Epidemiological Observations Regarding Balkan Endemic Nephropathy (BEN) in Romania in the Endemic Foci of the Mehedinti County

SUMMARY: The paper analyses the main focus of BEN in Romania, localized in the Mehedinti county, regarding GFR and proteinuria. It represents the data obtained from family physicians in 4 endemic villages (Hinova, Bistrita, Livezile and Husniciora), where the inhabitants of this BEN area are referred to. The main objective of this paper is to present some epidemiological data presently known in the BEN focus from the Mehedinti county in order to perform necessary measures that emerge from these observations. The majority of data was collected from a population participating in a screening organized in adult population by the Ministry of Health. Persons that came to the family physician were investigated through physical exam, laboratory exam comprise in a package that was also composed of urinalysis (proteinuria, urinary sediment). In persons over 50 the package comprised also serum creatinine. Some family physicians extended investigations regarding serum creatinine to persons below 50 years (18-50). The investigations carried out in persons over 50 revealed a reduction of the GFR in persons from two endemic villages as compared to the GFR from persons from the non-endemic region. In other two endemic villages no decline of the GFR as compared to non-endemic region has been noticed. Proteinuria didn’t differ in persons from the endemic region as compared to persons from the endemic region. The studies regarding GFR in persons with the age between 18 and 50 do not indicate an early decline of the GFR suggestive for an early onset of the disease. The investigation of patients from the endemic region dialedy in the two centers which subserves the population from the BEN region indicate an increased number of patients with end stage renal disease with BEN (51.34% in 2008 and 52.87% in 2009). Although some other countries report a decrease in the frequency of BEN cases this appears not to be the case in the BEN focus from Mehedinti county. BEN continues to represent a public health issue.

Key Words: Balkan Endemic Nephropathy, proteinuria, dialysis.

Observații epidemiologice privind nefropatia endemică balcanică (NEB) în județul Mehedinti

Rezumat: Lucrarea analizează principalul focar al NEB în România, localizat în județul Mehedinti, privind rata de filtrare glomerulară (RFG și proteinuria). Ea reprezintă datele obținute de la medicii de familie din 4 localități endemică (Hinova, Bistrița, Livezile și Husniciora) la care se adresează locuitorii din această arie. Principalul obiectiv al lucrării este a prezenta unele date epidemiologice în focarul NEB din județul Mehedinti, cu scopul de a efectua măsurile necesare care rezultă din aceste observații. Majoritatea datelor au fost colectate de la populația care a participat în screening-ul organizat în populația adultă de către Ministerul Sanătății. Persoanele care se adresează medicului de familie au fost investigate prin examen clinic, examenele de laborator care cuprind un pachet care a fost compus și din analizele de urină (proteinuria, sediment urinar). La persoanele peste 50 ani pachetul cuprinde de asemenea creatinina serică. Unii medicii de familie au extins investigațiile privind creatinina serica și la persoanele sub 50 de ani (18 – 50 ani). Investigațiile efectuate la persoanele peste 50 ani au relevat o scădere a RFG la persoanele din 2 sate endemic comparativ cu RFG de la persoanele dintr-o regiune non-endemică. În alte două localități endemic BEN nu a scăzut comparativ cu o regiune non-endemică. Proteinuria nu difere la persoanele din regiunea endemic comparativ cu regiunea non-endemică. Studiile privind RFG la persoanele cu varste cuprinse între 18 și 50 de ani nu indică un declin timpuriu al RFG, sugestiv pentru un debut timpuriu al bolii. Investigațiile pacienților dializați din 2 centre care deservesc populația din regiunea NEB au indicat un procent crescut al pacienților cu NEB (51,34 % în 2008 și 52,87 % în 2009). Deși în alte țări se raporteză o scădere a frecvenței cazurilor de NEB, aceasta afectiune continua să prezinte o problemă de sănătate publică.

