ORIGINAL

First influenza season after the 2009 pandemic influenza: report of the first 300 ICU admissions in Spain


Introduction: During the 2009 influenza pandemic, several reports were published, nevertheless, data on the clinical profiles of critically ill patients with the new virus infection during this second outbreak are still lacking.

Material methods: Prospective, observational, multi-center study conducted in 148 Spanish intensive care units (ICU) during epidemiological weeks 50-52 of 2010 and weeks 1-4 of 2011.

Results: Three hundred patients admitted to an intensive care unit (ICU) with confirmed An/H1N1 infection were analyzed. The median age was 49 years [IQR = 38-58] and 62% were male. The mean APACHE II score was 16.9 ± 7.5 and the mean SOFA score was 6.3 ± 3.5 on admission. Comorbidities were present in 76% (n = 228) of cases and 111 (37.4%) patients were male. The mean APACHE II score was 16.9 ± 7.5 and the mean SOFA score was 6.3 ± 3.5 on admission. Comorbidities were present in 76% (n = 228) of cases and 111 (37.4%) patients were male.

KEYWORDS
An/H1N1 influenza; Critically ill patients; Prognostic

Abstract

Introduction: During the 2009 influenza pandemic, several reports were published, nevertheless, data on the clinical profiles of critically ill patients with the new virus infection during this second outbreak are still lacking.

Material methods: Prospective, observational, multi-center study conducted in 148 Spanish intensive care units (ICU) during epidemiological weeks 50-52 of 2010 and weeks 1-4 of 2011.

Results: Three hundred patients admitted to an intensive care unit (ICU) with confirmed An/H1N1 infection were analyzed. The median age was 49 years [IQR = 38-58] and 62% were male. The mean APACHE II score was 16.9 ± 7.5 and the mean SOFA score was 6.3 ± 3.5 on admission. Comorbidities were present in 76% (n = 228) of cases and 111 (37.4%) patients were male. The mean APACHE II score was 16.9 ± 7.5 and the mean SOFA score was 6.3 ± 3.5 on admission. Comorbidities were present in 76% (n = 228) of cases and 111 (37.4%) patients were male.

Received 8 March 2011; accepted 10 March 2011
Available online 14 April 2011

0210-5691/$ - see front matter © 2011 Elsevier España, S.L. and SEMICYUC. All rights reserved.
doi:10.1016/j.medin.2011.03.001
Introduction

During the 2009 influenza pandemic caused by the A(H1N1) 2009 virus, several reports were published regarding the presentation of this disease with severe acute respiratory symptoms in hospitalized patients. Rapidly progressive viral pneumonia represents the primary cause of intensive care unit admission with mortality rates ranging from 17.3% to 46% among different sites. During the 2009 influenza pandemic caused by the A(H1N1) virus, several reports were published regarding the presentation of this disease with severe acute respiratory symptoms in hospitalized patients. Rapidly progressive viral pneumonia represents the primary cause of intensive care unit admission with mortality rates ranging from 17.3% to 46% among different sites. This disease represented a challenge for critical care physicians worldwide. In the 2010-11 winter a seasonal outbreak of influenza has been detected in Spain with most cases caused by the former A/H1N1 2009 pandemic virus, currently called "new A/H1N1 virus" (An/H1N1). Data on the clinical profiles of critically ill patients with the virus An/H1N1 infection during this outbreak are still lacking. Here, we present our experience in a series of the first 300 critically ill patients admitted to Spanish ICUs.

Material and methods

This prospective, observational cohort study of ICU patients was conducted across 148 ICUs in Spain. Data were obtained from a voluntary registry created by the Spanish Society for Research on Infectious Disease (REIPI) and the Spanish Biomedical Research Center Network for Research on Infectious Disease (CIBERES). The study was approved by the Joan XXIII University Hospital Ethics Committee (IRB NEUMAGRIP/11809). Patient identification remained anonymous and the informed consent requirement was waived due to the observational nature of the study.

Data were reported by the attending physician reviewing medical charts and radiological and laboratory records. In this case series, data on all patients within the cohort consecutively diagnosed with An/H1N1 influenza between epidemiological weeks 50-52 of 2010 and weeks 1-4 of 2011 are presented (fig. 1). Children under 15...
Patients who presented healthcare-associated infections occurring later were considered to be “vaccinated”. Definition of Hospital-Acquired Pneumonia (HAP) was based on current American Thoracic Society and Infectious Disease Society of America guidelines. Patients who presented healthcare-associated pneumonia (HCAP) were excluded from the present study. Obese patients were defined as those with a body mass index (BMI) over 30.

