



TREND OF BALKAN ENDEMIC NEPHROPATHY PATIENTS ON RENAL REPLACEMENT THERAPY IN BOSNIA FROM 2003 THROUGH 2005

GORAN IMAMOVIĆ^{1*}, ENVER ZEREM¹, SAFET OMEROVIĆ²

¹ Internal Medicine Hospital, University Medical Center Tuzla, Trnovac bb, 75 000 Tuzla, Bosnia and Herzegovina

² Department of Urology, General Hospital Mostar, Maršala Tita bb, 88 000 Mostar, Bosnia and Herzegovina

* Corresponding author

ABSTRACT

The aim of this study is to evaluate epidemiological status of Balkan endemic nephropathy (BEN) patients on renal replacement therapy (RRT) in Bosnia from 2003 through 2005. Incidence and prevalence rates of BEN, diabetes mellitus (DM) and RRT population and proportion of BEN RRT population in total RRT population were tracked in renal units covering the entire BEN endemic region in Bosnia. BEN incidence and prevalence rates were 52; 34;48 and 262; 265, 292, respectively. DM incidence and prevalence rates were 7; 13; 8 and 20; 28; 33, respectively. Total RRT population incidence and prevalence rates were 89; 82; 79 and 424; 436; 473, respectively. Proportions of incident BEN RRT population in incident total RRT population and proportions of incident BEN RRT population in incident total RRT population when incident diabetics were subtracted from incident total RRT population were 0,58; 0,41; 0,61, and 0,63; 0,49; 0,67; respectively. Proportions of prevalent BEN RRT population in prevalent total RRT population and proportions of prevalent BEN RRT population in prevalent total RRT population when prevalent diabetics were subtracted from prevalent total RRT population were 0,62; 0,61; 0,62, and 0,65; 0,65; 0,66, respectively. Trend of BEN RRT population was stable in Bosnia from 2003 through 2005.

KEY WORDS: incidence, prevalence, diabetes mellitus, epidemiology.

INTRODUCTION

Balkan endemic nephropathy (BEN) is an unknown kidney disease that can be encountered in rural areas of the Balkan Peninsula in Croatia, Bosnia and Herzegovina, Serbia, Romania and Bulgaria. The disease is progressive, functionally characterized with tubular proteinuria type and morphologically with focal tubular atrophy and interstitial sclerosis as predominant lesions. It is the leading cause of terminal renal failure in the affected region,

requiring some form of renal replacement therapy (RRT) (1). The prevailing opinion nowadays is in favor of slow intoxication in genetically susceptible subjects. There are three hypotheses attempting to explain the environmental cause of the disease: aristolochic acid, mycotoxins and the Pliocene lignite (2). BEN prevalence rates in former Yugoslavia oscillated through time since the endemic was first described in the 1950s, but the rates closest to reality seemed to range between 0,4 % - 8,3 % (3). In 1977 the extensive epidemiological surveys were conducted in all known endemic municipalities of north-eastern Bosnia and Herzegovina: Šamac, Brčko, Orašje, Odžak, Bijeljina and Modriča (4). Almost all the population from endemic region was tested, in total 244 016 inhabitants. Testing was done in the field applying widely accepted criteria (5): positive family history, farming in occupational history, proteinuria, anemia and/or raised creatinine. Prevalence rate was found to be 0,709% (1,730 diseased and 10,541 found to have proteinuria as a sole finding). Epidemiological status of BEN in Bosnia has neither been evaluated after the war 1992-95, nor has there been an evaluation of the trend of the disease in this country. Actual data that are available in health care facilities from the BEN region are based on the hospitals' and out-patients clinics' records as well as on the approximations in the field with respect to the affected families the patients are coming from. Epidemiological survey that would investigate trend of BEN in Bosnia is further complicated by migration of population that took place during the 1992-95 war. The evidence on RRT population in Bosnia and Herzegovina from 2003 through 2005 is available from European Dialysis and

Transplant Association (6). Incidence and prevalence rates were 414; 413; 399 and 1954; 2007; 2298, respectively. Likewise, the most reliable data on BEN that could be obtained at the moment are those provided by the same Association. So, we conducted this study in order to evaluate epidemiological status of BEN RRT population in Bosnia from 2003 through 2005.