Cuvinte-cheie: nefropatia endemică balcanică, dializă, proteinurie.
Balkan endemic nephropathy (BEN) is a disease of unknown etiology that has been described in some countries of the Balkan region in a geographical area near the Danube river: Romania, Bulgaria, Serbia, Croatia, Bosnia Hertzegovina.

The localities in which BEN is present are situated near the Danube.

In Romania the main focus of BEN is disposed in the Mehedinti county. Another focus has been described in the Caras Severin county in the neighborhood of Oravita, with the most affected town being Secaseni. There are no recent data regarding this focus.

The endemic focus of Mehedinti county comprises villages disposed around the city of Drobeta Turnu Severin. The focus comprises villages with BEN disposed on a surface of 1260 km2 of the 4933 km2 that represent the surface of the county.

From the data published by Trasca et al. it can be remarked that of the 382,344 inhabitants, 68,325 lived in the endemic area. This area comprises 19 communes with 108 villages.(

It has to be mentioned that BEN does not comprise all the localities of the BEN area, there exist endemic villages near non-endemic ones. In the same village there are patients with BEN in some families while other families, some neighboring the first ones do not present BEN cases.

The number of cases in the villages where BEN is described is not similar. There are villages with many cases of BEN defined as hyperendemic and others with less cases defined as hypoendemic. Another group of villages is defined as mesoendemic. Another observation is that BEN does not affect persons from the Roma population.

Because BEN is encountered in the rural areas in a population with modest sanitary education the existing data are relatively limited regarding BEN in the Mehedinti county focus.

Data regarding BEN epidemiology can be obtained from family physicians where the inhabitants from the BEN area are addressing. These participated in 2008 in a screening organized for the adult population by the Ministry of Health. Persons that came to the family physician were investigated through: physical exam, laboratory exam comprised in a package that was composed also of urinary exam (proteinuria, urinary sediment). In persons over 50 the package comprised also serum creatinine.

Some family physicians extended the investigations regarding serum creatinine to persons below 50 years. This action comprised only a relatively small number of persons existing persons even from families with BEN that did not show up for these investigations. In the BEN area persons from families with BEN, or even persons from zones where there are many cases with BEN consider themselves to be ostracized. They do not come to the doctor in order not to be suspected with BEN.

Despite this the mentioned screening could bring some data regarding renal affection of the population from the endemic zone compared to that from the non-endemic zone of the Mehedinti county. At the same time the family physicians from the area performed investigations of the persons that came to them: urinary exam, urea, serum creatinine. Therefore we asked them for the data regarding investigations in the BEN area.

We called to the family physicians from villages with increased endemicity. As control group we utilized data from a family physician from Drobeta Turnu Severin, a non-endemic locality.

In the Mehedinti county there are in Drobeta Turnu Severin 2 dialysis centers: a private center and a dialysis center belonging to the Hospital of the Romanian Railways.

Patients that reached the phase when dialysis was necessary presented to these centers in order to be treated. They can reflect the situation of the disease in the BEN area- is BEN endemicity is beginning to diminish, what is the number of BEN patients dialyzed as well as compared to nonBEN from the Mehedinti county, what is the disposition of patients regarding age, because there are observations that the disease is encountered presently in aged persons compared to previous years; what is the situation of urothelium tumors encountered in these patients, data regarding ethnicity of persons with BEN.

The main objective of this paper is to present some epidemiological data known presently in the BEN focus from the Mehedinti county in order to perform necessary measures that emerge from these observations.

MATERIALS AND METHODS

The following items have been studied:
1. observations of the dialysis centers regarding number of cases and the place where they belong in the endemic villages in order to study the endemicity of BEN in these villages.
2. Observations based on data provided by family physicians of 4 endemic villages: Hinova, Bistrita and Livezile, with increased endemicity and Husnicioara where there is a coal mine that functions, because in the hypothesis of BEN etiology
there have been discussed the production of disease through toxic substances that are originating from pliocen coal deposits.

3. The situation of dialyzed patients with BEN related to patients from non-endemic zones from dialysis centers from Drobeta Turnu Severin that are subserving this county including the BEN zone

We mention that eGFR has been calculated using MDRD4 formula, and proteinuria was performed using dipstick.