### Definitions

Primary viral pneumonia was defined in patients presenting illness with acute respiratory distress and unequivocal alveolar opacities involving two or more lobes with negative respiratory and blood bacterial cultures during the acute phase of influenza virus infection.

Community-Acquired Respiratory Co-infection (CARC) was defined as any infection diagnosed within the first 2 days of hospitalization. Infections occurring later were considered nosocomial. Definition of Hospital-Acquired Pneumoniae (HAP) was based on current American Thoracic Society and Infectious Disease Society of America guidelines. Patients who presented healthcare-associated pneumonia (HCAP) were excluded from the present study. Obese patients were defined as those with a body mass index (BMI) over 30.

Patient who had previously received Influenza A (H1N1) 2009 monovalent or seasonal influenza 2010-11 vaccination were considered to be "vaccinated".

### Statistical analysis

Discrete variables are expressed as counts (percentage) and continuous variables as means ± standard deviation (SD) or medians [25th to 75th interquartile range (IQR)]. For the demographic and clinical characteristics of the patients, differences between groups were assessed using the χ² test and Fisher’s exact test for categorical variables and the Student’s t-test or Mann-Whitney U test for continuous variables. Stepwise logistic regression analysis was used to determine the impact of each variable on ICU mortality. The variables included in the multivariate model were those that showed significant differences in the univariate analysis (Table 2), including the variable “vaccination condition” due to its potential clinical interest. Risk is expressed as odds ratio (OR) and its 95% confidence interval (CI).

Data analyses were performed using SPSS 15.0 for windows (SPSS, Chicago, IL, USA). Values of P < .05 were considered to indicate statistical significance.

### Results

Data from the first 300 adults admitted to Spanish ICUs during the winter of 2010-11 due to An/H1N1 infection are the focus of the present report. Patients were young (median 49 years) and 62% were male. The mean APACHE II score was 16.9 ± 7.5 and the mean SOFA score was 6.3 ± 3.5 on admission. The baseline characteristics of the population are shown in Table 1. Comorbidities were present in 76% (n = 228) of cases. The main comorbid condition reported was obesity in 111 patients (37.4%) followed by chronic obstructive pulmonary disease (COPD) (n = 59; 20%), diabetes mellitus (n = 45; 15.2%) and haematological disease (n = 37, 12.5%) (fig. 2).

The main presentation was viral pneumonia with severe hypoxemia that was present in 65.7% (n = 197) of the patients. Forty (13.3%) patients had COPD exacerbation or severe asthma, and CARC was identified in 54 (18%) patients. Streptococcus pneunmoniae (n = 21), Pseudomonas aeruginosa (n = 6), Staphylococcus aureus (n = 6) and Streptococcus pyogenes (n = 4) were the most frequent microorganisms isolated.

Two-hundred and thirty-seven patients (79%) required mechanical ventilation (MV). Non-invasive ventilation was used in 105 (35%), and failed in 53 patients (50.5%). One-hundred fifty-three patients (51.0%) received renal replacement techniques.

All patients received antiviral treatment for a median duration of 7 [6-10] days, which was initiated empirically in 194 patients (65.3%). Two-hundred and eighty-five (95%) received oseltamivir, whereas zanamivir was administered in 15 (5%) patients. Finally, eight patients (2.7%) received both antiviral drugs. The median time between the onset of symptoms and the first administered antiviral dose was 5 [3-7] days, with a dose of 75 mg/day in 50.3% (n = 151) of cases. Only 53 patients (17.6%) received early antiviral treatment (<48 h from symptoms onset).

One-hundred and thirty-one patients (43.6%) received early corticosteroid therapy at ICU admission for a median of 7 [4-11] days, with a dose of 400 mg/day in 95 patients (31.7%). The ICU admission criteria and treatment decisions for all patients, including determination of the need for intubation and type of antibiotic or antiviral therapy administered, were not standardized and were made by the attending physician. Systemic corticosteroid use was implemented when patients developed shock (hydrocortisone), or coadjuvant treatment was used for pneumonia (methylprednisolone). Orally administered oseltamivir (150 mg/24 h or 300 mg/24 h) or intravenous zanamivir (600 mg/12 h) was chosen by the attending physician.

### Figure 1

Number of confirmed cases of An/H1N1 virus infection admitted to intensive care unit and clinical attack rate in Spain (solid line).
duration of 7 [5-10], with 10.6% (n = 32) representing coadjuvant therapy for septic shock. Interestingly, 278 (92.6%) of the patients had not been vaccinated. Vaccinated patients were older ($P < .05$) and with higher delay between hospital and ICU admission (Table 1). No significant differences in comorbidities were observed between patients with or without vaccination (Fig. 2).

