Clinical and virological profile of patients with diagnosed HCV chronic infection in Italy: data from PITER (Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali) cohort study.

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Available in www.iss.it/piter

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INTRODUCTION

Italy has one of the highest prevalence rate of HCV infection in Europe, and HCV infection is the leading cause of cirrhosis, HCC, and liver-related deaths. Nevertheless, epidemiologic studies estimating the real prevalence, and severity of HCV related liver disease in the general Italian population were conducted during the years 1994-2006, in small towns or communities.

The introduction of the new DAAs for hepatitis C, whose use is expected to have a deep impact in terms of eradicating HCV and long-term morbidity and mortality, makes urgent the need to obtain representative real-life and long-term data on the HCV infected population, above all considering the high costs of these drugs and the need to adopt treatment priority rules to maximize cost-effectiveness.
The prospective Italian HCV cohort study, known as PITER, benefits from a structured network involving Italy's National Institute of Public Health (Istituto Superiore di Sanità), the Italian Society for the Study of the Liver (AISF), the Italian Society for Infectious Diseases (SIMIT), and their affiliated clinical centers.

Fig.1: Geographical distribution of PITER Network Clinical Centers.

AIM

The present analysis, based on baseline of patients in care, enrolled in the PITER cohort, has the following aims:

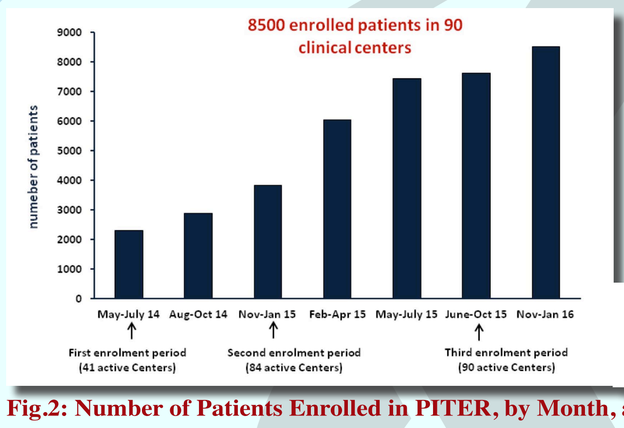
1. to evaluate the baseline characteristics of chronic liver disease of the enrolled patients
2. to evaluate factors correlated with liver disease severity
3. to evaluate gender peculiarities of cirrhosis and the overall impact of co-morbidities in patient with chronic HCV infection

MATERIALS AND METHODS

PITER network consists of more than 80 Clinical Centers distributed on the overall Italian area (Fig 1). The bespoke electronic data-collection system covers all clinical and therapeutic aspects of chronic HCV infection necessary for the main aims of the PITER study. The enrolled patients will be followed- up for at least 5 years, independently if they will be undergone an anti-HCV antiviral therapy.
The independent role of age, gender, genotype, BMI, co-morbidities , biochemical findings (AST, ALT PLT) on the advanced stage of liver disease (cirrhosis) were evaluated by univariate and logistic regression models. The regression model's goodness of fit (calibration and sensitivity) was also estimated.

RESULTS

- To date, the PITER-HCV cohort consists of 8500 enrolled patients in care in more than 80 Italian Clinical Centers distributed on the overall Italian area (Fig 2). In this analysis, data of 7237 patients with complete data entry were considered.



1470 therapy complete CRF are available (others will be completed after 24 weeks SVR data)
2395 follow-up CRF are available and related to patients of the first enrollment period

Fig.2: Number of Patients Enrolled in PITER, by Month, as of January 2016

- Mean age of enrolled patients is 59+-12 years; 56% are male.

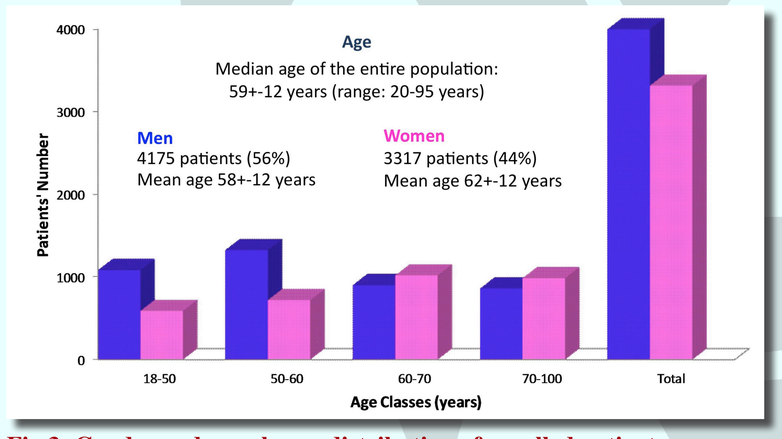


Fig.3: Gender and age classes distribution of enrolled patients

- Genotype distribution is as follows:
Gt1b-44%; Gt1a-11%; Gt2-15%; Gt3-10%; Gt4-6%.
Genotypes 1a, 3 and 4 are significantly more frequent among younger patients while Gt1b and Gt2 are significantly more frequent among older patients.

