

Chronic kidney disease:

**Assessment of current knowledge
and feasibility for regional research
collaboration in Central America**

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Presentation

Deficiencies in occupational health constitute a public health problem of epidemic proportions in the seven Central American Countries. The estimated two million occupational accidents per year in the Central American labor force mean that one out of every six workers has an accident at work sufficiently serious to require medical care. Occupational diseases are ignored or not diagnosed, and their socioeconomic consequences are seldom considered in policy formulation.

The Central American Health and Work Program (SALTRA), which works in collaboration with Central American and Swedish organizations and institutions, sponsored by the Central American Social Integration Secretariat (SISCA/SICA) with support from the Swedish Cooperation Development Agency for Development (ASDI) is addressing these problems. Its purpose is to develop national and regional public health skills for preventing occupational risks, to achieve sustainable improvements in production quality and efficiency.

Within this framework, the “Health and work” series is a response to the need for technical and conceptual tools in this vital area of Central American life, and as a way of disseminating information about these subjects to promote further investigation and improve the effects of actions taken in this field.

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Foreword

The number of patients with chronic kidney disease, CKD, and end-stage renal disease, ESRD, is increasing in both developed and developing countries, greatly expanding the need for chronic dialysis and renal transplantation. There are drastic differences in prognosis and outcome of a disease like ESRD in high- and low-income countries. When proper treatment is available the disease is usually not fatal but when there are few or no resources for dialysis or renal transplantation, death will soon follow. The potential influence from environmental, occupational and life-style risk factors is not well understood.

In Central America there is public concern about the increasing prevalence of CKD and ESRD, although this varies by country due to the lack of reliable information on the true rates of prevalence, incidence and related risk factors. Recently, several reports have been compiled, most notably in Nicaragua and El Salvador, on kidney disease and mortality in different populations. Due to lack of resources those reports are not conclusive, but they definitely seem to indicate a major problem in some of those subpopulations.

For several decades there has been collaboration between Central American and Swedish public and occupational health researchers. Several Sida-sponsored programs therefore have joined forces to collect and analyze existing information, and to design and perform pilot studies in preparation for applications for full-scale studies and effective interventions.

Impressive attempts to clarify the size of the problem and to identify risk factors have been made by concerned Central American researchers and clinicians, working with very limited resources. The support from Sida made it possible to bring together those people in a workshop where experiences could be shared, studies analyzed, different ways forward discussed, and bases laid for future information sharing and collaboration. The availability of modest sums for continued planning and pilot studies meant that no time was lost and that the workshop network could continue to keep in contact. This report summarizes the activities to date, and will be followed by others when the results of the ongoing studies are prepared for publication.

We are grateful to PAHO Nicaragua for constructive participation in the workshop and for summarizing some of the information, and to professor Carl-Gustav Elinder, Department of Renal Medicine, Karolinska University Hospital, for background information and suggestions for field study methods.

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SECTION I

Chronic kidney disease in Central America: An assessment of available information

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Introduction

Chronic kidney disease, CKD, is a major health issue in various parts of the world. The number of patients with end-stage kidney disease (ESRD) is increasing in both developed and developing countries, greatly expanding the need for chronic dialysis and renal transplantation (Meguid El Nahas & Bello, 2005; Rodriguez-Iturbe & Bellorin-Font, 2005).

Several risk factors for CKD have been reviewed previously (Atkins, 2005; McClellan, 2005). Diabetes and hypertension are well known risk factors, with solid epidemiologic evidence (Fox et al., 2004; Lea & Nicholas, 2002). There is little information on smoking as a risk factor for CKD (Fox et al., 2004). An increased risk of having renal damages has been associated with high alcohol intake but not with low intake (Perneger et al., 1999). There are also reports of alcohol consumption having a protective effect on renal function (Knight et al., 2003; Schaeffner et al., 2005).

Regarding frequent intake of analgesic drugs, there is solid clinical and good epidemiologic evidence of analgesic nephropathy caused by phenacetin (Delzell & Shapiro, 1998). However there is no convincing epidemiologic evidence that nonphenacetin-containing analgesics (including acetaminophen, aspirin and mixtures of these two compounds) or non-steroidal anti-inflammatory drugs cause CKD (Curhan et al., 2004; Delzell & Shapiro, 1998; Forel et al., 2001; Rexrode et al., 2001). Exposure to heavy metals such as lead, cadmium and arsenic, has been associated with chronic renal damage (Barbier et al., 2005; Van Vleet & Schnellmann, 2003). Renal toxicity after exposure to uranium has also been described (Kurtio et al., 2002).

Worldwide, there are some recognized endemic nephropathy regions such as Balkan (Cvorisec et al., 1998; Fuchs & Peraica, 2005; Pfohl-Leszkowicz et al., 2002) and Tunisia (Abid et al., 2003). The Balkan nephropathy is characterized by progressive renal failure, tubular microproteinuria, unremarkable urinary sediment, small and shrunken kidneys, and associated urothelial tumors. Some suggested agents are ochratoxin, aristolochic acids, heavy metals, and a complex interaction between sociocultural, genetic, and environmental factors (Djukanovic et al., 2001; Stoev, 1998; Tatu et al., 1998; Toncheva et al., 1998).

In Central America there is currently public concern about the prevalence of CKD and ESRD (Domínguez et al., 2003; Flores Reyna et al., 2003; Marín, 2003; MINSA-Nicaragua, 2003), although there is no reliable information about the prevalence of CKD and ESRD and related risk factors from one country to the next. The observed increase in demand for medical attention for patients with ESRD in hospitals in the region has supports the belief that there is in fact an increasing trend in the prevalence of CKD (Domínguez et al., 2003; García Trabanino et al., 2002). Many risk factors have been proposed to explain such an increase, e.g. agricultural work, pesticide exposure, and 'dirty' alcohol consumption. However, systematically collected evidence to support such these proposals

is scarce. The situation varies by country, with more information from countries such as El Salvador and Nicaragua, and almost no information from Honduras and Panama.

The present infrastructure in the region and the human resources are not enough to meet the demand for assistance for patients with ESRD. In countries such as El Salvador, around 15 million dollars per year are spent to pay the cost of renal replacement therapy (RRT) which covers only a small proportion of all existing cases in the country (Flores Reyna et al., 2003). Prevention and intervention measures are clearly and urgently needed. Epidemiological evidence is needed to design effective strategies for preventing CKD and ESRD, and to establish effective intervention measures.

This paper assesses and summarizes the available information on chronic kidney disease in Central America with respect to prevalence and related risk factors.

Methods

We used the following sources to identify data for consideration in this compilation:

- ❑ Data and reports available from official websites published by the Ministries of Health of each Central American country and The Pan American Health Organization (PAHO/WHO)
- ❑ Papers on renal studies performed in Central America included in the computerized database of PudMed. We searched this database for references to “chronic renal disease”, “CKD”, “end-stage renal disease”, “ESRD”, “kidney”, “renal damage”, “nephropathy”, and “Central America”. For each medical subject heading (MESH) searched, the scope was limited to human studies published in any language, and considered on a country-by-country basis.
- ❑ Other relevant data were identified from the reference lists in the publications thus identified.
- ❑ In addition, other relevant materials and unpublished data were identified by consultation with subject matter experts working in the region.

All identified sources of information were included. Results have been grouped by source of information. For each source investigated we provide a brief discussion on relevant observations, as well as a summary of methodological issues for all identified studies, such as study design, study population and outcomes. Finally we describe general limitations observed in each source of information as well as consistent findings.

Results and discussion

Sources of information

I. National statistics

Information available on chronic kidney disease (CKD) prevalence in Mexico and the Central American region is mainly based upon the official mortality figures published by the Ministries of Health of each country. The lack of access to detailed statistics was evident when a search through the official web sites of the Ministries of Health of the countries under study was performed. So far, we have only found a general report on the prevalence of CKD in Nicaragua (Marín Ruiz & Berroterán, 2002; MINSA-Nicaragua, 2003).

However, mortality statistics are also available from the WHO (www3.who.int/whosis) (WHOSI, 2005). Data from 1990, 1995/1996 and 1999/2000 for CKD and selected other causes of death are compiled in Annex 1. Country- and sex-specific time trends for CKD are given in Annex 2.

A striking male increase in CKD mortality during the 1990's was observed in El Salvador. There is an increasing male - female gap in El Salvador, and also in Nicaragua. Female rates seem to be stable and rather similar in Costa Rica and Nicaragua, but increasing in El Salvador. In Guatemala and Cuba no increase was observed. National mortality data are not available at all from Honduras. Within-country mortality data by regions have been reported for Nicaragua but not from other countries in Central America, to the best of our knowledge.

National statistics on chronic kidney disease from Nicaragua: official figures

In Nicaragua, CKD has been estimated to be the 7th leading cause of death. Official reports from MINSA-Nicaragua suggest a trend of increasing mortality rates due to CKD; the 2002-CKD mortality rate (CKD-MR) is 2.5 times greater than the CKD-MR in 1992 (MINSA-Nicaragua, 2000, 2003). However, the calculations showing these apparent increase in rates depend heavily on the baseline 1992-1994 data (See Figure 1). The yearly number of deaths was around 500 in the early 2000s.

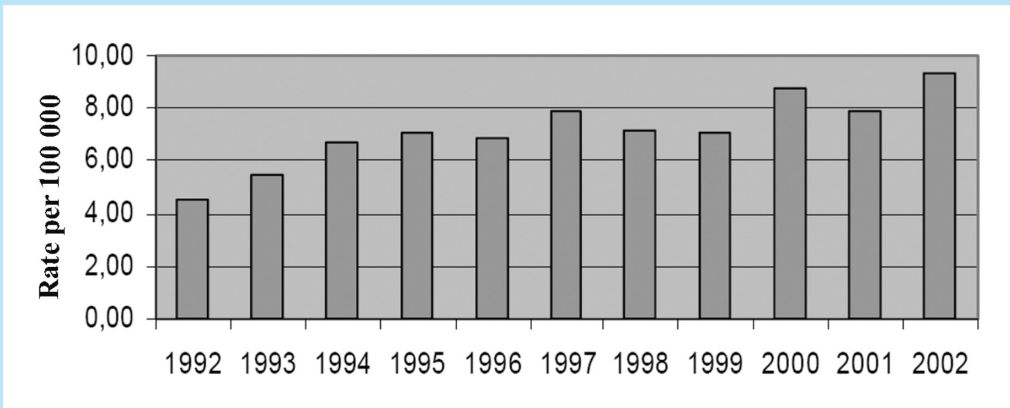


Figure 1: Annual chronic kidney disease (CKD) mortality rates in Nicaragua, 1992-2002. (Source: MINSA-Nicaragua, 2003)

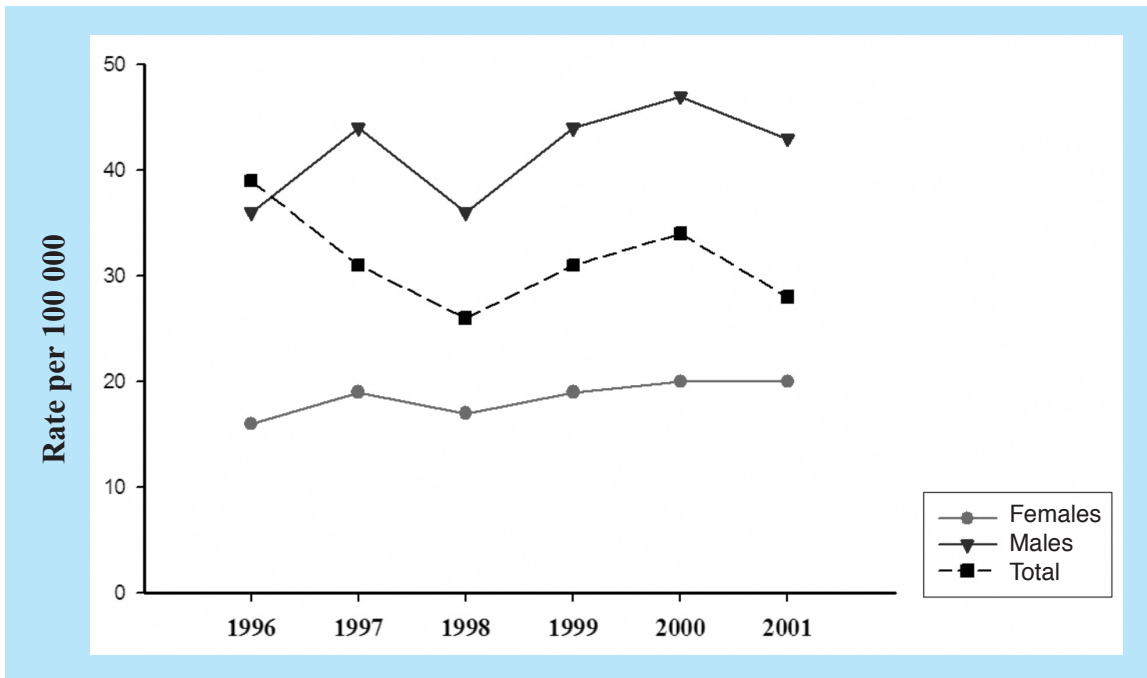
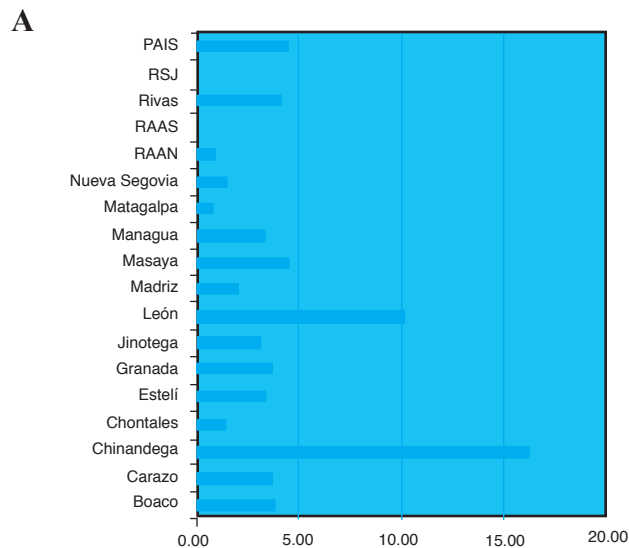


Figure 2: Annual rates of chronic renal insufficiency (CRI) morbidity by sex in Nicaragua. 1996-2001. (Source: Nicaraguan vital statistics, MINSA-Nicaragua; adapted from Marín Ruiz & Berroterán, 2002)

During the period 1996-2001 there was no convincing evidence for an upward trend for chronic renal insufficiency (CRI) morbidity (Figure 2) (Marín Ruiz & Berroterán, 2002). The rates clearly differ by sex, with males having CRI rate that is twice as high as that of females (Figure 2). However, it is not clear if these figures refer to prevalent or incident cases. Also, the definition of CRI is not given. (Note: the figure for years 96-97 seems to contain an error since the rates for both males and females presented upward trends but the total rate had a downward trend and does not reflect the combined male and female rates.)