![Figure 2](image-url)  
* Figure 2 Most common comorbidities reported in confirmed cases of An/H1N1 virus infections, differentiating vaccinated patients from those who were not. CF: cardiovascular disease; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; HD: hematological disease; HIV: human immunodeficiency virus infection; NM disease: neuromuscular disease.
Table 2  Clinical characteristics of patients with infection by influenza A(H1N1) virus (only in 200 patients discharged from ICU).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survival (n = 133)</th>
<th>Non-survival (n = 67)</th>
<th>P-value</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>48.7 (14.9)</td>
<td>50.0 (13.5)</td>
<td>.34</td>
<td>—</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>83 (62.4)</td>
<td>46 (68.7)</td>
<td>.38</td>
<td>—</td>
</tr>
<tr>
<td>APACHE II score at day 1, mean (SD)</td>
<td>14.2 (6)</td>
<td>21.8 (7.8)</td>
<td>&lt;.001</td>
<td>—</td>
</tr>
<tr>
<td>SOFA score at day 1, mean (SD)</td>
<td>4.6 (2.6)</td>
<td>8.6 (3.9)</td>
<td>&lt;.001</td>
<td>—</td>
</tr>
<tr>
<td>Time between onset symptoms and hospital admission in days, mean (SD)</td>
<td>4.5 (3.2)</td>
<td>5.2 (3.7)</td>
<td>.2</td>
<td>—</td>
</tr>
<tr>
<td>Time between hospital admission and ICU admission in days, mean (SD)</td>
<td>1.8 (2.2)</td>
<td>2.6 (3.4)</td>
<td>.06</td>
<td>—</td>
</tr>
<tr>
<td>Quadrants infiltrated in chest X-ray at ICU admission, mean (SD)</td>
<td>2 (1.2)</td>
<td>2.7 (1)</td>
<td>&lt;.001</td>
<td>—</td>
</tr>
<tr>
<td>Invasive Mechanical ventilation, n (%)</td>
<td>55 (42)</td>
<td>62 (92.5)</td>
<td>&lt;.001</td>
<td>1.9 (1.6-2.4)</td>
</tr>
<tr>
<td>Prone ventilation, n (%)</td>
<td>13 (9.8)</td>
<td>26 (38.8)</td>
<td>&lt;.001</td>
<td>2.2 (1.4-3.5)</td>
</tr>
<tr>
<td>Shock at ICU admission, n (%)</td>
<td>42 (31.6)</td>
<td>55 (82.1)</td>
<td>&lt;.001</td>
<td>2 (1.6-2.6)</td>
</tr>
<tr>
<td>Steroid therapy at ICU admission, n (%)</td>
<td>50 (37.6)</td>
<td>40 (59.7)</td>
<td>&lt;.05</td>
<td>1.3 (1.1-1.7)</td>
</tr>
<tr>
<td>Acute Kidney Injury, n (%)</td>
<td>21 (15.8)</td>
<td>33 (49.3)</td>
<td>&lt;.001</td>
<td>1.9 (1.4-2.8)</td>
</tr>
<tr>
<td>Community-acquired respiratory co-infection at ICU admission, n (%)</td>
<td>16 (12)</td>
<td>21 (31.3)</td>
<td>&lt;.05</td>
<td>1.6 (1.1-2.4)</td>
</tr>
<tr>
<td>Viral pneumonia, n (%)</td>
<td>84 (63.2)</td>
<td>44 (65.7)</td>
<td>.72</td>
<td>—</td>
</tr>
<tr>
<td>Time in days between onset of symptoms and first doses of antiviral received, mean (SD)</td>
<td>5.2 (3.2)</td>
<td>5.6 (3.1)</td>
<td>.33</td>
<td>—</td>
</tr>
</tbody>
</table>

### Comorbidities, n (%)

- Asthma: 16 (12.5) vs. 3 (4.5); P = .08
- Chronic Obstructive Pulmonary Disease: 26 (19.5) vs. 16 (23.9); P = .47
- Cardiovascular disease: 15 (11.3) vs. 8 (11.9); P = .89
- Chronic Renal Failure: 9 (6.8) vs. 6 (9); P = .57
- Hematologic disease: 9 (6.8) vs. 16 (23.9); P < .05; 1.9 (1.5-3.3)
- Pregnancy: 7 (5.3) vs. 1 (1.5); P = .2
- Obesity: 53 (39.8) vs. 17 (25.4); P < .05; 0.8 (0.6-0.9)
- Diabetes mellitus: 24 (18) vs. 8 (11.9); P = .26
- Human immunodeficiency virus: 1 (0.8) vs. 9 (13.4); P < .001; 6.9 (1.1-44.7)
- Vaccinated, n (%): 8 (6) vs. 4 (6); P = .99

