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**What is the Difference between Causes of ESRD in Iran and Developing Countries?**

Beladi Mousavi SS\*, Hayati F \*\*, Talebnejad M \*\*\*, Mousavi M ±.

\*Associate Professor, Department of internal medicine, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran, \*\*Assistant Professor, Department of internal medicine, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran, \*\*\*Department of Urology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran. ± Department of Chemistry, Islamic Azad University, Omidiyeh Branch, Omidiyeh, Iran.

Correspondence: Dr. F. Hayati, Assistant Professor, Department of internal medicine, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran, Telephone: +98(916) 311-4465, Fax: +98(611) 221-6504, E-mail: Fatemehhayati93@gmail.com

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**Abstract:**

**Introduction:** End stage renal disease (ESRD) is one of the most common life-threatening diseases. In the past two decades, there have been significant changes in the cause of ESRD around the world, and aim of the study was to determine its causes in Khouzestan province, Iran.

**Materials and Methods:** We retrospectively reviewed the medical records of our ESRD patients from January 1999 to March 2010. ESRD was defined as chronic and irreversible loss of kidney function requiring dialysis. We included only adult ESRD patients on maintenance hemodialysis, more than 2 months before entering the study. SPSS (version 15) software was used for data analysis.

**Results:** In our study, a total of 1000 adult ESRD patients, with mean age of  $51.54 \pm 16.39$  years were included. The male to female ratio was 1.3: 1 which had no significant changes during the period of study. The mean age of our patients at starting of hemodialysis was 41.23 years in 1999, but it increased to 56.91 years in 2010, which is up 15.68 years during this period.

In overall, the most common causes of ESRD were Diabetes Mellitus (n=282, 28.2%), Hypertension (n=265, 26.5%), unknown (n=242, 24.2%), Glomerulonephritis (n=79, 7.9%), Obstructive Uropathy (n=70, 7%), Cystic Kidney Disease (n=51, 5.1%) and unirenal (n=1, 0.1%). Although, two main causes of ESRD in patients aged 40 years and older (n=761)

were also Diabetes Mellitus (n=255, 33.5%) and Hypertension, however, in patients with less than 40 years of age (n=239), the most common causes were unknown and Glomerulonephritis. There were no significant difference in the main causes of ESRD (Diabetes Mellitus and Hypertension) between men and women (P= 0.26 and P= 0.48). But there was a significant association between mean age of diabetic ( $56.71 \pm 13.35$ ) versus non diabetic ( $49.51 \pm 17.03$ ) hemodialysis patients ( $p < 0.001$ ).

Conclusions: Based on our findings, the most common causes of ESRD in Khuzestan province, Iran were Diabetes Mellitus and Hypertension similar to developing countries. But, its causes are unknown in the significant percent of patients in contrast to these countries.

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**Keywords: End stage Renal Disease; Hemodialysis; Diabetes Mellitus; Hypertension**

### **Introduction:**

End stage renal disease (ESRD) is a public health problem and life-threatening diseases with significant health consequences and poor outcomes.<sup>(1-3)</sup>

As seen worldwide, the incidence and prevalence of ESRD have also significantly increased and cost of renal replacement therapy (RRT) imposes a major burden for health-care systems.<sup>(4-7)</sup>

Quality-of-life studies have shown that, although the life expectancy and outcome of patients with ESRD has improved since the introduction of dialysis, it is still far below that of the general population in developed and developing countries.<sup>(8-10)</sup> As an example, the mean life span at age 49 in the United States is 33 years in the general population but only seven years in patients on dialysis.<sup>(11)</sup> In addition, five-year survival of ESRD patients on HD in a study from Iran is only 46.8% that is very far below that of the general population.<sup>(10)</sup>

Improving outcomes in ESRD patients requires an integrated approach to prevention, detection and management of the different primary renal diseases causing ESRD. In the past two decades, there have been significant changes in the type of renal diseases causing ESRD in developed countries, and aim of the study was

to determine its causes in Khuzestan province, Iran as a developing country.

### **Material and Methods:**

This epidemiologic retrospective study was conducted on ESRD patients who referred to 9 hemodialysis centers in 8 cities of Khuzestan province, Iran from January 1999 to March 2010.

The ESRD was defined as patients who suffered from irreversible and permanent loss of renal function due to a state of uremia, requiring renal replacement therapy.