RESULTS

Results are presented in tables 1, 2, 3 and in figure 1.

Table 1 shows the prevalence of BEN in the dialysis centers of Drobeta Turnu Severin. Table 2 shows the glomerular filtration rate in the main endemic villages. Table 3 presents a comparative assessment of glomerular filtration rate in persons over 50 from the endemic villages Bistrita, Hinova, Livezile, Husniciaora with persons form a non-endemic area (Drobeta Turnu Severin). In figure 1 the dynamics of chronic kidney disease without BEN and with BEN in the Dialysis Centers from Drobeta Turnu Severin for period of 1990-2009 is shown.

The villages with the highest number of patients under dialysis are:

Erghevita is a village depending from the commune Simian. In the timeframe of 1972-1984 it had 1500 inhabitants. In 2007 the village had 200 inhabitants, 3 patients under dialysis. Other 11 patients with BEN originating from Erghevita live in Drobeta Turnu Severin where they perform dialysis. In 2010 Erghevita had 365 inhabitants.

Table 1 The prevalence of patients with Balkan Endemic Nephropathy in Dialysis Centers in Drobeta Turnu Severin (HD- hemodialysis, PD- peritoneal dialysis). * Since September 2007 the dialysed patients from the County Hospital are treated in the Private Dialysis Center "Renamed" (shadowed area in the table)

<table>
<thead>
<tr>
<th>Year</th>
<th>Hemodialysis Center County Hosp. Dr. Tr. Severin</th>
<th>Rom. Railway Hospital</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HD patients</td>
<td>BEN patients</td>
<td>PD patients</td>
</tr>
<tr>
<td>1990</td>
<td>30</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>1991</td>
<td>36</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>1992</td>
<td>42</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>1993</td>
<td>40</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>42</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>70</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td>72</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td>78</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>84</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>90</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>83</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>2001</td>
<td>88</td>
<td>38</td>
<td>30</td>
</tr>
<tr>
<td>2002</td>
<td>91</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>2003</td>
<td>98</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>2004</td>
<td>111</td>
<td>40</td>
<td>30</td>
</tr>
<tr>
<td>2005</td>
<td>122</td>
<td>59</td>
<td>28</td>
</tr>
<tr>
<td>2006</td>
<td>107</td>
<td>56</td>
<td>28</td>
</tr>
</tbody>
</table>

Table 2 shows the glomerular filtration rate in the main endemic villages.
Table 2: Assessment of renal function and proteinuria in persons from BEN area

<table>
<thead>
<tr>
<th></th>
<th>BISTRITA</th>
<th>HINOVA</th>
<th>HUSNICIOARA</th>
<th>LIVEZILE</th>
<th>TR. SEVERIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of explored patients &gt;50 years</td>
<td>224</td>
<td>243</td>
<td>77</td>
<td>326</td>
<td>254</td>
</tr>
<tr>
<td>Female</td>
<td>125</td>
<td>149</td>
<td>35</td>
<td>183</td>
<td>150</td>
</tr>
<tr>
<td>Male</td>
<td>99</td>
<td>94</td>
<td>42</td>
<td>143</td>
<td>104</td>
</tr>
<tr>
<td>Mean age: years</td>
<td>62.25±8.69</td>
<td>64.91±10.49</td>
<td>65.85±7.65</td>
<td>67.48±9.84</td>
<td>62.22±8.80</td>
</tr>
<tr>
<td>GFR ml/min</td>
<td>70.12±16.62</td>
<td>71.96±44.16</td>
<td>81.68±15.87</td>
<td>76.63±16.63</td>
<td>74.98±19.14</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>18pts (8.03%)</td>
<td>18pts (7.40%)</td>
<td>2pts (2.59%)</td>
<td>-</td>
<td>18pts (7.08%)</td>
</tr>
<tr>
<td>Number of explored patients 18-49 years</td>
<td>261pts</td>
<td>219pts</td>
<td>32pts</td>
<td>5pts</td>
<td>60 pts</td>
</tr>
<tr>
<td>Female</td>
<td>145</td>
<td>117</td>
<td>14</td>
<td>2</td>
<td>38</td>
</tr>
<tr>
<td>Male</td>
<td>116</td>
<td>102</td>
<td>18</td>
<td>3</td>
<td>22</td>
</tr>
<tr>
<td>Mean age: years</td>
<td>33.80±9.02</td>
<td>34.17±8.99</td>
<td>40.68±4.3</td>
<td>31.2±13.14</td>
<td>36.8±8.18</td>
</tr>
<tr>
<td>GFR ml/min</td>
<td>93.99±16.80</td>
<td>108.82±17.10</td>
<td>91.62±15.57</td>
<td>96.66±5.85</td>
<td>88.79±23.05</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>9pts (3.44%)</td>
<td>11pts (5.02%)</td>
<td>-</td>
<td>-</td>
<td>15pts (25%)</td>
</tr>
</tbody>
</table>