As of February 15 2011, 200 patients (66.6%) had been discharged from the ICU and 67 of them (33.5%) had died. The mortality rate was not different between patients who received vaccination (18.2%) compared to those who did not (22.6%; P = .79; OR = 1.32; 95%CI, 0.45-3.84). The 4 vaccinated patients who died had significant comorbidities (severe immunosuppression due to lung, bone marrow transplantation, and acute leukaemia). Among patients who underwent invasive mechanical ventilation (n = 117), the mortality was very high (n = 62; 53%).

The characteristics of patients at ICU admission according to survival or death (n = 200) are shown in Table 2. Patients who died presented higher APACHE II and SOFA scores at ICU admission. No differences in comorbidities were observed except for haematological disease (OR = 1.9; 95%CI, 1.5-3.3) and human immunodeficiency virus infection (OR = 6.9; 95%CI, 1.1-44.7) which were more frequent in non-survivors. Obesity was associated with a better prognosis (OR = 0.8; 95%CI, 0.6-0.9). Development of shock (OR = 2; 95%CI, 1.6-2.6); acute kidney injury (AKI) (OR = 1.9; 95%CI, 1.4-2.8), need for invasive MV (OR = 1.9; 95%CI, 1.6-2.4), number of quadrant infiltrates in chest X-ray (2.6 vs. 1.9; P < .05), steroid therapy (OR = 1.3; 95%CI, 1.1-1.7) and CARC (OR = 1.6; 95%CI, 1.1-2.4) were most frequent in non-survivors. APACHE II score, SOFA score, infiltrates in chest X-ray, invasive MV, shock at ICU admission, AKI, CARC, haematological disease, HIV infection and vaccination were variables included in the multivariate analysis to determine their association with the mortality. Stepwise logistic regression analysis showed that APACHE II score by point of increase (OR = 1.07; 95%CI, 1.01-1.14; P = .02), infiltrates in chest X-ray by quadrant (OR = 1.6; 95%CI, 1.08-2.4; P = .01), haematological disease (OR = 4.5; 95%CI, 1.2-17.5; P = .02) and invasive MV (OR = 9.4; 95%CI, 2.9-30.8; P < .001) were variables independently associated with mortality. The multivariate models had a Hosmer-Lemeshow goodness-of-fit test score of 13.04 (P = .11).

**Discussion**

To the best of our knowledge, this is the first study that presents a relatively large number of patients admitted to the ICU for severe infection due to the An/ H1N1 virus in the 2010-11 seasonal influenza outbreak, this being in the post-pandemic period.
In our series, the presenting features of An/H1N1 influenza during the winter of 2010-11 were quite similar to those described in the past 2009 A/H1N1 virus infection pandemic. Nevertheless some aspects need to be pointed out.

In this report, the severity of disease in patients (APACHE II score 16.9) was greater than that observed during the 2009 pandemic (APACHE II 13.8; *P* = .001) \(^5\). The frequency of comorbidities in the current series (76% of patients) was also higher than that observed in the 2009 pandemic (69.6%; *P* = .01) \(^5\)-\(^7\). While obesity remained the most frequent comorbidity, there was an increase in the number of patients with haematological disease during the 2010-11 seasonal influenza outbreak compared to the pandemic period. This was the fourth most frequent comorbidity and it was the only one independently associated with mortality in the multivariate analysis.

Primary viral pneumonia was significantly more frequent (63.2%) during the 2010-11 seasonal influenza outbreak compared with recently published data for the previous (2009 pandemic) outbreak (54.8%; *P* < .01) \(^10\). The rapid progression of pulmonary viral infection from respiratory failure to Acute Respiratory Distress Syndrome (ARDS) may be related to a significant increase in the need for MV in the current seasonal outbreak (79%) compared to the 2009 pandemic outbreak (61.5%; *P* = .01) \(^14\). The mortality rate of ventilated patients was very high (53%) in the present study and invasive MV was independently associated with mortality in the multivariate analysis.

The implementation of early (<2 days) antiviral therapy was associated with a lower mortality rate in ventilated patients with 2009 H1N1 \(^14\). While all patients received antiviral treatment, the present study showed a one-day delay (5 days instead of 4 days) in the administration of antiviral agents compared to previous studies \(^14\).