Tab.1: Genotypes distribution of enrolled patients per age classes

	Age Classes			
Genotype	18-50 (%)	51-60 (%)	61-70 (%)	>71 (%)
1	25	29	21	25
1a	41	45	10	4
1b	16	22	35	27
2	10	14	33	43
3	44	47	7	1
4	35	50	11	4
Other	33	29	22	16
ND	16	13	17	54

*analysis on 6211 patients

- The distribution of genotypes in different fibrosis stage was reported in Tab. 2. No association between genotypes and fibrosis stages is found. The evaluation of these distribution is of particular interest either for patients who are having access to antiviral therapy, particularly for GT 3 presented in 13% of patients with cirrhosis, or for patients who will be treated in the near future.

Tab.2: Genotypes distribution of enrolled patients per fibrosis stage

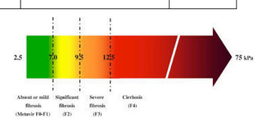
Genotype	F0-F1 (%)	F2 (%)	F3 (%)	F4/cirr (%)
1	59	66	67	66
2	19	13	12	11
3	9	10	9	13
4	7	7	6	6
Other/ND	6	4	5	5

- As reported in Tab.3, in 4282 patients for whom transient elastography data were available, fibrosis distribution is: F0-F1:39%, F2:14%; F3:12%;F4/cirrhosis:35%.
In 2955 patients fibroscan data were not available. In 47% of these patients cirrhosis was reported based on clinical and instrumental data .
Overall, within the 7237 enrolled patients with available fibrosis data, about 40% could be classified as having F4/cirrhosis.

Tab.3: Liver disease stages distribution

Fibrosis	Diagnosis with Fibroscan data N=4282	%	Diagnosis with clinical and instrumental data N=7237	%
F0-F1	1661	39		
F2	620	14		60
F3	520	12		
F4-Cirrosi	1481	35	2878	40

*analysis on 7237 patients



- As reported in Figure 4 , Fibrosis pattern was similar in the first and the second periods of enrollment which indicates that the population enrolled in PITER could be considered representative of the Italian HCV chronically infected patients in care.

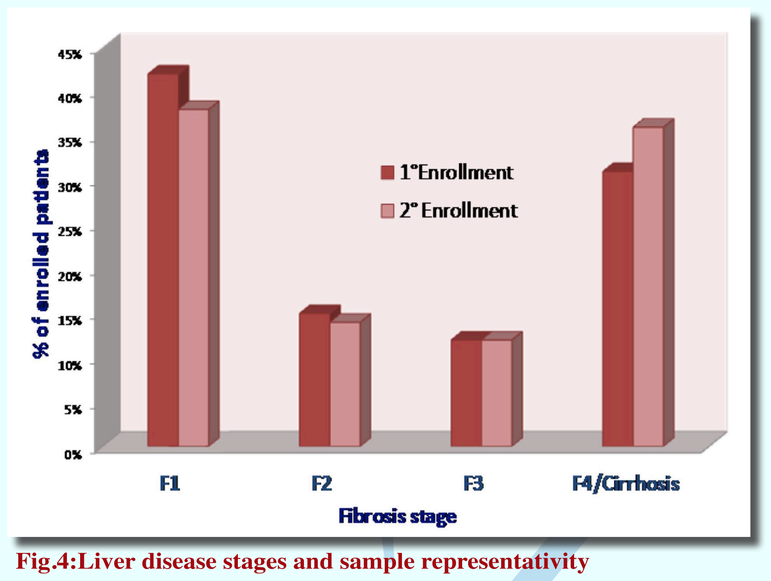


Fig.4:Liver disease stages and sample representativity

- Regarding the previous therapeutic history, about half of enrolled patients are treatment naïve. (Fig.5)
o Among treatment experienced patients, the fibrosis distribution is: F0-F1:32%, F2:15%, F3:13%; F4/cirrhosis:40%.
o Among treatment naïve patients, fibrosis distribution is : F0-F1:46%, F2:14%, F3:11%; F4/cirrhosis:29%.