According to clinical manifestation, patient and family history, lab data, radiology and sonography, the primary cause of ESRD had determined by nephrologists or internists. We also retrospectively reviewed the medical records of these patients for general information like age and sex.

We are included only hemodialysis (HD) patients older than 16 years of age who were dialysed more than 2 month before entering the study. Therefore, the child patients and patients who survived less than two months after starting of HD were excluded.

Patients who were hemodialysed because of acute renal failure, and patients with a

history of kidney transplantation were also excluded.

**Statistical analysis:** All the analyses were conducted using the statistical package for social sciences (SPSS) version 15 software. The mean and standard deviation of each characters and quantitative variables were calculated. For comparison two group's quantitative data, we were used student's t test and the significant differences between groups were determined at the  $< 0.05$  probability level in all analyses.

### Results:

A total of 1254 ESRD patients referred to our hemodialysis centers during the study period. From them, 353 patients had exclusion criteria and the study performed on 1000 HD patients, 574 males (57.4%) and 426 Females (42.6%) with male to female ratio of 1.3: 1 which had no significant changes during this period. The mean age of our patients was  $51.54 \pm 16.39$  years. It was in males  $51.87 \pm 15.96$  and in females  $51.09 \pm 16.98$  years. (Figure 1)

The mean age of ESRD patients at starting of renal replacement therapy was 41.23 years in 1999, but it increased to 56.91 years in 2009, which is up 15.68 years during the period of study

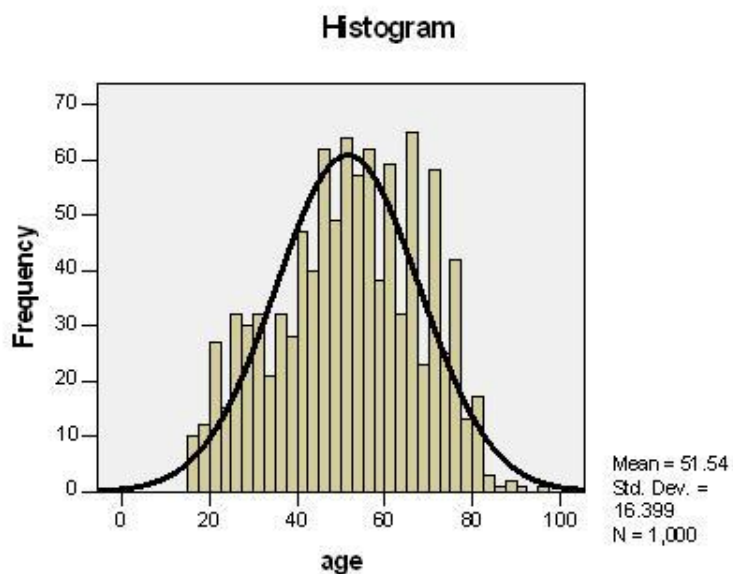
The most common blood type was blood group O (n=429, 42.9%) followed by A (n=278, 27.8%), B (n=251, 25.1%) and AB (n=42, 4.2%), 942 patients (94.2%) Rh positive and others (n=58, 5.8%) Rh negative.

In overall, the most common causes of ESRD were Diabetes Mellitus (n=282, 28.2%), Hypertension (n=265, 26.5%), unknown (n=242, 24.2%), Glomerulonephritis (n=79, 7.9%), Obstructive Uropathy (n=70, 7%), Cystic Kidney Disease (n=51, 5.1%) and unirenal (n=1, 0.1%) (Figure2). As the seen in Figure3, two main causes of ESRD in patients aged 40 years and older (n=761) were also Diabetes Mellitus (n=255, 33.5%) and Hypertension (n=219, 28.8%). In addition, the mean age of diabetic and hypertensive hemodialysis patients versus non diabetic and non hypertensive patients were  $56.71 \pm 13.35$ ,  $54.42 \pm 15.42$  and  $49.51 \pm 17.03$ ,  $50.50 \pm 16.62$  years respectively and there were a significant association between them ( $p < 0.001$  and  $p = 0.001$ ).

