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Review

# Autoimmune diseases in the intensive care unit. An update ☆

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ABSTRACT

Autoimmune diseases (ADs) are a challenge at the intensive care unit. The management of patients with these diseases in the critical care setting has improved over time since there are new and more aggressive alternatives to treat and diagnose them. We aimed to review the current causes of admission, clinical features, outcomes and variables associated with mortality of patients with ADs admitted to the intensive care unit (ICU). International classification criteria for ADs were used to include patients. Search was done through PubMed, SCOPUS, SciELO, and LILACS databases up to December of 2011.Twenty-nine case series and forty-one case reports were analyzed after quality assessment. Respiratory involvement was the leading cause of admission. Systemic lupus erythematosus (SLE) (33.5% of reported patients), rheumatoid arthritis (25%) and systemic vasculitis (15%) were the most frequent ADs in patients admitted to the ICU in the last decade. Mortality ranged from 17% to 55% in case series including all ADs, but in the ones that only included patients with a specific AD, such as SLE, it reached up to 79%. High APACHE score, multi-organ dysfunction, older age and cytopenia were the most reported variables associated with mortality. In conclusion, ADs should always be considered in patients with life threatening conditions that warrant critical care. Variables influencing mortality should be promptly identified in order to improve the patients' outcomes.



**Contents**



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## 1. Introduction

Systemic manifestations of autoimmune diseases (ADs), which are a heterogeneous group of entities, can become so severe that they endanger the lives of patients. Of all the patients with ADs presenting to the emergency room, the majority have a rheumatologic AD and up to 25% of them require hospitalization. Of these, up to one third will require care and support in an intensive care unit (ICU) [1]. The reported in-ICU mortality of patients with ADs reaches as high as 55% depending on the series [1–3]. Besides increased risk of mortality, critical illness is also associated with other long-term outcomes such as persistent cognitive impairment [4], which has a negative impact on quality of life and the ability of those who survived an illness that required ICU to reintegrate into daily life [5,6].

Patients with any of these diseases usually have multiple risk factors for in-hospital mortality and morbidity and are most likely to end up in the ICU, where they represent a challenge for the entire intensive care team. Moreover, it has been reported that, from 1996 to 2003, between 7 and 42% of individuals with an AD were first diagnosed during their ICU stay [7–11]. This supports our argument that this group of diseases should always be considered in the differential diagnosis in patients at ICU in order to not delay prompt and accurate treatment.

In 2005, we published a case series report and review of literature of patients with ADs requiring intensive care in a third level hospital [2]. Since then, there are no current reports that describe whether the AD situation in the ICU remains the same or if it has changed over time given the advances in the diagnostic procedures that allow an early diagnosis and aggressive treatment of ADs. The aim of the present study was to update the causes of admission, clinical features, and outcomes of patients with ADs requiring intensive care as well as variables associated with mortality that could be possible prognostic mortality factors. Another goal was to describe the state of the art of alternative therapeutic strategies in the ICU to manage life-threatening conditions and manifestations common to all ADs focusing on therapeutic plasma exchange (TPE) and intravenous immunoglobulins (IVIg).