Official statistics also show a gradient on the CRI annual mortality rates by regions that is consistent over time (see Figure 3 A-C) (MINSÁ-Nicaragua, 2003). It is obvious that the occurrence of CKD in the regions of León and Chinandega, located in the Pacific coast, is higher than elsewhere in the country, with a clear increase over time. In contrast, there were stable rates in Managua, an urban region, as well as in most other areas. Data on sex-specific regional time trends were unfortunately not available.

A difference in CRI morbidity rates between regions with and without presence of sugarcane plantations (see Figure 4), during the period 1996-2001 has also been observed (Marín Ruiz & Berroterán, 2002). The criteria for collapsing of areas were not reported. A higher rate for males was also observed in this report. (Note: there are inconsistencies in the given rates for males for the periods 1996-1997 and 2000-2001 and for females 2000-2001). An interesting observation is that mean rates for men and women over the period 1996-2001 seem to be similar in areas without sugarcane plantations, while the male/female ratio is higher in sugar growing areas (Marín Ruiz & Berroterán, 2002).



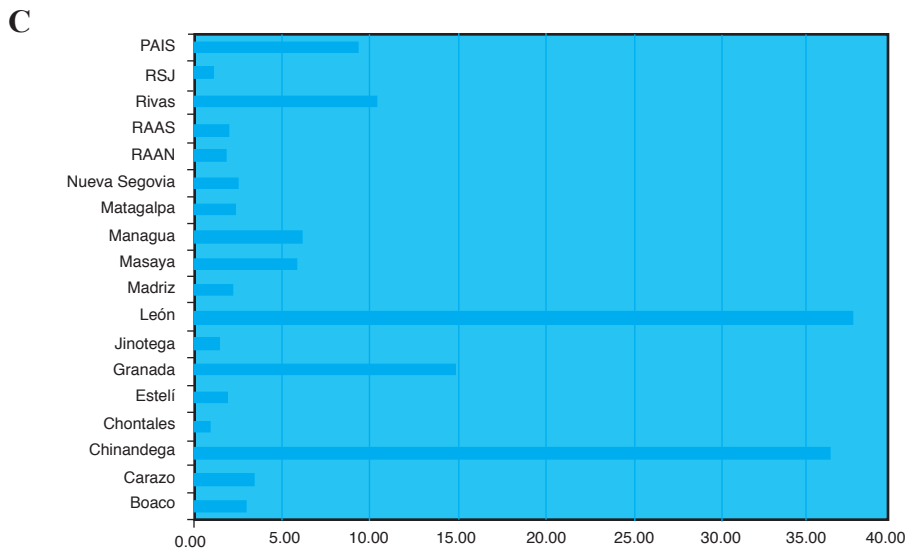
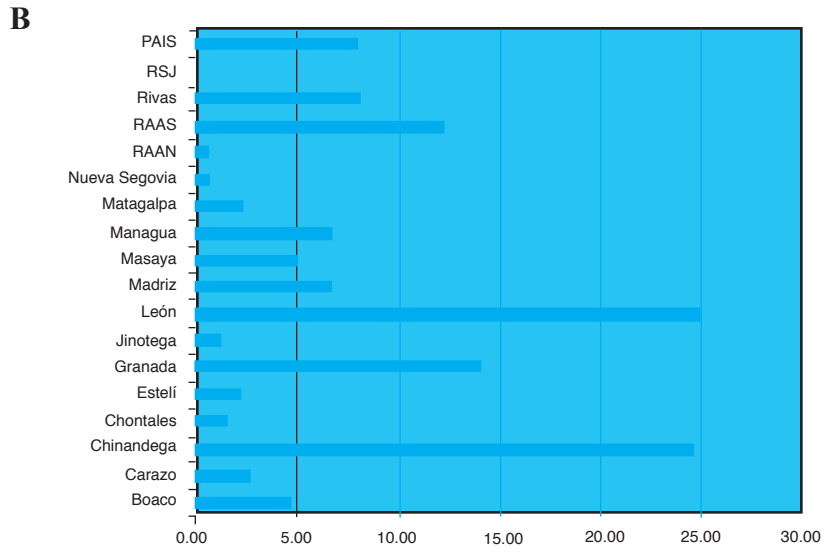


Figure 3. Chronic renal disease mortality per 100 000 in Nicaragua in 1992 (A), 1997 (B) and 2002 (C). (Source: MINSA-Nicaragua, 2003)

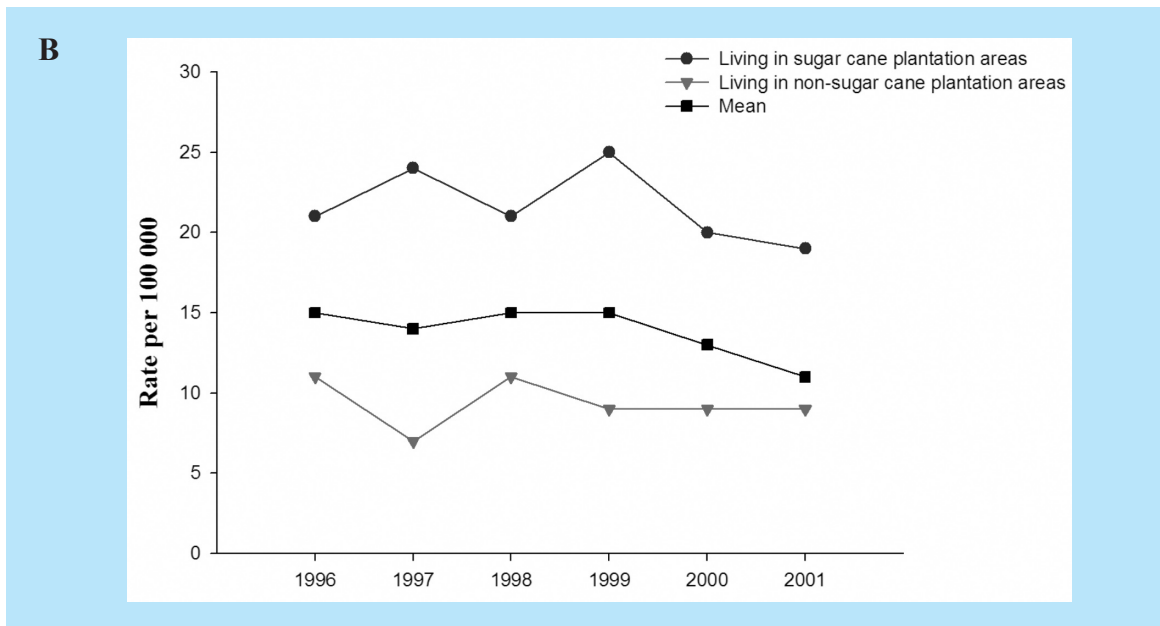
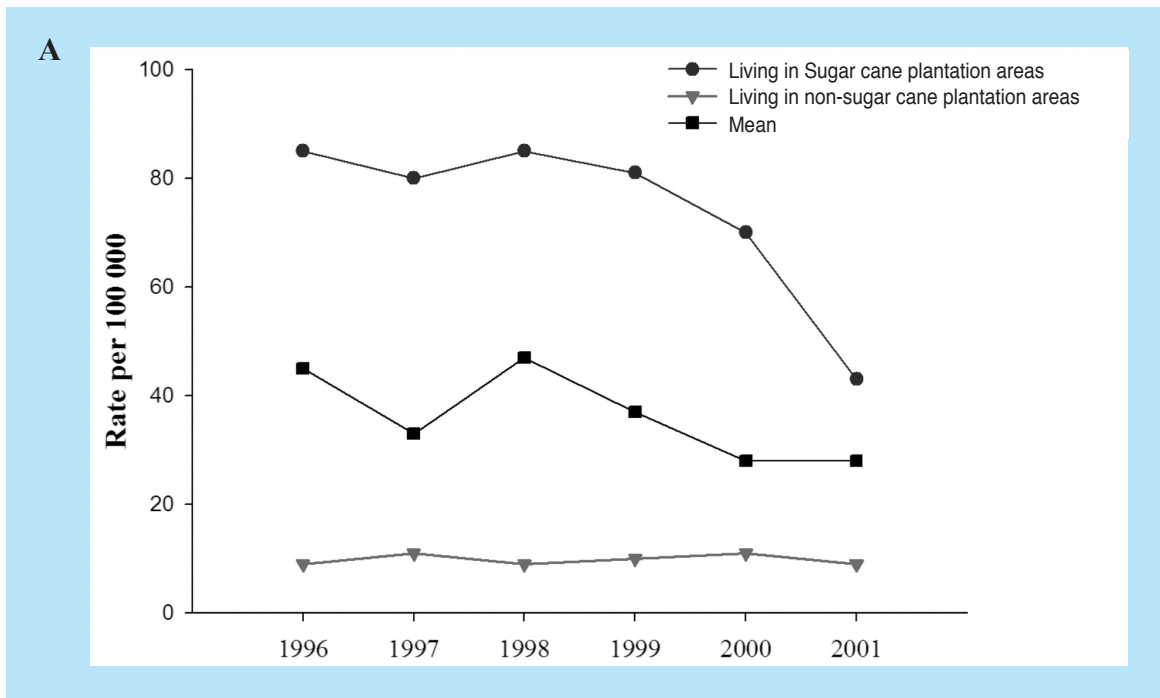


Figure 4. Annual rates of chronic renal insufficiency morbidity in males (A) and females (B) from areas with and without presence of sugarcane plantations, Nicaragua 1996-2001. Source: Nicaraguan vital statistics (Marín Ruiz & Berroterán, 2002)

A recent report on CKD in Chinandega (1995-2000) states a mortality rate in Nicaragua for CKD of 34/100000 in 2000 (MINSANicaragua, 2000). This figure is in contrast with the rate calculated from WHOSIS and supplementary population estimates from PAHO (cf Annex 2) (WHOSIS, 2005).

CKD was said to account for 13% of all deaths in the department of Chinandega. Within the department, the yearly rates (per 100,000) were highest in the municipalities of Chichigalpa and Posoltega, ranging from 47 to 89 and 42 to 61, respectively, between 1995 and 2000 (MINSANicaragua, 2000).

II. Hospital-based case series

Very little information is available from studies based upon hospital records or health care units of the third and fourth levels of attention to patients. Generally, these studies include interviews with patients with end-stage kidney disease (ESRD). A summary of primary disease in ESRD patients based upon published data is given in Table 1.

End stage renal disease: Preliminary findings of a recent study in El Salvador, 2004 (Flores Reyna et al., 2003)

A study of patients who were receiving renal replacement therapy during August-November 2003 at any of the 8 public hospitals in El Salvador which provide renal replacement therapy was performed in order to characterize the prevalence of cases of end-stage renal disease.

830 cases were identified (a period prevalence of 12.5 /100 000 persons). Among those, 64 % were males, 65% were living in urban areas, and 67% did not report previous predisposing diseases. Regional differences were encountered (a prevalence of 25 per 100,000 in La Paz vs. 4.4 and 5.0 per 100,000 in Cabañas and Cuscutlán).

Prevalence increased by age category from approximately 10 per 100,000 in the 20-29 age category up to 45 per 100,000 in the 50-59 age category. The time between diagnosis of renal disease and renal replacement therapy was short, with a median time of between 4-7 months. The interviews contained questions on work, type of drinking water used, and use of pesticides. The lack of a reference group precludes drawing any conclusions.

