

Chronic viral Hepatitis and liver diseases in Albania

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27, October 2016

Santantonio T, Lo Caputo S, Germinario C, Squarcione S,
Greco D, Laddago V, Pastore G.

**Prevalence of hepatitis virus infections in Albanian
refugees. Eur J Epidemiol. 1993 Sep;9(5):537-40.**

A sample of 393 Albanian refugees, including both children and adults, was tested for serological HAV, HBV, HDV and HCV markers.

A high prevalence of infection with both the hepatitis A and B viruses was found, while HDV and HCV infections were uncommon

One or more serological markers of HBV infection were found in **295 Albanians (75%)**, confirming the endemic nature of this virus in the Albanian community. **The overall prevalence of HBsAg was 19%**, and the carrier rate was higher in males than in females.

Ozaras, R., Inanc Balkan, I., Yemisen, M. and Tabak, F.
**"Epidemiology of HBV subgenotypes D." Clin Res Hepatol
Gastroenterol 2015 39(1): 28-37.**

D2 is seen in Albania, Turkey, Brazil, western India, Lebanon,
and Serbia

Zehender, G., Shkjezi, R., Ebranati, E., Gabanelli, E., Abazaj, Z., Tanzi, E., Kraja, D., Bino, S., Ciccozzi, M. and Galli, M.
"Reconstruction of the epidemic history of hepatitis B virus genotype D in Albania." Infect Genet Evol 2012 12(2): 291-298.

Despite a recent decrease in the prevalence of HBsAg in the general population, Albania is still highly endemic for HBV infection.

Genotype D is the most prevalent HBV strain in the Mediterranean area.

Study of prevalence and distribution of HBV genotypes and subgenotypes in a total of 73 HBsAg-positive patients living in Albania.

All of the Albanian subjects were infected with the HBV D genotype, and a percentage varying from 44.4% to 100% (depending on the ethnic or risk group) were infected with subgenotype D2, the most prevalent in the study population (72.4%). The other subgenotypes present in a minority of subjects were D1 (13.8%) and D3 (13.8%)

Zehender, G., Ebranati, E., Gabanelli, E., Shkjezi, R., Lai, A., Sorrentino, C., Lo Presti, A., Basho, M., Bruno, R., Tanzi, E., et al. "**Spatial and temporal dynamics of hepatitis B virus D genotype in Europe and the Mediterranean Basin.**" **PLoS One 2012 7(5): e37198.**

Subgenotypes D2 in Albania

Kondili, L. A., Cuko, L., Chionne, P., Candido, A., Madonna, E., Dentico, P., Resuli, B., Taliani, G., Brunetto, M. R. and Rapicetta, M. **"Hepatitis B, C and Delta virus infections in Albanian patients with chronic liver disease: evaluation of possible changes during the last 10 years."** **Eur J Gastroenterol Hepatol 2010 22(2): 167-171.**

The prevalence of viral hepatitis markers and of alcohol intake was evaluated in 106 and 99 Albanian patients with the diagnosis of viral and/or alcoholic chronic liver disease who were consecutively admitted to the University Hospital Center of Tirana, during 1995 and 2005, respectively.

A slight decrease in HBsAg (78 vs. 70%) and HBeAg (18 vs. 12%) prevalences were observed in patients admitted to the hospital during 2005 compared with those admitted during 1995, respectively.

In both periods of time, hepatitis B virus (HBV) DNA (genotype D) tested positive in all HBsAg-positive patients and in 36% of HBsAg-negative patients.

Anti-hepatitis C virus (HCV) prevalence (mainly observed after 30 years of age) was 14 versus 11%;

anti-hepatitis Delta virus (HDV) prevalence (more frequently present in young age group patients) was 9 versus 7% during 1995 and 2005, respectively.

Among patients who reported alcohol intake, alcoholic liver disease (HBsAg and anti-HCV negative) was diagnosed in 35 and in 57% of patients admitted during 1995 and 2005, respectively ($P = 0.05$).

In Albanian patients with chronic liver disease:

- (i) HBV remained the most important aetiologic factor of chronic liver disease; HDV and HCV prevalences were still low,
- (ii) in HBsAg-positive patients, HBeAg-negative chronic hepatitis prevailed,
- (iii) in HBsAg-negative patients, HBV DNA prevalence was high,
- (iv) during the last decade, an increased prevalence of alcohol intake in the aetiology of chronic liver disease was observed.

Resuli, B., Prifti, S., Kraja, B., Nurka, T., Basho, M. and Sadiku, E. "**Epidemiology of hepatitis B virus infection in Albania.**" **World J Gastroenterol 2009 15(7): 849-852.**

To assess the prevalence and socio-demographic distribution of hepatitis B virus (HBV) infection in Albania.

Blood samples from 410 unselected schoolboys, 666 students, 500 military personnel, 1286 casual blood donors, 378 voluntary blood donors and 640 pregnant women (total **3880 non-vaccinated residents** of rural and metropolitan areas from all over Albania;

Resuli, B., Prifti, S., Kraja, B., Nurka, T., Basho, M. and Sadiku, E. "Epidemiology of hepatitis B virus infection in Albania." World J Gastroenterol 2009 15(7): 849-852

2354 (60.7%) male and 1526 (39.3%) female;
mean age of 26.3 years

tested during 2004-2006 for hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B virus (anti-HBs) by ELISA.

Resuli, B., Prifti, S., Kraja, B., Nurka, T., Basho, M. and Sadiku, E. "Epidemiology of hepatitis B virus infection in Albania." World J Gastroenterol 2009 15(7): 849-852

The HBsAg and anti-HBs prevalence were 9.5% and 28.7%, respectively.

The highest HBsAg prevalence was evident in the younger age group, such as in schoolchildren (11.8%) and the military (10.6%).

Consequently, the anti-HBs prevalence increased with age, from 21.2% in schoolchildren (mean age: 15.7 years), to 36.3% in pregnant women (mean age: 26.3 years) and 29.7% in voluntary blood donors (mean age: 40.1 years).

There were no significant differences between males and females.

Katsanos, K. H., Christodoulou, D. K., Zervou, E., Babameto, A., Kraja, B., Hyphantis, H., Karetos, V., Tsonis, G., Basho, J., Resuli, B. F., et al. **"Hepatitis B remains a major health priority in Western Balkans: results of a 4-year prospective Greek-Albanian collaborative study."** Eur J Intern Med 2009 20(7): 698-702.

To report on the results of two projects (HEPAGA I and HEPAGA II) which lasted 4 years on chronic hepatitis B in Western Balkans lead by Ioannina, Northwest Greece and Tirana, Albania.

In HEPAGA I, serum samples from 410 Albanians were tested for HBV.

HEPAGA I showed that 11.89% of the Albanians was HBsAg(+) and only 21.19% had HBV immunoprotection.

In HEPAGA II, health care consumption was recorded in hospitalized patients with chronic hepatitis B and included 101 patients.

There was a significant difference in hospitalization costs per patient between centers.

The Greek patients were significantly older ($p=0.027$) and there was a significant correlation between age >50 years and hospitalization costs ($p=0.035$).

The HEPAGA I study showed a decrease in the prevalence of chronic HBV infection in Albania compared to that of the previous decade.

The HEPAGA II study demonstrated that health care consumption due to HBV infection is still an important determinant of the overall health consumption in Western Balkans.

Kondili, L. A., Chionne, P., Porcaro, A., Madonna, E., Taffon, S., Resuli, B., Taliani, G. and Rapicetta, M. "Seroprevalence of hepatitis E virus (HEV) antibody and the possible association with chronic liver disease: a case-control study in Albania." *Epidemiol Infect* 2006 134(1): 95-101.

A case-control study involving 109 in-patients with chronic liver disease and 190 in-patients with no apparent liver disease was conducted to evaluate the seroprevalence of anti-HEV antibodies and the possible association with chronic liver disease.

Among cases, the anti-HEV prevalence was 36.6% which increased significantly by age;

among controls, the prevalence was 12.1% ($P < 0.05$) and was similar among age groups < 60 years. Among cases, aged > 50 years (OR 4.0, 95% CI 1.4-11) and the presence of end stage liver disease (ESLD) (OR 4.3, 95% CI 1.4-12.8) were associated independently with anti-HEV positivity.

Kondili, L. A., Chionne, P., Porcaro, A., Madonna, E., Taffon, S., Resuli, B., Taliani, G. and Rapicetta, M. **"Seroprevalence of hepatitis E virus (HEV) antibody and the possible association with chronic liver disease: a case-control study in Albania."** *Epidemiol Infect* 2006 134(1): 95-101.

The mean optical density, determined by anti-HEV immunoenzymatic test, was significantly higher among patients with ESLD, compared to the other patients.

These results indicate that there is a high seroprevalence of anti-HEV in patients with chronic liver disease and a possible association between HEV infection and/or anti-HEV production and advanced stage chronic liver disease.

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Tirana

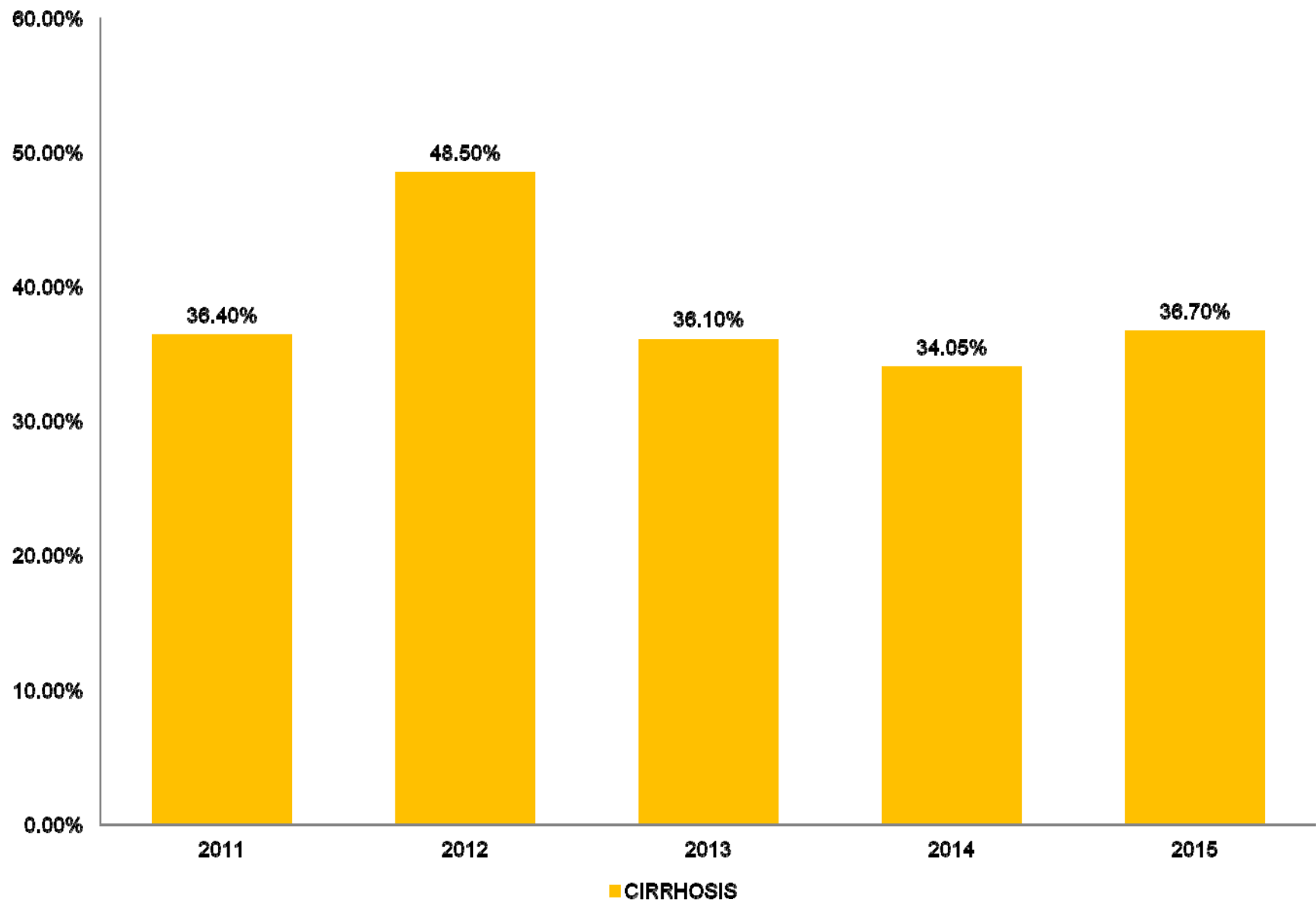
Structure of the diseases admitted

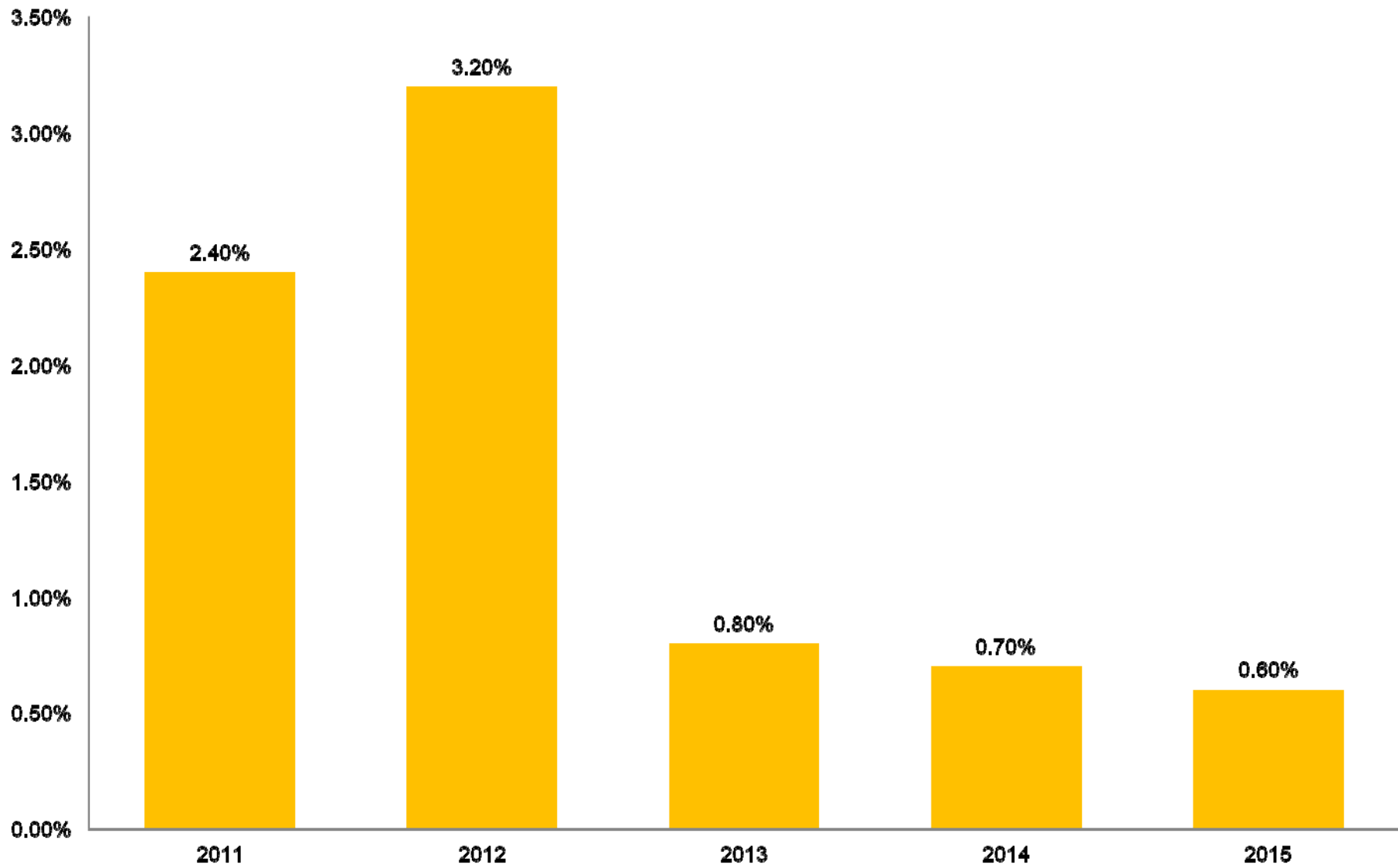
Around 70% liver diseases and 35% others.

Year 2011: Total 1107 .

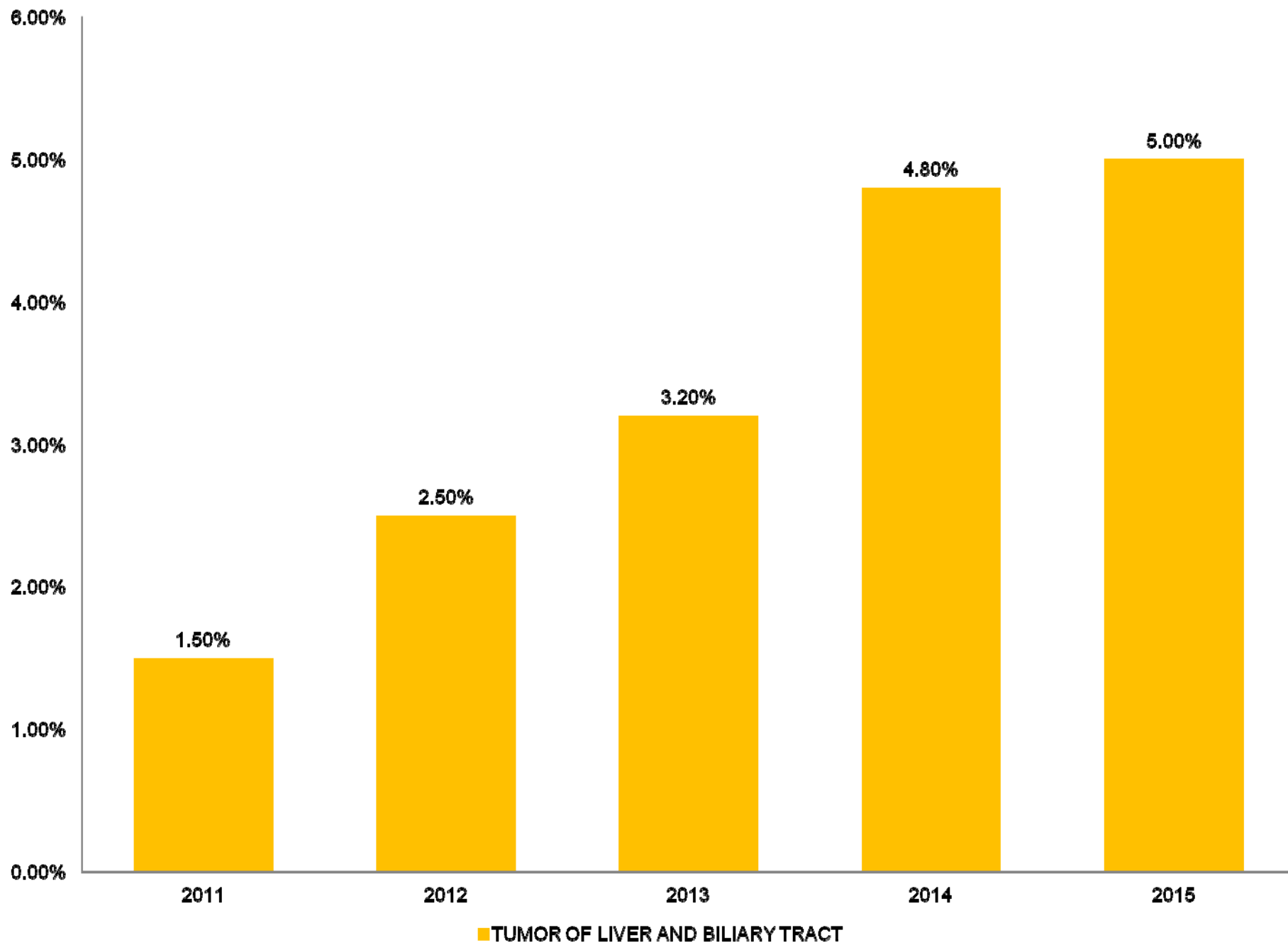
Liver cirrhosis 460 (41.55%);
decompensated 341 (74.1%)
compensated 119 (25.9%)

