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ORIGINAL ARTICLE | HEPATITIS C

Epidemiological, Clinical and Virological Characteristics of Patients with Hepatitis C in Morocco

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ABSTRACT

Objectives: In Morocco, the exact and recent prevalence of Hepatitis C Virus (HCV) infection is not well-known due to the lack of recent epidemiological studies of the general Moroccan population. The objective of this study was to determine the prevalence of HCV and to describe the epidemiological, clinical and virological characteristics of patients infected with HCV diagnosed at the Mohammed V Military Teaching Hospital in Rabat, Morocco.

Methods: This was a prospective study, spread over a period of 3 years (April 2015 - April 2018). All patients with a positive anti-HCV serology were included in the study except those on hemodialysis. In addition to HCV serology, all patients included were tested with HIV serology as well as the Hbs antigen by a Chemiluminescent type Microparticle Immunoassay technique (Architect[®], Abbott). RNA viral load and HCV genotyping were carried out using a real-time polymerase chain reaction.

Results: We collected 14,944 samples, of which 269 had positive anti-HCV antibodies (1.8%). The average age of patients with positive anti-HCV serology was 61 years, the sex ratio (Male/Female) was 1:4. Dental care was identified as the most common risk factor, (53% of the cases). Viral hepatitis C was identified in 82% of cases during a systematic check up. The main clinical signs reported in our series were asthenia (25% of cases) and subicterus (7% of cases).

Conclusion and Implications for Translation: In Morocco, the exact prevalence of HCV infection is not well known, due to the lack of recent epidemiological studies of the general Moroccan population. Our study showed a prevalence of about 1.8%, which is in accordance with the World Health Organization (WHO) estimation of between 1% and 2.49%. Our epidemiological study provides important information on the extent of the problem in Morocco, raises the interest in mass screening, and describes the populations at risk that will need to be identified as a priority.

Keywords: • Epidemiology • Diagnosis • Hepatitis C • Morocco • Risk factor • Military Hospital • Virology

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Résumé

Objectifs: Au Maroc, la prévalence exacte et actualisée de l'infection par le virus de l'hépatite C (VHC) n'est pas bien évaluée, en raison du manque d'études épidémiologiques récentes sur la population marocaine. L'objectif de cette étude a été de déterminer la prévalence du VHC et de décrire les caractéristiques épidémiologiques, cliniques et virologiques des patients infectés par le VHC diagnostiqués à l'Hôpital Militaire d'Instruction Mohammed V de Rabat, Maroc.

Méthodes: Il s'agit d'une étude prospective, menée sur une période de 3 ans (avril 2015 - avril 2018). Tous les patients avec une sérologie anti-VHC positive ont été inclus dans l'étude, sauf les patients hémodialysés. En plus de la sérologie VHC, tous les patients inclus ont bénéficié d'une sérologie VIH et d'une recherche de l'antigène Hbs par chimioluminescence (Architect®, Abbott). La charge virale du VHC le génotypage du VHC ont été effectués en utilisant une réaction en chaîne par polymérase en temps réel.

Résultats: Nous avons collecté 14,944 échantillons, dont 269 avaient des anticorps anti-VHC positifs (1,8%). L'âge moyen des patients avec une sérologie VHC positive était de 61 ans, le sex-ratio (Masculin/Féminin) était de 1,4. Les soins dentaires ont été identifiés dans 53% des cas. L'hépatite virale C a été identifiée dans 82% des cas lors d'un bilan systématique. Les principaux signes cliniques rapportés dans notre série étaient l'asthénie (25% des cas) et le sub-ictère (7% des cas).

Conclusion et implications pour la traduction: Notre étude a montré une prévalence d'environ 1,8% ce qui concorde à l'estimation de l'Organisation Mondiale de la Santé (OMS) comprise entre 1% et 2,49%. Notre étude épidémiologique fournit des informations importantes sur l'étendue du problème au Maroc, elle soulève l'intérêt du dépistage de masse et décrit les populations à risque qui devront être identifiées comme prioritaires.

