0.030	3.463	1.127	10.639
	Thrice	-	-	-	-
Serum calcium	> 10 mg dL^{-1}	0.934	0.954	0.311	2.923
	< 10 mg dL^{-1}	-	-	-	-

Table 4: Difference between number of patients with pre- and post- HD session hypertension among 5 studied HD centers

	Blood pressure after HD session N (%)				Blood pressure before HD session N (%)			
HD centers locations	Hypertension	Normal	Total	Sig.	Hypertension	Normal	Total	Sig.
				0.000				0.000
Tehran	12 (16.7)	60 (83.3)	72		32 (39.5)	49 (60.5)	81	
Shiraz	19 (51.4)	18 (48.6)	37		31 (79.5)	8 (20.5)	39	
Ahvaz	19 (30.6)	43 (69.4)	62		34 (54.8)	28 (45.2)	62	
Mashhad	20 (40.8)	29 (59.2)	49		34 (69.4)	15 (30.6)	49	
Kermanshah	8 (16.0)	42 (84.0)	50		32 (64.0)	18 (36.0)	50	
Total (%)	78 (28.9)	192 (71.1)	270		163 (58.0)	118 (42.0)	281	

Values in parentheses show percentage

availability and access to a specialist and/or a nephrologist in the area. This finding could alert us to pay more attention and to provide enough material and staff for all HD patients throughout the country (e.g., for example providing guidelines for management of serious complications attributed to HD practice, to be strictly implemented in all HD facilities).

In this study, factors were found contributing in hypertension in Iranian HD patients included acetate type of dialysate, hemodialysis duration over 6 months and thrice weekly program of HD (compared to twice weekly). Existence of higher blood pressure in patients on acetate type of dialysate compared to bicarbonate could be well explained for preference of using this type of dialysate in hypertensive HD patients; moreover, patients who underwent conventional thrice weekly HD program are generally in worse kidney function condition and this is typically the main reason for considering this HD program for ESRD patients.

According to logistic regression, hypotension during HD session and having a previous transplant history could not adversely affect hypertension in HD patients; although, the result reached nearly significance ($p = 0.053$ and 0.061, respectively). On the other hand, we interestingly did not detect a significant relationship between inter-dialysis weight gain in our patients and hypertension. Although, conflicting data exists regarding the correlation of inter-dialysis weight gain and blood pressure in HD, studies have shown that weight gain, observed in chronic HD patients has moderate to severe impact on pre-dialysis blood pressure in the majority of patients. Our data suggests that factors other than fluid overload contribute to high blood pressure in HD patients. Some other interesting findings in this study is that we didn't detect any relationship between age, gender and administering hypertonic sodium with pre-HD hypertension; we also didn't detected any relationship between hypercalciuria (serum calcium >10 mg dL^{-1}) and hypertension. Using erythropoietin was not associated with pre-HD high blood pressure, as well.

In this study, hypertension has a relatively moderate to low prevalence and often moderately controlled in the majority of patients. Reasons for uncontrolled blood pressure in HD population are multifactorial. Policies we can use for lowering blood pressure in patients on maintenance hemodialysis include: reducing salt intake, lowering dialysate sodium, ultra-filtration and patient education. Considering the results of this study, one may suppose that the only risk factor interfering in hypertension in our HD patient is time duration of HD therapy; however, there are several other factors which could effectively affect blood pressure control in HD patients-including structural abnormalities in central elastic arteries and peripheral arterioles, hyperparathyroidism, seasonal variations, chronic volume overload and circadian blood pressure profile abnormalities-which in this nationwide study we had not the possibility to detect them. In conclusion, this study revealed a relatively acceptable prevalence of hypertension in our HD population. Nevertheless, because of higher prevalence of HTN in HD centers out of capital city, it seems necessary that we should urgently pay more attention in promotion of these centers toward achieving better outcome with implementing strict guidelines to follow.

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