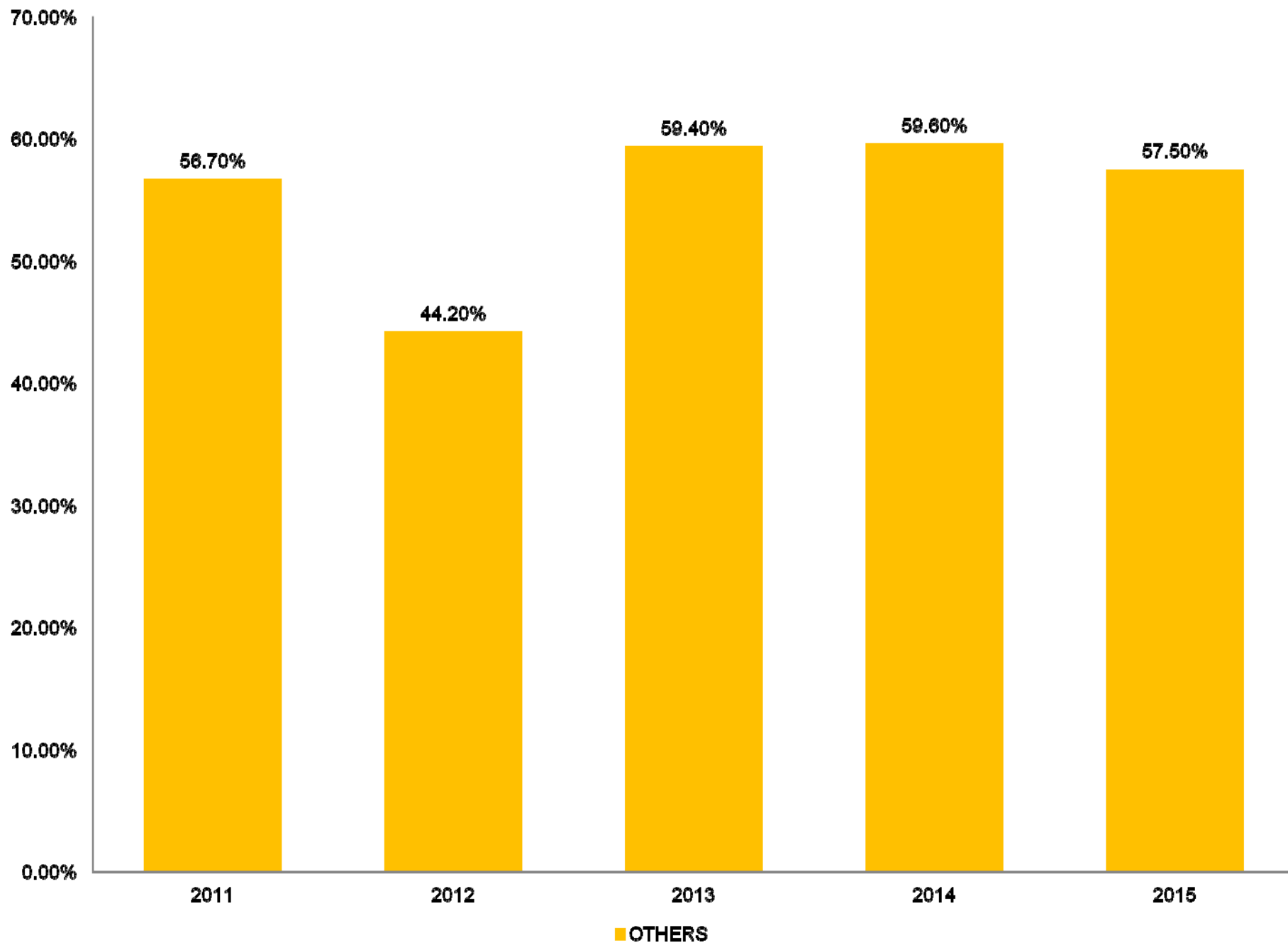
Related to the etiology it has the trend to narrow the difference between viral cause and alcoholic one, although the first etiological factor remains viral infections.





■ CRONIC HEPATITIS





Age groups according to years 2011 – 2015 and diseases

CIRRHOSIS	2011	2012	2013	2014	2015
5-14 vjc	0	0	0	0	0
15-24 vjc	4	5	2	5	7
25-34 vjc	24	16	13	19	13
35-44 vjc	56	53	46	42	37
45-54 vjc	144	153	169	161	147
55-64 vjc	112	143	166	190	194
65 =/<	62	90	82	89	81

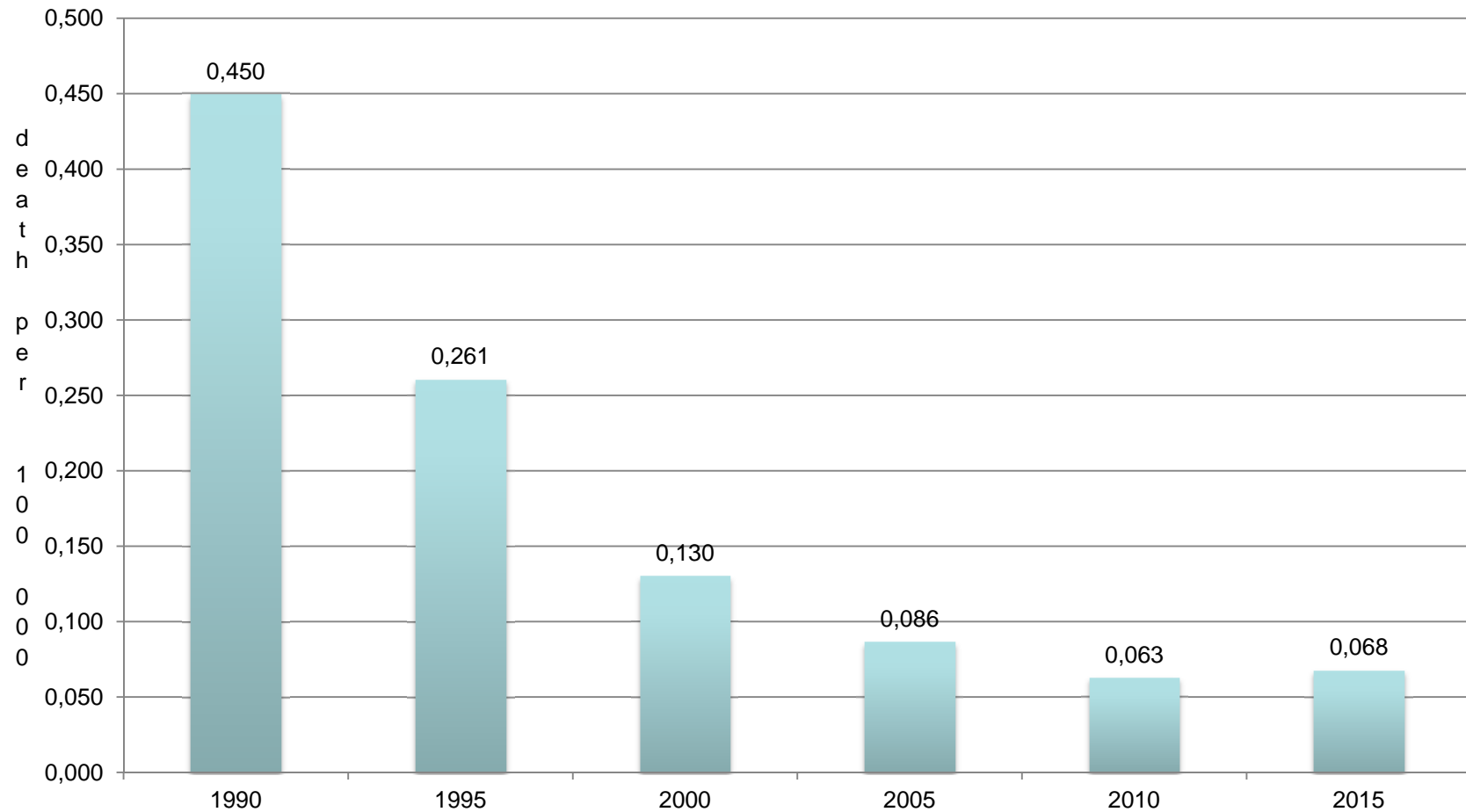
VIRAL HEPATITIS	2011	2012	2013	2014	2015
5-14 vjc	0	0	0	0	0
15-24 vjc	2	4	1	2	0
25-34 vjc	5	3	0	3	2
35-44 vjc	6	4	1	1	3
45-54 vjc	7	9	1	2	1
55-64 vjc	3	7	6	3	1
65 =/<	3	3	2	0	1

T. LIVER, BILIRIARY TRACT	2011	2012	2013	2014	2015
5-14 vjc	0	0	0	0	0
15-24 vjc	0	0	1	0	0
25-34 vjc	0	0	0	2	1
35-44 vjc	1	2	2	4	1
45-54 vjc	4	6	5	12	12
55-64 vjc	14	6	14	24	17
65 =/<	14	10	21	28	34

Mortality for the cases admitted to the hospital, service of Gastroenterology & Hepatology

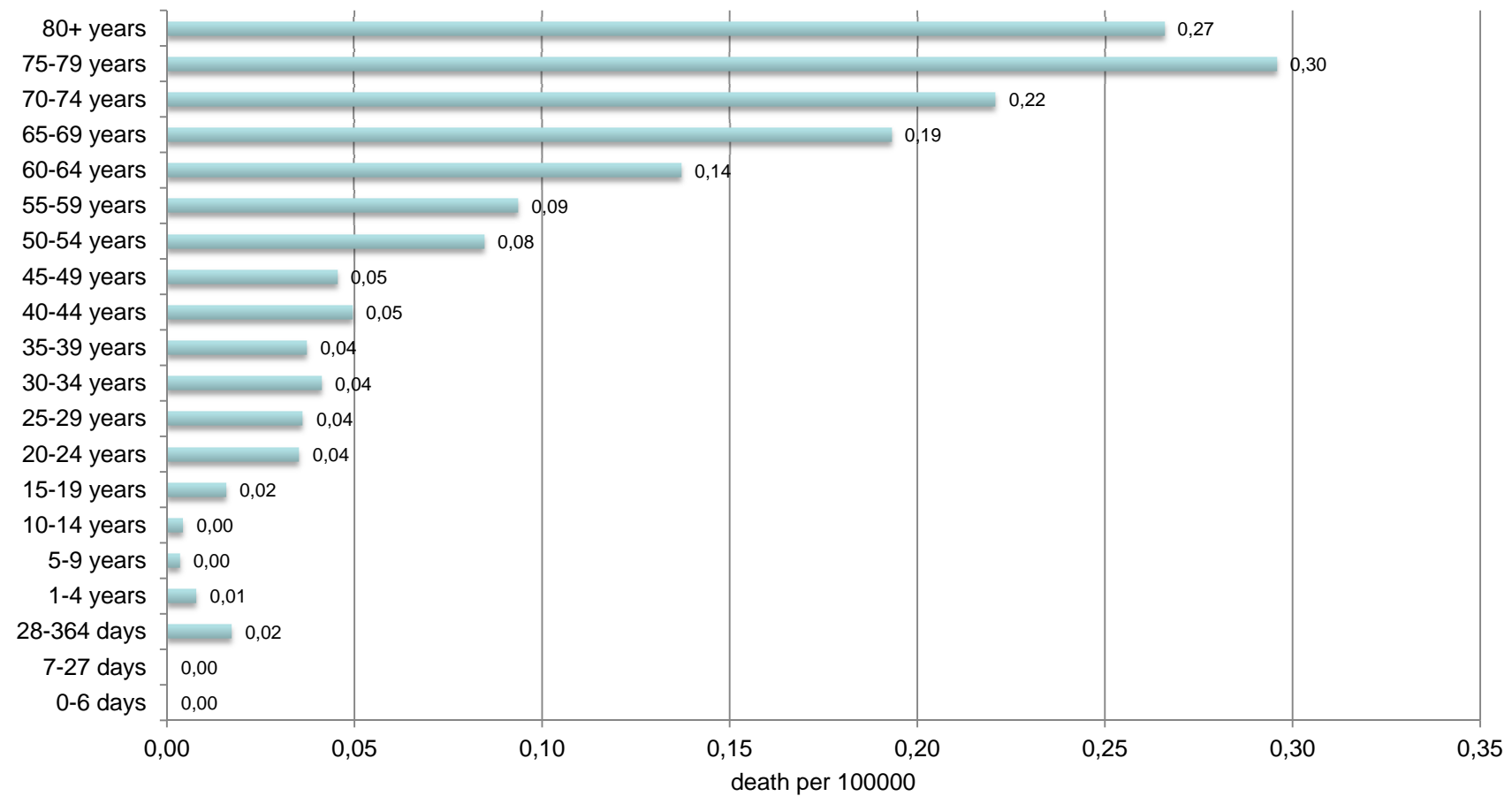
	2011	2012	2013	2014	2015
CIRRHOSIS	23 (5.72%)	17 (3.69%)	20 (4.58%)	26 (5.13%)	42 (8.76%)
V. HEPATITIS	0	0	0	0	0
T. GALLBLAD.	0	0	0	0	0
LIVER/BILIA R T	1 (3.03%)	2 (8.3%)	1 (2.32%)	0	0
OTHER	4 (0.63%)	2 (0.47%)	9 (1.14%)	10 (1.14%)	10 (1.33%)

Death due to hepatitis B over the years



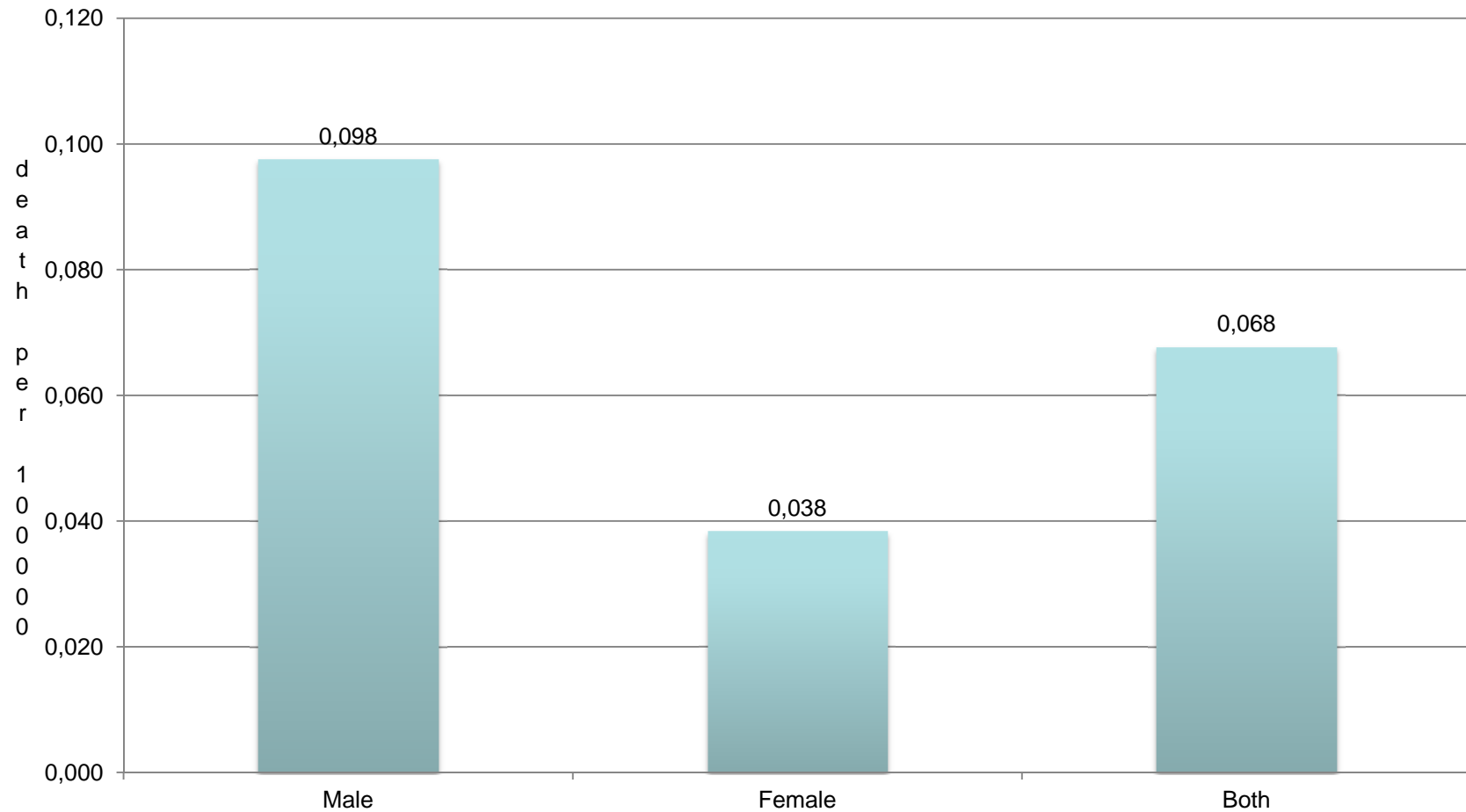
Global Burden of Disease Study 2015.

