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# Distribution of liver disease in a cohort of immigrants in Sicily: analysis of day-hospital admissions in a migration medicine unit

***Distribuzione delle malattie di fegato in una coorte di immigranti in Sicilia: analisi dei ricoveri in day hospital in un servizio di medicina delle migrazioni***

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## INTRODUCTION

In recent decades there has been a progressive decrease in the prevalence of hepatitis B virus (HBV)-related chronic hepatitis in the Italian population, thanks to the improved socio-economic conditions, which have led to changes in lifestyle, to new hygiene rules, blood screening and other precautions in the medical setting and, above all, to the national compulsory vaccination campaign, which started in 1991 [1, 2]. Although the incidence of hepatitis C virus (HCV) infection has also significantly decreased, again thanks to improved socio-economic conditions and smaller family size, as well as to compulsory screening for anti-HCV in blood banks and sexual educational campaigns, it is still the most frequent etiologic agent of chronic hepatitis, especially in the population aged over 60 [3-5].

The phenomenon of migration, which has recently begun to affect Italy (as well as the rest of Europe), has reached such high levels that to-

day there is an estimated regular immigrant population of around 5 million people in this country [6]. Recent estimates in population-based surveys in Italy indicate that the prevalence of HBV infection is below 1% in all group ranges in the general population, whereas among immigrants it has been estimated at around 9.3% and, even more recently, 11.7%, [7-9]. This difference in numbers is indeed expected to widen, as the national vaccination campaign has not yet been extended to immigrants, with the exception of those actually born in Italy.

Since 2000 there has been a day-hospital service with an outpatient clinic at the Policlinico University Hospital of Palermo. To facilitate healthcare access for irregular and/or illegal immigrants, our day-hospital has been given the authority to directly issue an STP (temporary resident foreigner status) certificate to patients who make an official *declaration of indigence*, which entitles them to receive free public medical care.

The objective of this study was to evaluate the distribution and etiology of liver disease in a cohort of our immigrant population who had been followed up as outpatients at our day-hospital service. The hypothesis was that a high

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prevalence of viral hepatitis could represent a potential danger both for the autochthonous population and for non-infected immigrants.

## ■ PATIENTS AND METHODS

We retrospectively examined the day-hospital discharge charts of all the immigrant patients presenting between 1/7/2009 and 30/6/2013. The charts used for the day-hospital management conformed with the Italian OSI (Epidemiological Observatory on Immigrant Health) project [10]. Briefly, the aim of the OSI project is to create an information network connecting the various Italian day-hospital structures - whether state-run or private - which give primary health care and assistance to irregular immigrants. It uses a uniform patient chart for collecting information, combined with a dedicated software package to record, process and analyze the data. It thus supplies information collected in a standardized and homogeneous way in areas as yet not reached by the present official systems.

From these patient charts it was possible to extract information about the overall activity of the day-hospital service offered to immigrants. We selected charts with any generic diagnosis of liver disease, based on elevated liver transaminases or on the positivity of any marker of hepatitis B or hepatitis C viruses, and the full details of each chart were then analyzed to determine etiology. Alcoholic liver disease was defined as the presence of transaminase alterations or evidence of fatty liver at ultrasound associated with an alcohol intake of at least 30 g per day for men and 25 g per day for women, while cryptogenic liver disease was any repeated alteration in liver transaminases in the absence of other known etiological factors of liver disease. From the following data at our disposal, we defined the pathological state of each patient:

- physical parameters (age, gender, weight, height, BMI);
- family history, early medical history and recent medical history, with particular attention to smoking habits, alcohol consumption, drug abuse and pharmacological history;
- blood tests (CBC, urinalysis, blood sugar, serum cholesterol, triglycerides, transaminases, gamma-GT, alkaline phosphatase, albumin);
- virological markers (HBsAg, HBsAb, HBeAg,

HBeAb, HBcAb, HBV-DNA, HCV-RNA, anti-HCV);

- specific and non-specific autoantibodies;
- ultrasound scan of the abdomen and other diagnostic imaging tests (esophagogastroduodenoscopy, CT scan);
- higher-level exams when necessary, including liver biopsy.

