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# *Aetiological Factors Associated With End Stage Renal Disease; Analysis of End Stage Renal Patients in Sri Lanka*

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**Abstract**

**Introduction: End stage renal disease (ESRD) can be considered as one of the growing health problems as well as a public health issue in Sri Lanka. The demographic and epidemiological transition currently the country undergoes, contribute significantly to this problem.**

**Methods: This study was conducted at the Nephrology Clinic, Kandy Teaching Hospital, a tertiary level medical institution. The study sample consisted of renal transplant patients satisfied the selection criteria. Considering the estimated sample size, no sampling techniques were used and a total of 305 patients interviewed using the study instrument, an interviewer-administered questionnaire.**

**Results: Investigation of possible aetiology of ESRD revealed that for 69.5% cases aetiology was not well established. Among the known aetiological factors, diabetes (38%) was the commonest followed by nephrotic syndrome (19%) and hypertension (18%). This distribution pattern differs from what was observed in other countries. The differences in the aetiology of ESRD in regard to sex of patients, ethnicity, educational status, occupation and income were statistically not significant.**

**Conclusion: Investigation of possible aetiology of ESRD revealed that for 69.5% cases aetiology was not well established. Among the known aetiological factors, diabetes (38%) was the commonest followed by nephrotic syndrome (19%) and hypertension (18%). The differences in the aetiology of ESRD in regard to sex of patients, ethnicity, educational status and occupation were statistically not significant.**

**Keywords – End Stage Renal Disease, Aetiological factors, Non Communicable Disease.**

## I. INTRODUCTION

The kidneys, which lie on either side of the lower vertebral column in the posterior part of the abdomen, are very important organs in our body. They excrete excess water, salts and waste products of metabolism. As such, kidneys have a major role in whole-body homeostasis. Among its homeostatic functions are acid-base balance, regulation of electrolyte concentrations, control of blood volume, and regulation of blood pressure. The kidneys accomplish these homeostatic functions independently and through coordination with other organs, particularly those of the endocrine system. Kidneys themselves are endocrine organs that produce and secrete hormones such as rennin, calcitriol and erythropoietin.[1]

Most kidney diseases attack the nephrons, the basic functional units of the kidney and causing them to lose their filtering capacity. Damage to the nephrons may happen quickly, often as the result of injury, poisoning, snake bite or acute infections such as leptospirosis. The sudden drop in kidney function is called acute renal failure (ARF). If timely and proper treatment is given, acute renal failure can be reversed.[1,2]

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Most kidney problems, however, happen slowly as in diabetes and hypertension. A person may have "silent" kidney disease for years. When the damaging process is slow, after years or even decades only the damage becomes apparent.[1,2] Gradual loss of kidney function is called chronic kidney disease (CKD) or chronic renal insufficiency. People with CKD may go on to permanent kidney failure. Total or nearly total and permanent kidney failure is called end-stage renal disease (ESRD).[2]

A cohort study of 9082 African-American and white adults of age 30 to 74 years showed that African Americans experience higher rates of chronic kidney disease (CKD) than do whites. The incidence of all-cause CKD was 2.7 times higher among African Americans, compared with whites.[3] It was hypothesized that racial differences in modifiable risk factors would account for much of the excess risk of CKD. Suggested explanations for this racial disparity include lower socioeconomic status among African Americans, higher prevalence and greater severity of diabetes mellitus and hypertension among African Americans, and increased inherited susceptibility of African Americans to kidney damage.[3,4]

Other than African Americans, People of Native American and Hispanic descent are also at an elevated risk for both kidney disease and diabetes.[5] Though the racial association remained strong and statistically significant across many studies, most of the excess risk of CKD experienced by certain ethnic groups remains unexplained by traditionally measured risk factors.[3,4.5] The excess risk of CKD among African Americans than whites was much greater among middle-aged adults (30 to 59 years of age; RR = 4.23) than among older adults (60 to 74 years of age; RR = 1.27), indicating an interaction between race and age.[3]

A case control study was conducted in Medawachchiya, SriLanka to find out the possible risk factors for CKD prevalent in that area. For this study ,84 CKD patients who were regularly followed up to the clinic and 155 age and sex matched controls were studied. This study showed that young male famers of low socioeconomic states were at a high risk. They were no associations with diabetes ,hypertension, agrochemicals snakebite, alcohol, medical drugs, traditional medians, water source, florid level of water and usage of aluminum utensils for cooking.[6,7]