Mots-clés: • Epidémiologie • Diagnostic • Hépatite C • Maroc • Facteur de risque • Hôpital Militaire

I. Background and Introduction

The Hepatitis C Virus (HCV) belongs to the family of *Flaviviridae*. It is an enveloped virus whose genome is a single-stranded RNA. Seven genotypes and several subtypes of HCV have been identified. Transmission of the virus is mainly parenteral and the infection will be chronic in 80% of cases,¹ which exposes patients to the risk of cirrhosis and hepatocellular carcinoma. Thus, hepatitis C is a major public health problem. The World Health Organization (WHO) estimates that 71 million people have chronic HCV.¹ Over the past five years, the management of HCV infection has been revolutionized by the advent of direct-acting antivirals (DAAs). These drugs, which inhibit the action of some viral proteins, such as the NS3 and NS5A protease inhibitors and the NS5B polymerase, have brought good tolerance and almost constant efficacy.¹ These therapeutic advances, as well as the significant morbidity and mortality from viral hepatitis, have motivated the establishment by WHO of a global strategy to combat viral hepatitis.¹

In Morocco, scattered studies report that seroprevalence of HCV in the general population

varies between 0.41 and 1.12%.² The objectives of this work were (1) to determine the prevalence of HCV in the population screened at the virology laboratory (Mohammed V Military Teaching Hospital (MVMTH), Rabat, Morocco), and (2) to describe the epidemiological and virological characteristics of patients infected by HCV.

2. Methods

2.1. Study Area

This was a prospective study carried out in the virology laboratory of the Mohamed V Military Instructional Hospital, spread over a period of 3 years (April 2015 - April 2018). All inpatients and outpatients with a positive "anti-HCV antibody" serology were included in the study. Hemodialysis patients affected by hepatitis C were excluded.

2.2. Study Design

The data were collected using a questionnaire comprise of the following items: last and first name, age, geographic origin, job, medical and surgical history, circumstances of HCV discovery,

initial symptomatology, and HCV risk factors. After informed, oral consent was obtained from each participant, we collected the data while respecting the anonymity of the patients.

2.3. Sampling and Data Analysis

During our study, we provided for all patients a dry tube for the detection of anti-HCV antibodies, HBs Antigen (HBsAg) as well as of the p24 Antigen and the anti-HIV antibodies 1 and 2 and two Ethylenediaminetetraacetic acid (EDTA) tubes for molecular biology tests (HCV RNA and genotyping). The samples were centrifuged for 20 min at 4000 rpm; the sera were stored at + 4 ° C; and the plasmas were stored at – 20°C. The investigation for anti-HCV antibodies was carried out by a Chemi-luminescent technique Microparticle Immunoassay (Architect®, Abbott) for hospitalized patients. HCV RNA viral load in blood was carried out using a real-time polymerase chain reaction (RT-PCR) on the Cobas Ampliprep/ Cobas Taq Man (Roche®) for patients with positive HCV serology. HCV genotyping was carried out using Cobas® HCV GT kit on the Cobas 4800 (Roche®) for patients with viral load of >250 copies/ml. Other biological data were extracted from the laboratory Information System (Alanine amino-transferase (ALT)). Statistical analysis was performed using SPSS® software version 13.0 (IBM). The comparative study was carried out by the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Sociodemographic Characteristics

We collected data for 14,944 samples of which 269 had positive anti-HCV antibodies which meant a seroprevalence of 1.8%. One hundred thirty two (0.88%) of these patients had a positive viral load which confirms current HCV infection. The average age of the patients was 61 years (28 – 95 years). Patients who were older than or equal to 50 years were the most affected by HCV. The 27-34 years and 35-49 years age groups were the least affected by HCV. No cases of HCV infection were found in patients younger than 24 years of age. Male

predominance (58%) was noted with a sex ratio of Male/Female of 1:4. The majority of the patients with positive anti-HCV antibodies (36%) were retirees from the Royal Armed Forces of Morocco.

3.2. Hepatitis C Infection

The discovery of the HCV infection was fortuitous (during a systematic screening, proficiency visit or pre-nuptial check-up) in 82% of the cases. Twenty patients (7%) were referred by the transfusion center following the discovery of a positive anti-HCV serology. The symptomatic form was found in 12% of the cases. The most frequently reported clinical sign in our study was asthenia (6%) followed by jaundice (3%).

Diabetic and hypertensive patients represented 37% and 18% of patients with positive anti-HCV antibodies, respectively. Diabetes was more common in patients over the age of 50 years ($p = 0.015$).