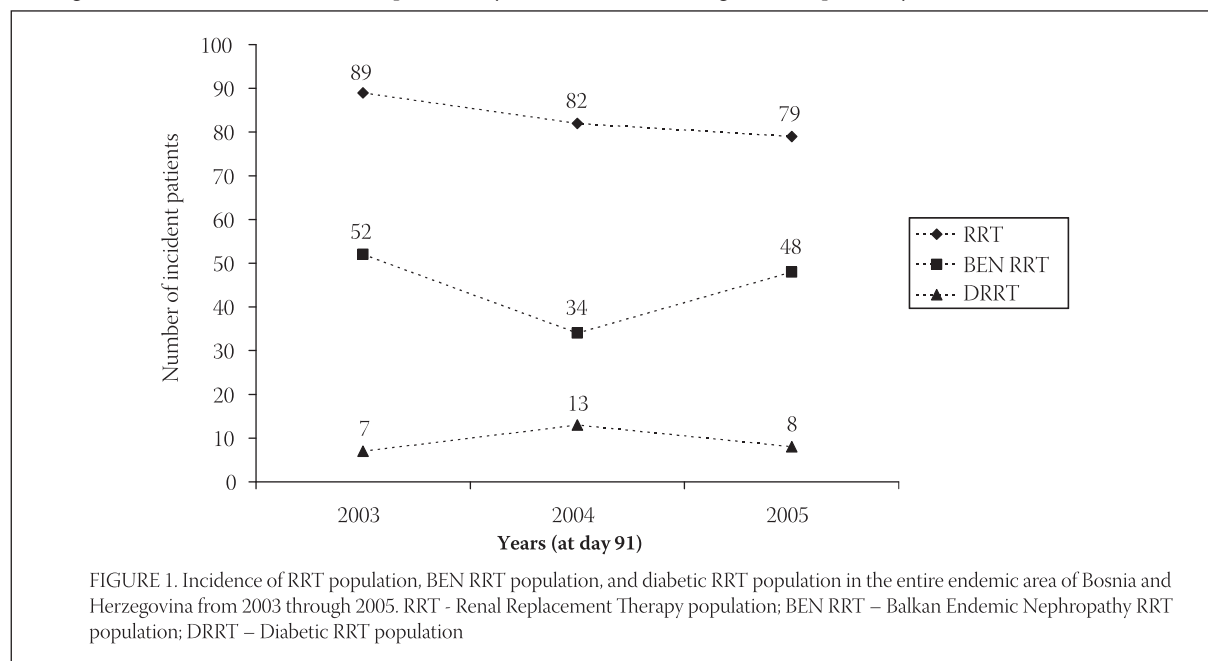
MATERIALS AND METHODS

This is the historical prospective observational study to track incidence and prevalence rates of BEN, diabetes mellitus and RRT population and to track the proportion of BEN RRT population in total RRT population in renal units covering the entire BEN endemic area of north-eastern Bosnia and Herzegovina settlements of Odžak, Bijeljina, Brčko and Šamac in the period from 2003 through 2005.

Data on RRT population were obtained from European Dialysis and Transplant Association (6) and from The Society for Nephrology, Dialysis and Kidney Transplantation in Bosnia and Herzegovina (7). BEN (5) and diabetes mellitus diagnoses were established on the basis of the widely accepted criteria. Descriptive statistical analysis was performed using MedCalc for Windows, version 8.1.0.0 (MedCalc Software, Mariakerke, Belgium).

RESULTS AND DISCUSSION

Incidence and prevalence data are shown in Figure 1 and Figure 2, respectively.



