

Environmental Factors Incriminated in the Development of End Stage Renal Disease in El-Minia Governorate, Upper Egypt

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Abstract

Background and Aims: End Stage Renal Disease (ESRD) has various causes that differ according to patient's country. In Egypt it is a huge health problem with high prevalence in El-Minia governorate as 308 per million population suffer from it. The aim of the work is to investigate the possible causes of ESRD with an unknown etiology in El-Minia Governorate.

Methods: A total number of 216 patients with an unknown etiology of ESRD as well as 220 controls were interviewed using a structured questionnaire including information about environmental factors predicted to cause ESRD such as occupation, pesticide handling, and source of drinking water.

Results: Distribution of patients by residence showed that most patients lived in rural areas (76%), compared to 57% in controls ($p < 0.001$). Drinking unsafe water was reported by 72% of patients and 48% of controls ($p < 0.001$). Family history of renal disease was found among 10% of patients and 4% of controls ($p < 0.001$). Exposure to pesticides and using herbs for the treatment were more among patients than controls (52% Vs 14% respectively) and (34% Vs 6% respectively) ($p < 0.001$).

Conclusions: ESRD with an unknown etiology may be attributed to environmental factors such as drinking unsafe water, exposure to pesticides and using herbs for treatment. Educational programs for common people should be strengthened. Lead pipes water supplies should be changed. Use of any herbs should be prohibited except under the supervision of Ministry of Health.

Keywords: ESRD, Unknown Etiology, Environmental Factors

Introduction

End stage renal disease (ESRD) is emerging as a major health problem in Egypt. The prevalence of dialysis patients is presumed to have increased from 10 per million in 1974 to about 165 per million in 1995 (1), and in 2005 it was 260 per million in El-Minia Governorate (2). The growing number of patients suffering from ESRD places a great demand on the health care resources in Egypt due to the high cost of dialysis and transplantation. The causes and risk factors for the development of ESRD vary worldwide. Diabetes and hypertension are the common

causes of ESRD in developed countries, whereas glomerulonephritis related to infections and obstructive uropathy are common in developing countries. The etiology of ESRD in El-Minia Governorate was

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unknown in 28% of patients (2) while it is only 3.7% in the United States (3).

During the year 2002, the unknown etiology of ESRD in El-Minia Governorate was 32.9% (4). Unrecognized environmental toxins or occupational exposures may lead to development and progression of chronic kidney disease in addition to the chronic pesticide exposure which could be an environmental risk factor for the development of CRF. Internists should be aware of the role of occupational and environmental exposures contributing to chronic kidney disease (5).

Water pollution is subdivided into fresh water pollution e.g. plant material, organic materials, minerals, etc and marine water pollution e.g. domestic sewerage, food processing wastes, pesticides, or organophosphorus compounds (6).

The aims of the current study was to investigate the possible causes of ESRD with unknown etiology and its relation to the environment.

Material and Methods

El Minia governorate is formed of 9 districts. 800 Patients with ESRD were interviewed and a structured questionnaire was used to obtain information about personal details, occupational history and exposure to possible risk factors for ESRD. The risk factors assessed were occupation and pesticide handling, family history of renal diseases, sources of drinking water at home and at the field, history of use herbal treatment for a long time and history of snake bites. All patients underwent complete clinical examination, ultrasonography, dialysis frequency and other data investigating the cause of ESRD were also investigated. Those who had a known cause for ESRD were excluded from the study.

The causes of ESRD were diagnosed in 584 patients (73%) which were hypertension in 160 patients (20%), obstructive uropathy 96 patients (12%), pyelonephritis 40 patients (5%), glomerulonephritis 88 patients (11%), diabetic nephropathy 64 patients

(8%), schistosomiasis 24 patients (3%) and analgesic nephropathy 40 patients (5%) and others such as lupus nephritis 72 patients (9%). Unknown causes were found in 216 (27%) patients who were recruited in this study and they were patients presenting to different dialysis centers in El-Minia Governorate.