The aetiology for CKD/ ESRD varies between regions, countries, sexes, races, age groups and across many other factors, but diabetes and hypertension are usually dominant factors, followed by glomerular and vascular causes.[3,4.5] Diabetes mellitus is the leading single cause of ESRD in United States. According to the 2002 Annual Data Report of the United States Renal Data System (USRDS), 42% of non-Hispanic dialysis patients in the United States had ESRD caused by diabetes.[5] Hypertension (high blood pressure) is the second leading cause of ESRD in adults, accounting for 25.5% of the patient population, followed by glomerulonephritis (8.4%). African Americans are more likely to develop hypertension-related ESRD than Caucasians and Hispanics.[5] Among children and young adults under 20 years on dialysis, glomerulonephritis is the leading cause of ESRD (31%), and hereditary, cystic, and congenital diseases account for 37%.[5]

A study done in United States also demonstrated similar sequence, but with different proportions. According to this survey, diabetes (34%), hypertension (25%), glomerulonephritis (6%), and kidney cysts (4%) were the leading causes for ESRD. However, in Australia a survey reported glomerulonephritis among more than a quarter of ESRD patients.[7] There leading causes for ESRD were glomerulonephritis (27%), diabetes (26%), hypertension (16%), and polycystic kidney disease (6%).

The aetiology of CKD in most parts of the Sri Lanka is similar to that descried in several studies conducted in various countries. Almost all CKD cases studied in a semi uran area in the Central Province had diabetes, long standing hypertension or both. For this study, a sample from randomly selected clusters (n=253) was screened and the prevalence of proteinuria (i.e. presence of protein n urine)which was considered as the disease marker for CKD in this study was 3.2%. [7,8] )However, it is not so for large number of cases reported from North Central Province in SriLanka. Regional clustering of cases seen in North Central Province of Sri Lanka and its surroundings suggests the possibility of environmental factors as aetiology.[6] According to available literature, although CKD gains epidemic dimensions worldwide, it is rarely directly caused by environmental factors.[3,4]

## II. METHODS

The study was a hospital-based descriptive study. It was conducted at the Kandy Teaching Hospital, a tertiary level medical institution. The study population comprised patients, who satisfied the following selection criteria:

- Underwent renal transplantation after year 1st of January 2000 at the Teaching Hospital, Kandy
- Following nephrology clinic at the Teaching Hospital, Kandy since renal transplantation
- Consented to participate in the study

Taking into cconsideration the total number of patients attending the nephrology clinic at the study setting, it was decided not to use any sampling methods. All the patients who satisfied the selection criteria were studied and the investigator was able to interview only 305 subjects during the study period.

The use of self-administered questionnaires demands some level of education and skill from the respondent. Since the educational level and the ability to understand questions varied among respondents, it was decided to use an interviewer-administered questionnaire for this study. The questionnaire was designed taking into consideration the variables identified from the objectives of the study.

The study instrument was pre-tested on a sample of renal transplant patients (n = 10) who were attending clinic at the National Hospital of Sri Lanka, Colombo. These patients were not part of the main study. The purpose of this pretest was to assess the feasibility of administering the questionnaire at a clinic set up, clarity and comprehensiveness of the questionnaire and the time taken to complete the same.

Measures were taken to minimize the possible biases during the designing stage of study instruments and during administration of questionnaire. All attempts were taken to keep the questionnaire simple. Except for a few, the majority of the questions had been structured and pre-coded. It was subjected to pre testing and shortcomings were rectified.

The selection criteria were strictly followed through out the study period. This helped to minimize the selection bias. The investigator administered the questionnaire in the same sequence using the same words with necessary explanation. These measures enabled minimization of interviewer bias.

Responses given by the participants of the study were cross checked whenever possible with the details written in the clinic records and diagnosis cards. This helped to reduce the recall bias. Questionnaires having omissions or discrepancies were identified at the end of clinic sessions and again cross checked with records kept at the clinic.

## III. Results

Among the participants of the study, 215 (70.5%) were males and the remaining 90 (29.5%) were females. The highest proportion of patients was Sinhalese (79.0%), followed by Moors (13.1%). About 21% of patients were unemployed and almost all of them were males, while almost equal number (20%) was housewives.

For majority of patients (79.3%), age of onset of end stage renal disease was in their productive age group of 25 to 54 years. The highest proportion of patients (31.5%) had their disease onset while they were in the 35 to 44 years.

Table 1: Age of onset of end stage renal disease (in years)

| Age of onset (years) | Number | % |
|---|---|---|
| 18- 24 | 50 | 16.4 |
| 25 - 34 | 81 | 26.5 |
| 35 - 44 | 96 | 31.5 |
| 45 - 54 | 65 | 21.3 |
| 55 - 64 | 11 | 3.6 |
| 65 and above | 02 | 0.7 |
| **Total** | **305** | **100.0** |

Bivariate analysis was done to find whether any association existed between the age of onset of end stage renal disease and factors such as sex, ethnicity, education and occupation.