End stage renal disease in patients from a national referent hospital in El Salvador (García Trabanino et al., 2002)

A study was conducted of all new cases that initiated chronic dialysis between November 1999 and March 2000. Through personal interviews, data were obtained on patient clinical conditions, demographic characteristics and occupational histories. 205 cases were identified, and 202 of these persons were interviewed. Around 22% had a history of diabetes or hypertension.

The proportions of males and females among those with a history of known risk factors for ESRD were similar. However, for those with no history of known risk factors there was a clear dominance of males (87%). Patients with unknown risk factors were also slightly younger. Additionally, in this group of patients the majority were farmers, residents of coastal areas or areas next to rivers, and reported more frequent occupational exposures to agricultural pesticides in the past (yes/no).

Characteristics of patients in the peritoneal dialysis program of the School Hospital, Tegucigalpa, Honduras (Durón et al., 2000)

Information about 66 cases of patients with chronic renal failure included in the peritoneal dialysis program at the Tegucigalpa School Hospital between January and June of 1999 was revised.

Known risk factors for chronic renal failure were not observed in 71% of cases. The rest of the cases were associated with diabetes, polycystic kidney, obstructive uropathy, and arterial hypertension. 49% were males. The majority of patients were from the Francisco Morazán region. Information on occupations was not recorded.

**Table 1:
Primary renal disease in end-stage renal disease (ESRD) patients reported from two Central American countries. For comparison, data from the Latin American Registry of Dialysis and Renal Transplantation are also given.**

SOURCE	UNKNOWN	DIABETES	APCKD*	ANALGESICS	GLOMERULO- NEPHRITIS
LATIN AMERICAN REGISTRY OF DIALYSIS AND RENAL TRANSPLANTATION, 1993 N = 6977 (MAZZUCHI ET AL 1997)	15 %	16%	3%	-	23%
EL SALVADOR, 1999/2000 N = 202 (GARCÍA TRABANINO ET AL 2002)	67%	15%	-	4%	0.5%
HONDURAS, 1999 N = 66 (DURÓN ET AL 2000)	73%	9%	9%	1.5%	-

* Adult polycystic kidney disease (APCKD)

III. Community-based studies

Several studies have been carried out in order to quantify the prevalence of chronic renal damage and to identify related risk factors.

Analysis of prevalence and determinants of chronic kidney disease (CKD) in the Pacific coast: Southern Mexico, Guatemala, El Salvador, and Honduras, 2003 (Domínguez et al., 2003) (see also separate data below for El Salvador)

A cross-sectional study assessed the prevalence of proteinuria as a marker of early renal damage among male residents from agricultural municipalities located in the Pacific coast regions of Southern Mexico, Guatemala, El Salvador and Honduras, no higher than 200 m above sea level. The year of the survey was not reported. The document was released in 2003.

806 males 18 years old or older were investigated, out of an estimated population of 100 354 males living in these regions. As reference groups, 104 females living in the same regions and 108 male agricultural workers living in areas located 500 meters or more above sea level were also investigated.

A background questionnaire on demographic characteristic, location of dwelling, water supply, alcohol consumption, smoking habits, work history, and known risk factors for CKD was applied. Urine analysis (morning sampling), determination of protein in urine, systolic blood pressure and glycemia were also measured.

The proportions of cases with proteinuria vary from country to country. Data from all the countries included in this study show that 40 % (range 36-45 %) of males and 14 % (4-22 %) of females living at the coastal municipalities, as well as 10 % (0-17 %) of males living in municipalities 500 m above sea level, had proteinuria. The majority of the male participants were between 45 and 60 years old.

The authors reported a negative relationship between the prevalence of cases with proteinuria and the altitude at which the municipalities are located: 11% of subjects from towns located ≥ 500 m above sea level, 21% of subjects from towns located between 100-300 m above sea level, and 41 % of subjects from towns located ≤ 100 m above sea level had proteinuria. This pattern was observed in Mexico, El Salvador and Honduras.

Migration is a common phenomenon in the countries under study. Between 21-39 % of the investigated subjects were not originally from the communities in which they were studied. Although the figures presented in the document are somewhat confusing, it seems that the prevalence of proteinuria among male migrants in the low altitude regions was considerably less than among the male natives in El Salvador (39 vs 61%), Guatemala (34 vs 66%) and Honduras (21 vs 79%).

The prevalence of hypertension and diabetes was estimated from the questionnaire and by measuring blood pressure on a single occasion, together with glycemia measurement. Overall, 71% of males living in the Pacific coast (low altitude; ≤ 200 m) with proteinuria had no indications of hypertension or diabetes.

In this study, the proportion of subjects with a history of alcoholism (defined as past or recent history of at least one work lost day per week due to alcohol drinking) was very high in males from the Pacific coast with proteinuria (55%), as well as in males from the same region without evidence of proteinuria (44%). Prevalence of alcoholism for the reference groups (females from the coast and males from municipalities ≥ 500 m above sea level) is not given in this document. Agricultural work and contact with pesticides was common; in total 73% of the men investigated reported frequent pesticide use (68% of those with proteinuria). The usual source of drinking water (river, well, bottled) also seemed similar between groups with and without proteinuria.

It is noted that high urine density (measured with Multistix10SG) was common; a total of 1/5 of individuals had values at the upper measurement limit (1030), and this condition was more prevalent in males from the coastal areas; however, figures were not given.

- **Investigations of the prevalence of chronic kidney damage in the Nicaraguan population**

The available information on CKD in the general population and in special groups of workers generally comes from community based studies. There are four studies, all based on cross-sectional samples.

These studies attempted to identify prevalent cases of individuals with decreased renal function. In a first step, sugarcane workers were enrolled (Study I), as well as residents of the local communities, who participated voluntarily after an invitation to the public (Study II, III and IV); serum creatinine (S-Cr) was determined.

In a second step, cases with renal damage were identified. Determination of S-Cr was used in almost all studies as a marker of renal damage. The usual cut-off point used to classify individuals as cases was established at S-Cr concentration ≥ 1.5 mg/dl, although in one study the cutoff point used was a S-Cr concentration ≥ 2.5 mg/dl (Study I). Referents were selected from participants having S-Cr concentration below 1.5 mg/dl. Prevalence odd ratios (PORs) were calculated.

Chronic kidney damage (CKD) in sugarcane workers, Chinandega, Nicaragua, February-March 2002 (Alonso Medrano & Perea, 2002)

This study is based on sugarcane workers at the Chichigalpa sugarcane plantation. In this study the number of workers is given (n= 2,164), but the sample selection process is not clearly described. It is not clear if a screening test to estimate S-Cr was performed in all workers.

Definition of cases: Sugarcane workers active until 1999, with symptoms of CKD and creatinine serum level ≥ 2.5 mg/dl (N=44). Definition of referents: active sugarcane worker (year not given), older than 15 years of age, with no symptoms of CKD and S-Cr ≤ 1.1 mg/dl (N=100). The selection procedure, however, is not clearly described.

A background questionnaire on demographic characteristic, location of dwelling, water supply, alcohol consumption, work history, and known risk factors for CKD was applied. Blood pressure, weight and height were also measured.

The proportion of cases and referents who had personal histories of hypertension or diabetes was similar, 10% and 8%, respectively. In contrast, 48% of cases and 29 % of referents reported a family history of chronic kidney disease.

Additionally, the authors reported an increased prevalence of CKD among those who reported consumption of home-made alcohol (guaro lija), POR 10.8 (95 % CI 3.6-30). No specification on the frequency or amount of alcohol intake was given.

Chronic kidney insufficiency (CKD) in sugarcane workers, El Viejo Chinandega, Nicaragua, March 2003 (Callejas Callejas et al., 2003a)

In a first step, a serum creatinine screening in 2000 workers at the sugarcane plant “Monte Rosa” was performed in March 2003. Among those, 200 (10%) workers had S-Cr ≥ 1.5 mg/dl. In a second step 38 cases (all individuals with serum creatinine level ≥ 2 mg/dl) and 111 referents (criteria for selection not given) were included for further study. A general questionnaire on work history, pesticide exposure, personal and family pathology profile, alcohol consumption, and use of non-steroidal analgesics was also applied. Physical examination included measurement of arterial blood pressure (AP), weight and height.

Elevated PORs (12.2; 95 % CI 4-39) were reported for individuals who consumed home-made alcohol beverages (guaro lija), but not for other types of alcohol consumption. A sugarcane work history of 10 years or more was associate with high S-Cr – in the case of cane cutting, a POR of 2.9 (95% CI 1.3-6.8) – but no association was observed with application of pesticides (POR 0.6, 95% CI 0.3 – 1.4).

Well-known risk factors for CKD such as family history of CKD and hypertension were not significantly associated with the occurrence of CKD in this study. A history of diabetes mellitus was not reported for any subject.

Chronic kidney damage (CKD) in non sugarcane workers, Chinandega, Nicaragua, July-August 2003: Preliminary results (Callejas Callejas et al., 2003b).

Workers older than 15 years of age living in non-sugarcane plantation areas were invited to participate in a study of renal function of non-sugarcane workers.

A questionnaire on work history, alcohol consumption and known risk factor for CKD was applied to 343 workers who voluntarily participated. S-Cr was also determined for all participants. Of the participants, 326 were included for data analysis. Seventeen (5%) subjects were not included, 16 due to a history of previous work at sugarcane plantations, and one with incomplete data. The prevalence of S-Cr ≥ 1.5 mg/dl was 7 %.

In a second step, cases were defined as all workers from Chinandega County, with no history of previous work at sugarcane plantations, with level S-Cr ≥ 1.5 mg/dl, regardless of the presence of CKD related symptoms (N=24). The rest (n=302) were considered as non-cases (referents)

Among cases, 5 subjects (20%) had personal histories of diabetes and arterial hypertension, in contrast to only 7 non-cases (45). A POR 4.8 (95% CI 1.7-13.7) was reported for cases who consumed home-made beverages.

Chronic kidney damage (CKD) in non sugarcane workers, Jinotega, May-Jun 2003 (Sequeira, 2003)

One thousand workers at 15 coffee farms in Jinotega were screened to determine creatinine serum levels. A questionnaire on work history, alcohol consumption and known risk factor for CKD was also applied. Seven subjects (0.7%) had serum creatinine levels ≥ 1.5 mg/dl.

Seventy-one % of all participants had a history of alcohol consumption, and 35% had also consumed home-made alcohol beverages. Further findings are not reported here, due to the very small number of cases (n=7).

Chronic kidney damage: A public health priority in the Pacific coastal region of Nicaragua, May-September 2003 (Callejas Callejas et al., 2003c)

This study included subjects with a history of current or previous work and current residence in the following communities:

- *Chinandega municipalities:* El Viejo, Corinto, Posoltega, El Realejo, Chichigalpa and Somotillo.
- *León municipalities:* Telica, Malpaisillo, and León

In a first step, participants were enrolled through an open (public) convocation and all subjects who agreed to participate and fulfilled the established criteria (see above) were included. A questionnaire on work history, alcohol consumption and known risk factor for CKD was applied to 1002 subjects from municipalities in Chinandega (n= 896) and León (101). Weight, height, and arterial pressure were also measured, as were S-Cr concentrations.

Among participants, 997 were included for data analysis. Five (0.5%) subjects were not included due to incomplete data. Overall, 849 (85%) were males, with a mean age of 39 years (range 14-88 years).

S-Cr \geq 1.5 mg/dl was observed in 10% (N=102). Of these, 100 subjects had an estimated creatinine clearance of \leq 80 ml/min (taking into account age, weight and sex). Overall, 24% of all subjects had histories of known risk factors for CKD (either personal history of hypertension or diabetes mellitus, or family history of CKD)

Prevalent cases were defined as individuals, regardless of age and sex, who had a creatinine serum level \geq 1.5 mg/dl (N=102). All others were considered as referents.

Cases were older (mean age 50 years) than referents (mean age 38 years) and had a higher presence of risk factors for CKD than referents – 40% vs 23%, respectively. Alcohol consumption, mainly consumption of home-made alcohol beverages, was more common in cases, POR 4.2 (95% CI 2.6-7.0).

The proportion of cases is greater among those who were involved in agricultural activities (13.8 %) than among those who were not (3.9 %). However, considering only agricultural workers, no difference in the proportion of cases was observed between non-sugarcane workers and sugarcane workers.

Agricultural work history as risk factor for renal function deterioration in the west region of the country, January 2003-January 2005 (López Arteaga, 2005)

This study attempted to compare male agricultural workers more than 15 years old and an estimated glomerular filtration rate (GFR) \leq 80 cc/min (cases) with similar subjects with a GFR $>$ 80 cc/min (referents), from several municipalities located in the regions of León and Chinandega, located in the west part of Nicaragua.

In order to obtain a ratio 1:3 between cases and referents, around 4076 agricultural workers were invited to participate. Participants were enrolled through an open (public) convocation. All subjects were interviewed following a structured questionnaire which included demographic data, current and past agricultural work (yes/no; years worked), current and past work at sugarcane plantation (yes/no; years worked), exposure to pesticides (ever; yes/no), personal history of pesticide intoxication (yes/no), and presence of known risk factors for CKD. Additionally, blood samples were taken from all subjects to determine serum creatinine. At the end, 3710 male subjects were included in the analysis (8 males subject $<$ 15 y and 358 females were excluded from the study).