The control group consisted of 220 subjects randomly recruited from patients with unrelated health problems from the general hospitals of the nine districts. Systematic random sample for controls were chosen from the nine districts of El-Minia governorate. All patients came to the general hospitals within the last three weeks of December 2006 were numbered and every fifth patients was included in the sample of the control group. Furthermore, the cases and controls were matched for sex, age, smoking habits and for being free from diabetes mellitus and hypertension. Controls with history of any renal disease were excluded from the study. The final number of the control group was 220 patients. All the subjects were recruited after obtaining informed verbal consents.

Storing pesticides at home, using pesticides at fields, selling or exposure to pesticides by any mean were investigated in this study and considered as an important risk factor. Pipe water was considered as the only safe drinking water in El-Minia governorate, while drinking water directly from the stream, tube wells or stored water was considered as unsafe water for drinking. Some unknown herbs are commonly used by Egyptians for treating different illness. These herbs are not standardised and have unknown compounds. These herbs are sold by non-medical personnels without manufacturing or expiry dates.

Statistics

Data collected from cases and controls were manipulated using an IBM compatible PC and SPSS program for windows release 13 for statistical analysis. Quantitative data were presented as mean \pm standard

Table 1. Characteristics of patients with ESRD of unknown etiology compared to controls in El-Minia Governorate, Egypt in 2006

Variables	Patients (n=216)	Controls (n=220)	Significant test	P-value
Males	141 (65%)	152 (69%)	Z= 0.85	0.20
Females	75 (35%)	68 (31%)	Z= 0.85	0.20
Age/y (x±s.d)	44±11	45.1±7.2	t = 1.23	0.22
Height/cm (x±s.d)	163.4±18.7	162.3±11.3	t = 0.74	0.53
Weight/kg (x±s.d)	70.7±6.3	71.1±5.9	t = 0.68	0.51
BMI (x±s.d)	25.2±2.6	25.8±3.5	t = 2.03	0.06

deviation, while qualitative data were presented as absolute numbers as well as percentages. Comparison between cases and controls were tested using unpaired t-test for quantitative data and test of proportion for qualitative data. Propability (p value) less than 0.05 was considered as statistically significant. Odds ratio were calculated for each risk factor for ESRD. The 95% CIs were calculated as mean ± 1.96SE, where SE is the standard error and the SE was calculated as s.d./√n, where n is the number of the subjects and s.d. is the standard deviation.

Results

In El-Minia governorate, there are 19 dialysis centers with variable capacities. This study included 216 patients with an unknown etiology of ESRD from patients presenting to all the dialysis units in El-Minia governorate, as well as 220 patients (control) with unrelated health problems from general hospitals in El-Minia governorate. Males were more than females in this study in both case and control groups, control

patients were slightly older than patients (45.1±7.2 and 44±11 years old respectively) with no statistically significant difference between the two groups. The mean height, weight and body mass index were similar in both groups (p>0.05) (Table 1).

Farmers were more among patients, while clerks were less than controls (p<0.001), and there was no significant difference between the two groups regarding other jobs (Table 2). Majority of patients (75.9%) came from rural areas compared to 56.8% of controls (p<0.001) (Table 3). Source of drinking water at home or work was investigated in this study. It was found that 71.8% of cases used to drink unsafe water (from stream or tube wells), while 47.5% of controls used to drink the same kind of water (Figure 1). The difference between cases and controls was statistically significant (p<0.001).

About 10% of patients reported that they had family history of renal dysfunction compared to 3.6% of controls (p<0.001). On the other hand, storing pesticides at home, using pesticides at fields, selling or exposure to pesticides by any mean were investigated

Table 2. Occupation of patients with ESRD of unknown etiology compared to controls in El-Minia Governorate, Egypt in 2006