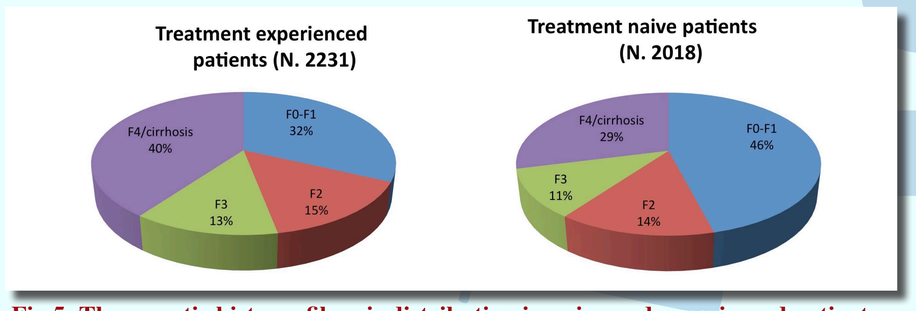


Fig.5: Therapeutic history: fibrosis distribution in naive and experienced patients

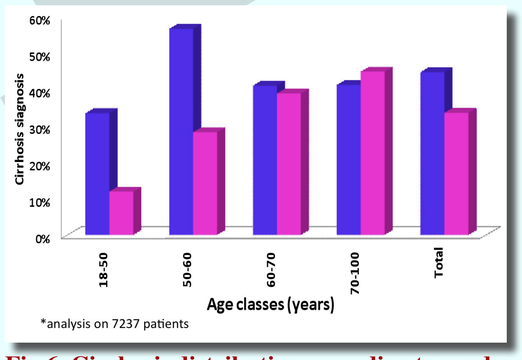
- The more frequent reported co-morbidities are cardiovascular diseases (32%) and diabetes (13%). Other co-morbidities were present in 4-8% of the enrolled patients. (Tab. 4)

Tab.4: Co-morbidities distribution

Co-morbidities	Age class		Total
	<=60 years N 3724 (49%)	>60 years N 3771(51 %)	N 7495 (100%)
Autoimmune/rheumatoid	132(3.5)	160(4.2)	292 (4)
Cardiovascular	614 (16.5)	1789(47.4)	2403 (32)
Diabetes	325 (8.7)	685(18.2)	1010 (13)
Haematologic	191(5.1)	179(4.7)	370 (5)
Neurologic	111 (3)	145(3.8)	256 (3)
Osteoarticular	134 (3.6)	341(9.0)	475 (6)
Psychiatric	322 (8.6)	158(6.8)	580 (8)
Renal	112 (3)	134(3.6)	246 (3)
Thiroid	223 (6)	414(11.0)	637 (8)
Tumors	137 (3.7)	349(9.3)	486 (7)
Other	527 (14.2)	664(17.6)	1191 (16)
None	1650(44.3)	777 (20.6)	2427 (32)

*analysis on 7495 patients

- Interestingly,
woman gender has less probability to develop liver cirrhosis, however risk of cirrhosis in females increased significantly in women older than 60 years;



*analysis on 7237 patients

Fig.6: Cirrhosis distribution according to gender and age groups

- women have more frequent hypertension , osteoarticular diseases and tumors, but less frequent diabetes than men.

Tab.5: Gender analysis of co-morbidities

Co-morbidities	Gender			
	Male N (4174)	%	Female N (3317)	%
Autoimmune	103	2.4	188	5.6
Cardiovascular*	**1251**	**29.9**	**1151**	**34.7***
Diabetes	**616**	**14.7**	**394**	**11.8***
Haematologic	214	5.1	156	4.7
Neurologic	143	3.4	113	3.4
Osteoarticular	**130**	**3.1**	**345**	**10.4***
Psychiatric	253	6	327	9.8
Renal	157	3.7	89	2.6
Tumors	**150**	**3.6**	**237**	**7.1***
Other	716	17.1	475	14.3

*Hypertension was more frequently present in women compared to men

CONCLUSIONS

PITER cohort constitutes a well representative sample of patients with chronic HCV infection in care in Italy.

- Enrolled patients have an advanced age and 56% are male
- Genotype 1b has the major prevalence
- F4/cirrhosis is diagnosed in about 40% of patients
- Co-morbidities are present with a prevalence between 3-32%

Among patients with chronic hepatitis C, allocation of DAA according to priority rules in Italy, based mainly on the fibrosis stage, will allow access to therapy to about 40% of patients in care. Following the overall treatment of these patients, PITER is a useful tool to estimate the burden of the remaining patients (based on the reported fibrosis stage) and could serve as predictive model to assess the impact of delaying treatment or not treating the remaining patients

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