## 2. Materials and methods

### 2.1. Search strategy

A search was done of PubMed (2005–2011), SCOPUS (2005–2011), SciELO (2005–2011), and LILACS (2005–2011) up to December of 2011 by two reviewers independently to identify studies that measured mortality and described causes of admission, clinical features, variables associated with mortality, alternative therapeutic strategies, and outcomes of patients with ADs. In the search strategy, the combinations of the following MeSH terms were used: "Systemic Vasculitis" [Mesh], "Vasculitis" [Mesh], "Arthritis, Rheumatoid" [Mesh], "Lupus Erythematosus, Systemic" [Mesh], "Multiple Sclerosis" [Mesh], "Scleroderma, Systemic" [Mesh], "Antiphospholipid Syndrome" [Mesh], "Sjogren's Syndrome" [Mesh], "Dermatomyositis" [Mesh], "Polymyositis" [Mesh], "Myasthenia Gravis" [Mesh], "Churg–Strauss Syndrome" [Mesh], "Giant Cell Arteritis" [Mesh], "Microscopic polyangiitis" [Mesh], "Cryoglobulinemia" [Mesh], "Polyarteritis nodosa" [Mesh], "Wegener granulomatosis" [Mesh], "Inflammatory Bowel Diseases" [Mesh], "Anemia, Pernicious" [Mesh], "Thyroiditis, Autoimmune" [Mesh], "Celiac Disease" [Mesh], "Arthritis, Juvenile Rheumatoid" [Mesh], "Vitiligo" [Mesh], "Primary biliary cirrhosis" [Mesh], "Liver Cirrhosis, Biliary" [Mesh], "Primary sclerosing cholangitis" [Mesh], "Hepatitis, Autoimmune" [Mesh], "Myelitis, Transverse" [Mesh], "Polychondritis, Relapsing" [Mesh], "Addison Disease" [Mesh], "Glomerulonephritis" [Mesh], "Purpura, Thrombocytopenic, Idiopathic" [Mesh], "Arthritis, Psoriatic" [Mesh], "Spondylitis, Ankylosing" [Mesh], "Sarcoidosis" [Mesh], "Mixed Connective Tissue Disease" [Mesh], "Raynaud Disease" [Mesh] and "Autoimmune diseases" [Mesh]; each one of them was cross-referenced with "Intensive Care Units" [Mesh] or "Intensive Care" [Mesh]. Each term was translated into DeCS (Health Sciences Descriptors) terms in order to search SciElo and LILACS databases. Human limit was applied. No limits regarding language or publication type were applied. In addition, a full-text evaluation was done of all articles retrieved. Those references from the articles that seemed to be relevant for our review were hand-searched.

### 2.2. Study selection, data extraction, and quality assessment

Inclusion criteria for the systematic review were as follows: any type of study done in an ICU that used international classification criteria for the selection of patients with ADs and that had information about in-ICU mortality, a description of clinical characteristics of ADs, cause of admission, variables associated with mortality, and/or description of the use of TPE and IVIg from 2005 to 2011. Articles published prior to 2005 that had already been included in other studies plus those that had not been included in previous systematic reviews were all brought together to compare pre-2005 data with the recent publicized data in order to find differences in the presentation and outcomes of ADs in the ICU over time. Citations, abstracts and full text articles were reviewed to select eligible studies. Two reviewers independently extracted data from each study using a standardized form.

Since a broad search strategy was used, an initial screening was done of all titles and abstracts to look for studies that would be likely to comply with inclusion criteria, following the PRISMA statement [12]. For foreign language articles, English translations of abstracts or the original article was reviewed in order to determine eligibility. For each eligible study, data on study design, patient characteristics at ICU admission, age, gender, ADs classification criteria, severity index scores, in-ICU mortality, TPE or IVIg use, possible variables associated with mortality, and study quality was abstracted. A chi square analysis for polytomous variables was performed to compare the causes of admission between each AD and within each AD. Cramer's V was calculated as a measure of the strength of association.

Additional information about evidence based guidelines on the indications for ICU admission and the use of TPE and IVIg was searched for specifically in order to complement information regarding these topics in the retrieved articles and construct informational tables that summarize their use in cases of patients with ADs.

### 2.3. Study quality

The study quality was assessed using the levels established by the Oxford Centre for Evidence-based Medicine as of August 2011 [13]. No study was excluded from the review based on the study quality assessment.

## 3. Results

### 3.1. Search results and study characteristics

Using our search strategy, 1240 articles were identified and, of these, 123 were chosen for full text review. One hundred and five articles met inclusion criteria and were included in the review (Fig. 1). The articles were grouped as case series reports [2,3,7,9–11,14–36] (Tables 1 and 2), case reports [37–77] (Table 3), and literature review articles that were used to enrich the discussion. Case series reports were divided into two groups: those that were specific for a single AD and those of ADs in general by chronological order. Case reports were grouped by AD. According to the 2011 Oxford Centre for Evidence-based Medicine Levels of Evidence all case series reports are level 4.