Deaths from Hepatitis B by age (2015)



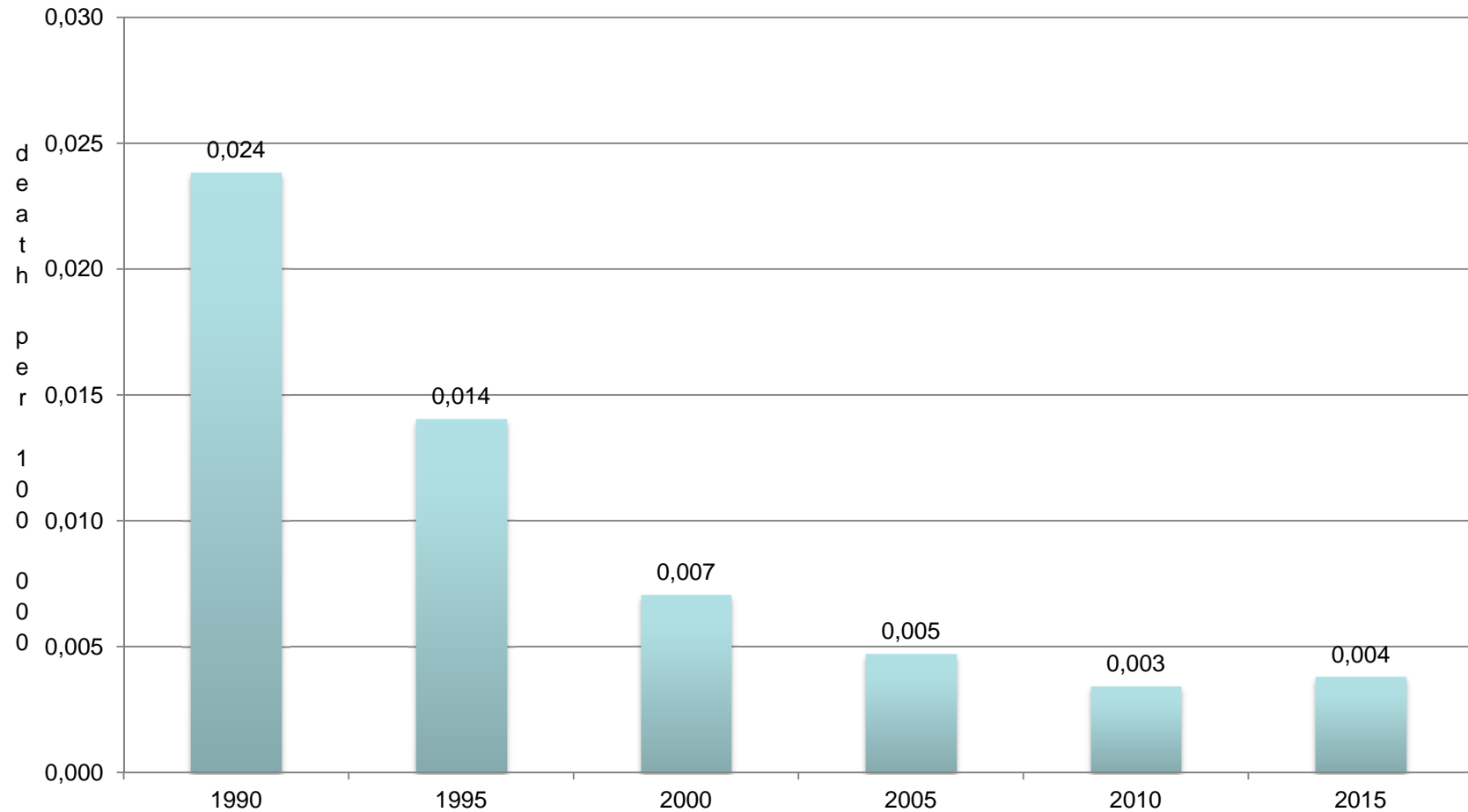
Global Burden of Disease Study 2015.

Death due to hepatitis B by sex (2015)



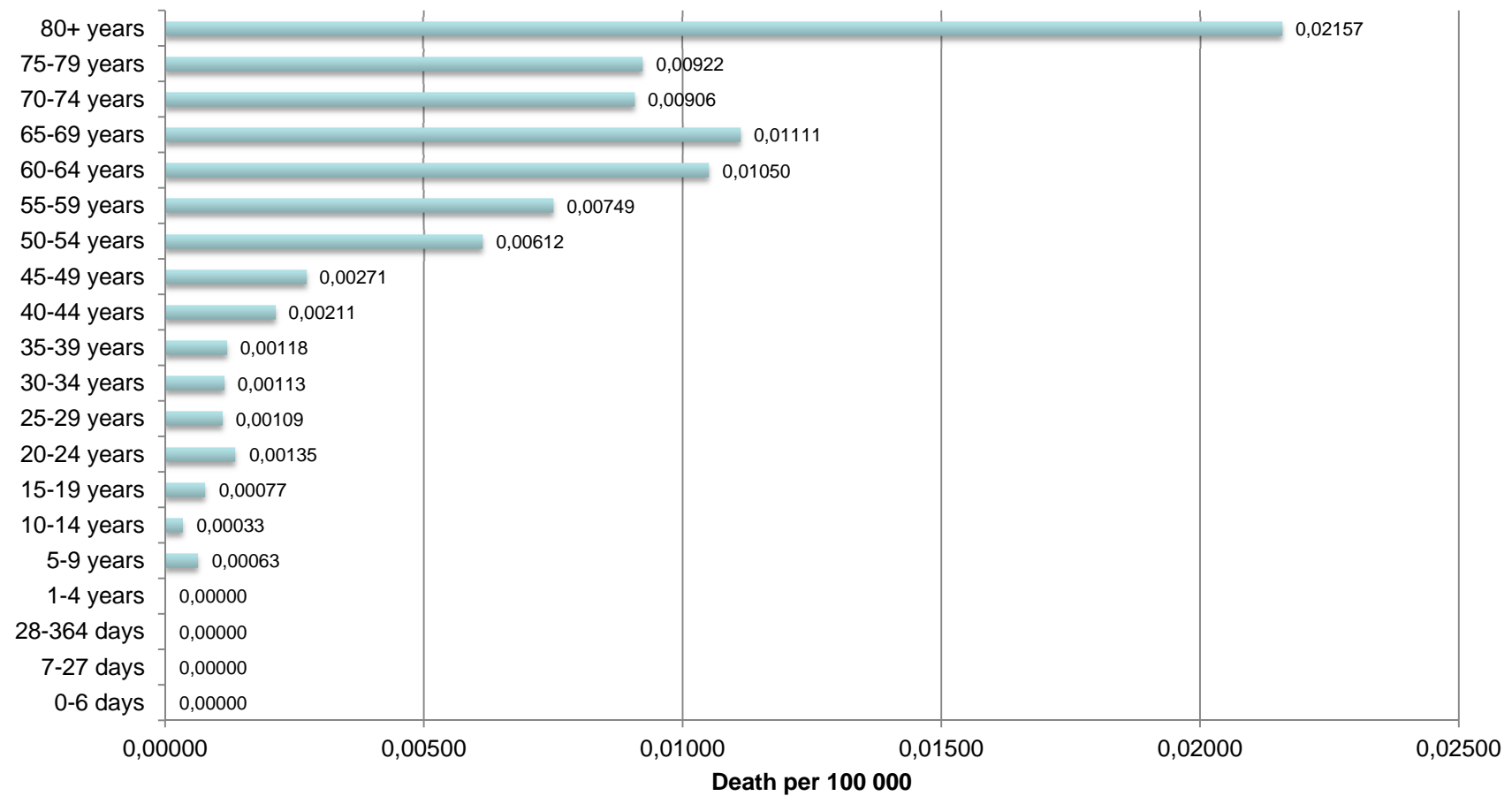
Global Burden of Disease Study 2015.

Deaths from Hepatitis C over the years



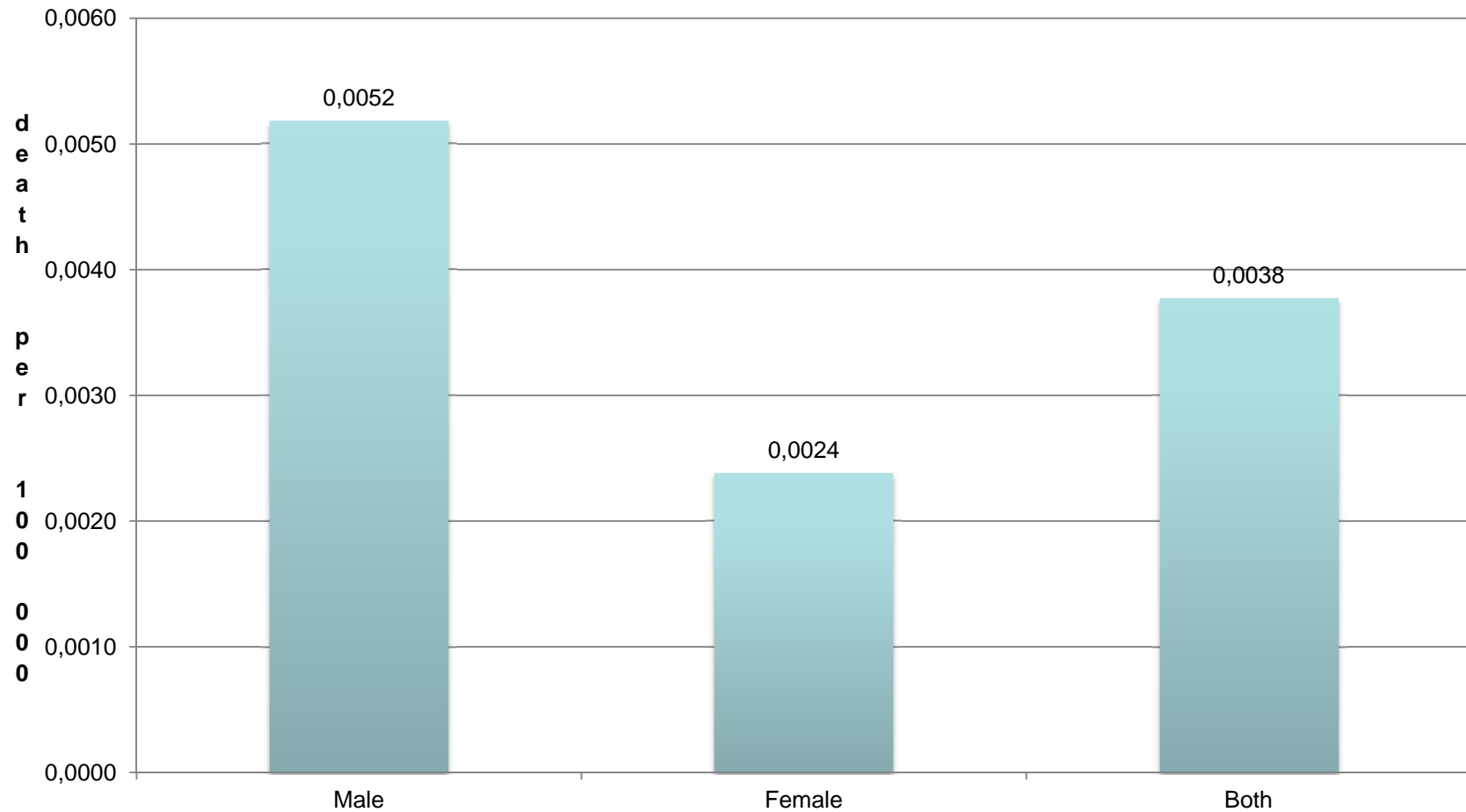
Global Burden of Disease Study 2015.

Deaths from Hepatitis C by age (2015)



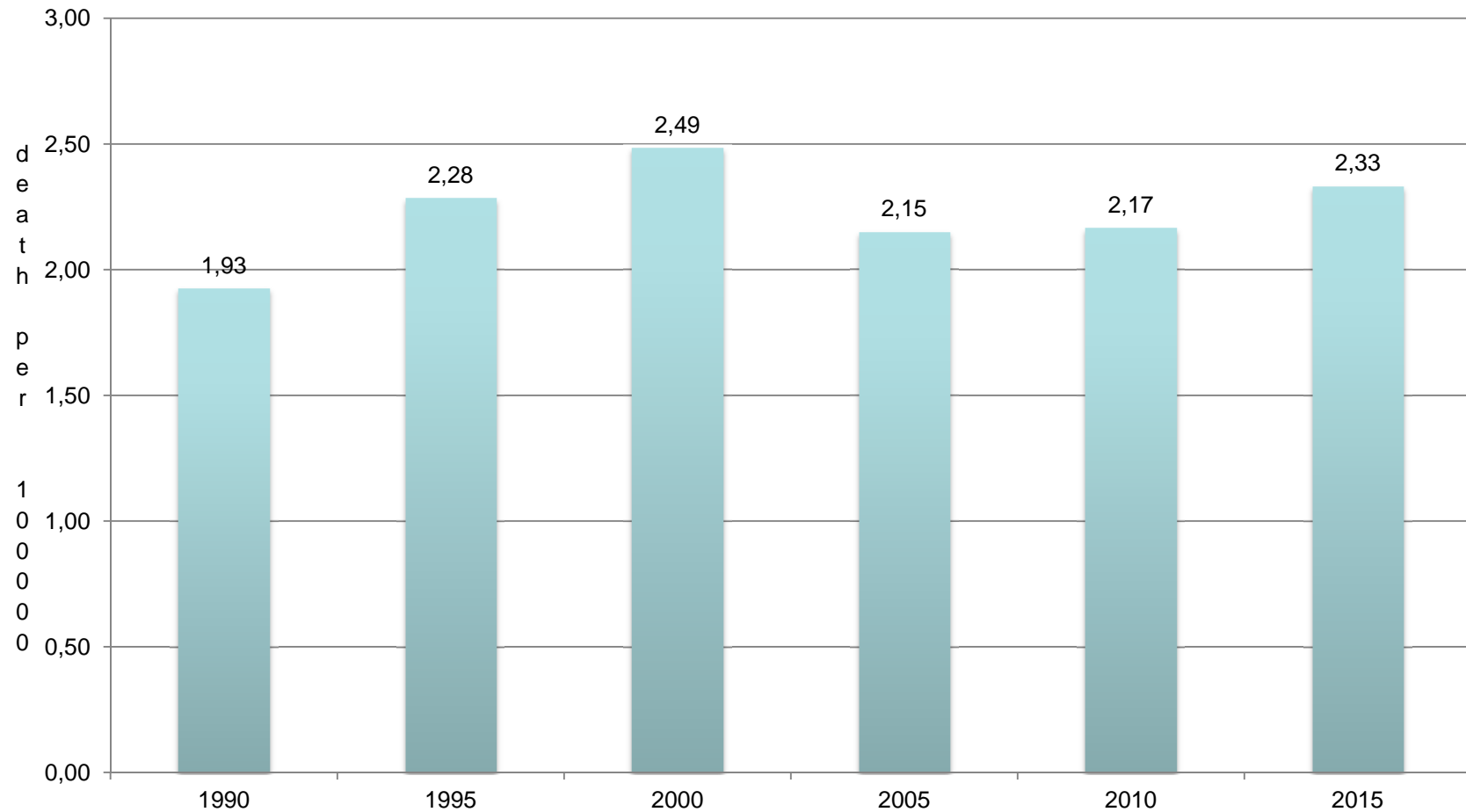
Global Burden of Disease Study 2015.

Death from hepatitis C by sex (2015)



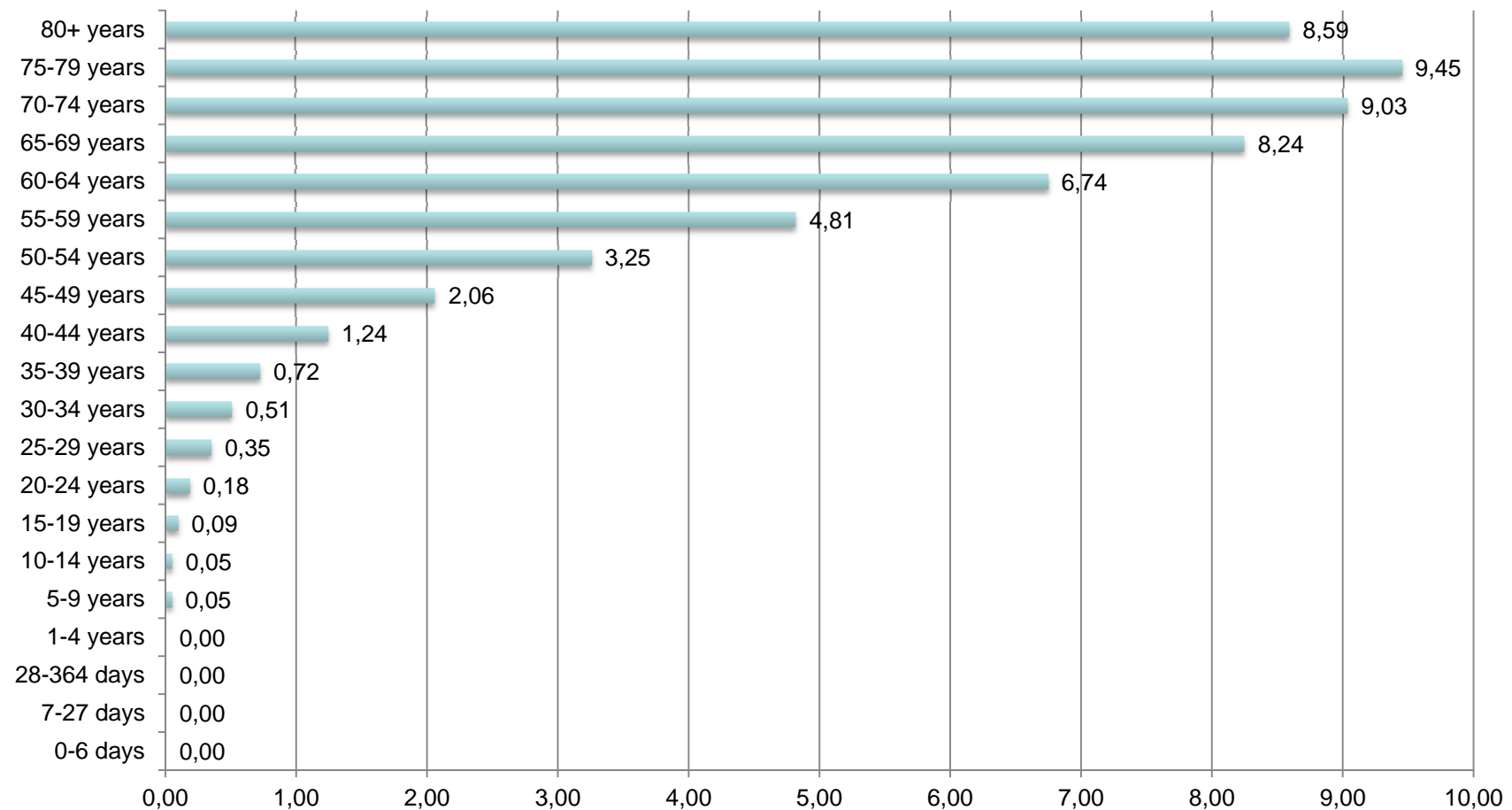
Global Burden of Disease Study 2015.