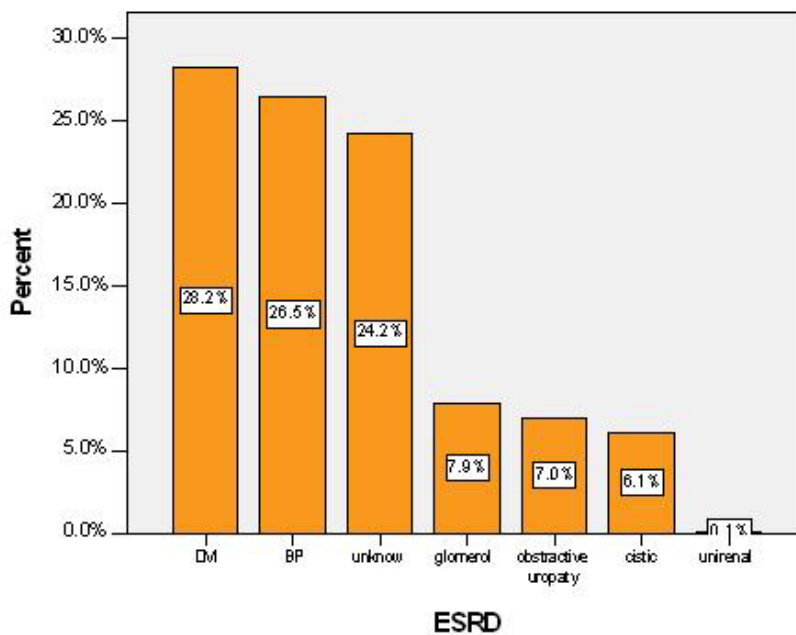
In patients with less than 40 years of age (n=239), the most common causes were unknown (n=74, 31%), and Glomerulonephritis (n=50, 20.9%), followed by Hypertension (n=46, 19.2%), Obstructive Uropathy (n=27, 11.3%), Diabetes Mellitus (n=27, 11.3%) and Cystic Kidney Disease (n=15, 6.3%) (Figure4).

Figure 5 and 6 show the causes of ESRD according to gender and there were no significant difference in the main causes of ESRD (Diabetes Mellitus and Hypertension) between men and women ( $P = 0.26$  and  $P = 0.48$ ).

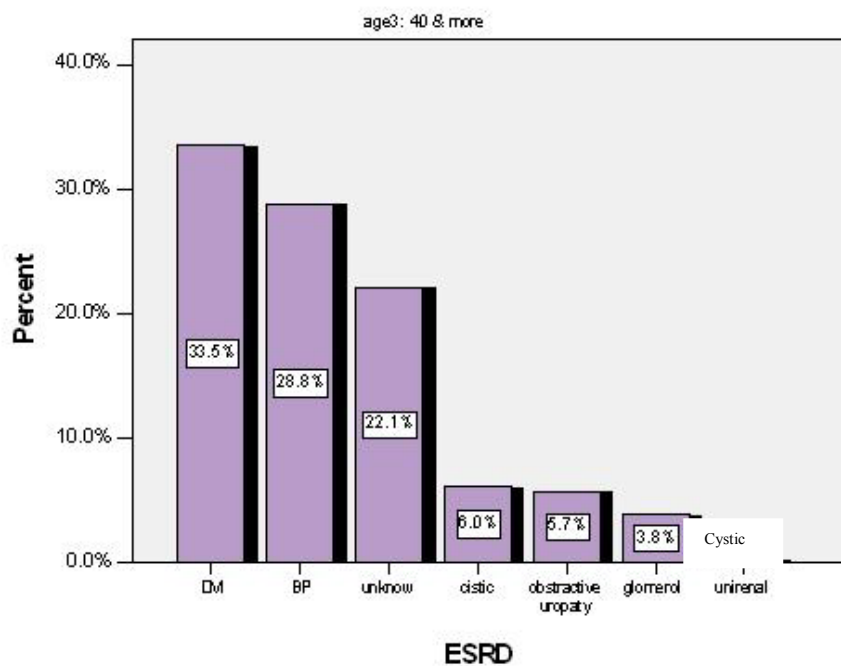
**Figure 1:** Age distribution of hemodialysis patients



