

# Serology for Hepatitis B and C, HIV and syphilis in the initial evaluation of diabetes patients referred for an external Nephrology consultation

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## ABSTRACT

**Introduction:** Information is available regarding the prevalence and incidence of positive microbiological serology results both in the general population and in patients on haemodialysis in Spain. Nevertheless, little information is known regarding patients with diabetes attended in external nephrology consultations. **Objective:** To evaluate the percentage of patients with positive serology results for hepatitis B and C, Human Immunodeficiency Virus (HIV), and syphilis in the initial assessment of patients referred to diabetic nephropathy external consultations. **Patients and method:** Retrospective study of 500 patients assessed over the course of 5 years with the diagnosis of diabetic nephropathy originating in external consultations and for which hepatitis B, C, HIV, and syphilis serology had been requested. **Results:** With regard to hepatitis B virus, 0.4% of patients had chronic hepatitis B, 10.2% had overcome the hepatitis and were in recovery, and 4.2% had received the hepatitis B vaccine. As for hepatitis C, 2.4% of the patients studied had antibodies against hepatitis C. With regard to syphilis, 0.8% of patients had positive serological results. No patients had positive HIV serology results. **Conclusions:** Despite major methodological limitations, this would be the first study to evaluate the microbiological serology of diabetic nephropathy patients treated in external consultations.

**Keywords:** Diabetic nephropathy. Hepatitis B. Hepatitis C. HIV. Syphilis.

*Serologías B, C, VIH y sífilis en la primera valoración de pacientes con diabetes remitidos a consulta externa de Nefrología*

## RESUMEN

**Antecedentes:** En España hay datos sobre prevalencia e incidencia de serologías microbiológicas positivas tanto en la población general como en pacientes en hemodiálisis. Sin embargo, se conocen pocos datos sobre los pacientes con diabetes atendidos en consulta externa de Nefrología. **Objetivo:** Valorar el porcentaje de pacientes con serologías positivas para hepatitis B y C, virus de inmunodeficiencia humana (VIH) y sífilis en la valoración inicial de los pacientes remitidos para estudio a la consulta externa de nefropatía diabética. **Pacientes y métodos:** Estudio retrospectivo de las serologías solicitadas con el diagnóstico de nefropatía diabética con origen en consultas externas de 500 pacientes valorados durante 5 años a los que se les había solicitado serologías de la hepatitis B, C, VIH y sífilis. **Resultados:** Respecto al virus de la hepatitis B, el 0,4 % de los pacientes tenían hepatitis B crónica, el 10,2 % había pasado la hepatitis y estaban curados y el 4,2 % había recibido la vacuna de la hepatitis B. En cuanto a la hepatitis C, el 2,4 % de los pacientes estudiados tenían anticuerpos frente hepatitis C. Respecto a la sífilis, el 0,8 % de los pacientes tenían serologías positivas. Ningún paciente presentó serologías positivas para VIH. **Conclusiones:** Si bien con grandes limitaciones metodológicas, este sería el primer estudio donde se revisan las serologías microbiológicas de pacientes con nefropatía diabética atendidos en consulta externa.

**Palabras clave:** Nefropatía diabética. Hepatitis B. Hepatitis C. VIH. Sífilis.

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## INTRODUCTION

In the general population in Spain, the prevalence of hepatitis C virus (HCV) antibodies ranges between 1.6% and

2.6%,<sup>1</sup> with rates of 2%-7% reported for hepatitis B virus (HBV).<sup>2</sup> The incidence rate of syphilis in 2010 was 6.39/100 000 inhabitants, and the Canary Islands had the highest syphilis rate in Spain (12.71/100 000).<sup>3</sup>

The prevalence of chronic HCV infection in patients with stage 5 chronic kidney disease is higher than in the general population. In patients on haemodialysis, the prevalence rate is estimated at 13%, with a wide variability among geographic regions (1%-70%)<sup>4</sup> and among dialysis units within the same country. In Spain, the prevalence of HCV infection in patients on haemodialysis in 1997-2001 was estimated at 22%.<sup>5</sup>

In Greece, 5% of patients on haemodialysis are positive for hepatitis B surface antigen.<sup>6</sup> In addition, a recent publication showed that all diabetic patients between the ages of 19 and 59 years should receive the hepatitis B vaccine, leaving the vaccination of patients older than 60 years of age up to the criteria of the attending physician.<sup>7</sup>

In a review of the relevant medical literature, we have found no information regarding the incidence of syphilis in chronic renal failure patients.