Fig. 1: The dynamics of chronic kidney disease without BEN and with BEN in the Dialysis Centers from Drobeta Turnu Severin for the period of 1990-2009

The commune Hinoa (2865 inhabitants in 2002) had 2 patients under dialysis in 2007 from the village Hinoa, 7 patients from the village Bistrita. From Cajei and and Ostrovul Corbului none of the patients were under dialysis. In 2010 Hinoa (1012 inhabitants) had 4 patients under dialysis, Bistrita (1370 inhabitants) had 8 patients under dialysis.

Livezile- the administrative center of the commune (1951 inhabitants in 2007). The village Livezile had 2 persons under dialysis, the village Valea Izvorului 10 patients under dialysis, one patient from the village Pietris, one patient from Izvorul Anestilor. From Izvoralul de Jos no patient was under dialysis treatment.

Poroina Mare (1375 inhabitants) in 2007 has 4 component villages: Fantanele Negre 5 patients under dialysis in 2007, while in Poroina Mare, Stigita and Sipotul no person under dialysis. In 2010 from Fantanele Negre (348 inhabitants) two patients are under dialysis treatment.

Rogova (1375 inhabitants) has 8 persons under dialysis and also two from the adjacent village of Poroinita (150 inhabitants), thus the total number of patients under dialysis from the commune of Rogova is 10 patients.

Other endemic important villages:
- Cioroboreni (1020 inhabitants)- 4 patients under dialysis
Table 3 Comparative assessment of glomerular filtration rate in persons over 50 from endemic villages Bistrita, Hinova, Livezile, Husnicioara with persons form a non-endemic zone (Drobeta Turnu Severin)

<table>
<thead>
<tr>
<th>Endemic village</th>
<th>GFR-endemic village</th>
<th>GFR-Drobeta Turnu Severin (nr patients=254)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bistrita (nr patients = 224)</td>
<td>70.12±16.62</td>
<td>74.28±19.14</td>
<td>P=0.003386</td>
</tr>
<tr>
<td>Hinova (nr patients = 243)</td>
<td>69.41±15.46</td>
<td>74.28±19.14</td>
<td>P=0.0004073</td>
</tr>
<tr>
<td>Husnicioara (nr patients = 77)</td>
<td>81.68±15.87</td>
<td>74.28±19.14</td>
<td>P=0.005519</td>
</tr>
<tr>
<td>Livezile (nr patients = 326)</td>
<td>76.63±16.63</td>
<td>74.28±19.14</td>
<td>P=0.2678</td>
</tr>
</tbody>
</table>

- Commune Prunisor: village Prunisor (803 inhabitants)- 4 persons under dialysis, Gelmingioaia (305 inhabitants) two patients under dialysis, Igiroasa one patient under dialysis.
- Husnicioara (320 inhabitants)- one patient under dialysis
- Corcova (1070 inhabitants)- 3 patients under dialysis

DISCUSSION

The localities with increased endemcity in the BEN zone are represented by Erghevita, Hinova, Livezile, Poroina Mare, Cioroboreni and Prunisor.