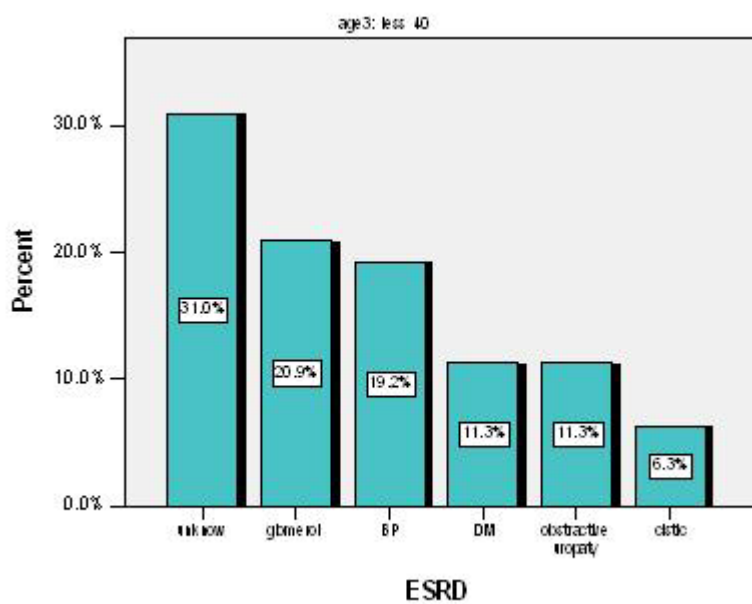
**Figure 2:** in overall Causes of ESRD



**Figure 3:** Causes of ESRD in patients with  $\geq 40$  years of age



**Figure 4:** Causes of ESRD in patients with < 40 years of age



**Figure 5:** Causes of ESRD in Men

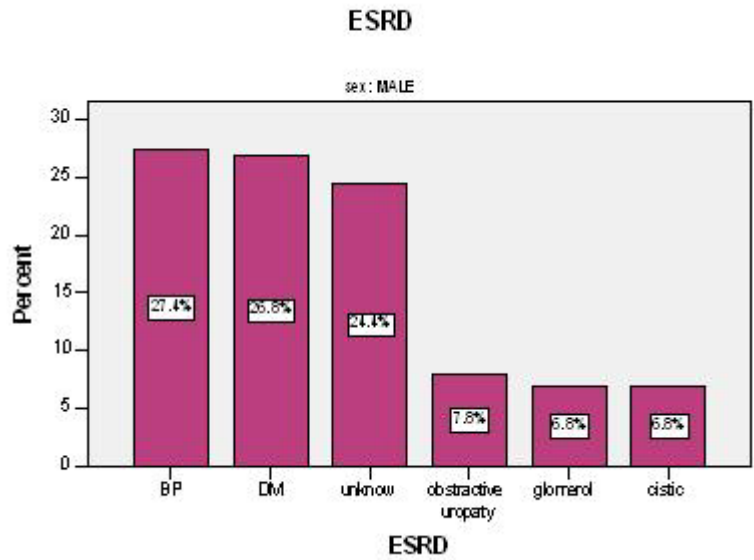
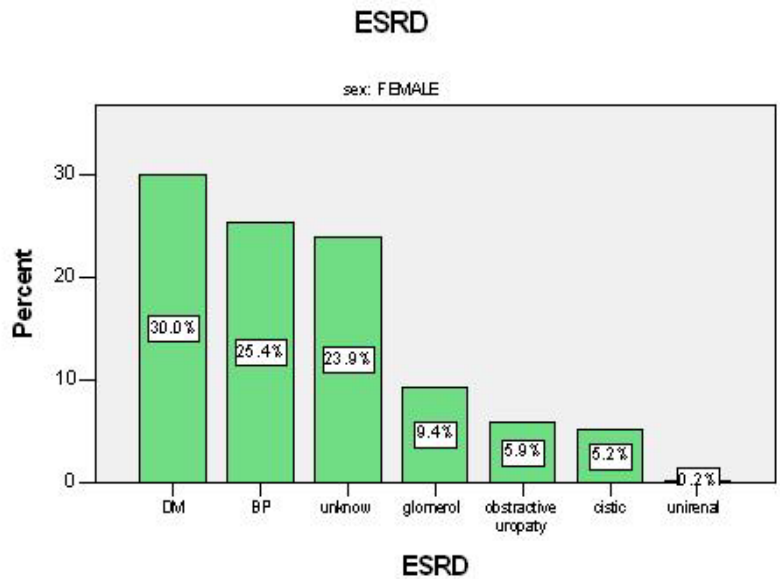


Figure 6: Causes of ESRD in Women



**Discussion:**

The evaluation and determination of primary renal diseases causing ESRD in each country and Comparison with other centers is very important. Some of the most common cause of ESRD is preventable, therefore it helps physicians for early detection, and good management

of these diseases; and it can a good guide for better prevention of ESRD.