In all age groups, there were more male patients. However, the difference in age of onset of End Stage renal Disease (ESRD) in regard to sex was found to be statistically not significant (chi-square = 5.87, p = 0.31).

Review of age of onset of ESRD in relation to ethnicity showed that Sinhalese were more in all age groups. However, the difference in age of onset of disease in regard to ethnicity was found to be statistically not significant (chi square = 29.33, p = 0.0815).

Analysis of the age of onset of end stage renal disease in relation to occupation showed that though most of the patients were either unemployed or house wives, in the age group of 35 to 44 years, most of the patients were self employed (small scale, including farming or cultivation). The difference in age of onset of end stage renal disease in regard to occupation was found to be statistically significant (chi-square 93.34, p = 0.000).

The source of water showed that more than half of the transplant patients (53.5%) were using water obtained from wells for drinking purposes.

Table 2: Renal transplant patients by source of drinking water

| **Source of water** | **Number** | **%** |
|---|---|---|
| Well | 163 | 53.5 |
| River stream | 05 | 1.6 |
| Pipe born | 124 | 40.7 |
| Mineral water (bottled) | 08 | 2.6 |
| Others | 05 | 1.6 |
| **Total** | **305** | **100** |

The review of possible aetiology of end stage renal disease revealed that for 69.5% of patients, aetiology was not well established. Among the known aetiological factors, diabetes (37.6%) was the commonest followed by nephrotic syndrome (19.4%) and hypertension (18.3%).

Table 3: Renal transplant patients by possible aetiology of end stage renal disease

| **Probable aetiology** | **Number** | **%** |
|---|---|---|
| Unknown aetiology | 212 | 69.5 |
| Diabetes mellitus | 35 | 11.5 |
| Hypertension | 17 | 5.6 |
| Nephrotic syndrome | 18 | 5.9 |
| Polycystic kidney disease | 04 | 1.3 |
| Alport Syndrome | 02 | 0.7 |
| Others | 17 | 5.6 |
| **Total** | **305** | **100.0** |

Bivariate analysis was done to find whether any association existed between the aetiology of end stage renal disease and factors such as age of the onset of ESRD, sex, ethnicity, educational status, and occupation and monthly family income..

The difference in the aetiology of end stage renal disease in regard to age of onset of end stage renal disease was found to be statistically significant (chi square = 84.83, p = 0.00).

Table 4: Aetiology of end stage renal disease by age of onset of end stage renal disease

| Age of onset | Aetiology of end stage renal disease | | | | | | Total |
|---|---|---|---|---|---|---|---|
| | Unknown | Diabetes | Hyper-tension | Nephrotic syndrome | Polycystic kidney | Others | |
| 18 - 24 | 37 | 0 | 1 | 6 | 0 | 6 | 50 |
| 25 – 34 | 68 | 2 | 1 | 5 | 0 | 5 | 81 |
| 35 – 44 | 69 | 11 | 3 | 6 | 2 | 5 | 96 |
| 45 – 54 | 33 | 16 | 11 | 1 | 2 | 2 | 65 |
| 55 – 64 | 5 | 5 | 0 | 0 | 0 | 1 | 11 |
| 65 + | 0 | 1 | 1 | 0 | 0 | 0 | 2 |
| **Total** | **212** | **35** | **17** | **18** | **4** | **19** | **305** |

The proportion of male patients with unknown as well as known aetiological factors except for polycystic kidney disease was more than that of females. However, for those with polycystic kidney disease both sexes had same number of patients. The difference in the aetiology of end stage renal disease in regard to sex of patients was found to be statistically not significant (chi square = 3.77, p = 0.58).

The proportion of Sinhalese patients was more for both unknown and known aetiological factors. The difference in the aetiology of end stage renal disease in regard to ethnicity of patients was found to be statistically not significant (chi squire = 34.00, p = 0.023).

The difference in the aetiology of end stage renal disease in regard to educational status of patients was found to be statistically not significant (chi squire = 25.84, df = 25, p = 0.418).The difference in the aetiology of end stage renal disease in regard to occupation of patients was found to be statistically not significant (chi squire = 25.81, df = 40, p = 0.410).