Informed consent was not requested because this study included only data gathered in an anonymous form from the hospital discharge charts. Furthermore, given that the study was retrospective and descriptive, it was not submitted to the Ethics Committee of our hospital.

### *Statistical analysis*

Since this was prevalently a study of descriptive epidemiology, no contrastive analysis was performed. Categorical variables are expressed as an absolute value and percentage.

## ■ RESULTS

### *Socio-demographic data*

Our immigrant population cohort presenting between July 2009 and June 2013 included 1218 patients (718 M and 500 F) with a mean age of  $35.6 \pm 11.4$  years. In 112 of them (72 M, 40 F: 9.2%) there was a diagnosis of "liver disease" on the SDO chart. Mean age of these subjects was  $36.4 \pm 10.2$  years (range 20-60). The percentage of patients with "liver disease" was almost constant over this period, with a slight increase in the last two years.

Table 1 shows the total number and relative percentages of all the immigrants and of the patients with chronic liver disease according to the three different areas of origin. More than two-thirds (67.8%) of the liver disease patients came from Africa, 15.2% were from Asia and 17.0% from Eastern Europe. The distribution of these patients by continent was identical to the continent distribution in the total immigrant population.

Table 2 shows the distribution of all liver disease patients by continent and subdivided according to etiology and sex. Seventy-two of the 112 patients were males and 40 females. These included 25 women and 51 men of African origin. Among the Asians there was only one woman and 16 men. In the Europeans, on the contrary, there were more women than men (14 women and 5 men), in line with the general epidemiological data on immigration from Eastern

**Table 1** - Total number and relative percentages of all immigrants and of patients with chronic liver disease in relation to the 3 different areas of origin.

	Africa		Asia		Eastern Europe	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Whole population	826	67.8	185	15.2	207	17.0
Pts with liver disease	76	67.8	17	15.2	19	17.0

**Table 2** - Distribution of patients by continent, sex and etiology.

Type/etiology	N.	Africa		Asia		Eastern Europe	
		M	F	M	F	M	F
HBV	50	23	11	7	0	1	8
HCV	17	6	4	4	0	1	2
Alcoholic	28	19	2	1	1	2	3
Cryptogenic	17	3	8	4	0	1	1
Total	112	51	25	16	1	5	14

European countries, which present a high majority of females. HBV-related liver disease was the most frequent etiology (44.6%), followed by alcoholic (25%) and HCV and cryptogenic causes (both 15.2%)

The most frequent African country (76 cases) was Ghana (35 cases), followed by Nigeria (9 cases) and the Ivory Coast (6 cases). 19 patients came from Eastern Europe (14 from Romania, 3 from Albania and 1 case each from both Poland and Serbia-Montenegro. The Asian patients (17 cases) came from Bangladesh (9 cases), Sri-Lanka (4 cases), Pakistan, India, China and the Philippines (1 case each).

#### ***Distribution of patients by etiology of liver disease***

**HBV** - Fifty patients (31M, 19F) were HBsAg positive. Thirty-four of these patients came from Africa, while only 16 were from other continents. The most frequent age range was from 20 to 40 years, corresponding to the general age of our immigrants.

**HCV** - Seventeen patients had a diagnosis of HCV-related chronic hepatitis. Ten were from Africa, four from Asia and three from Eastern Europe. Two patients were also alcoholics and were included in the alcoholic etiology group. The most frequent age range in this group of patients was also from 20 to 40, although 4 patients were aged over 50.

**Alcohol** - An unexpectedly high percentage of alcoholic liver disease was found: 28 out of 112

(25%). Men with ages ranging from 30 to 50 (23/28) were prevalent. Twenty-one came from Africa, two from Asia and 5 from Eastern Europe.