All these variables must be considered in order to explain the higher mortality observed in the current seasonal outbreak (33%) compared to that reported during the 2009 pandemic (21%; *P* = .01) \(^14\). Although in the present study only haematological disease, the need for MV, APACHE II score and number of quadrants infiltrates in chest X-ray were factors associated with mortality, other variables cannot be excluded given that the study may be underpowered to identify other factors also associated with mortality.

The use of corticosteroids in the present report was very high (43% of cases). WHO guidelines for the management of human infection with pandemic (H1N1) Influenza A infection recommend that corticosteroid therapy should not be used routinely. Recently, Martin-Loeches et al \(^15\) showed that the early use did not result in better outcomes and may be associated with an increased risk of super-imposed infections.

Many studies have demonstrated temporal relationships between influenza activity and CARC. During past pandemics, the bacteria most often recovered were common colonizers of the upper respiratory tracts of healthy persons, i.e., *Haemophilus influenzae*, *S. pneumoniae*, *S. pyogenes* or *Staphylococcus aureus* \(^16\)-\(^18\). Moreover, substantial laboratory evidence for synergism between influenza A and bacterial microorganisms has been suggested \(^19\). During the 2010-11 seasonal influenza outbreak, CARC was present in 18% of cases, this prevalence being similar to that reported in the 2009 outbreak (17.5%) \(^10\).

Finally, in the present report, 92.6% of the patients admitted to the ICU were not vaccinated. The presentation of ARDS with severe refractory hypoxemia is particularly common in patients with this disease process and might be linked to an abnormal immune response \(^20\). Vaccination induces broad and improved cross protection against severe illness of multiple subtypes of influenza A virus. While vaccination has been a matter of debate, there has nevertheless been no evidence of harm or serious side effects in the vaccine trials that were conducted. In our study, the 4 vaccinated patients who died had severe risk factors and death was related to serious underlying comorbidities; given their immunosuppression status, it is possible that an inadequate immune response to the influenza vaccine had occurred. Moreover, Pregnancy was significantly associated with primary viral pneumonia due to An/H1N1 \(^21\) and it was recognized as important risk factor for developed severe hypoxemia. However, all pregnant women included in the present report were not vaccinated. No definitive conclusions can be drawn about the impact of vaccination based on our results given the small number of vaccinated patients included in the study. However, vaccinated patients seemed to have a more favorable outcome as evidenced by briefer stays in the ICU (4 days) and hospital (5 days) and fewer day under mechanical ventilation (5 days) (Table 1). Further studies are needed to clarify the impact of vaccination on outcome in critically ill patients.

The short follow up of the patients is a limitation of this study that should be further addressed. Indeed, the mortality rate in the present series could be underestimated given that 100 patients remained in the ICU at the time of this report, with a median follow up of 30 days in those patients. However, it is important to report in a timely manner our clinical experience with patients infected with the An/H1N1 virus to be aware of their clinical characteristics and possible differences with the previous 2009 outbreak, all of them pointing to a greater severity of illness and higher mortality as seen in the current series. In addition, early information on how recommendations on the management of critically ill patients with An/H1N1 virus infection (i.e., on the use of antiviral agents or on the administration of corticosteroids) are being followed is of immediate practical relevance.

In conclusion, patients admitted to the ICU in the 2010-11 seasonal influenza outbreak appear to have a higher severity of illness, higher frequency of severe comorbidities, higher incidence of primary viral pneumonia and increased mortality compared with those observed in the 2009 pandemic outbreak. Hematological disease, severity of illness at ICU admission, number of quadrants infiltrates in chest X-ray and the requirement for mechanical ventilation were variables independently associated with mortality. Vaccination appears to be associated with improved outcomes. This report is aimed at providing a general description of the first An/H1N1 influenza patients admitted to Spanish ICUs. Further in-depth studies with a larger sample size are needed to confirm these preliminary results.

**Finance**

Supported by Instituto de Salud Carlos III (Ministry of Science and Innovation).
Conflict of interests

Authors declare no conflict of interests regarding the present manuscript.

Authors’ contributions

AR assisted in the design of the study, coordinated patient recruitment, analyzed and interpreted the data, and with IML assisted in writing the paper. JB, PO, FAL, RZ, JG, JB, FG, JR made an important contribution to acquisition and analysis of data. JC, JL, IML and EC were involved in revising it critically for important intellectual content. CL, FP and AE made a substantial contribution to the conception and interpretation of data, and revised the final manuscript version. They all approved the final version to be published.