Glomerular filtration rates (GFR) were estimated from serum creatinine concentration. The procedures and parameters used to calculate this concentration were not given in this report. The authors reported the following distribution: 490 agricultural workers with GFR < 80 cc/min and serum creatinine > 1.3 mg/dl, 3220 agricultural workers with GFR > 80 cc/min and serum creatinine < 1.3 mg/dl. Around 70% of cases and almost 100 % of referents were under age 50.

Here, the authors reported several adjusted odds ratios calculated by logistic regression. However, variables included in the models were not specified in the report. Family history of CKD (OR 1.58; 95 % CI 1.05-2.39), alcohol consumption (OR 1.39; 95 % CI 1.08-1.78), history of pesticide use (yes/no) (OR 2.3; 95 % CI 1.66-3.18), and history of pesticide intoxication (yes/no) (OR 2.6; 95 % CI 1.93-3.62) were significantly related. The authors also claimed that working at cotton, sugar, rice and corn plantation were positively associated with an increased risk of having a GFR < 80 cc/min. However, it is not clear if the authors were referring to current or past work, and how these variables were handled within the models.

Health profile of sugarcane workers from San Antonio Sugarcane Plantation with diagnosis of chronic renal insufficiency (Marín Ruiz & Berroterán, 2002)

This study provides descriptive data for 190 workers at the “San Antonio” sugarcane plantation, Chichigalpa, who were diagnosed with chronic renal insufficiency (CRI) during the period 1998-2000 (Marín Ruiz & Berroterán, 2002). The greatest proportion of subjects was aged 40-60 years, followed by those aged 15-40. Subjects who had worked there ≥ 21 years and between 10-20 years were the two groups which were most frequently diagnosed with CRI.

In this document, we also found a comparison between 39 subjects with diagnosis of CRI and 43 without CRI (Marín Ruiz & Berroterán, 2002). No data on study design, sample selection and criteria were given. However, some data presented here might indicate that there is an increased (around 1.5-fold) risk of developing CRI among those who are older than 42 years and those who worked more than 8 hours a day. Moreover, those who had worked for more than 15 years had a risk 3 times higher than that of those who had worked less than 15 years. These results must be interpreted with caution, since no further details are available.

Proteinuria and renal chronic insufficiency at the Pacific coast of El Salvador: related factors and detection by using a low cost method (García Trabanino et al., 2005). (See also Domínguez et al., 2003)

A screening for proteinuria was performed in males from a coastal area, Jiquilisco, and an area 500 m above sea level, Sesori. From estimated populations of 832 and 388 males, 291 (35%) and 62 (16%) participated, respectively. The proportion of agricultural workers was high in both areas, over 85%. Frequent consumption of alcohol (not defined) was more common in the high-altitude area, reported by 87% vs 65% in the coastal area. The men in the coastal area were somewhat younger than the men from the high altitude area, with median ages of 50 and 55 years, respectively.

Proteinuria was found in 46% of the participants from the coastal vs 13% of the participants from the high altitude area. Also elevated blood glucose was more common in the coastal area, 25% vs 8%. Agricultural work, pesticide use and alcohol were not significantly related to proteinuria.

In a second step, determinations of S-creatinine, B-Hemoglobin, B-glucose, and a quantitative analysis of proteinuria were carried out for 80 of the 133 men from the coastal area with proteinuria. Thirty-seven men subsequently had a diagnosis of CKD. Of these, 14 men had elevated B-glucose or arterial hypertension.

This corresponds to a prevalence of CKD of between 12% (assuming no diseased persons among non-participants with proteinuria in the second step, and no diseased persons among those negative in the screening) and 21% (assuming the same prevalence of diseased persons in all cases with proteinuria, and none among those screening negative) in the coastal area.

Limitations

Since the available documentation does not include detailed information regarding methodological issues, this critical assessment is based upon the information that is given in the documents (full reports or brief presentations only).

I. Limitations of national statistics (official reports)

This type of source is sensitive to several factors which might influence rate estimations:

1. Diagnostic changes over time
2. Resource availability, leading to detection bias varying by region
3. Rate estimation is dependent on correct estimation of the population (e.g., in Nicaragua the last national census was in 1995 and before that in the 1971).
4. Ecological information
5. Low frequency of autopsies and medical certification of the causes of death

II. Limitations of hospital series

These studies aimed at identifying end-stage kidney disease (ESRD). They are sensitive to several factors:

1. Differences in health care systems and attendance
2. Changes in inclusion criteria – may vary (for instance for males/females)
3. Quality of information

The underlying population for identification of cases is not clearly described in the studies reviewed.

III. Limitations of the community-based studies reviewed

1. In general, the studies presented here are based on cross-sectional samples from a population. Therefore, exposure and effects were measured at the same time. Data analysis compared cases with referents, including not incident but prevalent cases.
2. There is usually a lack of information on the underlying population.
3. Enrollment of participants was through self-selection, which may cause differential attendance.
4. No information on non-participants is given.
5. Very limited description on how referents were selected.
6. The data analysis is not always transparent, and there are inconsistencies between reported crude data and calculated prevalence odd ratios.
7. Exposure estimates are crude (mostly yes/no, and sparse or absent information on timing of exposures).
8. Little or no information for females!
9. Quality control methods, i.e. reproducibility, are not reported for clinical and laboratory tests

Concluding remarks

There is a need to scrutinize the information given as official figures from the ministries of health and related national and international organizations. For the reports described above, it remains unclear how much the incidence of CKD has increased or to what extent intensified attention paid to the disease during later years has resulted in more reports, especially of CKD as a cause of death. Given the poor bases in most cases for establishing the cause of death this could easily happen, and earlier under-reporting or over-reporting during later years are possible explanations for the observed time trends. However, the triggers for these studies were either workers (in Nicaragua) claiming that they were affected by kidney disease, or clinicians (in El Salvador) reporting a severely increased demand for renal replacement therapy and the inability of current health services to deliver proper treatment to so many patients.

All studies included in this compilation are essentially cross-sectional studies investigating prevalent cases of either end-stage renal disease or renal damage. In some studies, reference groups were also investigated and odds ratios for prevalence were calculated to identify possible associated risk factors. Investigated risk factors included:

1. Demographic characteristics: sex and age
2. Life style: alcohol consumption, smoking habits
3. Know risk factors for CKD: family history of chronic diseases, personal history of hypertension, diabetes, kidney stones, glomerulonephritis, and repeated urinary tract infection,
4. Occupational risk factors: type of work (especially agricultural activities), duration of work (years worked, working hours per day), crops, and contact with chemicals such as pesticides at work
5. Environmental factors: zones (urban, rural, agricultural areas, non-agricultural areas), water supply, and presence of sugarcane plantations in the area

A summary of reasonably consistent findings in the reports reviewed is given in Table 2.

In spite of the methodological limitations pointed out previously, especially those related to selection and reference groups, there seems to be an excess risk of CKD in several of the populations studied. However, it is not clear which specific risk factors could explain the apparent excess risk. Diabetes does not seem to be an obvious explanation, according to the observations in the cross-sectional studies, and in the clinical investigations in case series with ESRD from El Salvador and Honduras. Population-based cross-sectional studies using proteinuria as a marker of CKD indicated large differences between population groups in different regions, and between males and females. The prevalence of proteinuria was remarkably high in some study groups.

Several studies indicated an increased risk for CKD among agricultural workers, particularly sugarcane workers. *Suspected specific risk factors* included: long-term, extreme dehydration during work days, contaminated, home-made alcohol (“dirty alcohol”), and polluted drinking water, particularly pollution with heavy metals. It seems likely that the aetiology is multifactorial. The combination of extreme dehydration during workdays and polluted drinking water seems to be an important hypothesis to test.

Overall, there are clear indications that CKD is a serious problem in most, perhaps all, Central American countries, but there might be different risk factor combinations in different countries and populations, as well as differential vulnerability. A serious limitation is that most studies have included males only.

Table 2
Consistent findings from recent reports on chronic kidney disease in Central America.

Outcome	Source	Contribution	
Death	National statistics WHO	Changes over time not consistent between countries Male/Female ratio not consistent between countries Males are more affected than females	
	Nicaragua	Trends over time differ by region Increase in León and Chinandega, but no increase in Managua (urban) and most other rural areas.	
End-stage kidney disease	Hospital series (3 studies)	Around 2/3 of cases had no history of diabetes, hypertension or family history of CKD	
Renal function	Community based studies (9 studies)	Confirmed that diabetes and hypertension were not main risk factors for chronic renal disease.	
		Regional differences were indicated	
		S-Cr \geq 1.5 mg/dl	
		Chinandega, sugarcane	10 %
		Chinandega, not sugarcane	7.5 %
		Chinandega, León	10 %
		Jinotega, coffee	1 %
		Proteinuria	
		Pacific coast, low altitude (\leq 200 m asl)	40 %
		high altitude (\leq 500 m asl)	10 %
Generation of hypotheses of possible risk factors:			

Other questions to be considered

We list below, as a part of the discussion based on results of reading the available reports and documentation on CKD in Central America, other research questions and risk factors which can be considered for further investigation:

1. Low altitude could be consistent with toxic substances redistributed by flooding or greater humidity (molds?)
2. Is arsenic-containing soil more prevalent in Chinandega/León or have many new (deeper) wells recently been dug there?

However, 1 and 2 are not consistent with a sex difference; thus, much depends on the reality of the apparent gender difference.

3. What pesticides are used in cultivation of sugarcane but not in coffee growing?
4. Has the process (= chemicals) in sugarcane growing changed since the 90's?
5. Is anything known about production processes and consumption of home-made alcohol over time in Central America?

Susceptibility

Genetically determined susceptibility may interact with environmental exposures (cf. Balkan nephritis, metal toxicity). Is ethnic origin (Hispanic, indigenous) related to risk?

Disease entity

Is the damage glomerular or tubular? (A clue as to known risk factors)

Is it a rapidly or slowly progressive disease? (A clue as to time windows for exposure)

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APPENDIX # 2

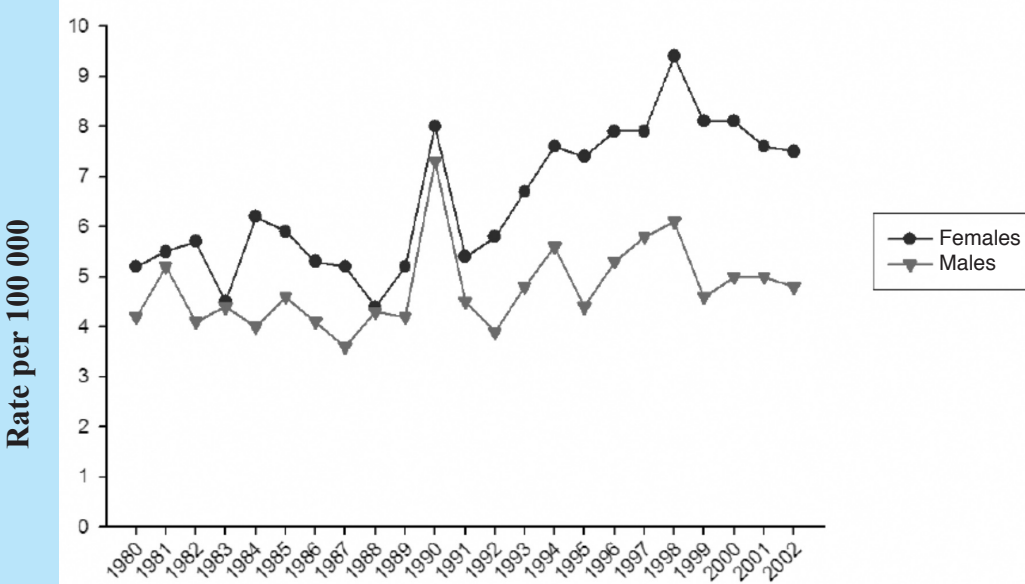


Figure 1: WHO Chronic Kidney disease (CKD) Mortality time trend: Costa Rica 1980-2002. Source: Appendix 1-Table 1; WHOSIS 2005. (<http://www.who.int/whosis/mort/en/>)

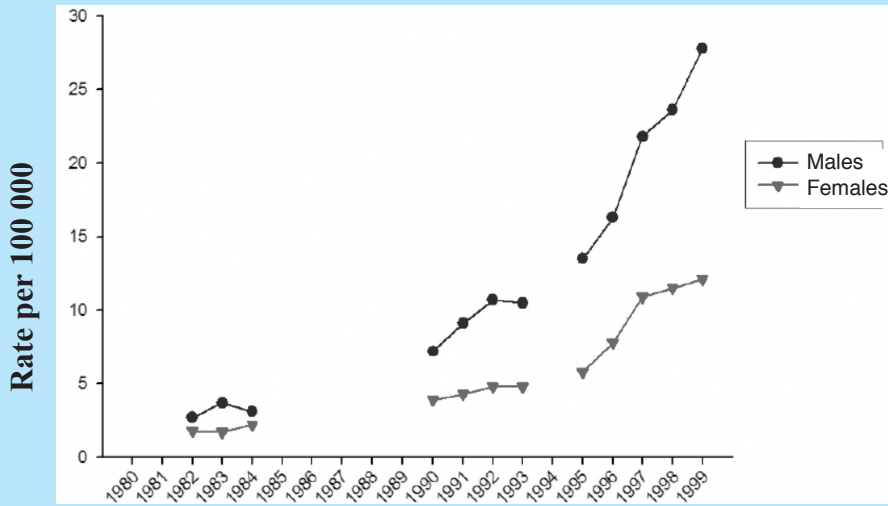


Figure 2: WHO Chronic Kidney disease (CKD) Mortality time trend: El Salvador 1982-1999. Source: Appendix 1-Table 1; WHOSIS 2005. (<http://www.who.int/whosis/mort/en/>)