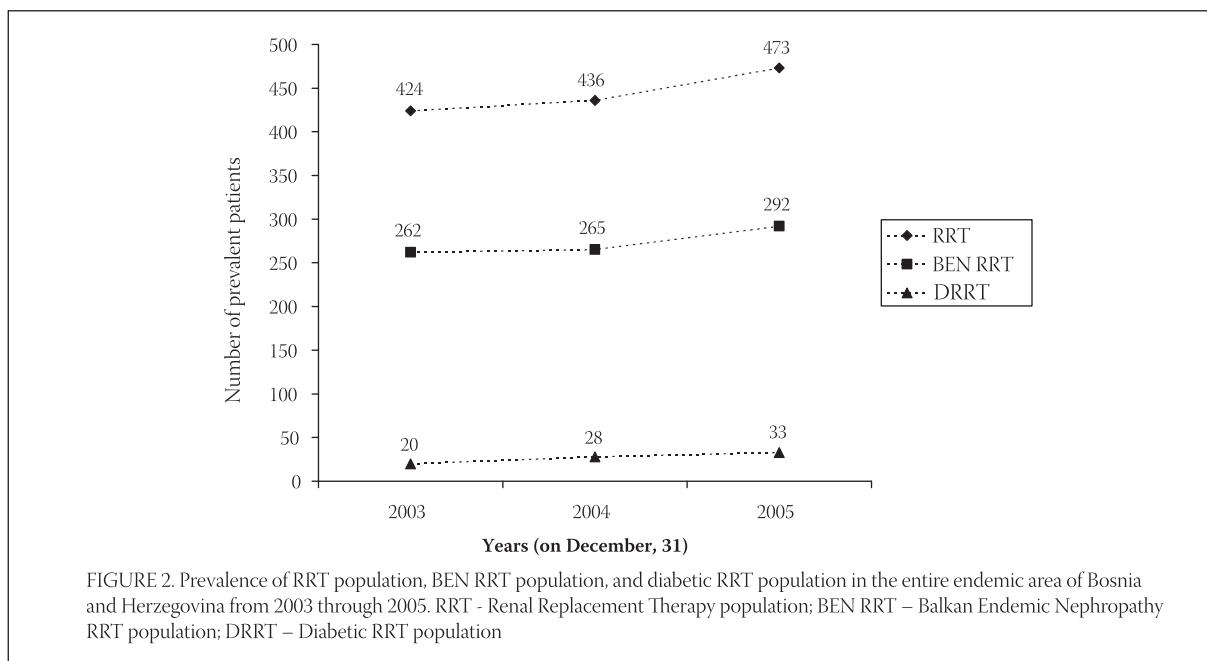


FIGURE 2. Prevalence of RRT population, BEN RRT population, and diabetic RRT population in the entire endemic area of Bosnia and Herzegovina from 2003 through 2005. RRT - Renal Replacement Therapy population; BEN RRT – Balkan Endemic Nephropathy RRT population; DRRT – Diabetic RRT population

Proportions of incident BEN RRT population in incident RRT population are shown in Figure 3. Proportions of prevalent BEN RRT population in prevalent RRT population are shown in Figure 4. Our results show that both incidence (Figure 1.) and prevalence (Figure 2.) of BEN RRT population are stable in Bosnia. They are still considerably higher than those pertaining to diabetes mellitus, which has shown remarkable increase worldwide. Trend of proportions of incident (Figure 3) and prevalent (Figure 4) BEN RRT population in RRT population when incident and prevalent diabetics were subtracted from incident and prevalent RRT population follows the trend of proportions without subtraction of diabetics.

There have been reports originating from the majority of the endemic countries that there is a trend to decrease in the intensity of BEN over the last two decades (8). On the basis of the recent epidemiological studies it seems that the incidence is decreasing and the onset of the disease has been moved towards older ages (9). However, Bukvić et al. reported the persistence of BEN in Serbia (10). It has been suggested that reversal of living standards to levels that existed before might have intensified exposure of the population to the presumed nephrotoxic agent(s) such that another epidemic wave of the disease could not be ruled out (11). In Bosnia, incidence of BEN RRT population dropped in 2004 (Figure 1.), even though prevalence kept on ris-