Occupation	Patients (n=216)	Controls (n=220)	Test of proportion	P-value
Farmers	87 (40%)	44 (20%)	3.64	0.001
Clerk	15 (7%)	67 (30%)	6.3	0.001
Manual work	20 (9%)	23 (11%)	0.42	0.34
No job	49 (23%)	46 (21%)	0.48	0.32
Housewife	45 (21%)	40 (18%)	0.69	0.25

in this study. It was found that 51.9% of patients exposed to pesticides compared to 34% of controls and this difference was statistically significant ($p < 0.001$). Using different types of herbs for traditional treatments were reported by 14.4% of cases and 5.9% of controls and this difference was also statistically significant ($p < 0.001$). History of snake bites were uncommon among patients (2.3%) and controls (0.9%) and this difference was not statistically significant ($p = 0.12$). In a multivariate logistic regression analysis, a family history of renal dysfunction, living in rural areas, exposure to pesticides and drinking unsafe water were significant predictors

of ESRD of unknown etiology (Table 4). Subjects with a family member with renal dysfunction were 3 times more likely to have ESRD of unknown etiology compared to those without such a family history. subjects drink unsafe water were 2.78 times more likely to have ESRD of unknown etiology compared to those who drink safe water. Subjects who live in rural areas were 2.4 times more likely to have ESRD of unknown etiology compared to those live in urban areas. Furthermore, subjects with history of exposure to pesticides were 2.08 times more likely to have ESRD of unknown etiology compared to those without such histories.

Table 3. Comparison between cases with ESRD of unknown etiology and controls regarding possible risk factors for ESRD in El-Minia Governorate, Egypt in 2006

	Patients n=216	Controls n=220	Test of proportion	P-value
From rural areas	164 (75.9%)	125 (56.8%)	4.22	0.001
Drinking unsafe water	155 (71.8%)	105 (47.5%)	5.17	0.001
Family history of renal disease	22 (10.5%)	8 (3.6%)	2.72	0.001
Exposure to pesticides	112 (51.9%)	75 (34%)	3.78	0.001
Use of herbs	31 (14.4%)	13 (5.9%)	2.9	0.001
History of snake bite	5 (2.3%)	2 (0.9%)	1.17	0.12

Figure 1. Possible causes of ESRD of unknown etiology

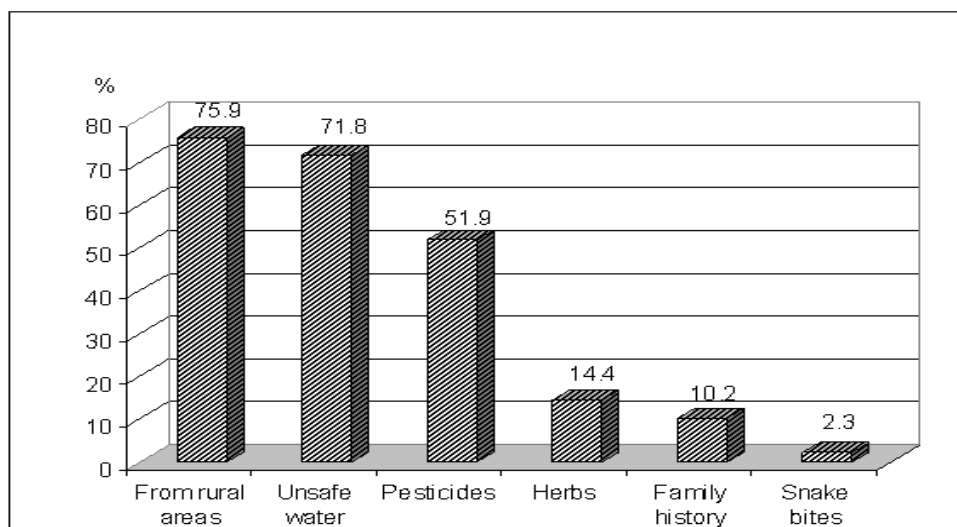


Table 4. Multivariate logistic regression of predictive risk factors of ESRD of unknown etiology in El-Minia Governorate, Egypt in 2006

	Odds Ratio	95% CI	P-value
Family history of renal disease	3.0	1.3 - 6.9	0.018
Drinking unsafe water	2.78	1.87 - 4.14	0.003
Living in rural areas	2.40	1.59 – 3.61	0.011
Exposure to pesticides	2.08	1.42 – 3.06	0.009

Discussion

The prevalence of ESRD is increasing in Egypt as well as as El-Minia Governorate and its etiology in many patients remains unknown. This study showed that the significant predictors of ESRD of unknown etiology are a family member with renal dysfunction, living in rural areas, drinking unsafe water, exposure to pesticides and using herbs for treating different illness. So, people with lower socioeconomic status, lower educational status and limited health care facilities may have more prevalence of ESRD with unknown etiology that may be attributed to environmental factors

A family history of renal dysfunction suggests a genetic etiology of the disease. However, given that only individuals in families living in this area develop the disease, it is suggested that the disease is triggered by an environmental factor in those that are genetically predisposed.