3.3. Hepatitis C Risk Factors

A potential risk factor for HCV infection was identified in 92% of patients with positive anti-HCV serology. The most common risk factor was dental care (53%) and surgical history (28%). In addition, blood transfusion, dental care and surgical history have been strongly associated with the acquisition of HCV infection in patients over the age of 50 years ($p < 0.05$) (Table I).

3.4. Viral Load

A high viral load ($\geq 800,000$ IU/ml) was found in 136 cases or 51% of the patients. A medium (2,000 – 800,000 IU/ml) or low viral load ($\leq 2,000$ IU/ml) was found in 21 (7%) patients. A high initial viremia was significantly more frequent in male patients with an age greater than or equal to 50 years ($p < 0.05$). A high viral load was strongly noted in patients with a history of surgery, transfusion or dental care ($p < 0.05$). Undetectable viremia was found in 112 (42%) patients.

3.5. Genotyping

Genotyping was performed in 269 patients. Genotype 1b was predominant (80% of cases) followed by genotypes 2a/2c and 1a (7%). Genotype 1b was significantly more common in

Table 1: Distribution of Hepatitis C serological markers and principal risk factors in the study population

Characteristic		HCV Positive Subjects		HCV Negative Subjects		p-value
		N	%	N	%	
Total: 14,944		269	1.8	14,675	98.2	
Age (years)	<23	0	0	1,614	11.0	p<0.05 (for patients aged 50 or over)
	24-34	11	4	3,669	25.0	
	35 – 49	43	16	7,924	54.0	
	≥50	215	80	1,468	10.0	
Sex	Female	113	42	5,723	39.0	p=0.1
	Male	156	58	8,952	61.0	
Dental care	No	126	47	4,256	29.0	p<0.05 (for patients aged 50 or over)
	Yes	143	53	10,419	71.0	
Blood transfusion	No	240	89	12,767	87.0	p<0.05 (for patients aged 50 or over)
	Yes	29	11	1,908	13.0	
Surgical history	No	194	72	6,017	41.0	p<0.05 (for patients aged 50 or over)
	Yes	75	28	8,658	59.0	
Tattoos	No	261	97	14,235	97.0	p<0.3
	Yes	8	3	440	3.0	

men than in women and in patients with a high viral load ($\geq 800,000$ IU/ml) ($p < 0.05$). More than half of the patients (56%) with positive anti-HCV serology had an ALT level ≥ 2 to 3 times, mainly in men aged 50 years or over ($p < 0.05$). In our study, only one case of HCV-HBV co-infection was diagnosed. No patient had a positive HIV serology.

4. Discussion

This was a single-center study carried out at the virology laboratory of the Mohammed V Military Teaching Hospital (MVMTH) and which concerned screening of 14,944 samples of which 269 patients has positive anti-HCV serology. The average age of patients with positive anti-HCV serology was 61 years. It is, therefore, an elderly population, which is consistent with published data in the literature.³ In our study, the advanced age of our patients could be explained by the nature of the population followed at the MVMTH, the latter being made up in large part of retired soldiers (33% in our series). Predominance of men has been reported with percentage up to 67%.⁴

In Morocco, the exact prevalence of HCV infection is not well known, due to the lack of recent epidemiological studies of the general Moroccan population. According to WHO data, the seroprevalence of HCV in Morocco varies between 1% and 2.49%.⁵ In our study, the seroprevalence of HCV was 1.8%. Benjelloun and colleagues reported that, in the general population, represented by parturient women and the military population, the seroprevalence of HCV was 1% and 0.5%, respectively.⁵ In another Moroccan study, where the general population was represented by people insured by the various national insurance funds, the seroprevalence of HCV varied from 0.9 to 1.2%.⁶ This rate remains close to that reported among Moroccan blood donors, which is 1.1%.⁷ The seroprevalence reported by our study remains lower than that reported in the Mediterranean region (2.4%) and close to that reported in the European region (1.5%).^{5,8}

In our study, viral hepatitis C was discovered in 82% of cases during a systematic assessment, in 11% of cases following a symptomatology, in 7%

of cases following a blood donation, and in 0.74% following a prenuptial check-up. In comparison, in Algeria, viral hepatitis C was discovered in 31% of cases following a systematic check-up, in 8% of cases following a prenuptial check-up, in 5% of cases following a blood donation, and in 28% of cases following symptomatology.⁹ In Tunisia, viral hepatitis C was discovered during a blood donation in 1.09% of cases.⁵ In France, hepatitis C was discovered in 46.2% of cases during a blood donation and in 56.8% of cases during a systematic assessment.¹⁰