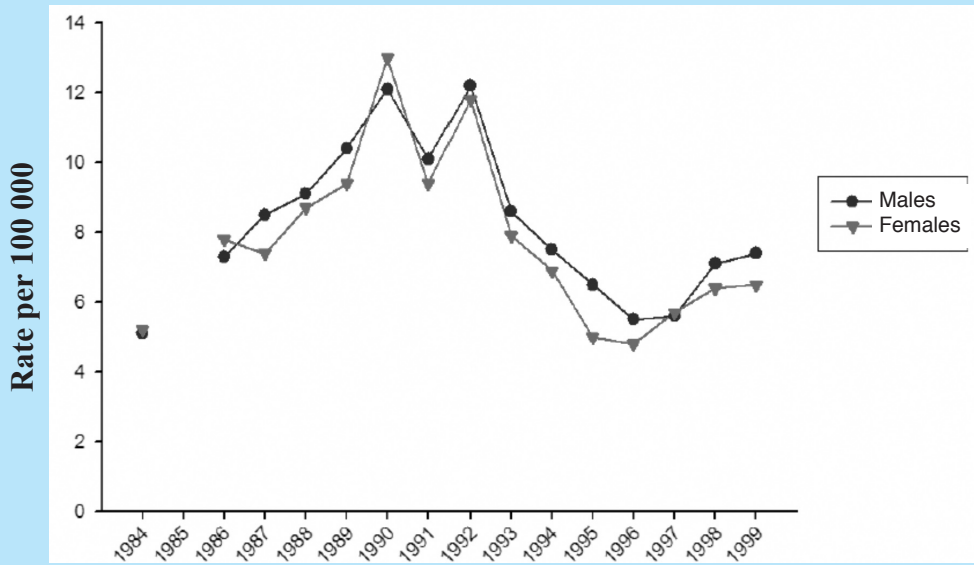


Figure 3: WHO Chronic Kidney disease (CKD) Mortality time trend: Guatemala 1984-1999. Source: Appendix 1-Table 1; WHOSIS 2005. (<http://www.who.int/whosis/mort/en/>)

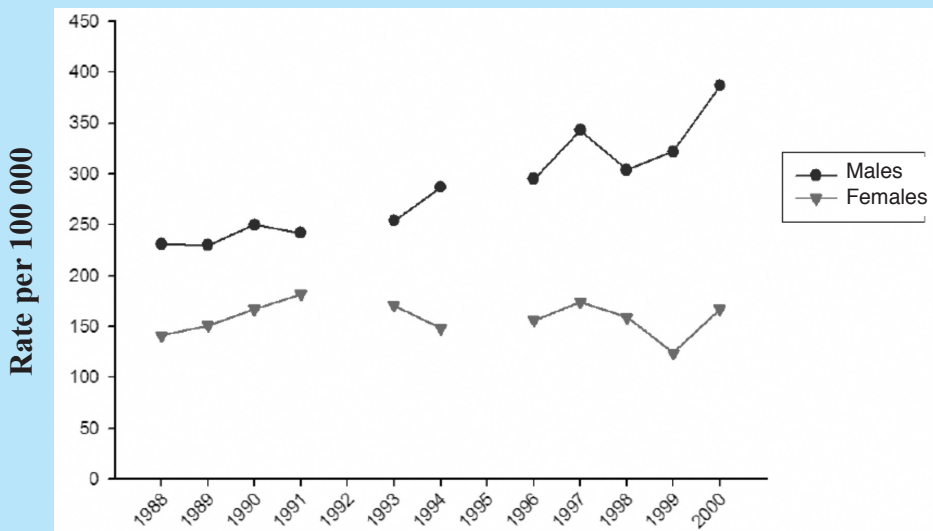


Figure 4: WHO Chronic Kidney disease (CKD) Mortality time trend: Nicaragua 1988-2000. Source: Appendix 1-Table 1; WHOSIS 2005. (<http://www.who.int/whosis/mort/en/>)

Table 1: WHO Chronic Kidney disease (CKD) Mortality time trend: Costa Rica 1980-2002.

Costa Rica								
Year	Population		Total deaths		Renal deaths		Rate	
	Males	Females	Males	Females	Males	Females	Males	Females
1980	1127000	1118000	5481	3792	59	47	5.2	4.2
1981	1139000	1132000	5084	3906	63	59	5.5	5.2
1982	1166000	1158000	5226	3942	67	48	5.7	4.1
1983	1184400	1194200	5313	4119	53	53	4.5	4.4
1984	1275700	1258000	5605	4326	79	50	6.2	4
1985	1313520	1286500	5950	4543	77	59	5.9	4.6
1986	1346800	1319100	5885	4564	72	54	5.3	4.1
1987	1410000	1381000	6064	4623	74	50	5.2	3.6
1988	1447900	1418400	6238	4706	63	61	4.4	4.3
1989	1494000	1416100	6447	4826	77	61	5.2	4.2
1990	1534000	1500000	6530	4836	122	110	8	7.3
1991	1574000	1539000	6655	5140	85	69	5.4	4.5
1992	1614100	1577700	7103	5152	93	62	5.8	3.9
1993	1653600	1616100	7124	5420	110	78	6.7	4.8
1994	1692800	1654300	7622	5692	129	93	7.6	5.6
1995	1800700	1753200	8052	6010	134	78	7.4	4.4
1996	1812532	1750990	7947	6046	143	92	7.9	5.3
1997	1859093	1796233	8242	6018	147	105	7.9	5.8
1998	1906303	1842121	8348	6360	179	112	9.4	6.1
1999	1952852	1887360	8699	6353	158	86	8.1	4.6
2000	1997785	1931012	8559	6385	162	97	8.1	5
2001	2040707	1972684	8836	6773	156	99	7.6	5
2002	2081834	2012617	8647	6357	156	96	7.5	4.8

Source: WHOSIS 2005 (<http://www.who.int/whosis/mort/en/>)**Table 2:** WHO Chronic Kidney disease (CKD) Mortality time trend: El Salvador 1982 -1999.

El Salvador								
Year	Population		Total deaths		Renal deaths		Rate	
	Males	Females	Males	Females	Males	Females	Males	Females
1980	-	-	-	-	-	-	-	-
1981	-	-	-	-	-	-	-	-
1982	2512000	2489000	20460	12849	68	44	2.7	1.8
1983	2627000	2602000	19805	12910	97	44	3.7	1.7
1984	2706300	2682300	17320	11550	85	59	3.1	2.2
1985	-	-	-	-	-	-	-	-
1986	-	-	-	-	-	-	-	-
1987	-	-	-	-	-	-	-	-
1988	-	-	-	-	-	-	-	-
1989	-	-	-	-	-	-	-	-
1990	2501837	2608331	16712	11512	181	101	7.2	3.9
1991	2549875	2659261	16369	10727	233	114	9.1	4.3
1992	2601400	2713400	16689	11211	279	130	10.7	4.8
1993	2657800	2771700	17237	11546	278	132	10.5	4.8
1994	-	-	-	-	-	-	-	-
1995	2776262	2892335	17672	11489	375	169	13.5	5.8
1996	2832187	2949106	16969	11935	462	229	16.3	7.8
1997	2886715	3004314	16938	12196	630	326	21.8	10.9
1998	2939995	3058194	17757	12177	694	353	23.6	11.5
1999	2992521	3111334	16483	11595	833	378	27.8	12.1
2000	-	-	-	-	-	-	-	-
2001	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-

Source: WHOSIS 2005 (<http://www.who.int/whosis/mort/en/>)

Not available (-)

Table 3: WHO Chronic Kidney disease (CKD) Mortality time trend: Guatemala 1984 -1999.

El Salvador								
Year	Population		Total deaths		Renal deaths		Rate	
	Males	Females	Males	Females	Males	Females	Males	Females
1980	-	-	-	-	-	-	-	-
1981	-	-	-	-	-	-	-	-
1982	-	-	-	-	-	-	-	-
1983	-	-	-	-	-	-	-	-
1984	3925000	3815000	35848	30412	200	200	5.1	5.2
1985	-	-	-	-	-	306	-	-
1986	4012034	3918635	36653	29652	291	299	7.3	7.8
1987	4109770	4015914	37134	29212	351	357	8.5	7.4
1988	4209811	4115630	35797	28265	382	395	9.1	8.7
1989	4313510	4219047	34023	27502	450	561	10.4	9.4
1990	4421885	4327116	40108	33192	535	419	12.1	13
1991	4535184	4440048	40155	32690	459	536	10.1	9.4
1992	4653241	4557699	40575	32543	569	372	12.2	11.8
1993	4776121	4680201	41320	32534	413	332	8.6	7.9
1994	4903771	4807603	41909	32843	366	249	7.5	6.9
1995	5036066	4939848	37394	27757	327	243	6.5	5
1996	5173056	5077009	34810	25802	287	299	5.5	4.8
1997	5314555	5218865	38743	28939	300	346	5.6	5.7
1998	5459874	5364658	40663	29819	386	356	7.1	6.4
1999	5608101	5513382	37062	27498	413	-	7.4	6.5
2000	-	-	-	-	-	-	-	-
2001	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-

Source: WHOSIS 2005 (<http://www.who.int/whosis/mort/en/>)

Not available (-)

Table 4: WHO Chronic Kidney disease (CKD) Mortality time trend: Nicaragua 1988 -2000.

Nicaragua								
Year	Population		Total deaths		Renal deaths		Rate	
	Males	Females	Males	Females	Males	Females	Males	Females
1980	-	-	-	-	-	-	-	-
1981	-	-	-	-	-	-	-	-
1982	-	-	-	-	-	-	-	-
1983	-	-	-	-	-	-	-	-
1984	-	-	-	-	-	-	-	-
1985	-	-	-	-	-	-	-	-
1986	-	-	-	-	-	-	-	-
1987	-	-	-	-	-	-	-	-
1988	-	-	7778	5591	231	141	-	-
1989	-	-	7154	5510	230	151	-	-
1990	-	-	7408	5813	250	167	-	-
1991	-	-	7113	5402	242	182	-	-
1992	-	-	-	-	-	-	-	-
1993	-	-	7458	5707	254	171	-	-
1994	-	-	7451	5643	287	148	-	-
1995	-	-	-	-	-	-	-	-
1996	-	-	7839	5962	295	156	-	-
1997	-	-	7923	5993	343	174	-	-
1998	-	-	8321	6431	304	159	-	-
1999	-	-	7977	5792	322	124	-	-
2000	-	-	7832	5766	387	167	-	-
2001	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-

Source: WHOSIS 2005 (<http://www.who.int/whosis/mort/en/>)

Not available (-)

SECTION II

Workshop on Chronic Kidney Disease in Central America

November 2-3, 2005
León, Nicaragua
SALTRA/ECOSAL

Introduction

The workshop on Chronic Kidney Disease (CKD) in Central America was supported and carried out within the framework of the SALTRA/ECOSAL regional projects. A [list of participants](#) is included in Appendix 1.

The aims of the workshop were

- To assess the available information on chronic kidney disease in Central America with respect to prevalence and related risk factors
- To establish a preliminary network, and enroll key contacts in each country in Central America
- To identify possibilities for research cooperation between and within countries with respect to the true incidence and prevalence of CKD in different geographical areas, identification of the etiology of CKD and implementation of intervention programs.

Based upon several published and unpublished documents, a working paper summarizing the available information on CKD in the Central American region was compiled and sent to all participants before the workshop (See Section 1).

During the first day the task for the workshop participants was to describe the situation of CKD in Central America, based on their experience in clinical medical settings, epidemiological studies, and public or occupational health activities. The second day of the workshop was dedicated to discussions of study design, planning and coordination. Three working groups were formed to discuss the feasibility of performing descriptive, case-control, and intervention studies on CKD in the region. The full group reports are found in Appendix 2.

Since the participants had different areas of expertise, the workshop also included short lectures on the clinical classification and pathophysiology of CKD (Dr. Ricardo Leiva), the global epidemiology of CKD and its risk factors (Dr. Kristina Jakobsson), disease markers used in epidemiological and clinical studies (Dr. Kristina Jakobsson), epidemiologic study designs (Dr. Christer Hogstedt, Dr. Patricia Monge), and exposure assessment (Dr. Berna van Wendel), to provide common background knowledge.

Summary of workshop plenary discussions

Short reports on the CKD situation in Central American countries

There is general concern about the prevalence of CKD and end-stage renal disease (ESRD) in *El Salvador*. Fifteen million dollars per year are spent to pay the cost of renal replacement therapy (RRT). Infrastructure and human resources are not sufficient to meet the increasing demand. Several studies indicate that there are regional differences within the country. Among the risk factors indicated in El Salvador work are agricultural work with dehydration and pesticide exposure, and alcohol consumption.