Past history of using herbs for treating different illness is a significant risk factor for ESRD of unknown etiology (Table 3). Most herbal preparation are not standardised and may have unknown compounds that result in ESRD. Chronic interstitial nephritis due to ingestion of Chinese herb *Stephania tetrandra* in a slimming regimen was described in Brussels, Belgium in 1993 (7). The withdrawal of this herb from the market caused reduction of ESRD in population of the affected area.

Snake bite is a recognised cause of acute renal failure because the toxins cause cortical necrosis that lead to renal failure. However, in the current study, only 5 out of the 216 patients (2.3%) and 2 out of the 220 controls (0.9%) reported snake bite in the past. The difference between cases and controls was not statistically significant and this point needs further investigations with large number of patients.

Most of the cases are from rural areas (75.6%) and 51.9% of cases were exposed to pesticides compared to 34% of controls ($p < 0.001$). Therefore, there is a serious concern whether exposure to pesticides is an etiological factor for ESRD. Previous study by Peiris–John et al, (8) reported an evidence of greater inhibition of acetylcholinesterase among patients with chronic renal dysfunction in the same study area compared with the patients with chronic renal dysfunction from non agricultural areas.

The current study indicated that being a farmer and exposure to pesticides were associated with ESRD. This suggests that long-term low-level (occupational or environmental) exposure to pesticides may have an impact on the development of ESRD.

Drinking unsafe water, mainly ground water, at home or field was significantly higher among patients than control groups. Ground water is high in mineral and heavy metals content and rich in fluoride. Dissolution of aluminium from poor-quality cooking utensils is high in the presence of fluoride

in water. The village folk use aluminium pots and utensils to store and boil water (9). Hence this study proposes that the high incidence of ESRD in El-Minia, Egypt is probably due to an environmental factor, with the clustering of patients within the families being due to a possible genetic predisposition to the potential environmental factor.

Several environmentally induced kidney diseases have been described in the literature (8, 10-12), Chronic heavy metal toxicity, such as that from lead and mercury is known to cause chronic renal damage. Cadmium is another heavy metal associated with renal disease (11). Industrial cadmium poisoning of several rivers in Japan caused contamination of locally produced rice, causing "Itai-itai disease" characterised by renal calculi and painful osteomalacia.

Balkan endemic nephropathy is a chronic kidney disease prevalent among settlers along the tributaries of the Danube River in Serbia, Bosnia, Bulgaria and Romania (13). First described in 1957, Balkan endemic nephropathy is a slowly progressive tubulointerstitial disease leading to ESRD. This disease has several factors similar to those of renal failure patients from rural areas, including the fact that the disease affects predominantly farmers, a familial aggregation of cases and interstitial nephropathy seen in renal biopsy (14).

Balkan endemic nephropathy has attracted the interest of researchers as a possible environmental disease, and many environmental and genetic factors have been evaluated as possible underlying causes (10, 11). One hypothesis considers that mycotoxins ingested in small amounts by individuals in the endemic regions might initiate the renal damage. Another theory considers the exposure to aromatic hydrocarbons leaching into well water in endemic areas as an etiologic factor (12).

The etiology of many patients of ESRD in El-Minia, Egypt still remains unknown. The current study strongly supports an environmentally induced disease. Further investigations should focus on

environmental factors and on the role of genetic factors.

Conclusions

ESRD with an unknown etiology may be attributed to environmental factors as, drinking unsafe water, exposure to pesticides and using herbs for treatment.

Recommendation

Education program for Nephrologists and practitioners should be strengthened with special emphasis on etiological factors leading to ESRD. In addition, educational programs for public should be strengthened to prevent drinking unsafe water and dealing with pesticides. Use of any herbs should be prohibited except under supervision of Ministry of Health.

Conflict of Interest

None declared.

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