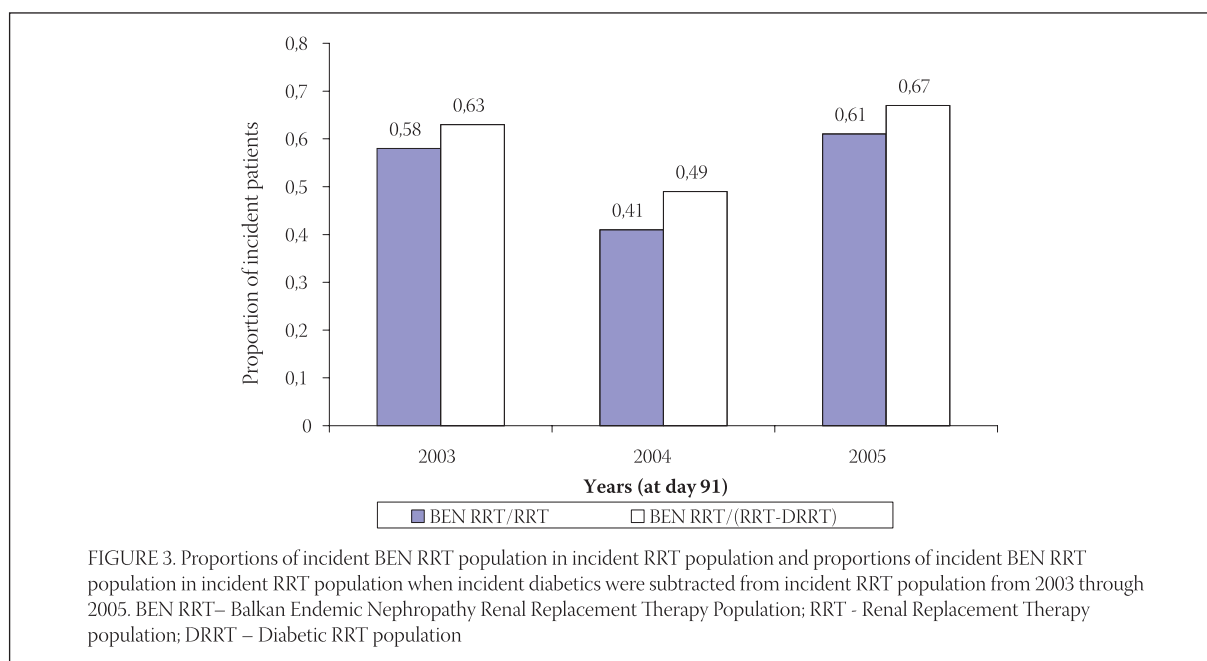
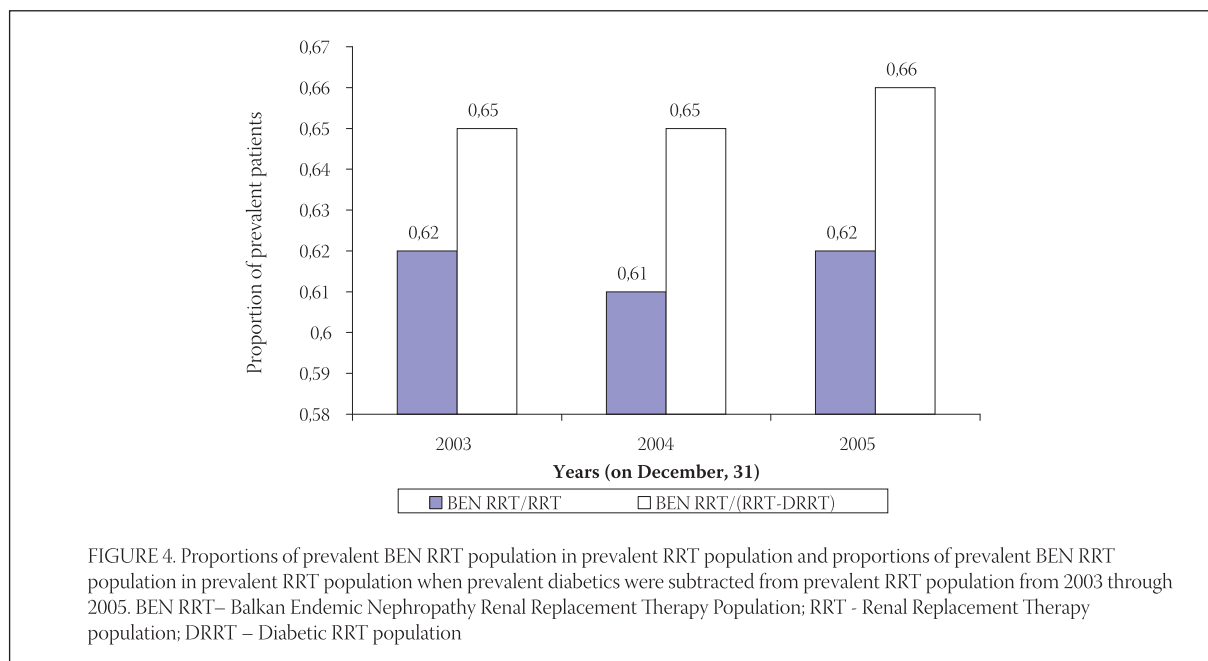