With this in mind, the objective of our study was to evaluate the percentage of patients with positive serological tests for hepatitis B and C, human immunodeficiency virus (HIV), and syphilis in the initial assessment of patients referred to external consultation for diabetic nephropathy.

## PATIENTS AND METHOD

Ours was a retrospective study of the serological tests requested for diabetic patients referred for an evaluation for diabetic nephropathy upon their first visit to nephrological external consultations (southern region of Grand Canary Island). We compiled the results of serological analyses supplied by the microbiology department at our hospital (started 5 July 2007) until the study date (10 November 2011). Serology tests had been requested for a total of 500 patients (297 males and 203 females) within this period. However, our study did not include all patients evaluated for the first time in external consultations for diabetic nephropathy during this period, only those requested in the name of the attending physician, since many requests are made by residents on rotation in various medical specialties. We also compiled biochemical results from urine and blood tests taken on the same date as the serology tests for each patient. For hepatitis B, we examined the results for hepatitis B surface antigen (HBsAg), total antibodies against core antigen (anti-HBc), IgM antibodies against core antigen of the hepatitis B virus (anti-HBcIgM), 'e' antigen (HBeAg), antibodies against e antigen (anti-HBe), and antibodies against hepatitis B surface antigen (anti-HBs). In cases in

which the value for HBsAg was very low and we had to rule out a false positive, we performed a confirmation test for surface antigen (neutralisation). For hepatitis C, we examined levels of hepatitis C antibodies (anti-HCV), and if the test was positive, we performed a confirmation test using a LIA<sup>®</sup> line immunoassay test in order to rule out a false positive. For HIV, some patients were only tested for antibodies (anti-HIV), and more recent patients were tested for both anti-HIV and p24 antigen, which allows for early detection of cases in which antibodies are still undetectable. In accordance with laboratory protocol, in cases of positive test results for anti-HIV, we performed a confirmation test using LIA<sup>®</sup> line immunoassay. For syphilis, a rapid plasma reagin test (RPR), was performed, as well as a fluorescent treponemal antibody test (FTA); to rule out false positives, a confirmation test using LIA<sup>®</sup> line immunoassays was performed.

Patients were subdivided into three categories based on hepatitis B serology results: chronic hepatitis B (HBsAg and anti-HBc positive, with or without HBeAg), resolved or cured hepatitis B (HBsAg negative and anti-HBc positive), and vaccinated against hepatitis B (anti-HBs positive with seronegativity for HBsAg and anti-HBc).

We reviewed the clinical histories of all patients with positive serology results (transaminase, whether or not treatment was given and response to treatment, and ultrasound with or without signs of portal hypertension).

We used SPSS statistical software, version 15.0, for all statistical analyses.

## RESULTS

We examined the serological results from tests requested upon the first evaluation of 500 patients (297 males and 203 females) with diabetes mellitus (95% with type 2 DM) referred for nephrological pathology analysis in nephrology external consultations. The mean patient age was  $61.58 \pm 13.97$  years (range: 15-87 years). From a nephrological point of view, 137 patients (27.4%) had an MDRD4 glomerular filtration rate (GFR) >60ml/min, and the rest had an MDRD4 GFR <60ml/min (mean:  $39.17 \pm 12.99$ ml/min) (57% with stage 3 chronic renal failure [CRF], 14.6% with stage 4 CRF, and 1% with stage 5 CRF); mean serum creatinine was  $1.56 \pm 0.67$ mg/dl, and mean proteinuria was  $1.20 \pm 2.13$ g/24 hours.

Seventeen patients were positive for anti-HCV, but only 12 were positive in the confirmation test. The 12 patients (7 males and 5 females) with positive anti-HCV and confirmation test results had a mean age of  $60.44 \pm 15.52$  years; only one patient had elevated transaminase levels, 2 patients had signs of portal hypertension in ultrasound tests, and only 2 patients received anti-viral treatment with

negative results from tests taken later for HCV. One patient was treated with interferon alpha and ribavirin, and the other was treated with pegylated interferon and ribavirin.

Positive FTA and RPR were observed in 5 patients (3 males and 2 females; mean age:  $61.80 \pm 10.52$  years). All five patients received treatment.

Two patients (one male and one female) had chronic hepatitis B, 51 patients (34 males and 17 females; mean age:  $61.70 \pm 13.26$  years) had resolved or cured hepatitis, and 21 patients (15 males and 16 females; mean age:  $60.20 \pm 16.58$  years) had been vaccinated. The two patients with chronic hepatitis B had normal transaminase levels.