In *Nicaragua*, official statistics suggest an increasing trend in CKD mortality, with higher rates among males. Regional differences have been observed, with the highest rates reported in León and Chinandega. Sugarcane work, pesticides and “dirty” alcohol are suspected risk factors which have been investigated in several cross-sectional studies. Due to public concern, the government, the Ministry of Health, PAHO, and other related institutions have promoted the implementation of intervention programs to assist patients with assumed work-related CKD (i.e. sugarcane workers). However, there is not a clear strategy for working to meet the demand for service and medical care of patients with CKD.

In *Costa Rica*, there is no evidence of an increasing trend of CKD in the population. Epidemiological studies on CKD have not been performed.

National statistics from *Honduras* on CKD are not available. Concern has arisen from the results of small clinical studies of patients with ESRD. ESRD is also a common diagnosis in hospital discharges.

In *Panama* there is neither compiled registry information on CKD morbidity nor information from epidemiological investigations.

No information was available from *Belize* or *Guatemala*.

Time trend data on CKD mortality

Mortality data obtained from WHO mortality statistics (www3.who.int/whosis) were compiled and analyzed. A striking male increase in CKD mortality during the 1990's was observed in El Salvador. There is an increasing male –female gap in both El Salvador and Nicaragua. Female rates seem to be stable and rather similar in Costa Rica and Nicaragua, but increasing in El Salvador. No increase is observed in Guatemala or Cuba. National mortality data are not available for Honduras.

For Nicaragua, mortality data have also been reported by regions, but such data are not available from the other countries in Central America, to the best knowledge of the participants.

The many limitations of the official mortality statistics were apparent – e.g. all deaths are not necessarily reported and very few autopsies are made (the cause of death is usually specified by a non-medical officer). In conclusion, there is a need to scrutinize the official figures from the ministries of health and related national and international organizations. It remains unclear if there is a truly increased incidence of CKD, or if the intensified attention paid to the disease during later years has resulted in more reports, especially as a cause of death. Given the poor basis in most cases for establishing causes of death, this could easily happen. There could be a true increase, but earlier under-reporting or over-reporting during later years are also possible explanations to the observed time trends.

During the workshop it was also pointed out that better information regarding the population under risk is needed. The population information is based on national censuses which may be out of date (El Salvador 1996, Nicaragua 1995, Costa Rica 2000). In Nicaragua a new national census, including a national household survey, will be carried out in 2006. A special problem is that migrant workers, especially those within the agricultural sector, are not included in censuses, and have very limited access to health services. These factors prevent obtaining more precise prevalence and incidence numbers.

Possible actions: Critical evaluation of national and regional CKD mortality data

Prevalence studies

Several exploratory cross-sectional studies have been performed with very low budgets, mainly in El Salvador and Nicaragua. The findings were presented at the workshop and are also available in published reports (for summaries and bibliography see section 1). The findings of the prevalence studies were eagerly discussed in an impressively open and generous atmosphere. It was concluded that in spite of methodological limitations, especially regarding selection and reference groups, there seems to be an excess risk of CKD in several of the populations studied. However, there was no consensus on the specific risk factors that could explain the assumed excess risk. Diabetes does not seem to be an obvious explanation, according to the observations in the cross-sectional studies, and the results of the clinical investigations of case series with ESRD from El Salvador and Honduras.

Population-based cross-sectional studies using proteinuria as a marker of CKD have indicated large differences between population groups in different regions, and between males and females. The prevalence of proteinuria was remarkably high in some study groups.

Several studies indicate an increased risk for CKD among agricultural workers, particularly sugarcane workers. *Suspected specific risk factors* were mentioned: long-term, extreme dehydration during work days; contaminated, home-made alcohol (“dirty alcohol”); and polluted drinking water, particularly water containing heavy metals. It seems likely that the etiology is multifactorial. The effects of a combination of extreme dehydration during workdays and polluted drinking water seems as an important topic for future investigation.

Overall, there are clear indications that CKD is a serious problem in most, perhaps all, Central American countries, but there might be different risk factor combinations in different countries and populations, as well as different vulnerability. A serious limitation is that most studies have only included males.

Possible actions: It was suggested that the existing data from studies on CKD should be reexamined. By sharing available data sets of the research projects that have been completed, an in-depth analysis of the material could be performed with acceptable statistical power. It was also suggested that available environmental data should be evaluated (such as the presence of heavy metals and pesticides in ground water).

Outcome measures

The participants expressed concern that there might be differences in the definitions of cases between countries and periods. National and regional practices vary considerably with respect to the terms and definitions used. However, it was clearly recognized that in many parts of the region only a minority of ESRD patients are ever diagnosed. In El Salvador it was estimated that 1 out of every 4 or 5 patients with ESRD reach the hospitals. Renal disease is seldom identified, since the patients receive medical attention in a late stage of the disease, and biopsies are not performed. Usually, the need for RRT is evident within a few months after the diagnosis of CKD. Thus, it is not known whether the increase of CKD is due to glomerular or tubular kidney damage.

For prevention, surveillance and research purposes CKD needs to be identified in its early stages, not only cases of ESRD. Hitherto, only simple diagnostics such as U-albumin and S-creatinine have been used in cross-sectional studies. For field investigations the circumstances under which the tests should be applied should be made clear (time of day, after resting or work, after proper rehydration, hours since last food and liquid intake, when repeated tests are necessary, etc). Furthermore, appropriate reference values for the Central American populations must be established. It is also important to pay adequate attention to the issue of gender.

Possible actions: Explore which of the kidney function tests which are available in the different countries are reliable, valid and economically and practically feasible.

Summary of group discussions on study design, planning and coordination

During the group discussion, attention was drawn to the need for the implementation of high-quality and more detailed descriptive studies to provide a better picture of CKD in the region. Implementation of a regional surveillance system should be considered, but would require standardization of criteria for case definition and diagnostic procedures.

Case-control (C-C) studies

Crucial questions for a C-C-study are:

- Is there access to ESRD patients? Where? When?
- Is it possible to identify all cases in specific areas?
- Is it possible to identify cases through the primary health care system?
- Can the national and local health authorities be involved in the identification of cases through the national health care system (including the social security system)?
- Will it be possible to recruit correctly selected referent persons?
- What is the availability of human resources for research?

A preliminary discussion of the situation by country indicated that it might be possible to identify all cases of ESRD in Costa Rica, which should be tried in the most affected region. In Nicaragua and El Salvador it might be possible to identify cases with available resources; however a serious commitment from the local health authorities is required. Despite the fact that in Costa Rica, Nicaragua, and El Salvador it is possible to identify cases of ESRD, the resource limitations of the national health care systems make it difficult to have an unbiased enrollment and follow up of all cases.

The establishment of CKD instead of ESRD as a research outcome was considered to be the most feasible option. In a first step a cross-sectional study to identify cases of CKD and a healthy cohort can be performed by screening a suitable population sample. A follow-up of the healthy cohort could be carried out by performing new screening tests. All new (incident) cases will be included in a second C-C study. A random sample from the cohort subjects that remain healthy could be selected as a control group

Different countries might have different predominant risk factors which should be taken into consideration. There was general agreement that the following factors should be investigated: socio-economic factors, environmental and occupational chemical exposures (heavy metals, pesticides, arsenic), occupational work load and dehydration, (illegal) alcohol consumption, and smoking habits. Chronic intake of analgesic drugs as a postulated risk factor was controversial.

Cross-sectional studies

There is evident underreporting of kidney disease in the region. There is a need for more prevalence studies on CKD in the general population as well as in certain occupational and regional populations. There is also need for more information on renal function in the general population, for females as well as males. The group proposed the use of existing public health programs as a rational and inexpensive way to collect such information. The population surveyed in León by Dr. Peña and co-workers was mentioned as an example.

Within such a program questions about exposures and effects related to renal disease could be included, as well as urinary samples for simple lab investigations (U-glucose, U-albumin). Blood samples for determination of s-creatinine are more specific, but would most likely decrease the participation rate. Also, the prevalence of diabetes and hypertension in the population needs to be investigated.

Hitherto, occupational CKD studies have focused on agricultural workers. Studies of occupational populations outside agriculture were also proposed, such as miners and construction workers, who share heavy manual workloads and probably also dehydration during work days, but without pesticide exposure. For miners silica and heavy metal exposure may be of additional importance. Also, maquila workers were mentioned as possible occupational groups to be investigated.

Intervention studies

Interventions on three different levels were identified and discussed: Some examples were:

Political level. The Nicaraguan national congress has approved new legislation which recognizes pesticide intoxication and renal disease in sugarcane workers as occupational diseases. The National Council of Occupational Health has emitted new guidelines (water supply, personal protective equipment, promotion of occupational health service).

Local level. In El Salvador limited training of physicians at some local health care centers has taken place.

Individual level. – Employers: The monitoring of renal function in sugarcane workers in Chinandega, Nicaragua, including a pre-employment test, has started. The employer must provide oral-hydration salt to agricultural workers and educational support to prevent renal problems. In Costa Rica some sugarcane companies have started supplying oral rehydration solutions to their workers. Due to pressure from a trade union at one company, medical examination for 200 workers for 2 continuous years has been enforced.

Individuals: A private initiative is capable of assisting 700 individuals from the region of Bajo-Lempa in El Salvador. The follow-up includes a medical examination (determination of protein in urine, measure of blood pressure). All individuals with diagnosis of CKD (n=70) are receiving medication, monitoring of cholesterol, diabetes and hypertension control, and monitoring of urological problems. It is expected that 6000 males will receive information on how to avoid renal problems (i.e. recommendations about adequate water intake, avoiding dirty alcohol consumption and auto-medication, and the need of a medical check-up).

Proposal for an intervention program in Nicaragua and El Salvador

This proposal was based on a screening for renal disease in the general population, treatment of identified cases and an intervention aiming at control of dehydration, drinking water and dirty alcohol (see Appendix 2 for details).

Closing remarks

It was evident that all participants were seriously concerned about CKD being an important public health issue in the region, even though its magnitude is unknown and probably variable. The discussions and sharing of experiences during the workshop were held in an impressively open and generous atmosphere which seems promising for future cooperation.

Valuable contacts were established for a future network. Circulation of information on and results from activities discussed for 2006 was encouraged, e.g. potentials for comparative analysis of the available, cross-sectional studies, the feasibility of screening studies in Nicaragua, Costa Rica, and El Salvador.

Identification of potential funding agencies for future studies is an urgent issue. The organizers of the workshop offered to function as a clearing house for collected, reported and future information on the issues that were discussed.

APPENDIX # 1

Program Workshop on Chronic Kidney Disease in Central America November 2 – 3, 2005 Venue: Hotel Austria, León		
Wednesday November 2 Situation of CKD in Central America and beyond		
8:30 – 9:00 hrs	Presentation of the workshop and participants	Ineke Wesseling, Regional Program Director SALTRA
9:00 – 10:30 hrs	Presentation of mortality and morbidity data by workshops of different countries	Participants from Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panamá
10:30 – 10:45 hrs	Coffee	
10:45 – 11:15 hrs	Continuation.....	
11:15 – 12:15	Summary of epidemiologic studies of CRD in Central America	Steven Cuadra, UNAM-Managua, University of Lund
12:15 – 14:00 hrs	Lunch	
14:00 – 15:00 hrs	Chronic renal disease: classifications and clinical aspects	Ricardo Leiva, Hospital Rosales, El Salvador
15:00 – 16:00 hrs	Global epidemiology of renal disease and known risk factors	Kristina Jacobsson, University of Lund
16:00 – 16:15 hrs	Coffee	
16:15 – 16:45 hrs	Summary	Christer Hogstedt, Research Director, National Institute of public health, Sweden
16:45 – 17:45 hrs	Discussions	Moderators Christer Hogstedt and Ineke Wesseling
17:45 – 18:00 hrs	Planning day 2	
	Relevant exposures and exposure assessment	

Thursday November 3		
Study designs, planning and coordination		
8:30 – 9:00 hrs	Relevant exposures and exposure assessment	Berna van Wendel de Joode, Christer Hogstedt
9:00 – 9:30 hrs	A caso – control design	Patricia Monge, Catharina Wesseling, IRET-UNA, Costa Rica
9:30 – 10:30 hrs	Cros-sectional studies for identification of high risk populations and cohort studies for follow-up of high risk populations	Group work by country
10:30 – 10:45 hrs	Coffee	
10:45 – 11:30 hrs	Plenary discussions	Christer Hogstedt, Ineke Wesseling
11:30 – 12:15 hrs	Questionnaires and other measurement instruments	Group work
12:15 – 14:00 hrs	Lunch	
14:00 – 14:45	Plenary discussions	Christer Hogstedt, Ineke Wesseling
14:45 – 15:30 hrs	Financing	Christer Hogstedt, Ineke Wesseling
15:30 – 15:45 hrs	Coffee	
15:45 – 16:30 hrs	Principles for collaboration	Christer Hogstedt, Ineke Wesseling
16:30 – 17:00 hrs	Defining tasks for different countries	
17:00 hrs	Closing	

APPENDIX # 2

Participants in workshop on chronic kidney disease

Country	Affiliation	E-mail
Costa Rica		
Ineke Wesseling	IRET, UNA-Costa Rica; SALTRA	Ineke_wesseling@yahoo.com
Patricia Monge	IRET, UNA-Costa Rica; SALTRA	pmonge@una.ac.cr
Berna van Wendel de Joode	IRET, UNA-Costa Rica; SALTRA	
El Salvador		
Ramon García-Trabanino	Clínica de Hemodiálisis	rgtrab@yahoo.com
Ricardo Leiva	Hospital Rosales	rleiva@integra.com.sv
Honduras		
Alex Padilla	CESCOO, Secretaría de Recursos Naturales y Ambiente-SERNA	aepadilla@gmail.com
Nicaragua		
Luis Callejas	Ministerio de Salud	lcallejas@tephinet.org
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Karina Kjällestahl	NIPH, University of Uppsala	carina.kallestal@fhi.se
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Scott Sanoff	Division of Nephrology & Hypertension, School of Medicine, UNC	

APPENDIX # 3

Group discussion reports

Group 1: Case-control studies

Group 2: Cross-sectional studies

Group 3: Intervention studies

Group 1: Case-control study - group report

<u>Participants:</u>	Luis Callejas Ricardo Leiva Scott Sanoff Luis Blanco Alex Padilla
<u>Rapporteur:</u>	Steven Cuadra
<u>Moderator:</u>	Ineke Wesseling

General discussion

During the group discussion, attention was drawn to the need for the implementation of high-quality and more detailed descriptive studies in order to provide a better picture of the situation of CKD in the region. On the other hand, the participants agreed that access to existing data bases should be of major concern, since this can give us the opportunity for re-analysis and new analyses of the available material.