H1N1 SEMICYUC/REIPI/CIBERES Working Group investigators

Andalusia: Pedro Cobo (Hospital Punta de Europa, Algeciras); Javier Martín (Hospital Santa Ana Motril, Granada); Cecilia Carbayo (Hospital Torrecárdenas, Almería); Emilio Robles-Musso, Antonio Cárdenas, Javier Fierro (Hospital del Poniente, Almería); Dolores Ocaña Fernández (Hospital Huercal, Ovira, Almería); Rafael Sierra (Hospital Puerta del Mar, Cádiz); M. Jesús Huertos (Hospital Puerto Real, Cádiz); Juan Carlos Pozo, R. Guerrero (Hospital Reina Sofía, Córdoba); Enrique Márquez (Hospital Infanta Elena, Huelva); Manuel Rodríguez-Carvajal (Hospital Juan Ramón Jiménez, Huelva); Ángel Estella (Hospital del SAS de Jerez, Jerez de la Frontera); José Pomares, José Luis Ballesteros (Hospital Universitario San Cecilio, Granada); Yolanda Fernández, Francisco Lobato, José F. Prieto, José Albofedo-Sánchez (Hospital Costa del Sol, Marbella); Pilar Martínez; María Victoria de la Torre; María Nieto (Hospital Virgen de la Victoria, Málaga); Miguel Ángel Díaz Castellanos (Hospital Santa Ana de Motril, Granada); Guillermo Sevilla (Clínica Sagrado Corazón, Sevilla); José Garnacho-Montero, Rafael Hinojosa, Esteban Fernández (Hospital Virgen del Rocio, Sevilla); Ana Loza, Cristóbal León (Hospital Universitario Nuestra Señora de Valme, Sevilla); Ángel Arenzana (Hospital Virgen del Rocio de la Macarena, Sevilla); Dolores Ocaña (Hospital de la Inmaculada, Sevilla); Inés Navarrete (Hospital Virgen de las Nieves, Granada); Medhi Zaheri Beryanaki (Hospital de Antequera); Ignacio Sánchez (Hospital NISA Sevilla ALJARAFE, Sevilla).

Aragón: Manuel Luis Avellanas, Arantxa Lander, S. Garrido Ramírez de Arellano, M.I. Marquina Lacueva (Hospital San Jorge, Huesca); Pilar Luque, Elena Plumed Serrano, Juan Francisco Martín Lázaro (Hospital Lozano Blesa, Zaragoza); Ignacio González (Hospital Miquel Servet, Zaragoza); Jose M. Montón (Hospital Obispo Polanco, Teruel); Paloma Dorado Regil (Hospital Rio Villanueva, Zaragoza).

Asturias: Lisardo Iglesias, Carmen Pascual González (Hospital Universitario Central de Asturias [HUC], Oviedo); Quiroga (Hospital De Cabueñas, Gijón); Águeda García-Rodríguez (Hospital Valle del Nalón, Langreo).

Balears: Lorenzo Socías, Pedro Ibáñez, Marcio Borges-Sa, A. Socras, A. Del Castillo (Hospital Son Llàtzer, Palma de Mallorca); Ricard Jordà Marcos (Clínica Rotger, Palma de Mallorca); José M. Bonell (USP, Clínica Palmmaplanas, Palma de Mallorca); Ignacio Amestaráñ (Hospital Son Dureta, Palma de Mallorca).

Canarias: Sergio Ruiz-Santana, Juan José Díaz (Hospital Dr. Negrín, Las Palmas de Gran Canaria); Sísón (Hospital Doctor José Molina, Lanzarote); David Hernández, Ana Trujillo, Luis Regalado (Hospital General La Palma, La Palma); Leonardo Lorente (Hospital Universitario de Canarias, Tenerife); Mar Martín (Hospital de La Candelaria, Tenerife); Sergio Martínez, J.J. Cáceres (Hospital Insular de Gran Canaria).

Cantabria: Borja Suberviola, P. Ugarte (Hospital Universitario Marqués de Valdecilla, Santander).

Castilla-La Mancha: Fernando García-López (Hospital General, Albacete); Ángel Álvaro Alonso, Antonio Pasilla (Hospital General La Mancha Centro, Alcázar de San Juan); M. Luisa Gómez Grande (Hospital General de Ciudad Real, Ciudad Real); Antonio Albaya (Hospital Universitario de Guadalajara, Guadalajara); Alfonso Canabal, Luis Martina, (Hospital Virgen de la Salud, Toledo); Almudena Simón (Hospital Nuestra Señora del Prado, Toledo); José María Áñón (Hospital Virgen de la Luz, Cuenca).