There are many studies about primary causes of ESRD in developed countries. According to these studies, glomerulonephritis (GN) in its several forms, is the most common initiating cause of ESRD in the past decades. However, possibly because of more aggressive treatment of glomerulonephritis and because

of changing practices in patient acceptance of ESRD programs, it is well established that diabetic nephropathy particularly type 2, and probably hypertensive nephrosclerosis are now the leading causes of ESRD in these countries.<sup>(12-15)</sup>

Unfortunately, there is lack of data about etiology of ESRD in developing countries like Iran and it appears that it may differ by factors such as genetic background, diet, life expectancy, and others. Therefore, there is an important question. Are the diabetes mellitus and hypertension are also the leading causes of ESRD in Iran?

We showed in the present study in Khouzestan province, Iran, that these two disease, diabetes mellitus and hypertension are the leading causes and they have in together 55% causative role.

Few other studies have done about causes of ESRD in Iran and they are also demonstrated similar results. For example Nobakht et al reported that ; Among the causes leading to ESRD in incident patients in Iran, diabetes mellitus and Hypertension/vascular disease are the most frequent.<sup>(16)</sup> Malekmakan et al also demonstrated that; hypertension and diabetes mellitus are the most common causes of ESRD in the Fars province of Iran.<sup>(17)</sup> Mahdavi-Mazdeh et al also shows that: Diabetic nephropathy and possibly hypertensive nephrosclerosis are the leading causes of ESRD in Iran.<sup>(18)</sup> However, in contrast to these studies, a study was done in Iran about 10 years ago that determined etiology of ESRD, which showed GN and hypertension, was the commonest causes.<sup>(19)</sup>

Therefore, although GN was the most common initiating cause of ESRD in the

past decade in Iran, possibly because of increasing prevalence of obesity, diabetes and hypertension in our country, as noted by Krzesinski et al, now diabetes mellitus and hypertension are the leading causes of ESRD similar to developed countries.<sup>(20)</sup> There is an other important question now. What is the difference between causes of ESRD in Iran and developing countries?

The results of our study show that significant proportion of patients with ESRD is due to unknown etiology (24%) similar to other studies in Iran for example Mohammad Aghighi et al study in 2009<sup>(18)</sup>, Leila Malekmakan et al study in 2009<sup>(17)</sup>, Ali Nobakht Haghighi et al study in 2002<sup>(16)</sup>, Salahi et al study in 2004<sup>(19)</sup> and in contrast to the united state (5.9%).<sup>(21)</sup>

We think it is due to the late presentation of patients when ESRD has already developed and late referral to the nephrologists in Iran. Unfortunately in most of developing countries like our country, probably because low socioeconomic status, people were not aware of signs and symptoms of chronic kidney diseases. Thus they are presented to the hospital when they have severe signs and symptoms of uremia and at this time determining the primary renal disease lead to ESRD is not possible.<sup>(19)</sup>

Although, renal biopsy is the most definitive method of differentiating acute kidney diseases from chronic kidney diseases, it is not helpful for differentiating different causes of ESRD. At the late stage of chronic kidney disease, histologic findings include glomerulosclerosis, tubular atrophy and interstitial fibrosis regardless of the etiology of kidney

failure and therefore renal biopsy is not helpful at the late stage. In addition, a significant proportion of patients with ESRD have very small kidneys. Therefore, kidney biopsy is also not possible to perform at the late stage of disease because of increment risk of complication and generally dose not recommended (22,23)

### Conclusion:

In conclusion, the results of our study demonstrated that Diabetic nephropathy and hypertensive nephrosclerosis are the leading causes of ESRD in Khuzestan province, Iran similar to developed countries. These two diseases in together have 55% causative role that could be prevented by an aggressive approach in controlling blood sugar and blood pressure. In addition, significant proportion of patients with ESRD in our country is due to unknown etiology (24%) in contrast to the united state (5.9%). We think it is due to the late presentation and late referral of patients with ESRD to the specialists and therefore general physicians, nurses and chronic kidney disease patients have to be educated about the benefits of early referral and presentation of these patients to the nephrologists.

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