**Cryptogenic** - In 17 of the 112 patients etiology was not determined and their liver disease was labeled as "cryptogenic". The proportions of these patients were the same in the three continents, with no prevalence in terms of age (range 20-60 years). They were included in this group as other known causes of liver disease were absent and hypertransaminasemia had persisted for more than 6 months.

Liver biopsy had been performed in 46 patients (41.1%). Eight patients (2 with HBV, 3 cryptogenic and 3 alcoholic etiology) had varying degrees of liver steatosis on histological analysis. Twenty-nine cases (22 HBV, 5 HCV and 2 alcoholic) presented varying degrees of chronic liver disease severity, eight cases (4 HBV, 1 HCV, 3 alcoholic) had a definite picture of liver cirrhosis and there was 1 case of alcoholic hepatitis. Biopsies were not performed in two other cases because there was a clinically evident picture of liver cirrhosis.

## **DISCUSSION**

Immigrants form a heterogeneous group of subjects who suffer from numerous disadvantages, and their health status can only be correctly assessed if detailed medical data are

available. Analysis of our data showed a spectrum of agents responsible for liver disease which is not entirely comparable to that of Italian patients, as immigrants have been reported to have a higher prevalence of HBV-related liver diseases than HCV-related forms [5, 11]. In the general Italian population there has been a significant reduction in HBV-infected patients since the introduction of compulsory vaccination and modifications in lifestyle, while HBV is still the most prevalent cause of viral liver disease in the populations from endemic areas not yet reached by vaccination campaigns [1, 9, 12-14].

These people could represent a considerable reservoir of viral strains new to the Italian host population. However, our immigrant patients with HBV-related chronic liver disease, as reported in other Italian studies, were mostly concentrated around the age of 30, reflecting the higher rate of vertically transmitted HBV infection in their country of origin, while in Italy people up to this age are already protected thanks to the vaccination campaign [11, 14, 15]. In the Italian population HCV infection is still the main cause of viral liver disease [5]. As expected, in the immigrant population we found a lower percentage of HCV- than of HBV- infection. This finding is also consistent with other reports from Italy and with epidemiological data from the countries of origin, where, as already mentioned, HBV is more prevalent [8, 9, 13, 14].

However, HCV infection should not be underestimated, both because it very frequently evolves into chronic liver disease and also because immigrants can introduce genotypes different to the Italian ones, thus modifying the current local epidemiological profile. In fact, the majority of our infected patients were originally from Asia (Taiwan, Mongolia, Pakistan), sub-Saharan Africa (Cameroon, Burundi, Gabon) and Eastern Mediterranean countries (Egypt, with over 20%, had by far the highest frequency), where HCV genotypes other than those most frequently found in Italy prevail [16]. Unfortunately, in this study we had no data about the genotypes of our immigrant patients, so this statement needs to be confirmed. The 17 cases of HCV positivity may seem a small number if the entire immigrant study population is considered (17/1218, 1.4%) and also when compared with the Italian prevalence figure (2.6%) [4]. However, anti-HCV assay was not performed in all our immigrants,

therefore we do not know if there were in fact any cases of anti-HCV positivity, even with normal transaminase levels, in the population termed "without liver disease".

The presence of alcoholic liver disease points to a trend of increased alcohol consumption among immigrants, even in groups traditionally alcohol-free, like the younger age groups and Islamic or Hindu subjects [17]. Unlike those countries where migration is not a new phenomenon (such as the United States, Germany, Britain, France and Holland) in Italy the knowledge available on alcohol dependence among immigrants is limited and it is difficult to obtain accurate updates on a phenomenon which is constantly changing.

Alcohol consumption has connotations which differ according to the countries and cultures of origin, thus making it difficult to fully understand the phenomenon, and abuse often remains concealed, due to the lack of appropriate means and methods of investigation. Several studies have highlighted the health and social problems originating from alcohol abuse in immigrants, a problem which is also present in the Italian population, and to the same extent. [17, 18].