Castilla y León: Juan B. López Messa (Complejo Asistencial de Palencia, Palencia); M. Jesús López Pueyo, M.V. Ortiz (Hospital General Yagüe, Burgos); Zulema Ferreras (Hospital Universitario de Salamanca, Salamanca); Santiago Macías (Hospital General de Segovia, Segovia); José Ángel Berezco, Jesús Blanco Varela (Hospital Universitario Rio Hortega, Valladolid); A. Andaluz Ojeda (Hospital Universitario, Valladolid); Antonio Álvarez Terrero (Hospital Virgen de la Concha, Zamora); Fabiola Tenza-Ezepeleta (Hospital Santa Bárbara, Soria); Zulema Páez, Álvaro García (Hospital Virgen Vega, Salamanca).

Cataluña: Rosa M. Catalán (Hospital General de Vic, Vic); Miquel Ferrer, Antoni Torres, Catia Cilloniz (Hospital Clinic, Barcelona); Sandra Barbadillo (Hospital General de Catalunya-CAPIO, Barcelona); Lluís Cabré, Ignacio Baez (Hospital de Barcelona, Barcelona); Assumpta Rovira (Hospital General de L’Hospitalet, L’Hospitalet de Llobregat); Francisco Álvarez-Lerma, Antonio Vázquez, Joan Nolla (Hospital del Mar, Barcelona); Francisco Fernández, Joaquim Ramón Cervelló; Raquel Iglesias (Centro Médico Delfos, Barcelona); Rafael Mañé, J. Ballús, Rosa M. Granada (Hospital de Bellvitge, L’Hospitalet de Llobregat); Jordi Vallès, Marta Ortiz, C. Guía (Hospital de Sabadell, Sabadell); Fernando Arméstar, Joaquim Páez (Hospital Dos de Mayo, Barcelona); Jordi Almirall, Xavier Balanzó (Hospital de Matarràs, Matarràs); Jordi Rello, Elena Arnau, Marcos Pérez, César Laborda, Joseca Souto, Mercedes Palomar (Hospital Vall d’Hebron, Barcelona); Inaki Catalán (Hospital Sant Joan de Déu, Manresa); Josep M. Sirvent, Cristina Ferri, Nerea López de Arbina (Hospital Josep Trueta, Girona); Mariona Badia, Montserrat Valverdú-Vidal, Fernando Barcenilla (Hospital Arnau de Vilanova, Lleida); Mónica Magret (Hospital Sant Joan de Reus, Reus); M.F. Esteban, José Luna (Hospital Verge de la Cinta, Tortosa); Juan M. Nava, J. González de Molina (Hospital Universitario Mutua de Terrassa, Terrassa); Zoran Josic (Hospital de Igualada, Igualada); Francisco Gurri, Paula Rodríguez (Hospital Quirón, Barcelona); Alejandra Rodríguez, Thiago Lisboa, Ángel Pobo, Sandra Trefler (Hospital Universitario Joan XXIII, Tarragona); Rosa María Diaz (Hospital San Camil, Sant Pere de Ribes, Barcelona).
Extremadura: Juliá-Narváez José (Hospital Infantia Cristina, Badajoz), Alberto Fernández-Zapata, Teresa Recio, Abilio Arrascaeta, M. José García-Ramos, Elena Gallego (Hospital San Pedro de Alcántara, Cáceres); Fernándo Bueno (Hospital Virgen del Puerto, Plasencia); Mercedes Díaz (Hospital de Mérida, Mérida).

Galicia: M. Lourdes Cordero, José A. Pastor, Luis Álvarez-Rocha (CHUAC, A Coruña); Dolores Vila (Hospital Do Meixoeiro, Vigo); Ana Díaz Lamas (Hospital Arquitecto Marcide, Ferrol); Javier Blanco Pérez, M. Ortiz Piquier (Hospital Xeral-Calde, Lugo); Eleuterio Merayo, Victor José López-Ciudad, Juan Cortes Cañones, Eva Vilaboy, José Vil lar Chao (Complejo Hospitalario de Ourense, Ourense); Eva Maria Saborido (Hospital Montecelo, Pontevedra); Raúl José González (H. Miguel Domínguez, Pontevedra); Santiago Freita, Enrique Alemán, Ana Ortega (Complejo Hospitalario de Pontevedra, Pontevedra); Ana María López, Julio Canabal, Enrique Ferres (Clínica Universitaria Santiago de Compostela, Santiago).

La Rioja: José Luis Monzón, Félix Goñi (Hospital San Pedro, Logroño).

