

**PREVALENCE OF ASYMPTOMATIC AVASCULAR NECROSIS OF THE HIP IN PATIENTS WITH KIDNEY TRANSPLANTATION**

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ABSTRACT

Introduction: Kidney transplant is one of the treatments in patients with ESRD (end stage renal disease) that increases the quality of life in patients. Following kidney transplant, patients need glucocorticoid and immunosuppressant drugs. These drugs put patients in risk of hip avascular necrosis. The purpose of this study was to evaluate the prevalence of asymptomatic avascular necrosis of the hip in patients with kidney transplantation.

Methods: This prospective descriptive cross-sectional study was conducted on all patients referred to the Shahid Mohammadi Hospital, Bandar Abbas, Iran, who had a kidney transplant at least six month before our study. All patients' information was collected with a questionnaire consisting of demographic information including age, sex, weight, height, history of hemodialysis, history of peritoneal dialysis, history of smoking, alcohol intake, history of prednisolone and the main variable data of the disease, including the causes of ESRD such as diabetes, hypertension and diabetes combined, polycystic kidney disease, IgA nephropathy reflux disease, focal segmental glomerulonephritis and time elapsed after the transplant. Magnetic resonance imaging (MRI) was used for the detection of avascular necrosis. Diagnosis of avascular necrosis was confirmed by two separate radiologists. Data was analyzed using IBM SPSS 21.0 software.

Results: In this study, 83 patients were studied. Among these patients, 45 (54.2%) were male and 38 (45.8%) were female. The average age of the subjects was 41.29 ± 13.72 years. Demographic variables were similar in two groups. There was no relation among the vertebrae and overall results densitometry with avascular necrosis ($p > 0.05$).

Based on this chart, prevalence of avascular necrosis in patients with osteoporotic hip based on densitometry, was significantly more than other people ($p = 0.008$).

Conclusion: According to results, prevalence of femoral head avascular necrosis is not higher in patients after transplant and it has no significant relation to age, sex, BMI, time passed after transplant, CMV infection, hospitalization, history of dialysis or type of donator. Also, there was no significant correlation between the vertebra densitometry and the overall results of densitometry with avascular necrosis on MRI. The only factor associated with avascular necrosis in this study, was osteoporosis in the hip densitometry.

KEYWORDS: Avascular necrosis, hip, kidney transplantation, magnetic resonance imaging

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1. INTRODUCTION

Kidney transplant is one of the treatments in patients with ESRD (end stage renal disease) that increases the quality of life in patients (1-3). Following kidney transplant, patients need glucocorticoid and immunosuppressant drugs (4, 5). These drugs put patients in risk of hip avascular necrosis (6, 7). Some studies in patients using glucocorticoids and immunosuppressant drugs like lupus, show that risk of femoral head avascular necrosis is high (8). One of the reasons that prevalence of femoral head avascular necrosis is higher in these patients is the use of glucocorticoids (9, 10). It also causes osteoporosis in addition to increasing the risk of femoral head avascular necrosis in these patients (11-14). Avascular necrosis is not always symptomatic and sometimes, it is recognizable before symptoms like pain and deformity and limited mobility with MRI (15, 16). Because of the costs of MRI, screening is cost effective if the prevalence of asymptomatic avascular necrosis is high. In kidney transplant patients, to prevent rejection, we use immunosuppressive drugs and glucocorticoids that can cause avascular necrosis of the femoral head in susceptible people (5). However, given that avascular necrosis of the femoral head can be asymptomatic in these patients, information about its prevalence is limited. If the prevalence of asymptomatic avascular necrosis is high after transplantation in patients, MRI screening in these patients is cost-effective.

The purpose of this study was to evaluate the prevalence of asymptomatic avascular necrosis of the hip in patients with kidney transplantation. Specific objectives of this study were prevalence of asymptomatic hip avascular necrosis in kidney transplant patients by age, gender, weight, time past the transplant, radiological symptoms, history of smoking, alcohol intake and history of hemodialysis.

2. MATERIAL AND METHODS

2.1. Research design and setting

This prospective descriptive cross-sectional study was conducted on all patients referred to the Shahid Mohammadi Hospital, Bandar Abbas, Iran, who had a kidney transplant at least six month before our study Census sampling was used.

2.2. Selection criteria

Inclusion criteria for the study included first time transplant patients and 6 months past their operation, between the ages of 18-70 years and therapy combined of steroids, cyclosporine or tacrolimus and mycophenolate mofetil. Exclusion criteria included secondary transplant patients, lupus patients, and patients with symptomatic AVN including inability to walk, pain, weakness and mobility limitations.