A total of 17 cases of liver disease (15.2%) were without a precise etiologic diagnosis, which is a substantial number. They included cases in which ultrasound scan showed varying degrees of fatty liver disease. Although the metabolic syndrome was not common in these patients (absence of obesity, hypertension, diabetes mellitus), steatosis was often present, therefore some of them may have presented a picture of this disease, which is now very common in western populations. The underlying cause of the other cases of steatosis may have been undeclared alcohol abuse.

At liver biopsy we found 8 cases of liver cirrhosis, which was only clinically evident in two cases. This confirmed that the migrant population is more often than not a healthy and young one and that there are few cases of clinically evident disease.

In conclusion, our study data show that liver disease was present in a sizeable proportion (9.2%) of our immigrant population cohort and that its principal cause is hepatitis B infection, which reflects epidemiology in the country of origin of these populations. Unfortunately, alcohol consumption is becoming more and more frequent among immigrants, likely related to the socio-cultural isolation experienced by

many of them, resulting from poor language skills, lack of friendship, economic resources and a family environment. We believe that it is therefore necessary to collect more precise information about the living and working conditions of immigrants if we wish to implement measures to prevent disease progression in individual patients, but also to prevent infection in their compatriots and in the host population. To this end, it would be advisable, for example,

to extend the hepatitis B vaccination campaign to include the immigrant populations that are permanently resident in Italy.

**Acknowledgement:** We wish to thank Ms. Carole Greenall for the revision of the English style.

**Keywords:** liver diseases, viral hepatitis, immigrants, developing countries, emerging infectious disease.

## SUMMARY

The objective of this study was to evaluate the frequency of liver disease and its aetiology in a cohort of immigrants. We retrospectively examined the hospital discharge charts of all the immigrant patients presenting at our day hospital from July 2009 to June 2013, and after evaluating the anamnestic, clinical and laboratory data on these charts we identified subjects with liver disease and its various aetiologies. The total sample population consisted of 1218 patients, of whom 112 (9.2%) had a diagnosis of liver disease. More than two-thirds of the latter (67.8%) came from Africa, while 15.2%

were from Asia and 17.0% from Eastern Europe. In most patients the disease was related to HBV (44.6%), followed by alcohol (25%) and then HCV or cryptogenic disease (both 15.2%). Forty-six patients had undergone liver biopsy, which showed eight cases of varying degrees of liver steatosis, 29 cases with a variable severity of chronic liver disease, eight cases with a definite picture of liver cirrhosis and one case of alcoholic hepatitis. These data show that a significant proportion of our immigrant population has liver disease and that the most frequent cause is hepatitis B infection.

## RIASSUNTO

*L'obiettivo di questo studio è stato quello di valutare la frequenza delle malattie di fegato e la loro etiologia in una coorte di popolazione immigrata.*

*Abbiamo analizzato retrospettivamente le cartelle cliniche di tutti i pazienti immigrati che si sono ricoverati in regime di day hospital tra luglio 2009 e giugno 2013 nel nostro servizio di Medicina delle migrazioni. Attraverso la rievitazione dei dati anamnestici, clinici e di laboratorio ci è stato possibile definire la frequenza e l'etiologia della malattia di fegato.*

*Il campione di popolazione totale è risultato di 1218 pazienti. Di essi, 112 (9,2%) avevano una diagnosi di malattia di fegato e poco più dei due terzi proveniva*

*dall'Africa (67,8%), il 15,2% dall'Asia ed il 17,0% dall'Est Europa. La malattia è risultata correlata con il virus dell'epatite B in quasi la metà dei casi (44,6%), seguita dall'abuso di alcool (25%) e poi dal virus dell'epatite C (15,2%) e da cause sconosciute (15,2%). Quarantasei pazienti sono stati sottoposti a biopsia del fegato che ha mostrato vari gradi di steatosi epatica in 8 casi, un grado variabile di epatite cronica in 29 casi, di epatite alcolica in 1 caso e di cirrosi epatica in 8 casi.*

*Questi dati dimostrano che una discreta proporzione della nostra popolazione di immigrati presenta una malattia di fegato e che la più importante causa di malattia è rappresentato dal virus dell'epatite B.*

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