Death from liver cancer due to hepatitis B over the years



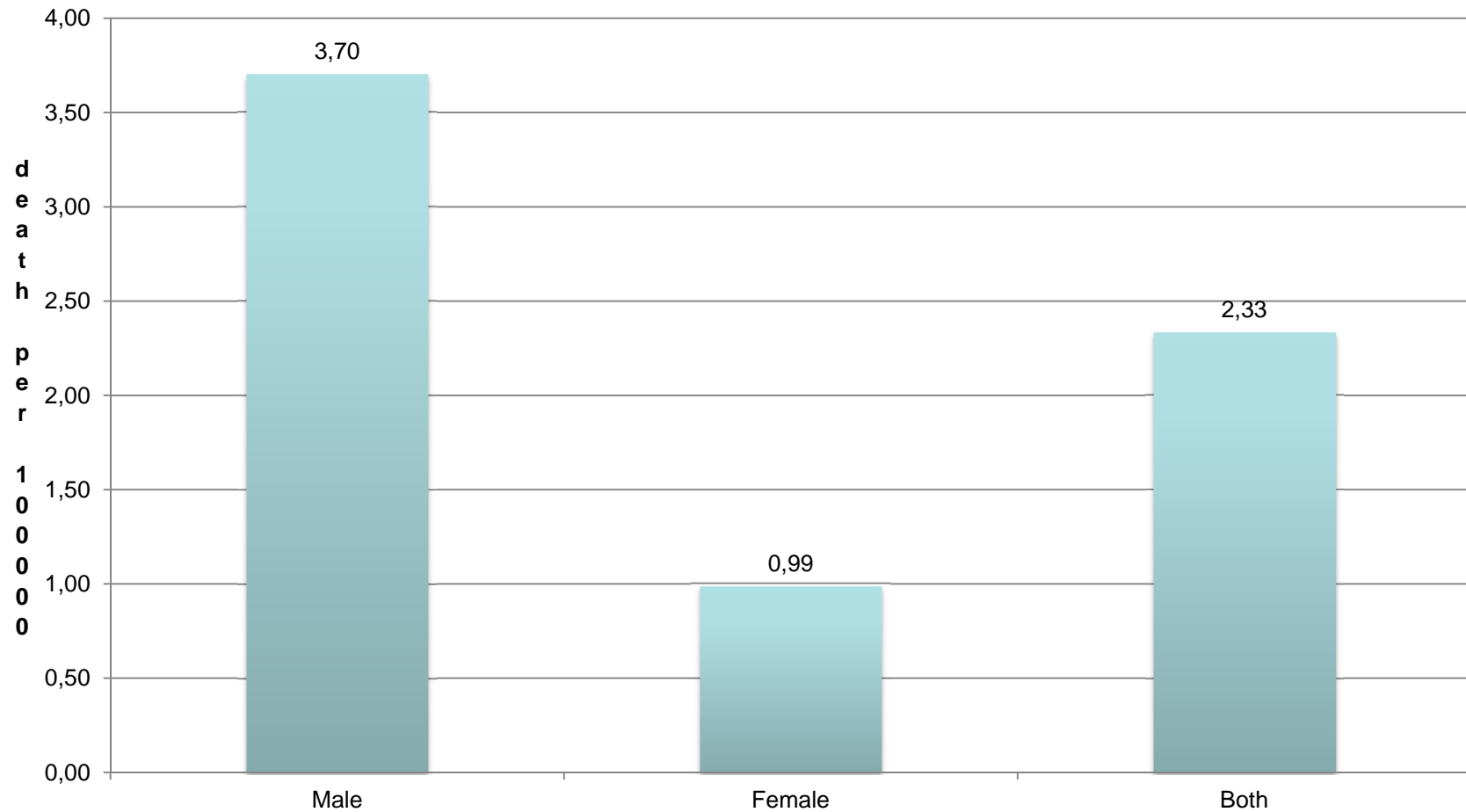
Global Burden of Disease Study 2015.

Death from liver cancer due to hepatitis B by age (2015)



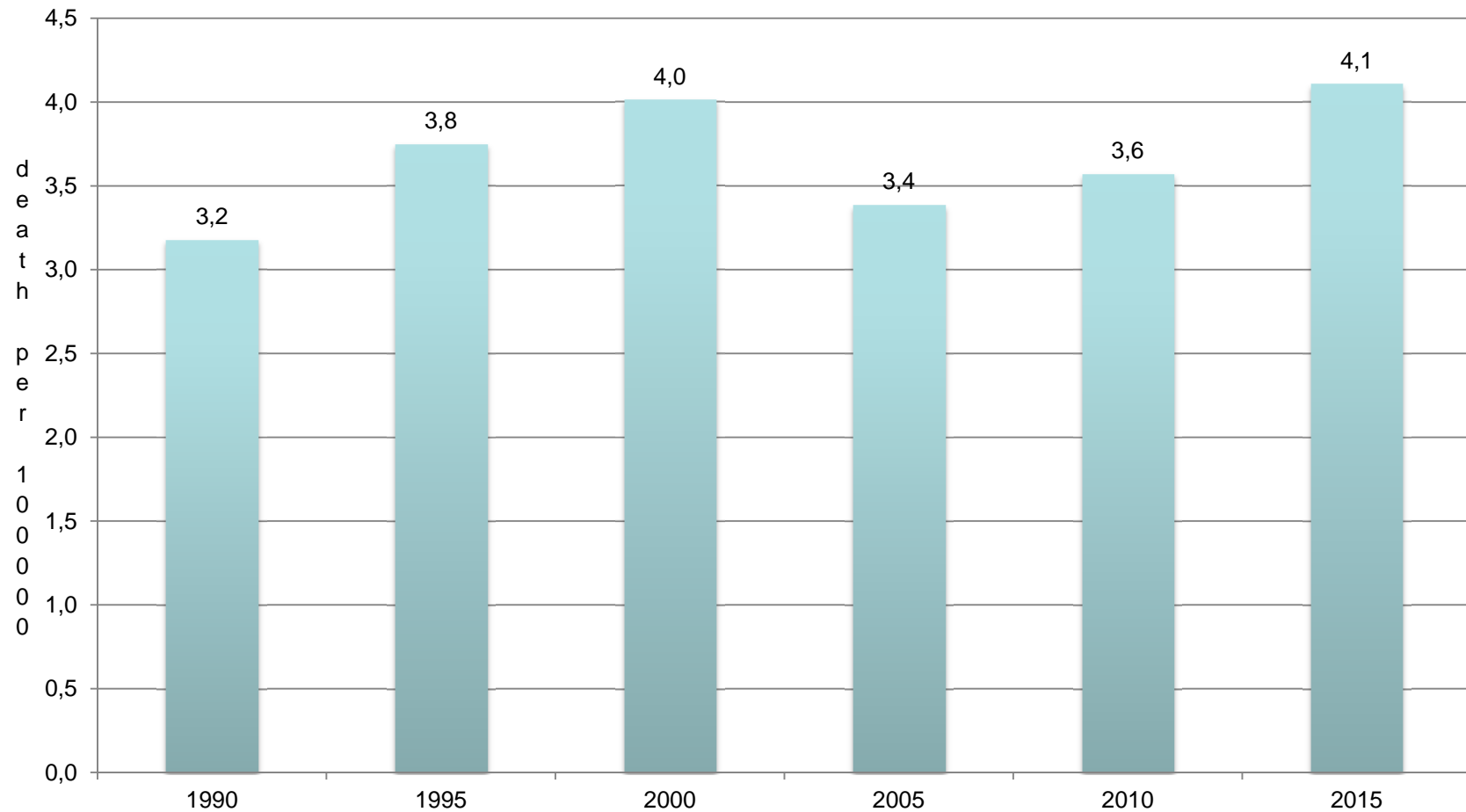
Global Burden of Disease Study 2015.

Death from liver cancer due to hepatitis B by sex (2015)



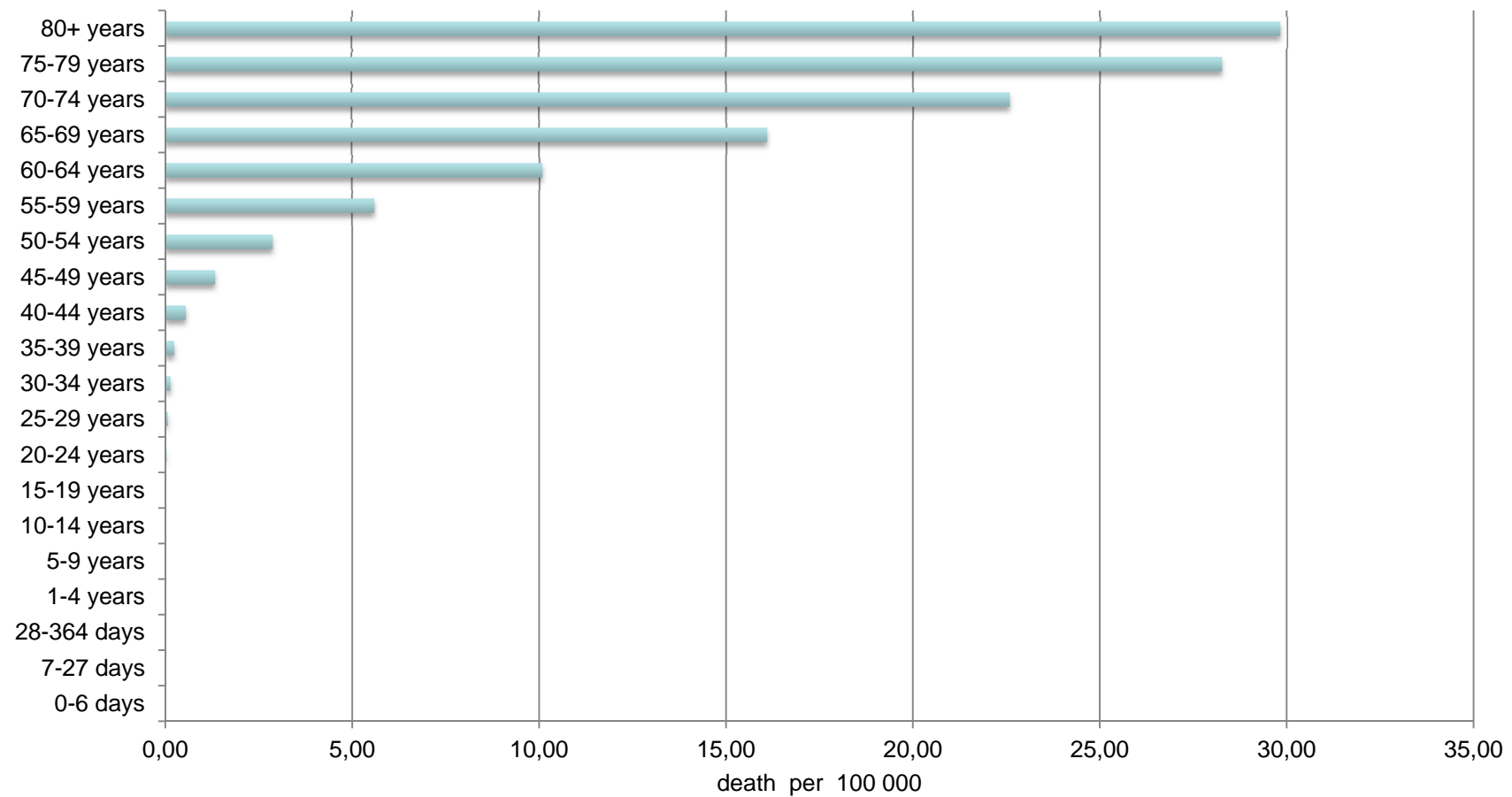
Global Burden of Disease Study 2015.

Death from liver cancer due to hepatitis C over years



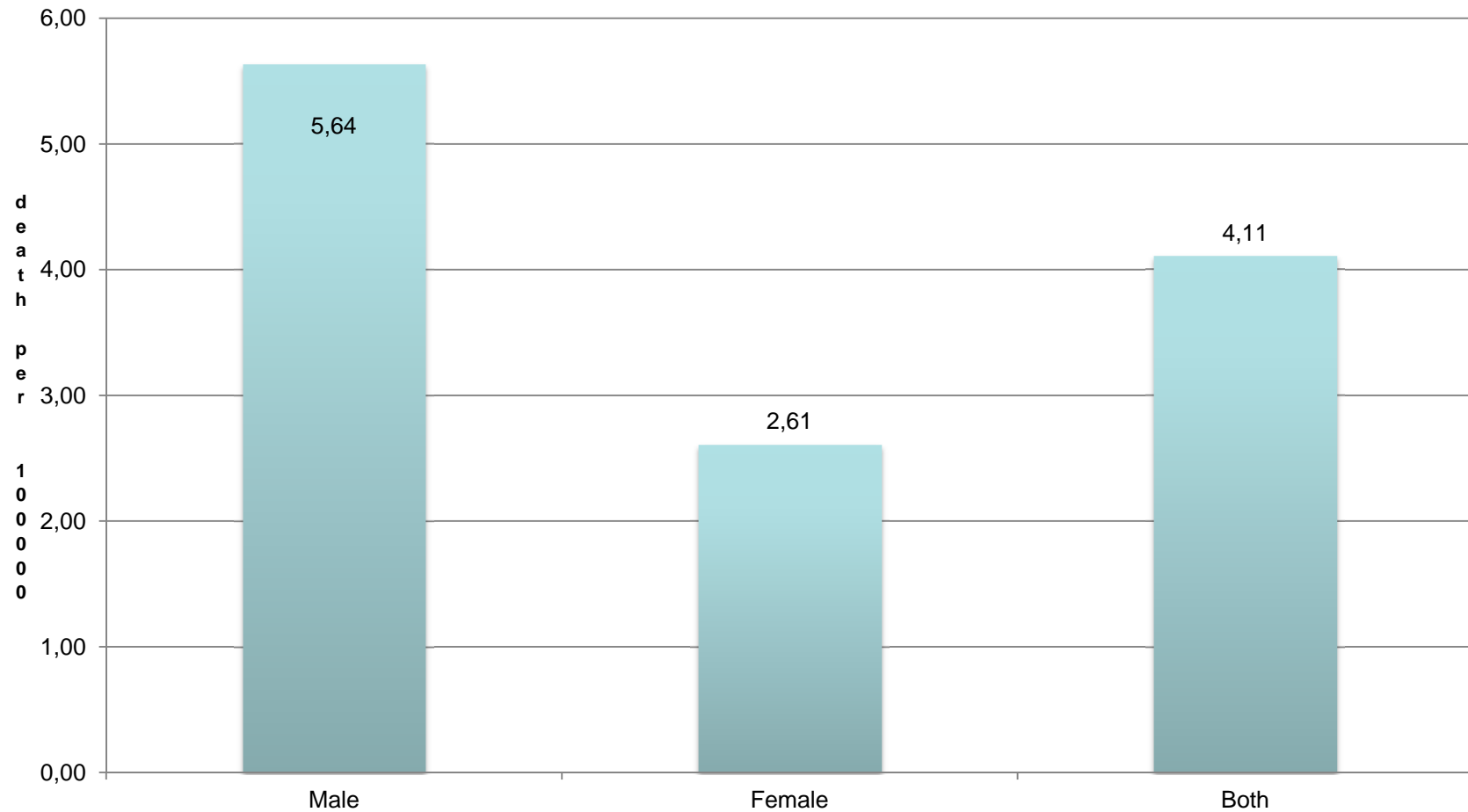
Global Burden of Disease Study 2015.

Death from liver cancer due to hepatitis C by age (2015)



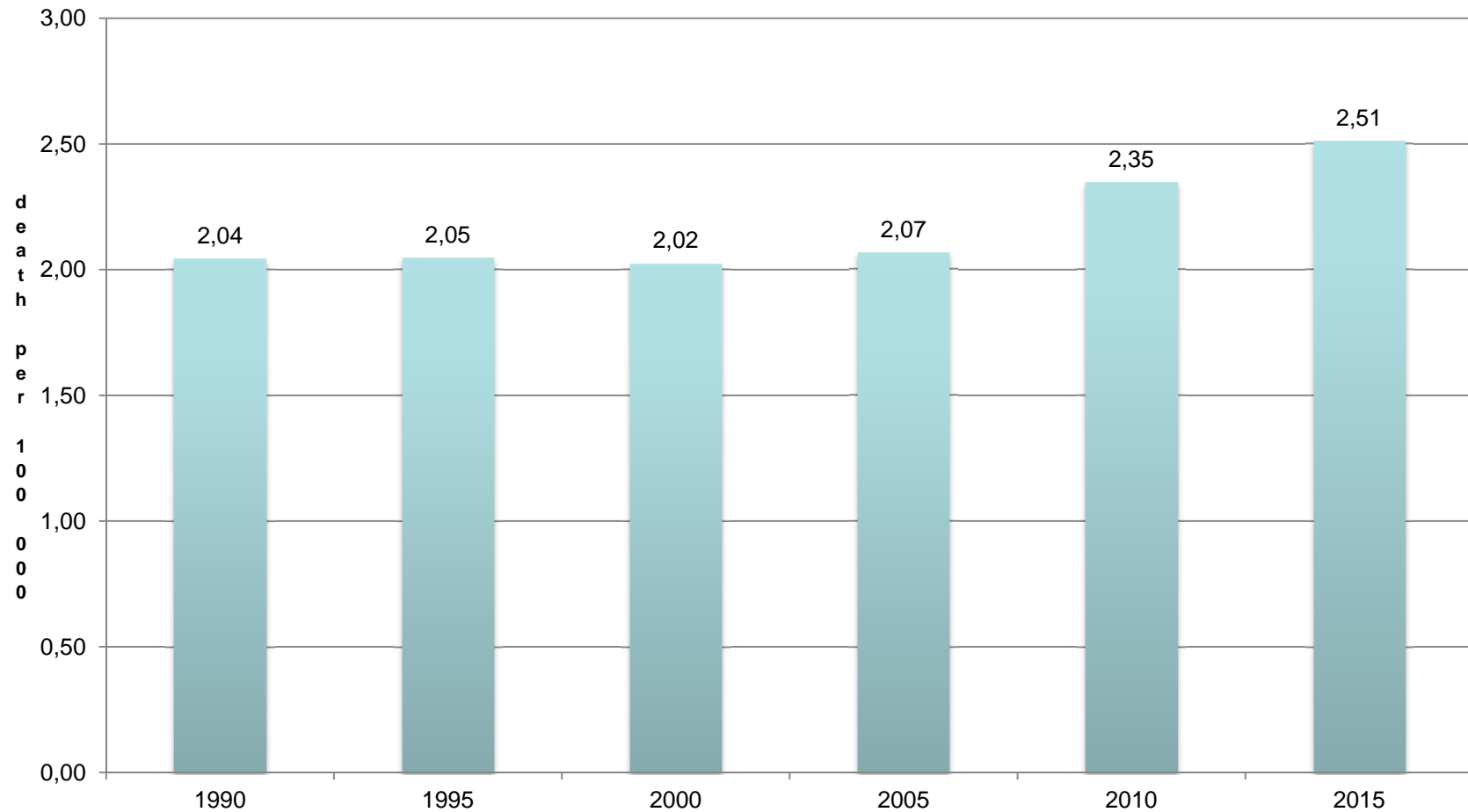
Global Burden of Disease Study 2015.