Implementation of a regional surveillance system should also be considered. Participants expressed concern that there might be contradictions in or differences between the definitions of cases between countries and periods. National practices vary considerably with respect the terms and definitions used. Thus, some aspects should be further discussed: standardization of criteria for case definition and diagnostic procedures, implementation of passive surveillance system at national levels com-

bined, when possible, with active investigation of cases, for instance through the application of diagnostic tools such as biopsies.

However, in order to evaluate the required conditions to carry out any research projects in the region, several questions need to be answered for each country:

- Is there access to ESKD patients? Where? When?
- Is it possible to identify all cases at specific areas?
- Is it possible to identify cases through the primary health care system?
- Can the national and local health authorities be involved in the identification of cases through the national health care system (including the social security system)?
- What is the availability of human resources?

Additionally, participants emphasized that some knowledge is required which depends on the improvement of national-level statistics and the identification of those regions which are most affected:

- In Nicaragua and Salvador, there are indications of regional differences in the prevalence of CKD, but they need to be confirmed
- In Costa Rica, problems have been observed in sugarcane plantation areas, but the influence of migrants is not clear.
- No information is available from Honduras, Belize, Guatemala and Panama. Descriptive studies are needed.
- The health care systems for each country should be described, and their capability for detection of cases should be verified.
- Based upon the available information from previous studies, it is important that the issue of gender is adequately covered. The types of data collected, how they were collected and how they were classified should reveal areas of importance to women as well as to men.

A preliminary discussion on the situation for each country showed that in Costa Rica it is possible to identify all cases of ESKD, but the most affected area needs to be defined first. In Nicaragua and El Salvador it is possible to identify cases with available resources, but a great commitment from the local health authorities is required.

Study design issues

Outcome:

Despite the fact that it is possible to identify cases of ESKD in Costa Rica, Nicaragua and El Salvador, limitations on resources in the national health care systems which can be used to attend these patients make the enrollment and follow up of all cases difficult. Thus, the establishment of CKD instead of ESKD as research outcome seems to be the most feasible option.

Exposures:

There was general agreement that the following factors should be investigated

- Socio-economic factors
- Chemical exposure: heavy metal, pesticides, arsenic
- Life style: alcohol consumption, smoking habits
- Work condition: work load, dehydration
- Known risk factors

Chronic intake of analgesic drugs as a risk factor was controversial. Thus a review of the scientific literature and consultations with experts in the field are needed. Participants remarked that different countries might have different predominant risk factors. This issue should be taken into consideration.

Study base:

The possibility that enrollment of subjects can be done through a random selection from the general population by using the electoral registration system was discussed (Subjects over 16 years).

In a first step, a cross-sectional study can identify cases of CKD and a healthy cohort can be established by screening of the selected sample (using results of renal function tests as markers of chronic renal damage). A follow-up of the healthy cohort will be carried out by performing new screening tests. All new (incident) cases will be included in a prospective case-control study. A sample from the cohort subject that remains healthy will be selected as control group (random sampling). Around 200 new cases are expected to be enrolled during one year.

There was a consensus regarding the countries that should be considered to carry out a case-control study: El Salvador and Nicaragua. Regional investigations can be performed in Nicaragua. For instance, in Nicaragua León, Chinandega, and Rivas will be included. More descriptive information is needed from the rest of the countries.

Other aspects:

Human resources available in El Salvador and Nicaragua

- Groups of Field Epidemiologists (Nicaragua)
- Epidemiologists at UNAN-León and UNAN-Managua
- Nephrologists (El Salvador and Nicaragua)
- Hygienists (Nicaragua)

Collaborators

- Societies of nephrologists
- Ministries of health
- Social security
- Universities
- PAHO

Obstacles and foreseeable problems

- Lack of support from national authorities (governments)
- Difficulties with the organization and structure of the research team
- Training of the personal to be involved
- Limitations of the local health care systems with regard to the detection of cases

Group 2: Cross sectional studies - group report

<u>Participants:</u>	Rodolfo Peña Teresa Rodríguez Susan Lynn Hogan Manuel Len
<u>Rapporteur:</u>	Patricia Monge
<u>Moderator:</u>	Kristina Jakobsson

Proposed agenda:

- Types of indicators to be used
- Populations or samples to be screened
- Case definition, selection of controls
- Possibilities of formation of cohorts
- Human resources
- Collaborators
- Rough costs
- Potential problems

Guideline for discussion:

The moderator proposed a guideline for discussion, based on the following five points:

1. What do we know
2. What do we want to know
3. Which study groups can be used
4. Which indicators of exposure
5. Which indicators of effects

1. What do we know

Renal disease in Central America is an important issue, mainly in males. There is an evident under-reporting of cases in the region, and a need for more prevalence information, but the numbers are definitely important, and not due to increased prevalence of Diabetes Mellitus. There could be a regional influence.

2. What do we want to know

Prevalence, the best definition of outcome and the possible exposures associated with the illness.

3. Which study groups can be used

There were two principal groups proposed: occupational vs regional, which were considered to be complementary. It is difficult to take a random sample. There is a need for more expertise and research.

For occupational populations outside agriculture, miners and construction workers were proposed, sharing heavy manual workload and probably also dehydration during work days, but without pesticide exposure. Also, maquila workers were mentioned as a possible occupational group to be investigated.

There is a need for more knowledge on renal function parameters in the general population. There was a proposal for using existing primary health care programs in the countries where visits to the population are performed by health care providers. As an example, the population surveilled in León by Dr. Peña and coworkers was mentioned. Within such a program questions on exposures and effects related to renal disease could be included, as well as the taking of samples for simple lab investigations. The prevalence of diabetes and hypertension in the population also needs to be investigated.

4. Which indicators of exposure

Pesticides, heavy metals, physical activity and silica were proposed as possible exposures to be studied. A directed questionnaire was proposed. Biomarkers of exposure are available for heavy metals and some pesticides.

5. Which indicators of effects

Blood creatinine and albuminuria were both proposed. Blood samples are highly specific, but would decrease the participation rate of subjects, due to venous puncture. Albuminuria modifies early, its sensitivity is high as well and its specificity moderate. Nonetheless, people with advanced kidney failure do not show albuminuria. Mortality data should not be used, since it is unlikely that existing registries provide good information.

Group 3: Intervention studies - group report

<u>Participants</u>	Ramón García-Trabanino Carina Kjälleståhl Lylliam López Berna van wendel de Joode
<u>Rapporteur:</u>	Marianela Corriols
<u>Moderator:</u>	Christer Hogstedt

Background

Participants indicated that any intervention effort must start with identification of the magnitude of the problem. Therefore a good register of mortality and morbidity is needed, as well as good information on the general population.

Participants pointed out that Costa Rica and El Salvador have a systematic death registry. But this is not case in Nicaragua. The registration of causes of death is not reliable in any of these countries. Information on the general population is based on estimations from national censuses (El Salvador 1996, Nicaragua 1995, Costa Rica 2000). In Nicaragua a new national census, including the national household survey, will be carried out in 2006.

Despite the fact that national registries are useful in identifying temporal and regional trends, this source of information has seldom been used.

Participants also stated that there is a lack of comparability of the diagnostic praxis between countries, and regions within countries, which is rather crucial when we deal with local data or data restricted to specific areas.

In countries such as Nicaragua and Costa Rica the local health care system network gives access to certain communities which make them suitable for some in-depth studies.

Ongoing intervention strategies in the region

El Salvador

At the present time there are three levels of intervention efforts: individual, local (limited training of physicians at local health care centers) and political (yearly reports from the Ministry of Health and PAHO). However there is lack of financial support for intervention programs at the individual and local levels (population based programs).

- There is a proposal to assist 9000 males from the region of Bajo-Lempa in El Salvador. However, due to lack of support, a private initiative is capable of assisting just 700 individuals with CKD. The individual follow-up includes medical examination (determination of protein in urine, measure of blood-pressure). All individuals with a diagnosis of CKD (n=70) are receiving medication (Pril or Sartan), monitoring of cholesterol, control of diabetes and hypertension, and monitoring of urological problems. On the other hand, It is expected that 6000 males will receive information on how to avoid renal problems (recommendations on adequate water intake, avoiding of dirty alcohol consumption and auto-medication, and the need of a yearly medical check-up including blood pressure measurement and urine protein determination)

Nicaragua

During recent years, great concern has emerged with regard to CKD and related problems. The public discussion promoted by society, non-governmental organizations and universities, as well as labor unions, led the government to make an official commitment to assist special populations such as sugarcane workers.

Political level: The Nicaraguan government, through the Ministry of Health, will create a special program to assist 4000 workers affected by Nemagon. Based on this example, the National Congress approved new legislation which recognizes pesticide-intoxication and renal disease in sugarcane workers as occupational diseases, so that medical care must be supplied for the employer.

Local level: A population-based screening of renal function in the Chinandega area has been carried out; however, financial support is needed to continue. On the other hand, the National Council of Occupational Health has emitted new guidelines (water supply, personal protective equipment, promoting OHS).

Individual level: Monitoring of renal function in sugarcane workers in Chinandega, which includes a pre-employment test (creatinine < 1.5). The employer must provide oral-hydration salt to agricultural workers and educational support to prevent renal problems.

Costa Rica

There is no special program at the national level to investigate CKD. Some sugarcane companies have started supplying oral rehydration solutions to their workers.

Due to pressure from a trade union at one company, medical examination for 200 workers for 2 continuous years has been enforced. This initiative has revealed that 14% of these workers had kidney problems, about 5% of them were severe.

Proposal for an intervention program in Nicaragua and El Salvador

The intervention program should aim at: prevention and treatment of dehydration, protection and treatment of drinking water sources, control of dirty alcohol, early treatment of cases, and detection of early and mild renal damage. The establishment of reference groups is also important.

- First phase: screening of the general population (10,000 subjects).
Second phase: All identified cases will receive early treatment to avoid progression.
Third phase: Additional intervention program for 10,000 subjects to control dehydration, drinking water sources and dirty alcohol.

Based on an incidence of 2% and a 50% effect we would see a reduction of about 100 cases due to the population based intervention after one year. The estimated cost is about €150,000 (probably less).

Financial possibilities

The participants discussed several alternatives as financial sources at the national, regional and international levels:

Local level:

- Local Non-Governmental Organizations
- Universities

Regional level:

- PAHO/WHO

International level:

- Sida/SAREC
- European Union
- German GTZ
- DANIDA
- World Bank

It was stressed that financial support from companies and industries should not be considered, to avoid conflicts of interest.

APPENDIX # 4

Potential for future collaboration – reexamination of cross-sectional studies

Existing data on CRD in the region should be explored by sharing the available data sets of the research projects that have been carried out in the region and performing an in-depth analysis of the material.

Dr. Ricardo Leiva (Department of Nephrology, Rosales Hospital, El Salvador University), Dr. Luis Callejas and Dr Steven Cuadra from Nicaragua plan to create a preliminary database during the spring of 2006.