Regarding the endemcity of these localities we can make the following remarks.

Erghevita has been considered as the most representative for BEN, this disease been known once as Erghevita nephritis. It is interesting to follow the demographic evolution of this village. If in the time-frame 1972-1984 it had 1500 inhabitants being identified 88 families with one many BEN patients, in 2007 the village had only 200 inhabitants. In 2007 there were only 3 patients under renal replacement therapy. Other 13 patients from Erghevita settled in the non-endemic zone of Drobeta Turnu Severin where they underwent dialysis treatment.

It has to be remarked that persons from the endemic zone that emigrate in nearby localities or even to other countries can make the disease. It has to be considered that a person that lives 20 years in the endemic zone can make the disease.(2) If it leaves the zone after this period, he can make the disease after many years in the locality where he moved.

An experiment has been performed in Bulgaria where an important group of persons from the village of Karach from the endemic zone has been moved in a locality near Sofia and Plevna, that are non-endemic localities. Although the risk to contract the disease has been diminished, cases with BEN occurred in some persons.

In our study the 11 patients from the endemic village of Erghevita show BEN, even if they left the village for many years. The disease can appear in immigrants that develop the disease after at least 25 years, period in which they stayed in the endemic zone.(3)

Regarding the sex of the patients with BEN it has been remarked that BEN is more frequent in women. This fact has been signaled by numerous authors. We have also found this in the BEN focus of Mehedinti.

This can be due to the fact that women live and work in the endemic zone where the main occupation is agriculture.

Men generally lived less in the endemic zone. They worked, and partially still work in factories from the neighborhood of the endemic zone, most in the town of Drobeta-Turnu Severin, being mainly commuters. Thus they are less exposed to a possible etiological agent in the endemic zone.

The age at which BEN is diagnosed is around 30-40 years, but presently this age increased. Generally many patients are over 50-60 years. Cukuranovic et al. analyzing patients with BEN under treatment with hemodialysis from 5 endemic localities from Serbia mentioned that they found the disease occurs in older ages, mean age being 72.5 years.(4) Mesic et al. found an increase of average of patients with BEN in Bosnia and Herzegovina.(5)

It is hard to explain this thing. In the case if the hypothesis of BEN etiology is due to aristolochic acid, for which there are many arguments, this increase of the age could be due to the fact that presently in the zone herbicides are used, and the modern milling procedures withdraw Aristolochia Clematitis seeds from the flour.

A longer time-frame could be necessary for the accumulation of nephrotoxic doses of aristolochic acid. Despite this the etiology of BEN is not yet established.

The administrative unit named commune of Hinova is comprises 2865 inhabitants in 2002. It is composed of 4 villages: Hinova, Bistrita, Carjei and Ostrovu Corbului. We
have in 2007, 2 patients under dialysis from the village Hinova and 7 patients under dialysis from Bistrita, while in other two villages (Carjei and Ostrovu Corbului) we have no patient under dialysis.

It can be signaled that there are localities in the endemic zone where many persons are under dialysis treatment while others do not have any persons under dialysis.

This is signaled in other localities from the BEN area. Thus in the commune Livezile, composed of 5 villages (1951 inhabitants in 2007) 2 patients from the village Livezile undergo treatment with dialysis and 10 patients from the village Valea Izvorului. In the village Petris one patient undergoes dialysis, in the village Izvorul Anestilor one patient undergoes dialysis, while in Izvorul de Jos no patient is under dialysis.

In the BEN area of Mehedinti there is no clear evidence of BEN cases. This is due to many causes:
- a reduced addressability of patients suspected to have BEN, mainly due to the fact that in the area there is the belief that a person with BEN is a already condemned person to have an unfavorable evolution, despite the fact that there are two dialysis centers in the area.
- Family physicians do not have a clear evidence of these patients, and neither of the potential patients that can origin from these families.
- In the last 30 years epidemiological studies in the area have not been performed in order to detect BEN in the population of the endemic zone; there were only sporadical studies on limited groups of patients.