Death from liver cancer due to hepatitis C by sex (2015)



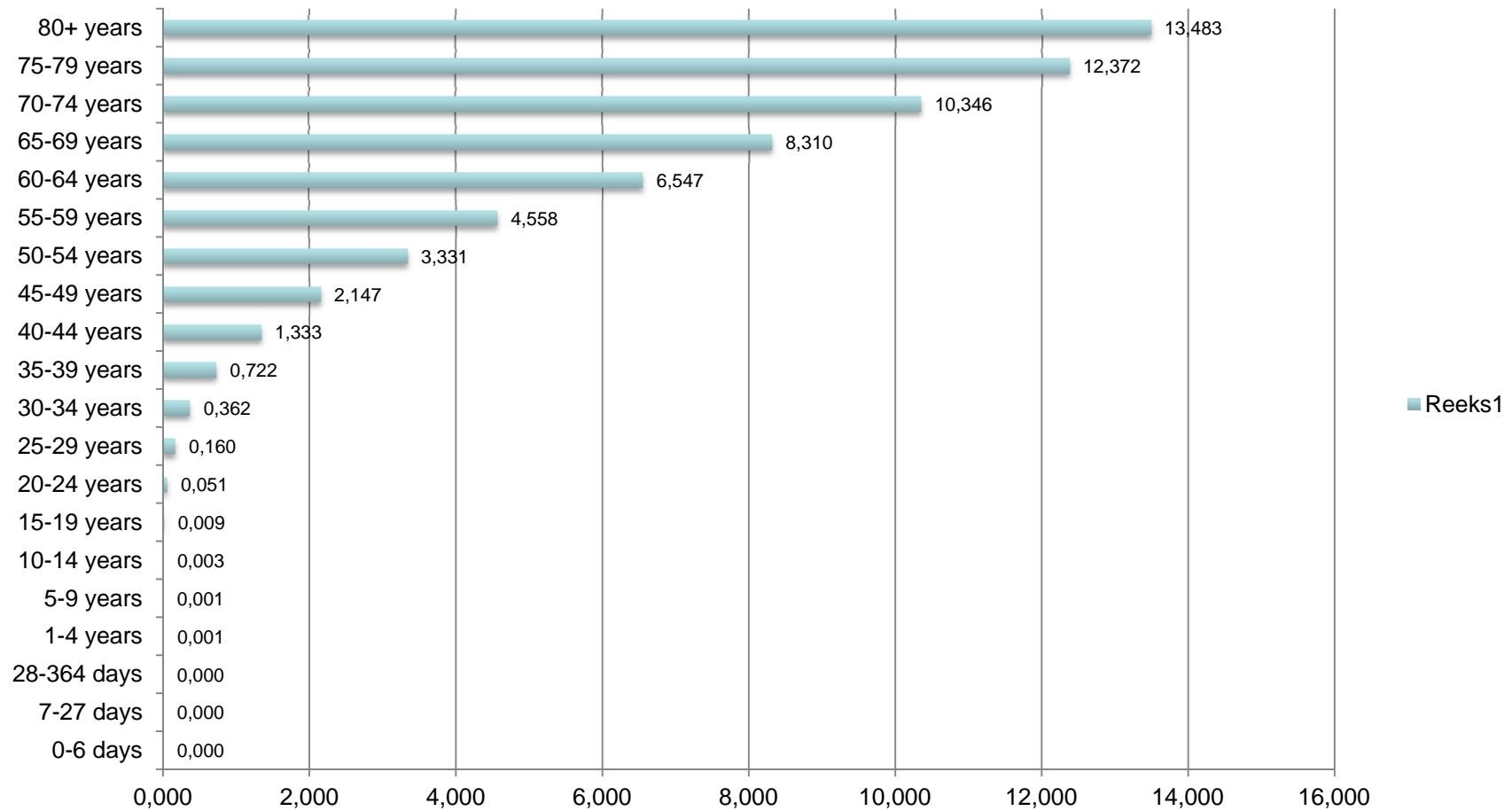
Global Burden of Disease Study 2015.

Death from cirrhosis due to hepatitis B over the years



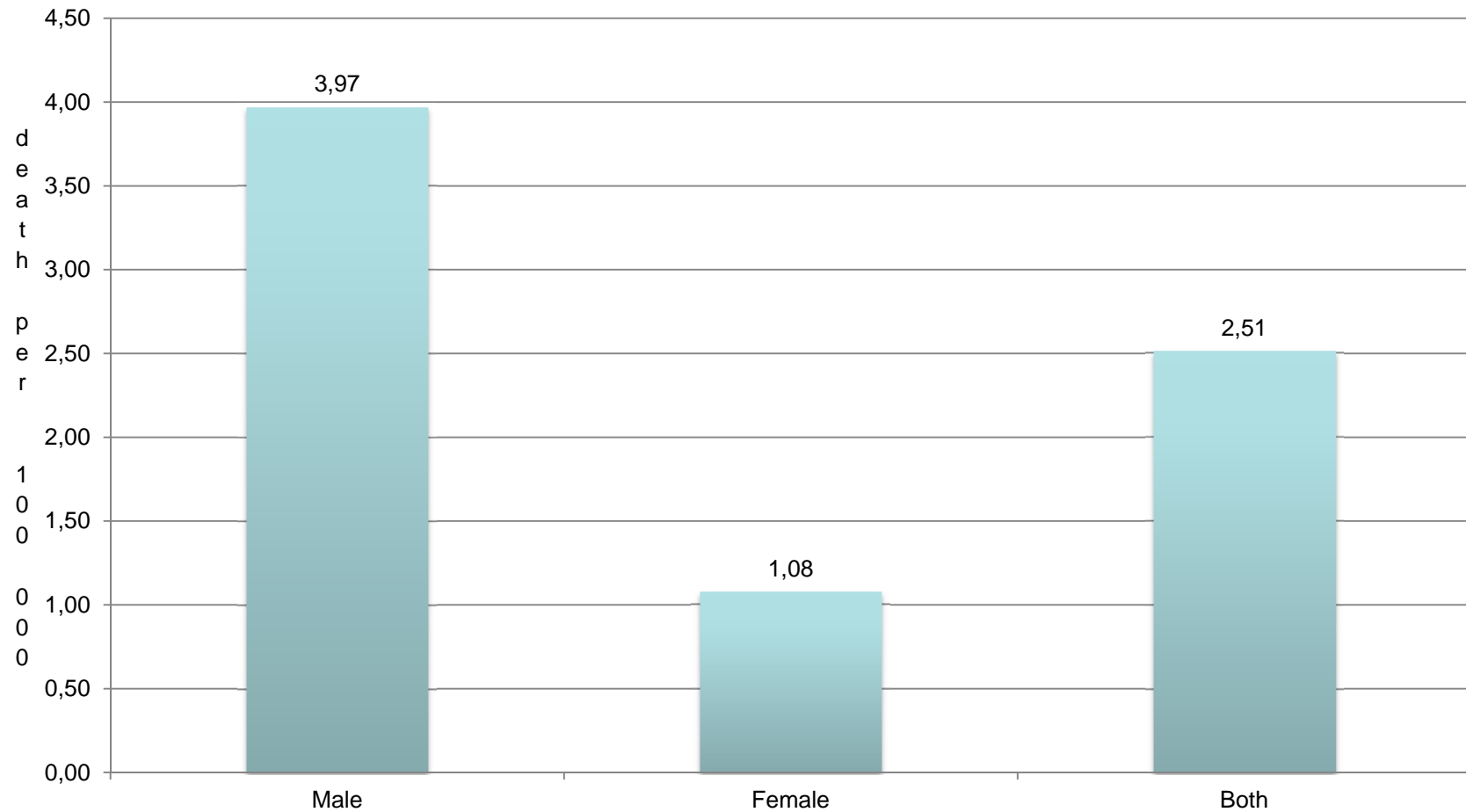
Global Burden of Disease Study 2015.

Death from cirrhosis due to hepatitis B by age (2015)



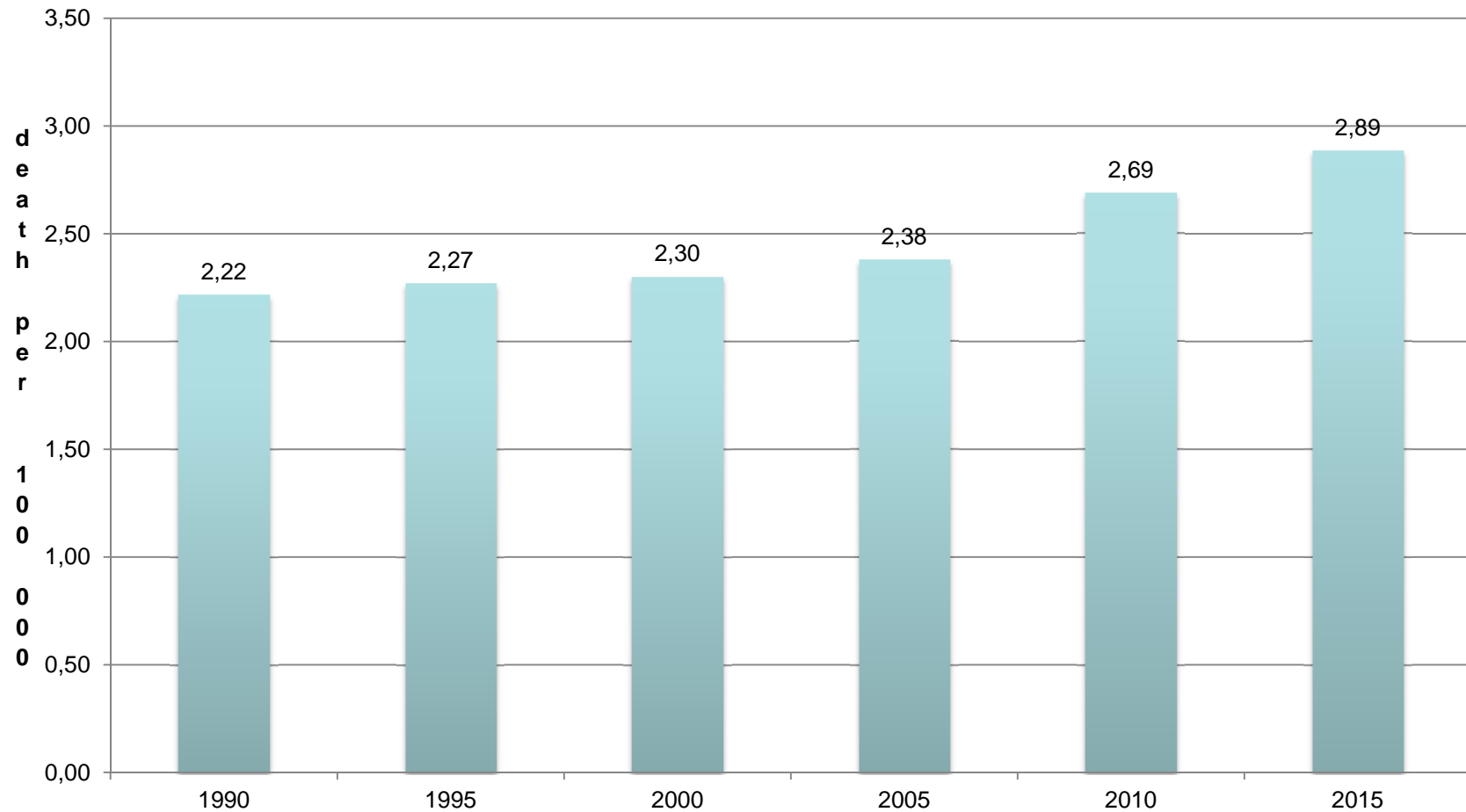
Global Burden of Disease Study 2015.

Death from cirrhosis due to hepatitis B by sex (2015)



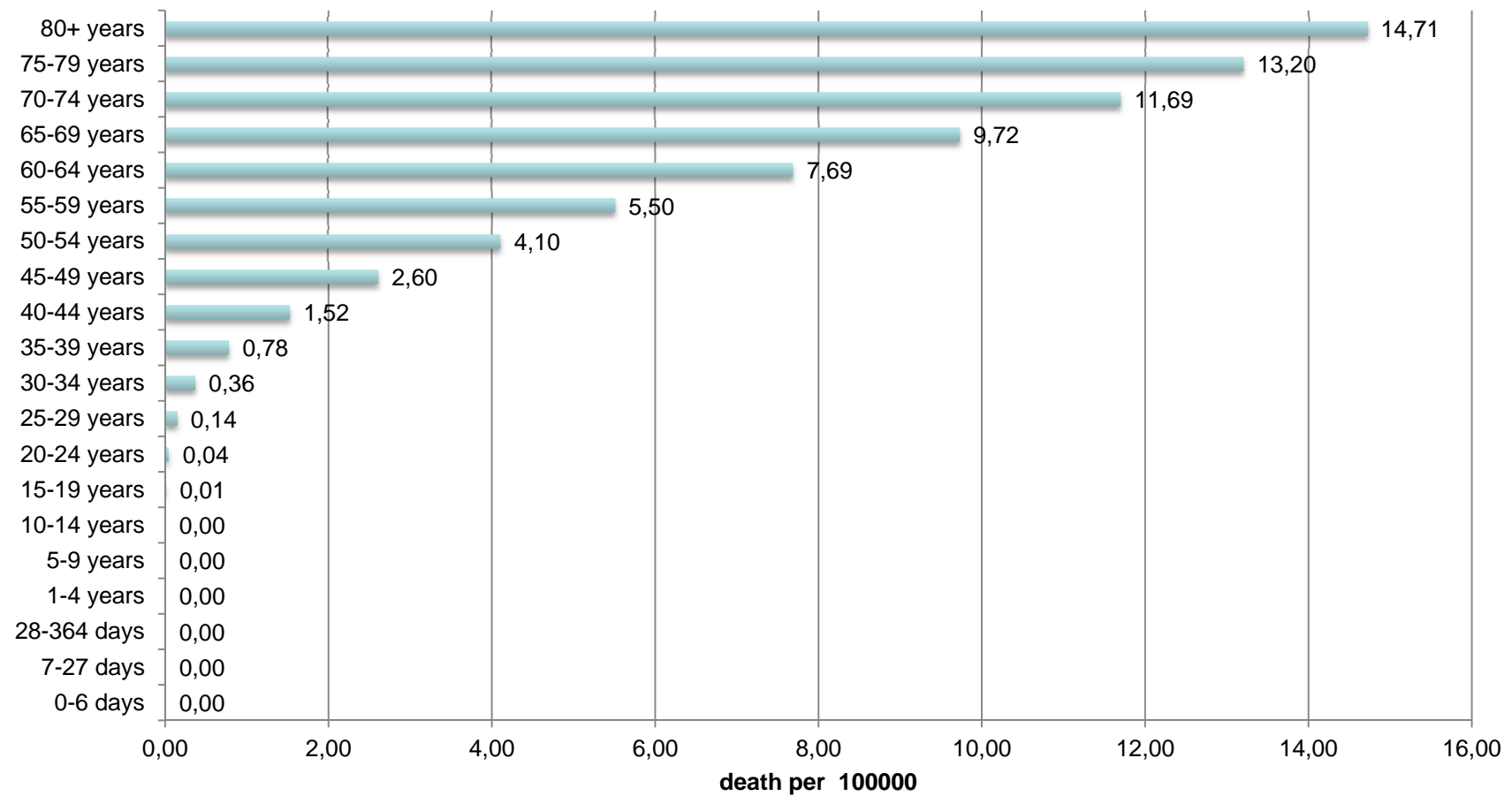
Global Burden of Disease Study 2015.

Death from cirrhosis due to hepatitis C over the years



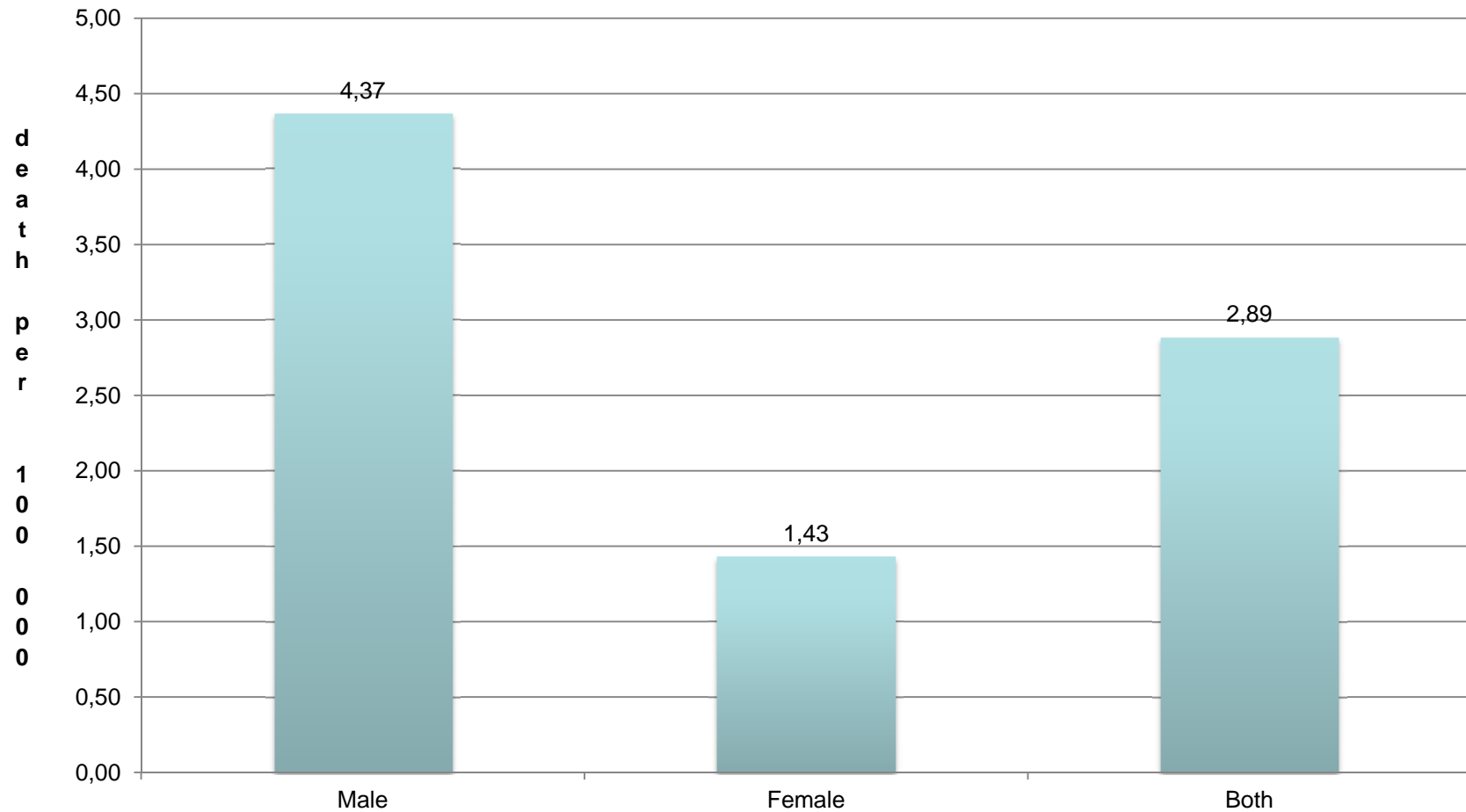
Global Burden of Disease Study 2015.

Death from cirrhosis due to hepatitis C by age (2015)



Global Burden of Disease Study 2015.

Death from cirrhosis due to hepatitis C by sex (2015)



Global Burden of Disease Study 2015.

Availability and reimbursement of the drugs: Lamivudine

Lamivudine is a drug that in Albania was introduced in 2002
In 2007, were introduced the generics.

During 2015 , there were 466 patients taking Lamivudine and they are mostly with Liver Cirrhosis.

1.Effect of Lamivudine in the patients with decompensated cirrhosis

B.Resuli, J.Basho, A.Babameto, V.Demiraj, L.Cuko.

Service of Gastroenterology& Hepatology, University Hospital "Mother Theresa" Tirana. (2006)

16 patients with decompensated HBV (anti-HBe positive) cirrhosis.
11 M and 5 F; average age 51.2 ± 7.6 yr.treated for a period 1 – 5 years
(2.9 ± 1.4 yr.)with Lamivudine 100mg/day

The response to therapy was evaluated by normalisation of ALT, suppression of HBV-DNA (less than 250 copies/ml), and amelioration of Child-Pugh score > 2 points.

ALT significantly lower ($p < 0.001$) on the end of first and second year of treatment versus the base line , HBV-DNA negative in 87.5% and 93.7% after first and second year. Child-Pugh score significantly ameliorated ($p < 0.001$) after one and two years after treatment.

2.Treatment of chronic hepatitis and liver cirrhosis (HBeAg negative) with Lamivudine

L.Cuko. B.Resuli, J.Basho, A.Babameto

Service of Gastroenterology & Hepatology

2006

Results of treatment of chronic hepatitis HBeAg negative 12 months with Lamivudine

Biochemical and virological response 24 weeks after ending of therapy

*123 pts. (70.6%) with Chronic Hepatitis (CH) age 37.42±15.7
(12-68); 93 (75.6%) M and 30 (24.3%) F*

*51 pts. (29.3%)With Liver Cirrhosis (LC); age 47.1±19.8
(18-70) ; 38 (74.5%) M and 13 (25.4%) F*

2.Treatment of chronic hepatitis and liver cirrhosis (HBeAg negative) with Lamivudine

Lamivudine 100 mg/day for 12 – 36 months

Naive patients

51 patients with CH treated for 48 weeks , the others until 3 years.