Madrid: Frutos Del Nogal Sáez, M. Blasco Navalpoto (Hospital Severo Ochoa, Madrid); M. Carmen García-Torrejón (Hospital Infanta Elena, Madrid); César Pérez-Calvo, Diego López (Fundación Jiménez Díaz, Madrid); Luis Arnaiz, S. Sánchez-Alonso, Carlos Velayos, (Hospital Fuenlabrada, Madrid); Francisco del Río, Miguel Ángel González (Hospital Clínico San Carlos, Madrid); María Cruz Martín, José M. Molina (Hospital Nuestra Señora de América, Madrid); Juan Carlos Montejo, Mercedes Catalán (Hospital Universitario 12 de Octubre, Madrid); Patricia Albert, Ana de Pablo (Hospital del Sureste, Arganda del Rey); José Eugenio Guerrero, María Zurita, Jaime Benitez Peyrat (Hospital Gregorio Marañón, Madrid); Enrique Cerdá, Manuel Alvarez, Carlos Pey (Hospital Infanta Cristina, Madrid); Montse Rodriguez, Eduardo Palencia (Hospital Infanta Leonor, Madrid); Rafael Caballero (Hospital de San Rafael, Madrid); Concepción Vaquero, Francisco Mariscal, S. García, (Hospital Infanta Sofía, Madrid); Nieves Carrasco (Hospital Universitario La Princesa, Madrid); Isidro Prieto, A. Lié tor, R. Ramos (Hospital Ramón y Cajal, Madrid); Beatriz Galván, Juan C. Figueras, M. Cruz Soriano (Hospital La Paz, Madrid); P. Galdós, Bárbara Balandín Moreno (Hospital Puerta de Hierro, Madrid); Fernández del Cabo (Hospital Monte Príncipe, Madrid); Cecilia Hermosa, Federico Gordo (Hospital de Henares, Madrid); Alejandro Algora (Hospital Universitario Fundación Alcorcón, Madrid); Amapro Paredes (Hospital Sur de Alcorcón, Madrid); J.A. Cambronero (Hospital Universitario Príncipe de Asturias, Madrid); Sonia Gómez-Rosado (Hospital de Móstoles, Madrid); Luis Miguel Prado López (Hospital Sanitas La Zarzuela, Madrid); A. Esteban, J.A. Lorente, N. Nin (Hospital de Getafe, Madrid).

Murcia: Sofía Martínez (Hospital Santa María del Rosell, Murcia); F. Felices Abad (Hospital Universitario Reina Sofía, Murcia); Mariano Martínez (Hospital Universitario Virgen de la Arrixaca, Murcia); Sergio Manuel Buti, Bernardo Gil Rueda, Francisco García (Hospital Morales Meseguer, Murcia).

Navarra: Laura Macaya, Enrique Maravi-Poma, I. Jiménez Urria, L. Macaya Redín, A. Tellería (Hospital Virgen del Camino, Pamplona); Josu Insanisti (Hospital de Navarra, Pamplona).

País Vasco: Nagore González, Pilar Marco, Loreto Vidaur (Hospital de Donostia, San Sebastián); B. Santamaria, Tomás Rodríguez (Hospital de Basurto, Bilbao); Juan Carlos Vergara, Jose Ramon Irurtagoyena Amiano (Hospital de Cruces, Bilbao); Alberto Manzano (Hospital Santiago Apóstol, Vitoria); Carlos Castillo Arenal (Hospital Txagorritxu, Vitoria); Pedro Maria Olaechea, Higinio Martin (Hospital Galdakao-Usansolo, Vizcaya).

Valencia: José Blanquer (Hospital Clinic Universitari, Valencia); Roberto Reig Valero, A. Belenger, Susana Altaba (Hospital General de Castellón, Castellón); Bernabé Álvarez-Sánchez (Hospital General de Alicante, Alicante); Santiago Alberto Picos (Hospital Torrevieja Salud, Alicante); Ángel Sánchez-Miralles (Hospital San Juan, Alicante); Juan Bonastre, M. Palamo, Javier Cebrián, José Cuñat (Hospital La Fe, Valencia); Belén Romero (Hospital de Manises, Valencia); Rafael Zaragoza, Constantino Torno (Hospital Dr. Peset, Valencia); Virgilio Paricio (Hospital de Requena, Valencia); Asunción Marques, S. Sánchez-Morcillo, S. Torno (Hospital de la Ribera, Valencia); J. Litour (H.G. Universitario Elche, Valencia); M. Ángel García (Hospital de Sagunto, Castellón).

Andorra: Antoli Ribas (Hospital Nuestra Señora de Meritxell, Andorra).

References