The single action performed on a large scale was in 2009, when investigations have been performed in the area regarding urinary exam in the whole adult population, investigation that comprised proteinuria; and serum creatinine in the population over 50 years. In all persons a survey has been performed regarding past diseases, as well as a general set of investigations.

Although the addressability of the population was limited, being possible that many persons from families with BEN or with symptoms of the disease avoided these investigations.

On the other hand investigations performed in the BEN area did not have as a determinant objective this disease. Therefore we consider that investigation of the cases with BEN in the Dialysis centers from the area can offer us useful data regarding epidemiology of the disease as well as dynamic evolution of the morbidity due to this disease.

Not all patients with BEN, as well as other patients with renal failure, reach dialysis centers. They can decease of other diseases: cardiovascular and neurological or tumours etc. Chronic renal insufficiency is complicated frequently with cardiovascular and neurological diseases. Patients with BEN often present urothelium tumours, some before the start of dialysis treatment.

Analyzing the cases from the dialysis centers from Drobeta Turnu Severin for 20 years we remarked a reduced addressability of patients with BEN as well as of those without BEN in the first years of functioning.

In the first 10 years there was only the Dialysis Center of the County Hospital of Drobeta Turnu Severin.

In the first year of functioning 1990, 30 patients have been dialyzed of which 6 with BEN representing 20% of the total number of dialyzed patients. The number of dialyzed patients increased progressively, thus in 1999 there have been 90 patients dialyzed of which 27 with BEN, representing 30% of the patients.

In 2000 when the dialysis center at the Romanian Railways Hospital was established the number of dialysed patients in the dialysis centers of Drobeta Turnu Severin increased. So in the Romanian Railways Hospitals and in Drobeta Turnu Severin County Hospital Center together were 139 patients of whom 36.69% had BEN. This reflected a better addressability of patients with chronic renal failure including BEN patients.

Over the years 2001-2009 the number of dialyzed patients in the two centers increased, reaching a peak in 2005 when 185 patients were dialyzed, of whom 47.03% had BEN; another peak was reached in 2008 when 187 patients were dialyzed of whom 96 (51.34%) had BEN.

At the end of 2009, 174 patients were under dialysis, of whom 96 (52.87%) had BEN.

Other authors too, such as Cukuranovic et al. have noticed that during the first years of functioning of the dialysis center the patients addressability was lower, and it increased gradually.

The dynamics of dialyzed patients, including BEN ones, over this period and also the fact that some of them have left the area.

The Mehedinti county is at the top of the counties in the area as concerns dialyzed patients.

Thus, in 2003 the number of the dialyzed patients in one million inhabitants in the Mehedinti county was of 428, as against 198 in the Caras-Severin county, 327 in the Timis county, 169 in the Dolj county and 189 in the Arad county.

The presence of BEN is the cause for that county’s having the largest number of patients under dialysis.

An analysis of BEN patients from Bosnia in 2003 on the basis of the renal registry report noticed that they
represent 14.79% of dialysed patients, the prevalence being much higher in north-eastern Bosnia where the main endemic villages lie, accounting for 61.61% of patients.

In Europe, the incidence rates of renal replacement therapy for end-stage renal disease (ERA-EDTA Register data from 1997 to 2006) was in 2006 of 125.4 patients/million of inhabitants.(6)

Actually two types of observations exist concerning the present stage of BEN:
- one stating that the number of BEN cases is decreasing and another one, stating that BEN continues in the BEN area. These observations are based on two types of studies:
  - analysis of patients under dialysis coming from the BEN area.
  - epidemiological studies carried out in the area.

These studies have been performed in the countries where the disease is present. Radovanovic has mentioned that the prevalence of BEN was stable over many years, but now it appears to decline in most affected settlements.(7)

Cukuranovic et al. have found, in dialysed patients from 5 villages in South Morava in Serbia, that end-stage renal failure in BEN patients has become less frequent over the 2004-2006 period and they attribute this to diminution of exposure to environmental toxicants.