HBe Ag positive 9.7% (13.8% for CH) and HBeAg negative in 90.23%)

HBV-DNA 2.3×10^8 dhe 1.97×10^9 copies/ml

HBV and HDV 8.04%

HBV and HCV 4.02%

HBV and Alcohol 13.2%

2.Treatment of chronic hepatitis and liver cirrhosis (HBeAg negative) with Lamivudine

Study from 1-3 years (in total 36 months)

72 patients, treated with standard doses of lamivudine (in monotherapy): 100mg/daily orally administered.

After 12 months the treatment was stopped only to the patients that had reached the normal range of biochemical and virological tests.

The treatment with lamivudine was never suspended to none of the patient with chronic hepatitis B (HbeAg-neg) that demonstrates the lack of collateral effects of this drug

2.Treatment of chronic hepatitis and liver cirrhosis (HBeAg negative) with Lamivudine

HBeAg negative/anti-HBe positive in 90.2%

Biochemical response (ALT < 40 UI/l) and virological one (HBV-DNA < 250 copies/ml), 12 months after treatment was found in 70.8%

After three months, ALT from 133.65 ± 53 UI/l was found 30.06 ± 11.20 UI/l

Recidive (ALT > 2 x ULN) and increase of HBV-DNA > 10^5 copies/ml, 24 weeks after stopping treatment at the group treated for 12 months, was found in 54.5%

The positive biochemical and virological response was found to be 70.8%, 55.3% and 50 % respectively after first , second and third year.

For the patients with Liver Cirrhosis (LC), normalization of ALT , HBV-DNA and Child-Pugh decreased with 2 points, was seen 28.5%, 32% and 47% respectively after the first , second and third year of treatment.

Tenefovir

October 2009 it was registered as Viread (7 years)

April 2014 was classified as reimbursable drug.

From 2009 to 2014 was used for 250 patients.

From May 2014 and now on, 803 patients are in therapy with Tenefovir; one quarter of them suffer from liver cirrhosis.

Tenefovir

Total 803 pts. (May 2014 - September 2016)

F= 201 (25%) **M**= 602 (75%)

Age: 46.72 ± 11.47 (range 16 - 85 yr.)

LC 201 (25.03%);

HBV Chronic Hepatitis 600 (74.71%)

HBV+C/D 2 (0.25%)

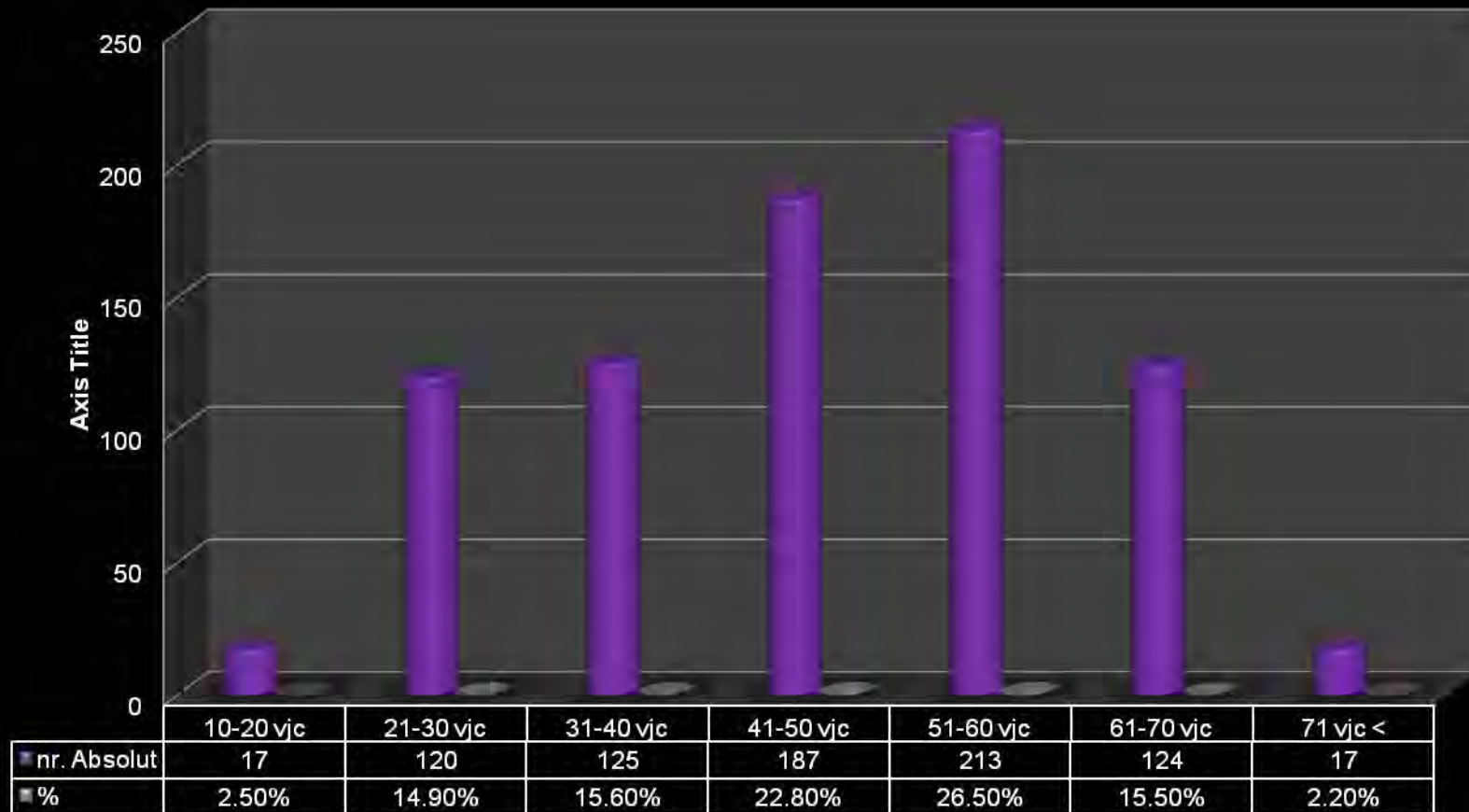
Chronic Hepatitis native patients and Lamivudine –resistance cases

Compensated Liver Cirrhosis

Decompensated Liver Cirrhosis

After transplant

USE OF TENOFOVIR ACCORDING TO THE AGE-GROUPS



Tenefovir

The control

HBV-DNA	every one year
Quantitative HBsAg	every 6 months
ALT, AST	every 3 months

After one year HBV-DNA negative in approximately 95%, until three years negative 98-99%

Quantitative HBsAg	10%	> 10 000 UI/mL
	60-65%	2000-5000 UI/mL
	25%	<1000 UI/mL

4 patients became HBsAg negative

5 patients HBsAg <100 UI/mL

First experience 2009

55 patients treated with Tenefovir and it was found HBV-DNA negative in 54 (85.71%) after one year of treatment. Only one positive after first year.

Epidemiology, clinical, biochemical and virologic features of hepatitis Delta

Edite Sadiku

University Hospital Center , Service of Gastroenterology&Hepatology

In 2005 the prevalence of HDV in our country was reported around 11%.

Study: 405 patients HBsAg positive (Service of Gastroenterology&Hepatology and Service of Internal Diseases) during 2007 - 2011

323 (79.75%) Chronic Hepatitis B

72 (17.77%) Liver cirrhosis B

9 (2.2%) Hepatocarcinoma of the liver

All the patients negative for anti-HCV and anti-HIV

Prevalence of HDV resulted 9.13%; prevalence according to gender : female 2.22%; male 6.91%.

Incidence for 4 year period (2007-2011) : I=1.16/100.000

In patients with anti-HDV positive :

5.4% compensated cirrhosis,

13.51% decompensated cirrhosis

81.08% chronic hepatitis B+D.

Average values of AST, ALT, GGT, FA, Gama-globuline and bilirubin resulted more increased in the Delta group patients.

Average values of protrombine level and albumine resulted lower in in the Delta group patients

All the patients with hepatitis Delta resulted HBeAg negative and anti-HBeAg positive, B mutant virus.

Were treated 15 patients with Peginterferon 180 µg/week for 48 weeks.

(one was excluded due to thrombocytopenia at the end of the 12 week)

Biochemical response: At the end of 24 week, ALT was normal in 2 patient (13.3%) and at the end of the treatment ALT was normal in 4/15 patients (26.6%).

Virological response: At the end of 24 weeks HDV RNA negative in 20% and at the end of the treatment after 48 weeks HDV RNA negative in 33.3%.

In 72 week, SVR was found in 13.32% of the patients.

Treatment with Interferon Alfa-2a of chronic Hepatitis, HBeAg negative (Preliminary data)

Jovan BASHO, Eriola GJIKÀ

University Servis of Gastroenterology & Hepatology, "Mother Theresa" Hospital, Tirana

20 cases (18 M and 2 F)

Average age: $32.8 \pm 13,5$ vjet

Study during 2007

Diagnosis: Active Chronic Hepatitis B, HBeAg negative

Negative for anti-HCV and for anti-HDV and no alcohol consumption

Treatment: Interferon alfa-2a (Roferon) 4.5 MU x 3 javë x 24 javë

Follow up: ALT week 0, 4, 12, 24, 48

HBV DNA week 0, -, 12, 24, 48

Treatment with Interferon Alfa-2a of chronic Hepatitis, HBeAg negative (Preliminary data)

At the beginning of the treatment:

AST 83.4 ± 53.06 U/l, ALT 147.7 ± 106.25 U/l and

HBV DNA 4.3×10^7 kopje/ml

ALT level

Week	4	12	24	48
ALT normal	20%	50%	50%	40%

HBV DNA level

Week	12	24	48
HBV DNA < 60 U/ml	50%	40%	30%

Treatment with Interferon Alfa-2a of chronic Hepatitis, HBeAg negative (Preliminary data)

Week 48

Normalization at the same time of ALT and HBV DNA
(sustained biochemical and virological response in 3 cases (30%))

HBsAg not negative in all the cases.

All the patients tolerated good the therapy and finished treatment

Adverse events not important

Peginterferon and Ribavirin are in reimbursement scheme from April 2014.

Under therapy with peginterferon are actually 160 patients. 418 patients total treated, from which 63 are HBV (+), 355 are HCV liver disease.

Actually 150 are in treatment with peginterferon.

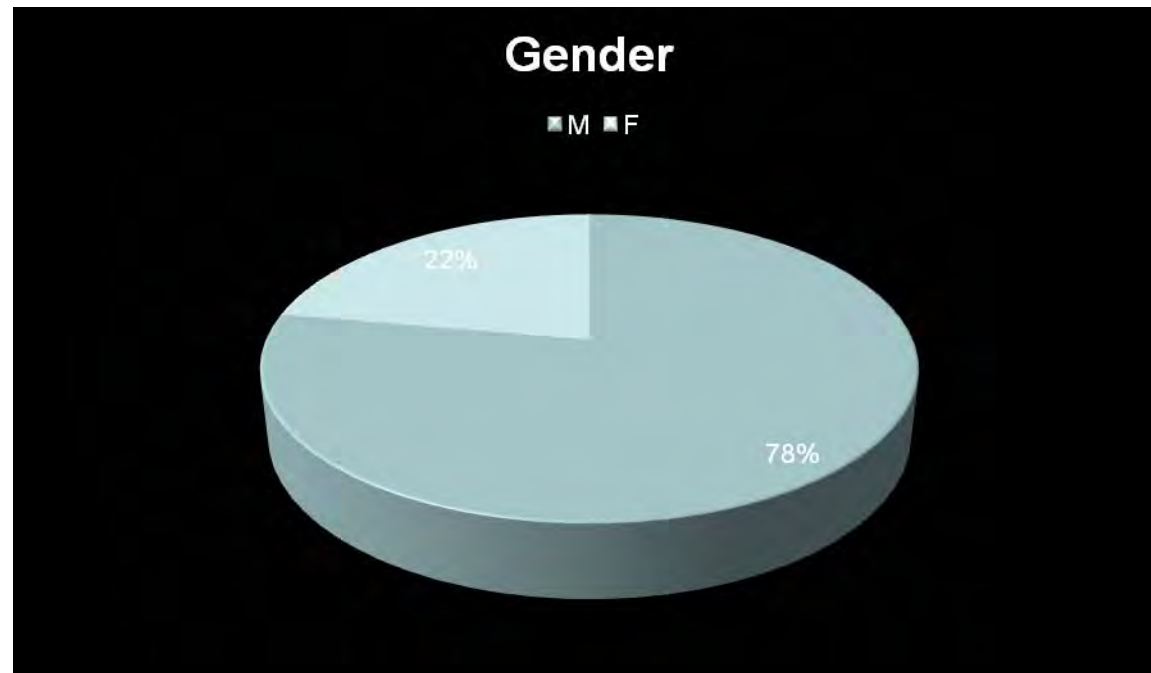
Under therapy with Sofosbuvir, Harvon, and Dasabuvir and Ombitasvir/ Paritaprevir /Viekirax are 49 patients with HCV.

Total 63 Patients

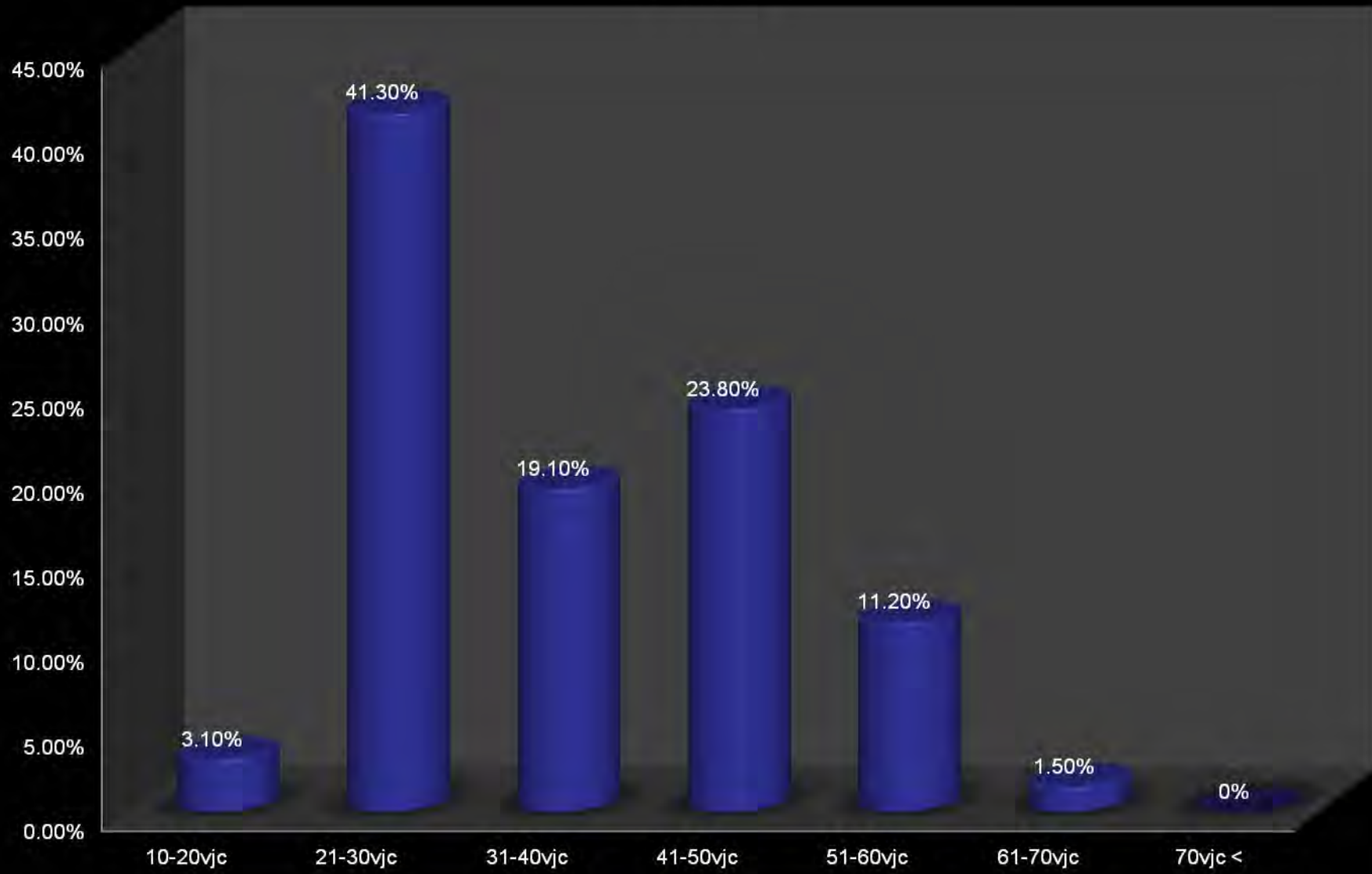
F= 14 (22.5%)

M= 49 (77.8%)

Average age 36.4 ± 9.59 (range 19 – 63 yr)

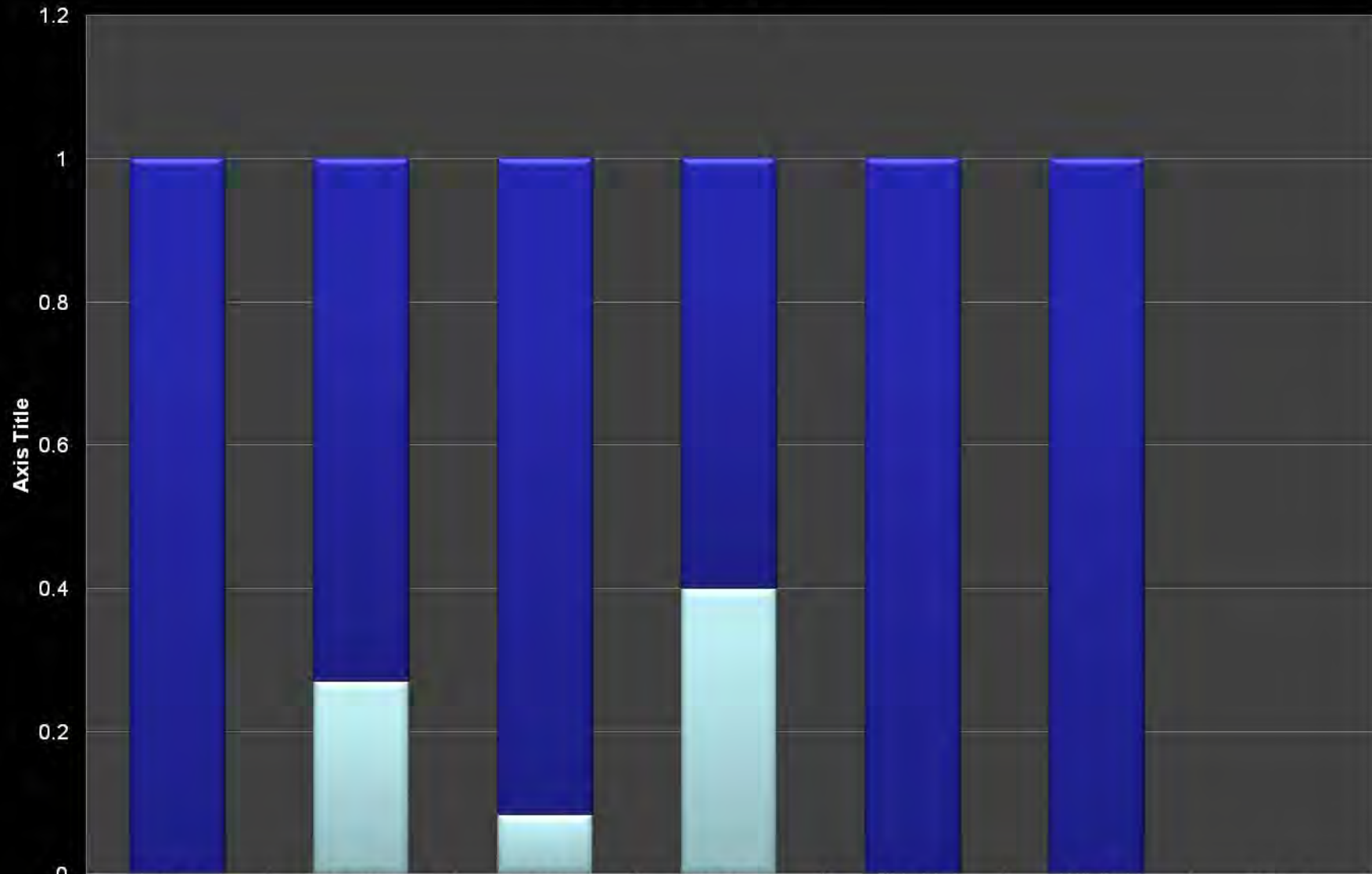


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Chart Title



	0vjc	21-30vjc	31-40vjc	41-50vjc	51-60vjc	61-70vjc	71vjc <
M	100%	73.10%	91.70%	60%	100%	100%	
F		26.90%	8.30%	40%			0

Liver Cirrhosis and complications

**Predictive Value of the Model of End-Stage Liver
Disease in Cirrhotic Patients with and
without Spontaneous Bacterial Peritonitis
(Clinical study)**

Bledar Kraja,¹ Marsela Sina,¹ Iris Mone,² Fatjona
Pupuleku,³ Adriana Babameto,¹ Skerdi Prifti,¹ and
Genc Burazeri⁴

*Gastroenterology Research and Practice, Volume 2012,
Article ID 539059, 5 pages doi:10.1155/2012/539059*

MELD in Cirrhotic Patients with and without Spontaneous Bacterial Peritonitis

- Spontaneous bacterial peritonitis (SBP) is a common and serious infection occurring in patients with cirrhosis and ascites which may be complicated by renal failure, systemic sepsis, and poor survival

(A. Rimola, et al. Journal of Hepatology, 2000).