FIGURE 3. Proportions of incident BEN RRT population in incident RRT population and proportions of incident BEN RRT population in incident RRT population when incident diabetics were subtracted from incident RRT population from 2003 through 2005. BEN RRT– Balkan Endemic Nephropathy Renal Replacement Therapy Population; RRT - Renal Replacement Therapy population; DRRT – Diabetic RRT population



ing (Figure 2.). This might reflect better access to health care services, including dialysis and renal transplantation. However, the incidence went up in 2005, again. This could be accounted for by process of repatriation of war refugees from exile in 2005, even though we can

not support this presumption with official demographic data. On the other hand, this could also be accounted for by the limitation of this study, since BEN is a chronic disease and it is difficult to judge about its evolution in certain area over the period of three years, only.

CONCLUSION

Trend of BEN RRT population was stable in Bosnia from 2003 through 2005. It takes ongoing study and extensive epidemiological survey in the field again in order to get overall picture of current BEN status in Bosnia.

List of Abbreviations

BEN	-	Balkan Endemic Nephropathy
BEN RRT	-	Balkan Endemic Nephropathy Renal Replacement Therapy population
DM	-	Diabetes mellitus
DRRT	-	Diabetic Renal Replacement Therapy population
RRT	-	Renal Replacement Therapy total population

REFERENCES

- (1) Polenaković M., Stefanović V. Balkan Nephropathy. In: Oxford Textbook of Clinical Nephrology (Cameron J.S., Davison A.M., Grunfeld J.P., Kerr D., Ritz E., editors), Oxford: Oxford University Press. 1992; pp.: 857-866.
- (2) Stefanović V., Toncheva D., Atanasova S., Polenaković M. Etiology of Balkan endemic nephropathy and associated urothelial cancer. *Am. J. Nephrol.* 2006; 26: 1-11.
- (3) Čeović S., Pleština R., Miletić-Medved M., Stavljenić A., Mitar J., Vukelić M. Epidemiological aspects of Balkan endemic nephropathy in a typical focus in Yugoslavia. In: *Mycotoxins, Endemic Nephropathy and Urinary Tract Tumours* (Castegnaro M. et al., editors). Lyon: IARC Scientific Publications. 1991; pp.: 5-10.
- (4) Gaon J., Dedić I., Telebak B., Turić A. Occurrence of endemic nephropathy in SR B&H. *Proceedings of the 5th Symposium on Endemic (Balkan) Nephropathy*. Niš: University Press. 1983; pp.: 263-267.
- (5) Danilović V. Endemic nephropathy in Yugoslavia. *Proceedings of the 4th Symposium on Endemic (Balkan) Nephropathy*. Niš: University Press. 1981; pp.: 1-5.
- (6) Amsterdam: European Dialysis and Transplant Association. <http://era-edta-reg.org/index.jsp> [accessed Apr 7, 2007].
- (7) Mešić E., Lukić L., Dolenc L., Petković N., Stipančić Z., Resić H. Balkan endemic nephropathy in Bosnia and Herzegovina-renal registry report. *Med. Arh.* 2006; 60(4): 240-242.
- (8) Čukuranović R., Petrović B., Čukuranović Z., Stephanotis V. Balkan endemic nephropathy: A decreasing incidence of the disease. *Pathol. Biol.* 2000; 48:558-561.
- (9) Radovanović Z. Epidemiology and etiology of endemic nephropathy. In: *Endemic Nephropathy*. (Radovanović Z., Sindjić M., Polenaković M., Đukanović Lj., Petronić V., editors), Belgrade: Office for Textbooks and Teaching Aids. 2000; pp.: 81-83.
- (10) Bukvić D., Janković S., Arsenović A., Đukanović L. Balkan endemic nephropathy is still present in the Kolubara region, Serbia. *Ren. Fail.* 2005; 27: 565-569.
- (11) Radovanović Z. Epidemiological characteristics of Balkan endemic nephropathy in eastern regions of Yugoslavia. In: *Mycotoxins, Endemic Nephropathy and Urinary Tract Tumors* Castegnaro M. editor), Lyon: IARC Scientific Publications. 1991; pp.: 11-20.