2.3. Data collection

All patients' information was collected with a questionnaire consisting of demographic information including age, sex, weight, height, history of hemodialysis, history of peritoneal dialysis, history of smoking, alcohol intake, history of prednisolone and the main variable data of the disease, including the causes of ESRD such as diabetes, hypertension and diabetes combined, polycystic kidney disease, IgA nephropathy reflux disease, focal segmental glomerulonephritis and time elapsed after the transplant. Magnetic resonance imaging (MRI) was used for the detection of avascular necrosis. Diagnosis of avascular necrosis was confirmed by two separate radiologists in two different centers. Densitometry findings were examined in three parts. The first was spine densitometry. The next part was the hip bone densitometry and finally the overall results were presented.

2.4. Research ethics

Research design was approved by the Scientific and Ethical Committee of the Medical School of Hormozgan University of Medical Sciences, and from all patients an informed consent was obtained after explaining the conditions for participation in the research study.

2.5. Statistical analyses

After collecting the information, the data were entered into the computer by IBM SPSS Statistics for Windows (Version 21.0. Armonk, NY: IBM Corp. Released 2012), and analyzed with this program. To perform analysis of the chi-square test, Fisher's exact test frequency, percentage, mean and standard deviation and independent samples t-test was used. The significance level for P-value was defined <0.05.

3. RESULTS

3.1. Demographics

In this study, 83 patients were studied. Among these patients, 45 (54.2%) were male and 38 (45.8%) were female.

The average age of the subjects was 41.29 ± 13.72 years ranging from 13 to 68 years. The mean weight of the subjects was 92.29 ± 15.11 kg. Their average height was 163.16 ± 10.16 cm. The average BMI of the subjects was 13.27 ± 5.12 kg/m². The time since the transplantation varied from 2 years to 29 years and the average was 8.67 ± 4.95 years. None of the subjects did not use cigarettes or alcohol or opium. Of the subjects, 77 patients (92.8%) were on dialysis before transplantation. All the patients' dialysis type was hemodialysis.

3.2. Study main results

Among the participants, 1 patient (2.1%) was IgA nephropathy and 11 cases (13.3%) were glomerulonephritis, 3 (6.3%) kidney stones, 3 (3.6%) diabetes 11 (13.3%) hypertension, 3 (3.6%) adult polycystic kidney disease, 1 (1.2%) MCK and 1 (1.2%) neurogenic bladder mentioned as the causes of kidney failure. The cause of kidney failure in 49 patients (59%) was unknown. Among those surveyed, in 7 patients (8.4%) had transplanted kidney from living relatives and 76 (91.6%) had received their kidney from deceased donors. In addition, among those surveyed, in 4 patients (4.8%) cytomegalovirus infection was reported. Furthermore, 57 patients (31.3%) had a history of hospitalization. Among subjects, the kidney donor in 7 patients (8.4%) was a living relative, and in 76 cases (91.6%) was deceased. Vertebrae densitometry result in 29 cases (34.9%) was normal, in 33 cases (39.8%) was osteopenia and in 21 patients (25.3%) was osteoporosis. The hips densitometry result in 41 patients (49.4%) was normal, in 38 cases (45.8%) was osteopenia and in 4 patients (4.8%) was osteoporosis. The overall densitometry result in 24 (28.9%) was normal, in 37 patients (44.6%) was osteopenia and in 22 patients (26.5%) was osteoporosis. MRI results in 81 patients (97.6%) were normal, and in 2 patients (2.4%) were in favor of avascular necrosis. In Table 1 the relation between avascular necrosis and demographic variables is discussed. Avascular necrosis has a significant statistical relation with gender, history of dialysis before transplantation, donor type and those with no history of CMV and hospitalization (Table 1).

The mean age in the group with normal MRI was 63.13 ± 9.40 years and in patients with avascular necrosis was 45.8 ± 57 years, the difference was not significant statistically ($p=0.102$). The average BMI in patients with normal MRI was 24.59 ± 5.12 and in patients with avascular necrosis was 20.29 ± 3.84 kg per square meter, this difference was not statistically significant ($p=0.243$). The mean time since transplantation in patients with normal MRI was 8.59 ± 4.98 and in patients with avascular necrosis was 12 years that statistically, this difference was significant ($p<0.001$). No relationship between bone densitometry and avascular necrosis was observed ($p>0.05$) and the prevalence of avascular necrosis patients with hip osteoporosis was significantly higher ($p=0.008$) (Table 2). There is no relationship among the vertebrae and overall results densitometry with avascular necrosis ($p>0.05$) (Table 2). Also, the prevalence of avascular necrosis in patients with osteoporotic hip based on densitometry, was significantly more than other people ($p = 0.008$) (Table 2).