(T. A. Sheer Digestive Diseases, 2005).

- Numerous studies suggest that 10–30% of hospitalized patients with cirrhosis and ascites have SBP, with in-hospital mortality ranging from 20–40%.

(G. Garcia-Tsao, Journal of Hepatology, 2005).

P. J. Thuluvath, The American Journal of Gastroenterology, 2001)

MELD SCORE

Outcome prediction of patients with chronic end-stage liver disease (ESLD)

In 2001, the Mayo Clinic group suggested a novel model to predict the outcome of patients with ESLD, which they named MELD

*(L. M. Forman "Hepatology, 2001.
P. S. Kamath, et al. Hepatology,2001).*

In 2003, MELD was formally adopted by the UNOS (United Network of Organ Sharing) for allocation and quality control.

It has since been validated in many other aspects of terminal liver disease:

- prediction of prognosis in viral or alcoholic hepatitis
- risk of mortality among cirrhotic patients
- outcome following liver transplantation
- recently, also as a prognostic tool for patients with acute liver failure

(A. Said, et al. Journal of Hepatology,2004.

N. Chalasani,et al.Hepatology,2002.

N. N. Onaca,et al.,Liver Transplantation,2003.

S. E. Yantorno, et al. Liver Transplantation,2007).

MELD SCORE

Outcome prediction of patients with chronic end-stage liver disease (ESLD)

Because of the significant morbidity and mortality related to SBP, identifying predisposing factors is of great interest.

MELD score is a measure of mortality risk in patients with ESLD

(H. L. Chan, et al. The American Journal of Gastroenterology, 2006).

Development of **ascites and encephalopathy**, two complications of ESLD that are not used in the MELD score calculation, has generally correlated with higher MELD scores

(F. Botta, Gut, 2003)

MELD SCORE

Outcome prediction of patients with chronic end-stage liver disease
(ESLD)

Because of low social economic level, poor sanitary conditions, and lack of hepatitis B vaccination of the population over 12-13 years old, the Albanian population is highly infected with hepatitis B virus.

(L. A. Kondili, M. R. Brunetto, et al. Journal of Medical Virology,2005).

In our country we find also a high rate of alcohol abuse.

(G. Burazeri, J. D. Kark, Alcohol and Alcoholism,2010).

Due to these two main factors, we have an important number of patients with hepatic cirrhosis, SBP, and liver failure.

Study Population

Cross-sectional study included 256 consecutive patients (199 men and 57 women), diagnosed with liver cirrhosis and ascites, hospitalized at the University Hospital Center in Tirana from January 2008 to December 2009.

SBP was found as a complication in 64 (25%)

MELD score was based on laboratory parameters (bilirubin, creatinine levels and INR) collected at admission and determined by using the UNOS Internet site MELD calculator (<http://www.unos.org/>).

Model of end-stage liver disease (MELD) score was used in hospitalized patients with liver cirrhosis to predict the occurrence of SBP and fatal outcome.

The etiologic factors of cirrhosis

alcoholic liver disease	(53.1%)
viral hepatitis B	(29.7%)
viral hepatitis C virus	(2.3%)
viral hepatitis with alcohol use	(4.7%)
and other etiologies	(10.2%).

Of 64 cases with SBP, the etiology of cirrhosis was

alcohol consumption	(56.3%)
HBV infection	(23.4%)
HCV infection	(7.8%)
alcohol + HBV	(1.6%)
other etiologies	(10.9%)

Results

There were no significant differences with regard to age, gender, diabetes mellitus between two groups.

Alcohol-related etiology was the most common causes of cirrhosis in both groups (52.1% versus 56.3%, $P = 0.11$).

MELD score was significantly higher in SBP patients than non-SBP patients (age-adjusted mean score: 23.2 versus 19.5, $P = 0.003$).

There were no significant differences in mean levels of bilirubin, creatinine, and INR ($P = 0.37$, $P = 0.22$ and $P = 0.36$, resp.).

The prevalence of SBP was significantly higher among patients with a higher MELD score (≥ 25): 37.5% versus 24.5%, $P = 0.013$.

In multivariable-adjusted logistic regression models controlling for age, sex, diabetes, and etiology, there was evidence of a statistically significant difference in SBP rates by MELD score: the OR for developing SBP by each MELD point was 1.06 (95% CI = 1.02–1.09, $P = 0.002$)

Results

Variable	Without SBP (<i>N</i> = 192)	With SBP (<i>N</i> = 64)	<i>P</i> value
MELD score	19.49 (18.38–20.60)	23.20 (21.27–25.12)	0.001
MELD group			0.046
≤15	64 (33.3)	12 (18.8)	—
16–24	81 (42.2)	28 (43.8)	0.111
≥25	47 (24.5)	24 (37.5)	0.013

Results

The main causes of death	SBP	non-SBP
▶ Variceal bleeding	(27%)	(30%)
▶ hepatorenal syndrome	(27%)	(10%)
▶ liverfailure	(20%)	(22%)
▶ hepatopulmonary syndrome	(13%)	(5%)
▶ Other causes of death	(13%)	(33%)

Case-fatality rate was significantly higher in SBP patients than non-SBP patients (23.4% versus 12.0%, $P = 0.024$).

Results

MELD score was significantly higher in fatal cases versus nonfatal patients (mean age-adjusted score was 32.7 versus 18.4 overall, 34.8 versus 18.0 in SBP patients, and 32.0 versus 18.5 in non-SBP patients; all $P < 0.001$).

Mean MELD score was significantly different in patients who died in the group of SBP compared to those who died in the group without SBP ($P = 0.01$).

A higher MELD score was independently associated with a higher risk of SBP.

In this Albanian sample of hospitalized cirrhotic patients, MELD score was confirmed as a significant predictor of both SBP and fatal outcome.

The prevalence of SBP as a complication of the ascitic cirrhotic patients included in the study was 25%.

This may be due to relatively high percentage of alcoholic cirrhosis in our country, which is more disposed to develop SBP.

In the present study, SBP is more frequent in alcoholic-related cirrhosis patients.

Prevalence of SBP is higher in the cirrhosis patients whose ascites is caused by alcohol consumption rather than by viral hepatitis

J. Lata, et al., European Journal of Gastroenterology and Hepatology, 2003.

The patients with moderate to high MELD scores have a substantially greater risk of SBP indicating that MELD score may be a useful tool to predict the development of SBP.

The mean MELD score of 19.1 in patients with ascites without SPB is lower than the mean MELD score (24.8) of patients with SBP

(M. Malinchoc, al., Gastroenterology, 2001)

Severe liver cirrhosis with MELD score ≥ 18 was associated with an increase risk of SBP

(A. A. Gayatri, Acta Medica Indonesiana, 2007).

The MELD score has a predictive value in hospital mortality in patients with end-stage liver disease of diverse etiologies and severity

(H. L. Chan, et al. The American Journal of Gastroenterology, 2006).

(F. Botta, et al. Gut, 2003).

MELD score is an independent predictor of hospital mortality in SBP.

(S. R. Nobre, et al, European Journal of Gastroenterology and Hepatology, 2008)

The findings can be useful for increasing suspicions for SBP development in hospitalized cirrhotic patients with elevated MELD score.

The renal failure, due to further reduction of effective circulating volume, is still a common cause of death in the patients with SBP

(E. S´anchez, et al. *The American Journal of Gastroenterology*, 2007).

The serum creatinine has been shown to have a determinant impact on the prognosis of cirrhosis

This parameter is not included in the Child-Turcotte-Pugh score.

*(G. Fern´andez-Esparrach, et al. *Journal of Hepatology*, 2001)*

The MELD score has advantages when compared with the Child-Pugh score.

- it uses objective parameters
- its objective parameters are less subject to center-to-center variability such as the Child classification,
- the MELD score increases as the three constituent parameters deteriorate, whereas the individual scoring elements in the Child score remain fixed once a defined threshold has been reached

(L. M. Forman et al Hepatology,2001).

**P0663 HEPATORENAL SYNDROME (HRS): INCIDENCE,
PRECIPITATING EVENTS AND SHORT-TERM PROGNOSIS**

B. Resuli, J. Basho, A. Kristo, J.Çela, A. Babameto, L.Çuko,
E.Shagla, E.Petrela

19th United European Gastroenterology Week, October 2011

To assess the incidence, precipitating events and factors associated with an increasing risk of in-hospital mortality in cirrhotics with HRS.

600 consecutive patients with advanced liver cirrhosis and ascitis admitted to service during January 1st 2008 and December 31, 2010 were retrospectively evaluated.

HRS was defined according to consensus-based diagnostic criteria proposed by the International Ascites Club in 1996.

Seventy eligible patients for HRS, 62 male and 8 female, mean age 55±4.9 y/old, were managed with a similar treatment protocol including general supportive measures and treatment of associating complications, such as infections, hepatic encephalopathy and gastrointestinal bleeding.

HEPATORENAL SYNDROME (HRS)

The etiology of cirrhosis was:

alcoholic (68.5%),

HBV infection in (21.5%)

others in (10%).

MELD score, serum albumin and serum sodium were analyzed as possible predictors of survival at 3 weeks.

HRS was diagnosed in 11.7 % of the patients with cirrhosis and ascites.

Comparison of variables between patients who dies during the first 3 weeks (group A) and those who have survived (group B) were made.

HEPATORENAL SYNDROME (HRS)

The most frequent precipitating event of HRS was:

- spontaneous bacterial peritonitis (62.7%),
- followed by gastrointestinal bleeding (23.6%),
- diuretic-induced volume depletion (8.3%)
- and therapeutic paracentesis without plasma expansion (2.54%).

In 2.9% of the cases HRS was developed spontaneously without known precipitating factors.

50% of the patients died during the first 3 weeks.

Statistically significant difference in MELD score (31.97 ± 0.66 of the group A versus 24.31 ± 5.78 of the group B, $p < 0.0001$) and serum albumin (2.49 ± 0.33 g/dl of the group A versus 2.68 ± 0.25 g/dl of the group B, $p < 0.03$) was observed.

No significant difference as regards the serum sodium (127.4 ± 7.58 mmol/L of the group A versus 128 ± 5.16 mmol/L of the group B, $p = 0.49$).

HEPATORENAL SYNDROME (HRS)

HRS is a relatively common complication in cirrhotic patients with ascites.

The most frequent precipitating factor was spontaneous bacterial peritonitis.

High MELD score (>31) and low serum albumin (<2.4 g/dl) were strongly associated with very short patients survival.

P0682 THE ASSOCIATION BETWEEN THE SERUM SODIUM LEVEL AND THE SEVERITY OF COMPLICATIONS IN PATIENTS WITH LIVER CIRRHOSIS

L.Çuko, A. Babameto, J. Basho, J.Çela, A. Kristo, I.Tafaj, E.Petrela

19th United European Gastroenterology Week, October 2011

Hyponatremia is a common problem in patients with advanced cirrhosis and an independent predictor of mortality in these patients.

Little is known, however, regarding the relationship between the degree of dilutional hyponatremia and development of cirrhotic complications.

Aim was to evaluate the prevalence of hyponatremia and its association with the severity of complications in liver cirrhosis.

186 inpatients (2009-2010) with cirrhotic complications such as simple ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, hepatic encephalopathy, variceal bleeding and infection.

Three pts. groups according to serum sodium concentration as follows:

- (1) serum sodium \leq 130mmol/L
- (2) serum sodium between 131mmol/L and 135mmol/L
- (3) serum sodium \geq 136 mmol/L.

The liver function impairment is assessed by Child-Pugh and MELD scores.

THE ASSOCIATION BETWEEN THE SERUM SODIUM LEVEL AND THE SEVERITY OF COMPLICATIONS IN PATIENTS WITH LIVER CIRRHOSIS

Study Population (n=186)

Gender (M/F)

Values

153 / 33

Age (m ± SD)

57.3 ± 12.8 vjeç

Etiology

HBV

51 (27.4%)

HCV

12 (6.4%)

Alcohol

118 (63%)

Cryptogenic

5 (2.6%)

Child-Pugh

n (%)

Child A

20 (10.7%)

Child B

75 (40.3%)

Child C

91 (48.9%)

MELD score (m ± SD)

17.5 ± 6.04

Na në serum (mmol/L, m ± SD)

132.3 ± 6.08 mmol/L

Complications

Ascites

154 (82.7%)

Hepatic Encephalopathy

86 (46.2%)

SBP

62 (33.3%)

Hepatorenal syndrome

24 (12.9 %)

Esophageal varices

140 (75.2%)

G/I Hemorrhage (varices)

40 (21.5%)

THE ASSOCIATION BETWEEN THE SERUM SODIUM LEVEL AND THE SEVERITY OF COMPLICATIONS IN PATIENTS WITH LIVER CIRRHOSIS

The prevalence of hyponatremia, classified as serum concentration of ≤ 135 mmol/L, ≤ 130 mmol/L, and ≤ 125 mmol/L, were 59.09 %; 19.3 % and 4.2 %, respectively.

Variable	≤ 130 mmol/L (n = 50)	131-135 mmol/L (n = 70)	≥ 136 mmol/L (n = 66)	p
Child-Pugh	10.8 \pm 1.7	9.7 \pm 1.9	9.0 \pm 1.6	< 0.001
MELD score	19.7 \pm 5.6	18.1 \pm 5.3	15.3 \pm 5.4	< 0.001

These score indicate that as hyponatremia became more severe, liver function declined.

Patients with a serum sodium < 130 mmol/L had a significantly increased risk for developing complications:

hepatic encephalopathy	(OR 10.4, CI, 4.337-5.307, p<0-001),
spontaneous bacterial peritonitis	(OR 4.6; CI, 1.923-10.95; p=0.002),
hepatorenal syndrome	(OR 9.4; CI, 2.032-13.947; p,<0.001).

THE ASSOCIATION BETWEEN THE SERUM SODIUM LEVEL AND THE SEVERITY OF COMPLICATIONS IN PATIENTS WITH LIVER CIRRHOSIS

Complications	≤ 130 mmol/L (n = 50)	131-135 mmol/L(n = 70)	≥ 136mmol/L (n =66)	p
PBS 62 (33. 3%)	27 (43.5)	25 (40.3)	10 (16.1)	0.002
HRS 23 (12.36%)	14 (60.9)	7 (30.4)	2 (8.7)	0.001
EH 86 (46.23%)	40 (46.5)	34 (39.5)	12 (14)	0.001

No correlation between serum sodium level and gastrointestinal bleeding.

Prevalence of hyponatremia is significantly high in patients with liver cirrhosis (59.09%).

Serum sodium levels <130mmol/L were strongly associated with the occurrence of some of major complications.

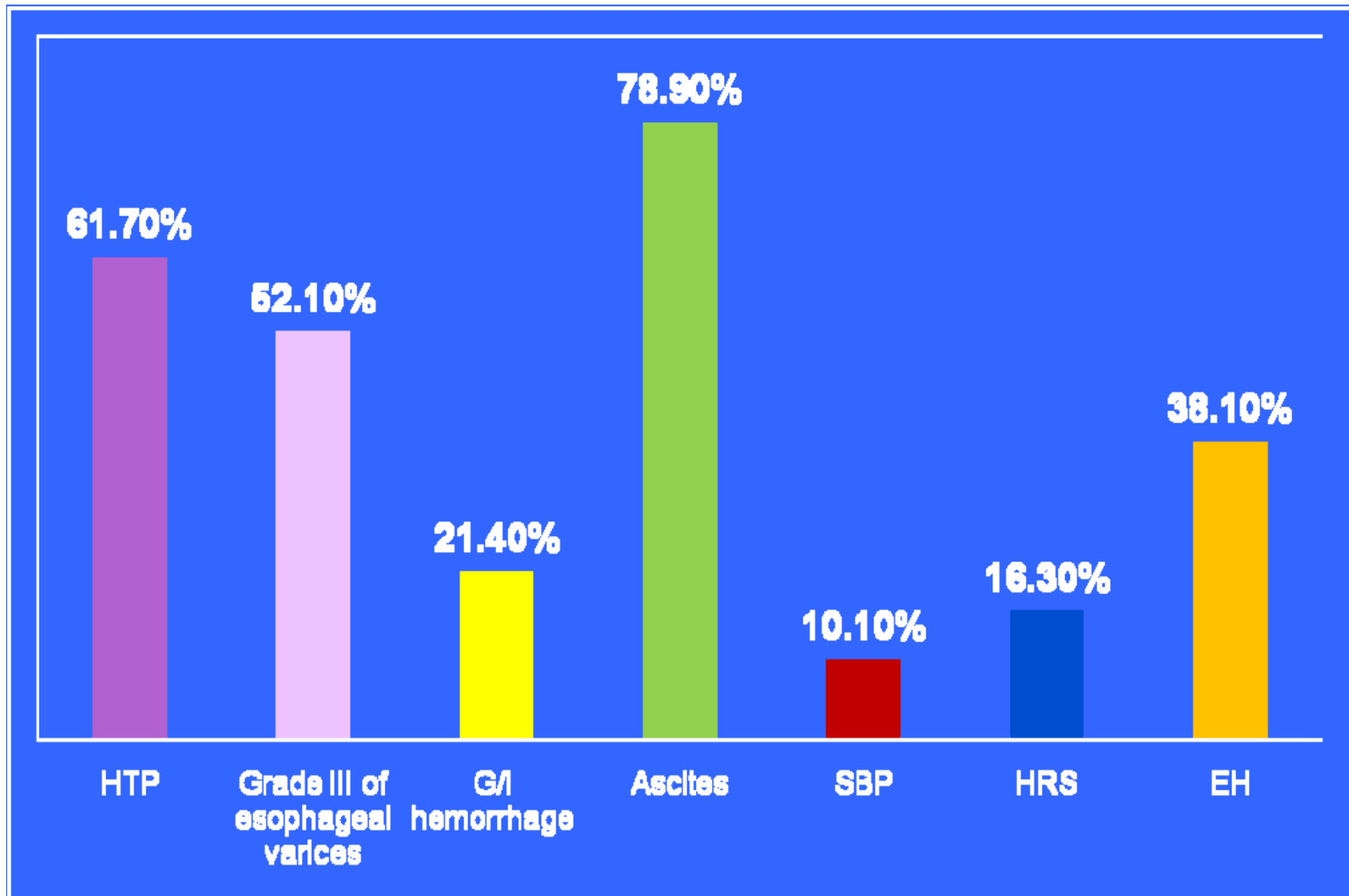
Alcoholic liver cirrhosis (Complications and Prognosis)

A. Carkanji, B. Resuli

September 2012

- The prevalence of the major complications of alcoholic cirrhosis as : HTP and gastrointestinal hemorrhage, ascites and SBP, HRS and Hepatic encephalopathy
- Evaluate the short term prognosis of the cirrhotic patients according to the Child-Pugh and MELD criteria.
- Retrospective study of 168 patients with alcoholic liver cirrhosis admitted to the service of Gastroenterology and Hepatology from January 2009 to March 2010.
- All the patients were male , from 28 to 80 yr.old, mean age 54 yr. old
- According to the age groups, it was found 10.2% of the cases in the age interval 31 to 40years old, and 26.8% in the interval 41 to 50 years old. The most number of patients belong to the interval age from 51 to 60 years old (33.9%).