One patient who disappeared from the follow-up programme had positive anti-HCV and HBsAg. No patients had positive anti-HIV serology.

## DISCUSSION

In a recent study from the United States, of 29 patients diagnosed with acute hepatitis B, 25 were diabetic,<sup>7</sup> which led to the analysis of risk of infection by hepatitis B virus (HBV) among diabetic patients. The authors found that, in patients with no risk behaviours for HBV and aged 23-59 years, diabetics were 1.2 times more likely to be infected than those without diabetes.<sup>7</sup> On 25 October 2011, the Hepatitis Vaccines Work Group of the Advisory Committee on Immunization Practices (ACIP) of the United States recommended that all patients with diabetes mellitus (types 1 and 2) between the ages of 19 and 59 years should receive the hepatitis B vaccine as soon as possible after being diagnosed with diabetes mellitus (category A recommendation). Given the fact that data regarding HBV infection in patients older than 60 years of age are still unclear, the ACIP left the choice of whether or not to vaccinate these patients in the hands of the attending physician. Approximately 15% of patients with chronic HBV infection will develop cirrhosis or hepatocarcinoma.<sup>8</sup> In our study population, 10.6% of patients had been in contact with HBV, 0.4% became chronic carriers and the rest recovered. No patients had cirrhosis or hepatocarcinoma. Only 4.2% had received vaccines, a very small percentage for an at-risk population such as diabetic patients.

As regards HCV, only 2.4% of patients studied over the 5-year period had positive hepatitis C antibodies. Since our study did not examine annual prevalence or cumulative incidence, our results would not be compared with the results from the general population or with results from chronic renal failure patients. If we suppose that the number of new cases is the same every year, we would obtain 0.48% of new patients per year. We must point out that two (16.6%) of the patients with hepatitis C already had signs of cirrhosis

or portal hypertension in the abdominal ultrasound. The first observation that patients with cirrhosis and HCV infections had diabetes at a greater frequency than patients with cirrhosis of another aetiology was published in 1994,<sup>9</sup> and later studies also confirmed this finding.<sup>10-12</sup> In this context, elevated levels of glycaemia as hyperinsulinaemia and insulin resistance have been associated with increased fibrosis in chronic hepatitis C; in addition, the progression of hepatitis C is faster in diabetic patients.<sup>13-16</sup>

Finally, only 4 of the 500 patients studied over the 5-year period had positive serology results for syphilis. Syphilis must be included in the differential diagnosis for diabetic patients with diabetic nephropathy and with distal and symmetrical motor and sensory deficits.<sup>17</sup> From a cardiovascular point of view, 10% of patients with syphilis can develop aortic insufficiency, coronary ostial stenosis, or aortic aneurysms.<sup>18</sup> From a nephrological point of view, nephropathy can arise both in congenital syphilis and secondary syphilis. The most common form is nephrotic syndrome secondary to membranous glomerulonephritis with subepithelial IgG and complement deposits, having previously demonstrated the presence of both treponemal antigen and anti-treponemal antibodies in glomerular lesions.<sup>19,20</sup> Tubulo-interstitial nephritis is also common, and treatment with penicillin leads to a rapid resolution of the nephropathy.

In summary, the primary findings of this study are that 0.4% of patients had chronic hepatitis B, 10.2% had been cured of hepatitis B, 4.2% had received the hepatitis B vaccine, 2.4% had antibodies against hepatitis C, and 0.8% had positive serology tests for syphilis. As such, while the frequency of hepatitis C is similar to that of the general population, the percentage of patients with antibodies against HBV is greater than in the general population. The two patients with cirrhosis and portal hypertension had hepatitis C.

In the medical literature reviewed, we have not found any studies that examine the microbiological serology of diabetic patients with nephrological pathologies that are attended in external consultations. As such, and despite the major methodological limitations implied, this would be the first study in which these components are studied. Diabetic nephropathy is an ever-increasing preoccupation for nephrologists, and well-designed studies that aid in the in-depth analysis of these patients could be very helpful. It would also be interesting to evaluate the response of patients with diabetic nephropathy to antiviral treatment.

To conclude, diabetic patients referred to nephrology external consultations in the southern region of Grand Canary Island have a similar percentage of individuals with HCV antibodies as the general population, but the percentage of individuals with HBV antibodies is greater than in the general population. Given that only two patients

had HBsAg, we must still examine whether this would justify the vaccination of all diabetic patients referred to our practice.

### Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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