Given their availability, the following data sets should be checked in the first step:

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Callejas Callejas, L., Alonso Medrano, C.D. and Mendoza, B. 2003. *Insuficiencia renal crónica (IRC) en trabajadores de caña de azúcar, El Viejo, Chinandega, Nicaragua*. US Cenetr for Disease Control and Prevention (CDC)-Ministerio de Salud Nicaragua (MINSa Nicaragua), Managua

Callejas Callejas, L., Alonso Medrano, C.D. and Mendoza Canales, B. 2003. *Estudio de IRC en trabajadores no relacionados al cultivo de la caña de azúcar, Chinandega, July-August 2003: Resultados preliminares*. US Cenetr for Disease Control and Prevention (CDC)-Ministerio de Salud Nicaragua (MINSa Nicaragua)

Callejas Callejas, L., AlonsoMedrano, C. and Mendoza Canales, B. 2003. *Insuficiencia renal crónica: una prioridad en salud pública, en la zona de la costa del pacífico de Nicaragua, Mayo - Septiembre 2003*. US Cenetr for Disease Control and Prevention (CDC)-Ministerio de Salud Nicaragua (MINSa Nicaragua)

SECTION III

Kidney disease research in El Salvador – report from exploratory field visits

22-24 February 2006

Ineke Wesseling,
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Sandra Peraza,
in collaboration with
Dr. Ricardo Leiva and
Dr. Ramón García-Trabanino

Introduction

Chronic renal disease is a very serious disease that leads to death unless the patient has access to dialysis or transplantation of a new kidney. The reported annual incidence in high-income countries of renal replacement therapy, RRT, which could be crudely regarded as the incidence of End-stage Renal disease, ESRD, in such countries, is reported to be 5 – 20/100.000 population (all ages). In middle- and low-income countries the detection of this disease is far from complete and it is likely that many or most cases are never detected, neither within the health system nor in the mortality statistics. The reported prevalence rates for RRT in Latin America varies between 1.7 – 61/100.000 with a strong relationship to GNP.

Case reports from El Salvador and Nicaragua (1,2) have indicated dramatically increased mortality as well as prevalence of renal disease in certain areas, especially among agriculture workers including sugarcane cutters. Those studies were discussed at a workshop organized by SALTRA in Leon, Nicaragua, in November 2005, c.f. workshop report. One of the conclusions reached in the workshop was that the possibilities for improved studies on the prevalence of renal insufficiency at different stages in different areas and trades should be explored, as should the possibility of direct future studies on causal factors and interventions. The El Salvadorian participants invited SALTRA participation in on-going planning for such studies. This report concerns visits between the 22 – 24 of February 2006 to hospitals, health units, agriculture cooperatives etc. to explore the conditions for epidemiological studies and the suggestions for continued planning.

El Salvador

The population of El Salvador is about 7 million persons. The capital city of San Salvador has more than 2 million people: an estimated 42 % of the population lives in rural areas. The majority of the population is young: 36.5 % of inhabitants are between 0-14 years old and 5.1 % are older than 65 years.

Life expectancy is around 71.2 years, infant mortality 25.1 per 1000 newborns. About one-half of the population lives at or below the poverty line, concentrated in the countryside. One-fifth of the population is illiterate, with a higher percentage of illiteracy among females. An estimated 2 million El Salvadorians live and work outside the country.

El Salvador has a health budget of about \$250 million, which is 9% of the national budget and 1.6 % of the gross domestic product. Medical coverage is provided by the Ministry of Public Health and Social Assistance (MSPAS). The Salvadoran Institute of Social Security (ISSS), which is a labor-market insurance scheme paid by employers and employees, covers 17 % of the population.

End-stage Renal Disease in El Salvador (3)

El Salvador has no system to collect data at a national level for the identification of renal incidence and prevalence with demographic characteristics. However, the national system has 13 hemodialysis centers, 7 peritoneal dialysis centers and 4 kidney transplant centers.

In a case study published by Garcia-Trabanino, et al. (1) the risk factors for ESRD in Rosales Hospital among 205 patients were in 33% of the cases diabetes mellitus, arterial hypertension and chronic use of non-steroid anti-inflammatory drugs, while the rest of the patients (67%) did not present an etiologic diagnosis; 63% of those were agricultural workers (vs 21% in the first group). The majority of the patients in this second group were males, farmers, residents of coastal areas or areas next to rivers and who some years previously had been exposed to pesticides through their work.

Another study performed during 2003 by PAHO and MSPAS described 830 patients with renal replacement therapy (RRT) at MSPAS and ISSS (4). 65% of the patients lived in urban areas, while 71.4% were men between 20 and 60. The most frequent occupation was day laborer in the agricultural sector. Many used to drink water from wells, had been exposed to pesticides and fertilizers, and drank alcohol. The etiology of the ESRD was unknown in most of the cases, and the type of dialysis most used was peritoneal dialysis.

Treatment with hemodialysis in a private clinic costs 500 – 1.000 USD/month. The average income in ES is 200 USD/month.

Wednesday 22 February – visits to Hospital Rosales, and Santa Clara

On the first day of the three-day exploratory visit to El Salvador, Christer Hogstedt and Ineke Wesseling met with SALTRA's national coordinator, Sandra Peraza, and other counterparts at the University of El Salvador (UES). The plans for a pilot study on chronic renal disease were conveyed to the Board of the Faculty of Chemistry and Pharmacy, presided over by the Dean, Dr. Salvador Castillo. One point discussed was the need for assignment of faculty member time to SALTRA activities, among them outbreak studies such as the chronic kidney disease epidemic, which fits well with the UES goal to reach out to Communities.

Later, CH, IW and SP visited the Hospital Rosales, the main public hospital, where patients from the entire country are referred. At Hospital Rosales, Dr. Ricardo Leiva is head of the Department of Nephrology with a staff of specialists and residents in nephrology (Drs. Silvia Lazo de Leiva, Zulma Cruz de Trujillo, Luis Trujillo, Lidia Benítez, Ana Aguilar and Cristina Campos). Hundreds of patients with end-stage renal disease (ESRD) receive renal replacement therapy – some hemodialysis and kidney transplants, but mostly peritoneal dialysis (4). The Department of Nephrology provided figures of 20-50 new patients per month. Many patients consult only once or twice, due to poverty (no money for transportation to the hospital), fear of dying from peritoneal dialysis, and simply because there is no room available. Without treatment, these patients are assumed to die within a

short period of time. Exact mortality rates are uncertain. It is not uncommon that death certificates are issued by nonmedical personnel such as municipal office workers. Dr. Zulma Cruz de Trujillo handed over a recent paper presented at an international conference for prevention of chronic kidney disease, which highlights these issues (3).

Clinicians are under high pressure to do something for their dying patients. The Department of Nephrology is planning to carry out a study in part of the municipality of San Luis Talpa, in the Department of La Paz, which was identified by the PAHO study as the region with the highest incidence (25 per 100,000) (4). The trigger was a request by the general physician employed at the Santa Clara sugarcane cooperative in the Municipality of San Luis Talpa, Dr. Bibiana Cruz, who was struck by the high frequency of renal problems among her patients. Dr. Cruz has started to collect data on renal function of consulting patients and to refer cooperative members to the Hospital Rosales. About 60 cases of CDR in different stages have been detected, including 2 cases of ESRD and approximately 8-9 cases with advanced kidney disease. All these patients are being extensively studied at the Rosales Hospital. The collaboration between the Hospital Rosales and the Cooperative is also intending to provide surveillance to detect early cases for more opportune and less costly treatment.

In the afternoon SALTRA members, together with staff of the Hospital Rosales, visited the health center at the Cooperative of Santa Clara, in the Caserío de Santa Clara, a former hacienda. Members and their families had gathered to discuss their concerns with the clinicians of the Hospital Rosales and to hear about steps to be taken to address the epidemic. Pastor Antonio Carbajal Escobar, leader of the cooperative, headed the meeting, with words of among others by Dr. Leiva and Dr. Cruz de Trujillo, and observations by a number of cooperative members and SALTRA visitors.

In addition, an interview was held with Dr. Bibiana Cruz. The cooperative of Santa Clara has existed since 1980 and has members in 2 of the 11 counties of the Municipality of San Luis Talpa. There has been some turnover, but since 1997 membership has been stable. Besides the health center in Santa Clara, there are two public health centers in the municipality, one in San Luis and one in La Esmeralda. In Santa Clara, most medical services are free for members, but non-members have to pay and therefore often attend the public health centers. The physician comes four times a week and attends about 200 patients per month. The nurse also provides medical services. The proportion of families of Santa Clara that are members of the Cooperative is unclear, but there are 414 associated families, with one person being a member and the other family members beneficiaries. It is possible to obtain lists of members and nonmembers. Both members and non-members are farmers and the populations are considered to be similar, although non-members produce some cotton in addition to sugarcane. Most cooperative members have lived in the area for over 20 years. During the sugarcane harvest season (December – May), the cooperative population is stable and there is immigration of workers from outside the area; after the harvest season members of the population may look for work outside Santa Clara.

All cooperative members are sugarcane farmers. They can read and write at an educational level of approximately 3-4th grade. Dr. Cruz estimates about 3 adults over age 20 per family. Today, children are not allowed to work on the sugarcane farms, and, women are therefore increasingly involved in agricultural field work. Dr. Cruz has diagnosed RCD almost exclusively in men, but in both members and nonmembers. There is a clinical laboratory in San Luis, but its capacity seems insufficient, with results of various renal function tests not being consistent for the same patient and different from those obtained at the Hospital Rosales. The level of concern about renal disease is very high in the community and Dr. Cruz believes both sick and healthy people will participate in an epidemiologic study.

Municipio de Jiquilisco – 23 February 2006

After a short visit to the private Centro de Hemodiálisis where Dr. Ramon García-Trabanino works, we went together to a meeting in Tierra Blanca with the Fondo Social de Emergencia de Salud Zona Costa de Usulután and were received by the founder Padre Pedro, the director, Julio Miranda, Dr. Carolina Hernández and other co-workers and members of the Board of the Fondo. For many years Dr. Ramon García has responded to requests for information, advice and some patient examinations from the Fondo.

The Fondo is a religious NGO which has about 1000 families as members. They pay 16-18 cents/month to receive health support of various kinds, e.g. health advice, some medications and transportation to hospitals. The Fondo also argues for actions on certain health concerns for the benefit of the member families. It receives donations from religious groups in other countries. There are a total of 7,500 persons in Tierra Blanca. The last census was performed in 2000.

There has been concern for more than a decade about renal disease in the area, which started with the observations of two Belgian nurses at the Fondo centre. Dr Jesus Dominguez from Spain worked here for four years and performed a field study on proteinuria (5) together with Dr Ramon García and others. Exposure from pesticide spraying on the cotton fields that earlier covered Tierra Blanca has been suspected as the cause of the many kidney deaths.

Based on the information and discussion it seems quite possible to perform a cross-sectional study with blood and urine samples at the health centre. A nearby new private laboratory has recently analyzed Se-Creatinine and urine tests with dip sticks in 60 persons for 5 USD/person at the initiative of Dr García. These tests demonstrated proteinuria in more than half of the tests and urinary infections in a large number.

A suggestion was made to examine all men and women aged 35 – 60 from the Concordia cooperative, where most members are agricultural workers and participate in the sugarcane harvests from November to April, in an extended pilot study on approximately 150 persons. Membership in the cooperative is very clear and lists can be created. Director Miranda offered to organize the transport of the subjects to be examined to the Fondo center or a health unit, and estimated that participation would be very high, given the existing worries about the subject.

We also visited the Unidad de Salud in Tierra Blanca and the Hospital de Jiquilisco (see map). There was a great concern at both institutions about the number of renal failures. The possible causes that were mentioned included dehydration, dirty drinking and washing water, urinary tract infections, and pesticides.

The Jiquilisco hospital has 19 physicians, 50 beds and a laboratory which can perform a restricted number of basic tests. Dr Gerardo Cruz, head of the hospital, presented figures on new cases of chronic renal disease. During 2002 – 2005 90 – 120 patients were diagnosed annually as new cases of Insuficiencia Renal Crónica, IRC, which would correspond to an estimated incidence of 120 – 177/100,000, although there is some uncertainty about the exact catchment area for the hospital. It also seems most likely that a considerable proportion of sick persons die without ever having been referred to the hospital for diagnosis. According to Dr. Cruz, IRC is the most common cause of death for men in Jiquilisco with an average of two deaths per week. IRC is less frequent among women.

Most patients that are diagnosed and informed about the conditions for dialysis, which would either mean peritoneal dialysis at San Miguel hospital or traveling to San Salvador 1-2 times/week (if even accepted at the public dialysis centers), refrain from even being referred. Very few could afford treatment at a private clinic (basically, only those persons that can receive substantial support from abroad)



Concluding suggestions and plans – 24 February 2006-03-04

At a meeting with representatives from the university (UES), the hospital (Rosales), SISCA, the Ministry of Health and others, the following was suggested and discussed after initial presentations by Drs. Leiva and García-Trabanino on the problem and earlier studies.

Aims

- To establish validated prevalence and incidence of mild and severe kidney disorders among men and women in El Salvador
- To identify the causes of potential excess risks and links in the causal chain
- To suggest, perform and study the effects of feasible interventions
- To identify cases for treatment

Potential study designs to be initiated during 2006

- Pilot investigations of all men and women aged 35 – 60 years in two agricultural cooperatives in the coastal area (Tierra Blanca and Santa Clara, approximately 100 – 200 persons in each) where some testing already has begun and support exists for such an investigation.
- Reference populations of 150 – 300 agricultural workers in cooler areas and non-agricultural workers
- Prospective hospital-based case – control study from the Rosales hospital

Later studies

- Large population study – 5,000 – 10,000 individuals - with follow up
- Intervention studies

Next steps

1. Develop and agree upon study protocols during March – April 2006 for the prevalence studies and the hospital-based case – control study
2. Organize the logistics for the studies – May 2006.
3. Carry out investigation June – October 2006, c.f. protocol
4. Organize the data sets, analyze, report and communicate the results November 2006 – June 2007
5. Apply for funding of larger studies and follow the activities in other countries

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