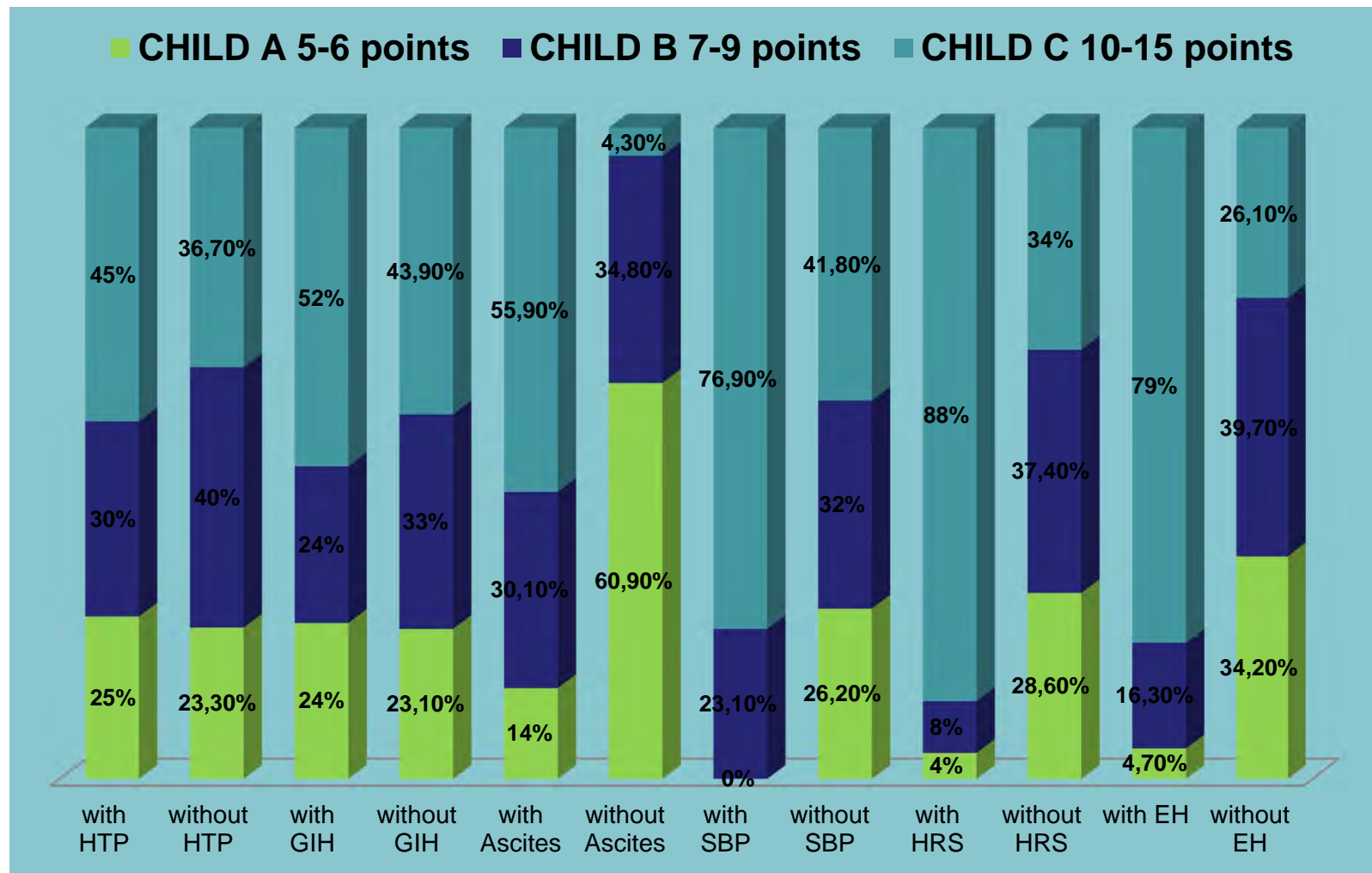
Complications



CHILD-PUGH class related to the major complications

Complications			CHILD A 5-6 points	CHILD B 7-9 points	CHILD C 10-15 points	P value
HTP	with	80	25%	30%	45%	0.08
	without	30	23.3%	40%	36.7%	
GIH	with	25	24%	24%	52%	0.2
	without	91	23.1%	33%	43.9%	
Ascites	with	93	14%	30.1%	55.9%	0.001
	without	23	60.9%	34.8%	4.3%	
SBP	with	134	0%	23.1%	76.9%	0.001
	without	103	26.2%	32%	41.8%	
HRS	with	25	4%	8%	88%	0.001
	without	91	28.6%	37.4%	34%	
EH	with	43	4.7%	16.3%	79%	0.001
	without	73	34.2%	39.7%	26.1%	

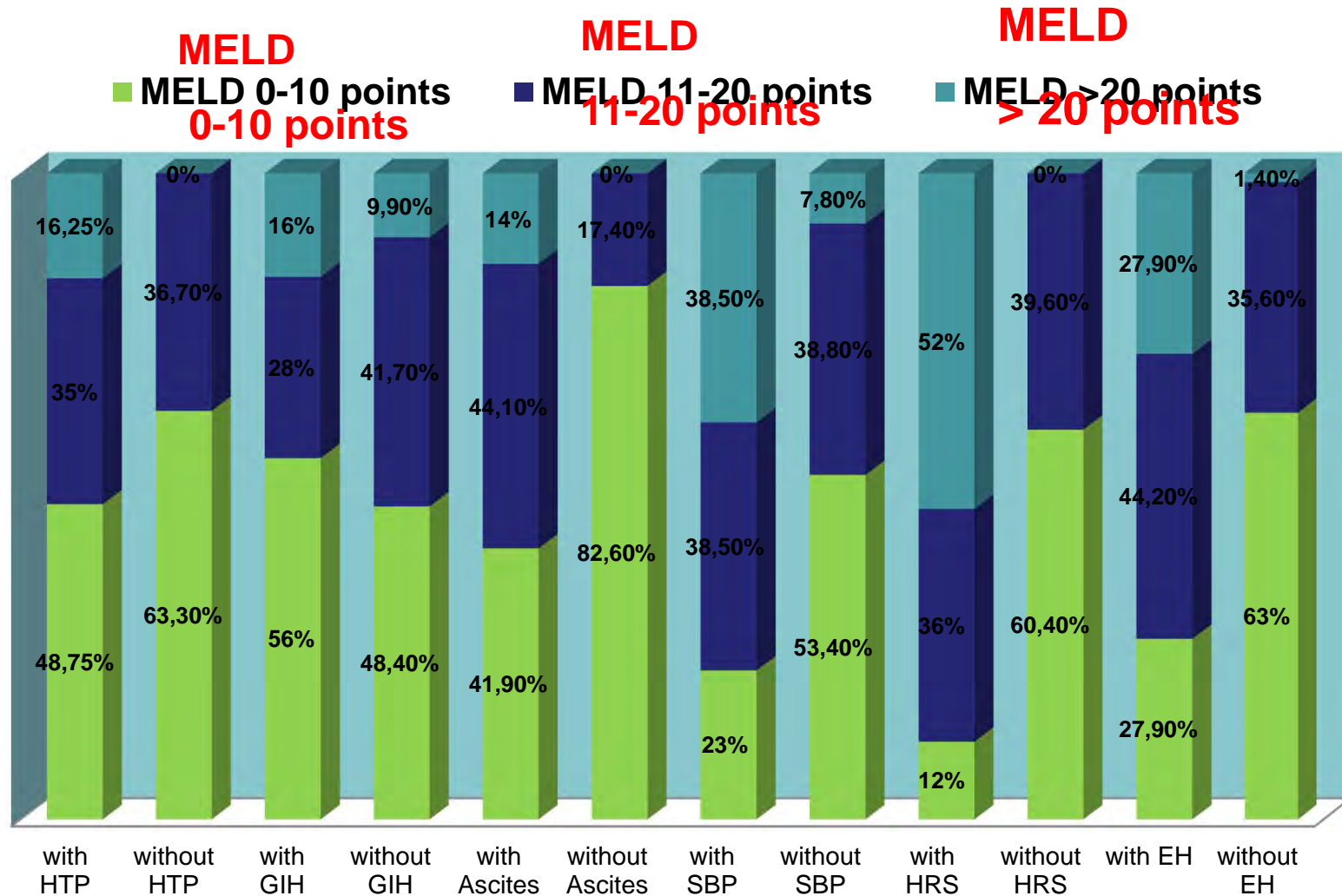
CHILD-PUGH class related to the major complications



MELD related to the major complications in the patients with alcoholic liver cirrhosis

Complications			MELD 0-10 points	MELD 11-20 points	MELD >20 points	P value
HTP	with	80	48.75%	35%	16.25%	0.006
	without	30	63.3%	36.7%	0%	
GIH	with	25	56%	28%	16%	0.5
	without	91	48.4%	41.7%	9.9%	
Ascites	with	93	41.9%	44.1%	14%	0.001
	without	23	82.6%	17.4%	0%	
SBP	with	134	23%	38.5%	38.5%	0.001
	without	103	53.4%	38.8%	7.8%	
HRS	with	25	12%	36%	52%	0.001
	without	91	60.4%	39.6%	0%	
EH	with	43	27.9%	44.2%	27.9%	0.001
	without	73	63%	35.6%	1.4%	

MELD related to the major complications in the patients with alcoholic liver cirrhosis



GI Hemorrhage

- Approximately *25% of the cirrhotic patients* with esophageal varices have GIH during 2 following years after diagnosis.
- The hemorrhagic risk with varices < 5 mm diameter is 7% in 2 years, while with varices > 5 mm is until 30%.
- In end-stage liver disease it is the risk of repeated GIH in 30-35% during the following 6 weeks after the first episode.
- Death risk varies from 5% to 8% during the first week, 20-30% in the period of 2 weeks.
- The 2 year survival of the patients with liver cirrhosis and ascites varies from 40 to 50%, while the 5 year survival arrives until 20%.
- SBP is found in around 15-25% of the patients with liver cirrhosis. The mortality continues to be a high one , until 70% and it is one of the most severe complications of liver cirrhosis.

- 25% of the patients with HTP were included in CHILD A class , while 30% and 45% respectively in B and C class.
- Related to the MELD criteria was found that 51.25% of the patients with HTP had > 10 points, while in patients without HTP 63.3%, 36.7% and 0% belong respectively to 0-10, 11-20, >20 points intervals. Change was statistically significant.
- The most part of the cirrhotic patients with complications belong to CHILD B and C class respectively 30% and 45% for HTP, 24% and 52% for GIH, 30.1% and 55.9% for ascites, 23.1% and 76.9% for SBP, 8% and 88% for HRS, 16.3 and 79% for EH.
- The short term prognosis related to the MELD criteria resulted the worst for patients with major liver cirrhosis complications as: HTP (p= 0.006), GIH (p=0.5), ascites (p=0.001), SBP (p=0.001), HRS (p= 0.001) and EH (p=0.001).

Hepatocellular Carcinoma(Etiological and clinical characteristics in the moment of presentation : retrospective analysis of 145 cases.

Adriana Babameto¹, Ilir Bibolli¹, Liri Hoxha¹, Jovan Basho¹, Klerida Shehaj¹, Bashkim Resuli¹

Revista Shqiptare e Gastroenterologjise dhe Hepatologjise,Nr.6 2011

To analyze the putative etiologic factors of HCC and its baseline characteristics.

Retrospective study of a cohort of 145 consecutive patients (81.6% male and 18.4% female, median age 59.4 ± 10.8 years old; range 26-82 years old) seen in our service of gastrohepatology between January 2005 to December 2009, fulfilling diagnostic criteria for HCC adopted by Barcelona EASL conference.

Liver cirrhosis was found in 26 patients (87%), with ascites in 62.7% and without ascites in 37.3%

Underlying cirrhosis was seen in 87% cases with ascites in 62.7% and without ascites in 37.3%

Hepatitis B being the most common etiologic agent (55.3%), followed by alcohol (27.7%) and HCV (1.6%)

HCC caused new onset ascites and recent worsening in three-fourth cases with ascites.

Paraneoplastic syndrome was a rare event in HCC.

Okuda stage II and III was found in 55% and 45% respectively.

Vascular invasion was seen in 23% by the time they presented with extra hepatic spread of tumor in 14% of the cases.

Ca-cirrhosis was found to be 12.43 % of total number of liver cirrhosis, with a yearly incidence from 4% to 6.6%.

HCC cases in the study were found to be 2.8 % of total number of the hospitalized patients, 11.17 % of the total number of the patients with chronic liver diseases, 19.56 % of the total number of hospitalized patients with malignant

Chronic infection with hepatitis B virus and alcohol abuse are the major risk factors for development of HCC in Albania. The prevalence of advanced stage HCC makes most of the detectable lesions unsuitable for curative resection. However, universal hepatitis B vaccination program may become the most effective preventive measure. Occult HBV infection may account for a proportion of cases of HCC in unknown etiological group.

DIFFERENT PATTERN OF DECOMPENSATION IN ALCOHOLIC VERSUS NONALCOHOLIC CIRRHOTIC PATIENTS

P. Kristani¹, F. Kurti², S. Xinxo³, A. Babameto²

National Conference of Gastrohepatology, March 2016

The aim of the study is to evaluate the different models of decompensation in relation to the etiology of liver cirrhosis.

- **200 cirrhotic patients** hospitalized during 2011 - 2014 in regional Durres hospital, divided in two main groups (alcoholic and non-alcoholic patients), were retrospectively analyzed.
- **172 males(84%) and 28 females(16 %) p<0.05), mean age was 58 yrs**
- **According to the etiology: alcoholic cirrhosis was present in 51% of patients.**

Male dominated in alcoholic cirrhosis 98% vs 62% in nonalcoholic group (HBV, HCV, cryptogenic, autoimmune), while female dominated in non-alcoholics (38% vs. 2%), $p < 0.05$).

According complications: ascites is the main complications in alcoholic cirrhosis (93% vs. 73% , $p < 0.05$), while HCC and death dominated in nonalcoholic group (24% vs. 5.8% and 36.7% vs. 23.5%; $p < 0.05$) respectively.

ALCOHOL, OBESITY AND TOBACCO AS RISK FACTORS
FOR HEPATOCELLULAR CARCINOMA

Adriana Babameto 1, Klerida Shehu 2, Edlira Ibro 3, Pranvera
Kristani 4

EASL HCC SUMMIT GENEVA, SWITZERLAND FEBRUARY 13 - 16, 2014

To evaluate the role of alcohol, tobacco and obesity as risk factors for HCC in Albanian patients.

Patients with HCC, cirrhosis with HCC and cirrhosis without HCC were enrolled in the study.

Were enrolled 65 patients with HCC and 100 patients with cirrhosis without HCC.

It was found significant correlation between alcohol, tobacco and obesity.

Comparing HCC cases to the cirrhotic group without HCC, it was found that the risk of HCC increased 4-fold for alcohol, 2-fold for tobacco and 2.5-fold with obesity.

Also a dose-dependent relationship between alcohol and tobacco exposure with risk of HCC was noted.

P-242 Mortality trend for hepatocellular carcinoma in Albania: a hepatitis B virus endemic area
F. Kraja, I. Akshija, I. Harizi, J. Millo, S. Kullolli, E. Karauli, O. Spahiu, B. Kraja
(Annals of Oncology · June 2016)

To investigate the mortality from HCC in a high-risk area. The aim of this study was to describe the trend of HCC mortality among different age groups in Albania, an endemic area of hepatitis B virus infection in South-eastern Europe.

Official death certification data for liver cancer (ICD-9 code: 155.0) from 2006 till 2010 based on the official information from the Institute of Statistics.

Were calculated age-standardized mortality rates per 100,000 persons by sex in separate age groups and overall using the world standard population as reference.

Overall, HCC mortality (per 100,000 persons) was 5.4, 5.3, 5.8, 4.9 and 4.2 for the years 2006, 2007, 2008, 2009 and 2010, respectively.

During these five years HCC has declined (APC = -8.3%) even though it is not significant (p trend= 0.23).

There was a similar decline in men and women (APC = -7.6% and APC = -8.1%, respectively).

HCC mortality decreased in all age groups with different annual percentage change (APC).

There was decreasing significant trend in the youngest age group (APC = -18.8% at age 20-49, p trend < 0.05)

whereas a decreasing not significant trend was observed in the middle-aged and the oldest age group (APC = -4.6% at age 50-69, p trend = 0.4 and APC = -7.5% at age 70-79, p trend = 0.5).

HCC mortality has shown a decreasing but not significant trend in Albania during 2006-2010.

However, these findings indicate that thanks to hepatitis B vaccination program a decline began with the more favourable significant trend in the youngest age group.

Furthermore, results suggest that public health strategies for HCC screening should differ by age-groups in an endemic area of hepatitis B virus.

Needs

In patients with chronic hepatitis, antiviral therapies leading to maintained HBV suppression in chronic hepatitis B and sustained viral response in hepatitis C are recommended since they have been shown to prevent progression to cirrhosis, and hence HCC development

Surveillance of the patients with chronic liver diseases with virus B and C infections.

Better access to treatment for Hepatitis C chronic diseases

National registry for chronic Hepatitis and cirrhosis from B and C infections

A better collaboration between all structures in order to have national database for liver cancer

Improvement of reporting from all districts and correct completion of new case report form is required.

Strengthening of the public health laboratory capacities for the diagnosis of these diseases ,



FUTURE

PAST

PRESENT

Thank you