## IV. Discussion

The mean age of study sample was 40.3 years (95% CI: 39.1 - 41.6) and the median was 41 years. The youngest person interviewed was 19 years old and the oldest was 69 years old. Sex distribution of the study sample showed a male preponderance (70.5%). The male preponderance of ESRD/ CKD patients was observed in other studies also.[9]

Distribution of ethnicity and religion of patients reflected the ethnic and religious composition of the general population. About 76% of patients were married and living with their spouses. 75% of patients admitted that their main caregiver was their spouses and almost all remaining patients were looked after by their parents or other relatives. As these patients need support throughout their remaining life, while planning rehabilitation services the need for providing it in the family environment should be taken into consideration.

The variables described under sociodemographic characteristics were mostly constitutional factors and therefore the recall bias was minimal. Under sociodemographic characteristics, details of drinking water were also obtained and the intention for this inclusion was to find any relationship between drinking water and CKD/ ESRD, as postulated in an unpublished report (6). The data showed that 54% used well water and another 41% used pipe born water for drinking purposes. However, the analysis was not done, because the resources available for the investigator did not allow obtaining information on the chemical contents of water such as fluoride and the duration of use of water from different resources since the childhood of these patients.

According to the responses given, almost 99% used water for drinking after some form of treatment such as boiling or filtering. Definitely, it did not represent the behaviour and practices mostly prevalent in the general population. This shows that these patients changed their practices with the onset of kidney disease or since transplantation.

As the study population was only those accessible to the kidney transplantation program of the Teaching Hospital, Kandy, the sociodemographic characteristics described here did not truly reflect the characteristics of end stage renal disease patients in Sri Lanka.

For almost four fifth of patients (79%), age of onset of end stage renal disease was in the productive age group of 25 to 54 years. This finding was consistent with what was described in literature.[8] The economic consequences of this to the patients, their families, society and country should be analyzed further.

Bivariate analysis showed that the differences in age of onset of end stage renal disease in relation to sex (chi-square = 5.87, p = 0.31) and ethnicity (chi square = 29.33, p = 0.0815) were statistically not significant. However, differences in age of onset of ESRD in regard to educational status (chi-square =39.47, p = 0.033), and occupation (chi-square 93.34, p = 0.000) were statistically significant.

While interpreting above results, the influence of confounding factors should be considered. Only those who were accessible to the transplantation program of the Teaching Hospital, Kandy were studied. Factors such as income, educational status and availability of donors influence the accessibility of ESRD patients to any renal transplantation program. Further, as the onset of CKD/ ESRD is insidious, it is very difficult for both clinicians and patients to exactly state the age at the onset.

In Sri Lanka, many preliminary research studies reported high prevalence of chronic kidney disease due to unknown etiology especially in North Central Province and its surroundings.[6] In this study also, investigation of possible aetiology of ESRD revealed that for 69.5% cases aetiology was not clear.

It should be noted that even for cases with a known history of hypertension and/ or diabetes mellitus, some times the aetiology was recorded as “unknown” in the relevant medical records by the treating physicians. About 40% of patients had hypertension at least for one year before the diagnosis of ESRD and 12% had diabetes (Some of the patients had both illnesses). However, according to the physicians these diseases could not be the reason for ESRD in some patients, as they were in the early stage or they were well controlled throughout. They strongly believe there should be some unknown factors contributing to the occurrence of CKD/ ESRD in these patients.

According to this study, among the known aetiological factors, diabetes (38%) was the commonest followed by nephrotic syndrome (19%) and hypertension (18%). This distribution pattern also differs from what was observed in other countries. According to global studies, diabetes mellitus (43%) and hypertension (23%) were the leading causes for CKD/ ESRD, followed by glomerular nephritis (12%) and cystic disease (3%) (5). In future, global epidemic of diabetes mellitus and obesity will invariably lead to high proportion of CKD/ ESRD cases secondary to diabetes. In America, prevalence of ESRD due to diabetes was 34% in 1999 and this proportion increased to 44% in 2003.[10]

Bivariate analysis showed that the differences in the aetiology of ESRD in regard to age of onset of ESRD was statistically significant (chi square = 84.83, p = 0.00). However, the differences in the aetiology of ESRD in regard to sex of patients(chi square = 3.77, p = 0.58), ethnicity (chi squire = 34.00, p = 0.023), educational status (chi squire = 25.84, p = 0.418) and occupation (chi squire = 25.81, p = 0.410) were statistically not significant.

## V. Conclusions

Investigation of possible aetiology of ESRD revealed that for 69.5% cases aetiology was not well established. Among the known aetiological factors, diabetes (38%) was the commonest followed by nephrotic syndrome (19%) and hypertension (18%). The differences in the aetiology of ESRD in regard to sex of patients, ethnicity, educational status and occupation were statistically not significant.

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