Bukvic et al. in 2005 noticed that BEN is still present in Kolubara region in the village of Sopic, but the clinical course of the disease become more protracted over time. They observe that new cases of BEN appear only in the affected families.(8)

A diminution of the incidence of the disease in Bosnia Hertegovina has been found. However, Imamovic et al. have remarked that the trend of BEN renal replacement therapy population was stable in Bosnia from 2003 through 2005.(9)

In Croatia Miletic-Medved found out that prevalence of BEN is approximately the same as it was in the last decades(10)

In Bulgaria, Dimitrov et al. have found a decline of the incidence of BEN in 8 villages in the Vratsa district after 1984. According to these authors the migration of the population might have contributed to this decline.(11)

In Romania the number of dialyzed patients with BEN increased till 2008 (96 patients) with BEN dialyzed with a slight decrease of their number in 2009 (92 patients). The observations concerning the BEN dialyzed patients as against those without BEN reflect the fact that the disease continues in the area.

Observations concerning the glomerular filtration rate in the persons under study revealed a lower GFR in patients aged over 50 in two villages (Hinova and Bistrita) as against in patients in a family doctor’s office in Drobeta Turnu Severin.

Thus GFR was significantly lower in the population of the Bistrita endemic village and Hinova endemic village than in patients of a family doctor’s office in Drobeta Turnu Severin (p=0.0033 in the first case and p=0.0004 in the second one). But in the endemic village of Livezile in the population under analysis the GFR was higher but insignificantly as against that in Drobeta Turnu Severin. (p=0.2678). The population under analysis in the endemic village of Husnicioara show the GFR which was significantly higher then that in Drobeta Turnu Severin. (p=0.0055)

It results from the above that this study was not conclusive as concerns the GFR affection in the population in the endemic area, some villages showing a lower GFR than controls while others do not.

The results of investigations carried out in the endemic places we have studied are hard to analyze as compared with those of investigations carried out in other BEN areas, because determinations of the renal function were indicated by carried out persons aged over 50.

Stasevic et al. analysed 510 persons aged between 18 and 90 have remarked that elderly patients show lower values of the renal function.(12)

Explanations for this are difficult to offer:
- CRF, and BEN, in less frequently observed in some area of the endemic zone.

A variable addressability of the population of renal function evaluation has existed.

Actually, we found this in the area itself, one member of our team going there, where he observed a total reticence of patients to undergoing the investigation.

Determination of proteinuria has not revealed differences in the patients analysed, coming from two places in the endemic zone (Bistrita and Hinova) and Drobeta Turnu Severin.

In the population aged 18 through 49, the GFR average in Bistrita and Hinova was 107.29 +/- 13.95 ml/min and 106.05 +/- 12.53 respectively, while in Drobeta Turnu Severin it was 113.38 +/- 17.77 ml/min/1.73sqm.

The village of Livezile showed a GFR average of 96.66 +/- 5.88 and Husnicioara 104 +/- 10.13 ml/min as against that in the patients explored in Drobeta Turnu Severin.

The investigations carried out in persons from the endemic zone (age range 18-50) revealed mean values of the GFR above 100ml/min/1.73sqm. These values are
within reference range and are comparable to those from the non-endemic region studied by us.

Only in the village Livezile from the endemic region reduced GFR values as compared to other BEN villages and other non endemic areas were noticed.

Studies performed don’t indicate an early GFR decline of persons from the BEN region, the disease being currently encountered in persons over 40-50 years. On the other hand Stefanovic et al. mention that the early stages of BEN are not easily detectable clinically, as the disease is asymptomatic until a significant decline in function occurs, and even then symptoms are usually non-specific.(13)

Proteinuria in the patients explored was more frequent in controls.

From the above study of data existing in family doctors offices in BEN areas an accurate assessment of the status of BEN can not be performed.

It should be followed by further studies focused on BEN assessment.

The epidemiological observations in the BEN area of the Mehedi County argue in favor for the persistence of BEN, the disease continues to represent a public health issue.

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