In the current study, transfusion was implicated in 11% of patients over the age of 50 years and in males ($p < 0.05$). In a previous Moroccan study, this mode of transmission was identified in 21.7% of cases.¹¹ The development of transfusion safety measures based essentially on serological techniques has made it possible to considerably reduce the risks of HCV transmission. Nevertheless, a residual risk, although very low, remains to this day due to the existence of a silent window, a period during which the serological markers systematically screened are not detectable. New molecular techniques have made it possible to envisage viral genomic screening. This approach ensures earlier detection of viral RNA in a subject carrying the virus. The use of these technologies in Morocco could detect DNA or RNA when the antigen/antibody serology tests may be negative.^{12,13}

Dental care was implicated in 53% of the cases. This factor was significantly linked to the acquisition of HCV infection in patients ≥ 50 years of age ($p < 0.05$). A Maghrebian study has reported that this mode of contamination was suspected respectively in 24.7% of cases.¹⁴ For our study, this could be explained by the use in the past decade of non-sterile equipment for surgical procedures in situations of peacekeeping operations. The tattoo represents in our sample only a small proportion. This is probably the consequence of the significant regression of this habit due to a change in the conception of beauty and improvement in socio-cultural level. In some countries where tattooing is experiencing a renewed interest, this mode of HCV transmission was widely described (51% of cases in Canada).¹⁵ Furthermore, intravenous drug addiction generally constitutes a major mode of contamination with frequencies of

up to 81% of cases according to studies carried out in Europe and Canada.^{14,15,16} In our study, no case of intravenous drug use was identified, which could be explained by the fact that drug addiction constitutes a taboo that is difficult to admit.

French studies have reported 20% of HIV-HCV co-infection; this high rate can be explained by the fact that the modes of transmission are similar, in particular in drug addiction and unprotected sex.¹⁷ The HCV-HIV association frequently reported in the literature was rare in our context, probably because drug addiction or unprotected sex were underreported in our context. The rate of HCV-HBV co-infections in our study was 0.4%. This may be explained by the systematic vaccination against hepatitis B of young military recruits and also by the awareness campaigns against sexually transmitted diseases at the level of military units. In our study, the most common genotype was 1b (80% of cases). In Morocco, the most common genotype is genotype 1, followed by genotypes 2 and 4.¹⁸ Our study had some limitations. It was a single-center study. Access to clinical records was often difficult, making it impossible to analyze certain variables (virological response to treatment, histological data, adverse effects and resistance to treatment). Nevertheless, our study made it possible to describe the main epidemiological, clinical and virological characteristics of our study population. The aim is to better meet the WHO objective of eradicating this disease in 2030.¹

5. Conclusion and Implications for Translation

Viral hepatitis C is a major public health problem, on the one hand because of its frequency and on the other hand because of its complications with the risks of progression to cirrhosis and hepatocellular carcinoma. WHO has proposed a global strategy for the eradication of HCV in 2030. Faced with this international commitment to viral hepatitis (VH), Morocco has developed the first National Strategic Plan against VH for the period 2016-2021. The aim of this plan is to reduce the transmission of VH, as well as the mortality linked to VH by 30% and the prevalence of chronic HCV infections by 35% in 2021

with a view to eliminating HCV in Morocco in 2030. In this context, epidemiological studies are of major importance, since they provide a clear picture of the extent of the problem in our country. Our study promotes interest in mass screening and describes the populations at risk that will need to be identified as a priority. Prevention, in particular respecting the universal recommendations for the use of medical and paramedical equipment, as well as education and awareness-raising, are the best methods to halt the spread of this virus.

Compliance with Ethical Standards

Conflicts of interest: None. **Financial Disclosure:** Nothing to declare. **Funding/Support:** None. **Ethics Approval:** Ethics approval was not required for this study. **Acknowledgments:** None. **Disclaimer:** None.

Key Messages

- ▶ Mass screening with priority to people at risk can be a potential key for eradicating Hepatitis C Virus (HCV) in Morocco.
- ▶ In Morocco, viral genomic detection must be generalized with a view to eradication of HCV.
- ▶ Prevention measures, in particular in medical environment, as well as education are important to halt the spread of HCV.

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