Table 1. Comparison of demographic variables between two groups

Parameters	Subgroups	MRI results		p-value
		Normal (n = 81)	Avascular necrosis (n = 2)	
Sex, n (%)	Male	44 (54.3%)	1 (50%)	0.709
	female	37 (45.7%)	1 (50%)	
History of previous dialysis before transplant, n (%)	Positive	75 (92.6%)	2 (100%)	0.86
	Negative	6 (7.4%)	0 (0%)	
Donor, n (%)	Corpse	7 (8.6%)	0 (0%)	0.83
	Non-family member (live)	74 (91.3%)	2 (100%)	
CMV infection, n (%)	Positive	4 (5%)	0 (0%)	0.905
	Negative	77 (95%)	2 (100%)	
History of hospitalization, n (%)	Positive	56 (69.1%)	1 (50%)	0.531
	Negative	25 (30.9%)	1 (50%)	

Table 2. Relationship between the results of densitometry and MRI findings

Bone densitometry results		MRI results		p-value
		Normal (n = 81)	Avascular necrosis (n = 2)	
Spine densitometry, n (%)	Normal	28 (96.6%)	1 (3.4%)	0.486
	Osteopenia	33 (100%)	0 (0%)	
	Osteoporosis	20 (95.2%)	1 (4.8%)	
Hip densitometry, n (%)	Normal	40 (97.6%)	1 (2.4%)	0.008
	Osteopenia	38 (100%)	0 (0%)	
	Osteoporosis	3 (75%)	1 (25%)	
Overall results, n (%)	Normal	23 (59.8%)	1 (4.2%)	0.437
	Osteopenia	37 (100%)	0 (0%)	
	Osteoporosis	21 (95.5%)	1 (4.5%)	

4. DISCUSSION

The results of this study indicate that the prevalence of avascular necrosis is low in patients who have undergone a kidney transplant. However, its causes can be linked to the drugs mentioned in these patients (4, 5). In addition, some bone deformities which may result in kidney failure have occurred in these patients (17-19). Among the other reasons that can be cited in this context, there are also underlying diseases that patients are suffering from. For example, diabetes or blood pressure can be the patient's underlying disease that is susceptible to avascular necrosis. Our study showed higher prevalence of avascular necrosis in osteoporotic patients. Some studies in lupus patients treated with cytotoxic drugs and corticosteroids have been carried out, which have shown that the prevalence of asymptomatic avascular necrosis is high in these patients (8). One of the things that justifies the difference between our study and these studies, is that avascular necrosis can be caused by lupus in lupus patients. In this study, no significant association was observed between gender and age and femoral avascular necrosis. The most important reason could be the small size of understudy population. In this study, we examined all patients who had surgery. Because of the low prevalence of avascular necrosis that was seen in only two patients, analyzing this problem in patients and comparison to demographic factors, and things such as history of dialyses, hospitalization and CMV was not possible. In this study, only two patients had avascular necrosis. The only factor that was statistically significantly associated with avascular necrosis of the femoral head was osteoporosis in hip densitometry, which in patients with osteoporosis in hip densitometry there was a 25% chance of avascular necrosis. Although because of small size of patients with avascular necrosis that only one had hip osteoporosis, the results are not reliable. Based on the results, the prevalence of asymptomatic avascular necrosis of the hip in patients after kidney transplant is not so high; MRI screening is not cost-effective or reasonable. And it's better to use it on symptomatic patients or with abnormal findings in physical exam. Of the factors studied, the only factor in kidney transplant patients that was associated with avascular necrosis of the hip was densitometry osteoporosis in the hip. So, MRI in these patients is recommended to evaluate the risk of avascular necrosis. The interpretation of MRI results depends on the radiologist. The results may be variable, based on the radiologist which interprets the information. Therefore, in this study, we have requested two separate radiologists to interpret the MRI findings. When the results were incompatible, a third radiologist interpreted the MRI.

5. CONCLUSIONS

According to results, prevalence of femoral head avascular necrosis is not higher in patients after transplant and it has no significant relation to age, sex, BMI, time passed after transplant, CMV infection, hospitalization, history of dialysis or type of donator. Also, there was no significant correlation between the vertebra densitometry and the overall results of densitometry with avascular necrosis on MRI. The only factor associated with avascular necrosis in this study was osteoporosis in the hip densitometry.

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CONFLICT OF INTEREST:

There is no conflict of interest to be declared.

AUTHORS' CONTRIBUTIONS:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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