

Mortality in Systemic Lupus Erythematosus seen in Antananarivo University Hospitals

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ABSTRACT

Systemic lupus erythematosus is a potentially life-threatening autoimmune disease. The aim of this study was to describe the epidemiology-clinical profile and identify the causes of death of lupus patients in Antananarivo University Hospital.

This was a retrospective descriptive and analytical study from January 2010 to January 2021, including all lupus patients who died during hospitalisation.

During this period, 32 deaths were recorded, with an estimated mortality rate of 17.77%. The mean age of the patients was 41.18 years. The sex ratio was 0.14. Dermatological, rheumatological and renal disorders accounted for 96.8%, 75.0% and 71.9% of patients respectively. ESR and CRP were elevated in 68.7% and 59.4% of patients respectively. Antinuclear antibody and anti-native DNA antibody were positive in 71.8% and 62.5% respectively. Lupus cases were mainly attributable to complications of disease evolution (46.8%) and infectious events (37.5%).

Mortality in systemic lupus erythematosus remains high in emerging countries. Lupus nephropathy was one of the most common causes of death in lupus patients, followed by infectious complications. The factors associated with mortality identified in our series were: a history of arterial hypertension, tuberculosis infection, the presence of altered general condition, cardiovascular and nephrological impairment ($p \leq 0.05$).

Keywords: Cause of death; Systemic lupus erythematosus; Madagascar

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune disease with multi-organ involvement. Its course is unpredictable and depends on the severity of the organs affected [1]. Systemic lupus erythematosus remains associated with excess mortality compared with the general population [2]. Many factors with a poor prognosis have been identified in the literature: demographic, clinical and biological data. The causes of death in lupus patients are multiple. The aim of this study is to describe the epidemiological profile and identify the causes and factors related to death in lupus patients at Antananarivo University Hospital.

METHODS

This study was conducted in eight medical departments caring for lupus patients in three hospitals in Antananarivo, Madagascar. This was a retrospective descriptive and analytical study of a lupus case population hospitalized and/or followed up in these centers from January 2010 to January 2021. The diagnosis of SLE was based on the criteria of the American College of Rheumatology (ACR) 1997. Lupus patients who died in hospital were included. Data were collected from medical registers and medical records of patients seen in hospital.

Data collected from medical records during the study period were transcribed onto Microsoft Excel, then imported and analyzed using Epi info software version 7.1.3.

Lupus patients who died outside hospital were not included in this study. Information on clinico-biological data was not exhaustive and differed from one center to another.

RESULTS

During the study period, thirty-two deaths occurred in 180 lupus patients, representing a case-fatality rate of 17.77%.

The mean age of deceased lupus patients was 41.18 years (\pm 16.27 years), with a minimum of 14 years and a maximum of 87 years. The majority were aged between 30 and 39, with a proportion of 43.8%.

At the time of lupus diagnosis, the average age of the patient was 36.62 years, with a minimum of 14 years and a maximum of 67 years, and those aged between 30 and 39 represented 53.13% of the population.

Women represented 87.50% and men 12.50%, with a sex ratio of 0.14.

Arterial Hypertension (AH) was present in 53.1% of patients. Tuberculosis was diagnosed in 9.4% of patients, and 12.5% had a history of other autoimmune diseases.

On average, lupus was diagnosed 5.25 months (\pm 6.02) after the onset of symptoms. This was less than 6 months in 71.8% of cases, and more than 6 months in 28.1%. General lupus symptoms such as asthenia and weight loss were encountered in 81.3% of patients.

In general, dermatological, rheumatological and renal disorders were present in 96.8%, 75% and 71.9% of patients respectively.

Red cell sedimentation rate (ESR) and C-Reactive Protein (CRP) were elevated in 68.7% and 59.4% of patients respectively. Serum protein electrophoresis showed polyclonal hypergammaglobulinemia in 53.3% of cases, and increased α_2 globulinemia in 26.7% of patients.

A blood count abnormality was noted in all patients. Anemia was present in all cases. Leukopenia was present in 31.25% of cases, and hyperleukocytosis in 34.38%. Thrombocytopenia was present in 21.88% of patients.

Antinuclear antibody and anti-native DNA antibody were positive in 71.8% and 62.5% respectively.

Regarding lupus treatment, hydroxychloroquine was administered in 96.9% of patients; eighty-four percent of these patients were on systemic corticosteroids, and immunosuppressants (notably methotrexate, cyclophosphamide, and mycophenolate mofetil) were prescribed in 25% of patients.

Lupus patients mainly died of complications related to the progression of the disease in 46.8% of cases, and of infectious complications in 37.5% (Table 1).

Table 1: Distribution of sample by diagnosis of death.

Death diagnosis	n	Proportion (%)
Infectious complications	12	37,5
Complications related to disease progression	15	46,8
Cardiovascular events	3	9,4
Unknown	2	6,3

In terms of infectious complications, urinary tract infection affected 16.67% of cases; bacterial pneumonitis was diagnosed in 16.67% of patients; genital, digestive and oral infections were each observed in 8.34% of cases; postoperative infectious complication was reported in 8.33% of cases; pulmonary tuberculosis was revealed in 8.33% of cases. Severe SARS-COV2 infection was found in 25% of cases (Figure 1).

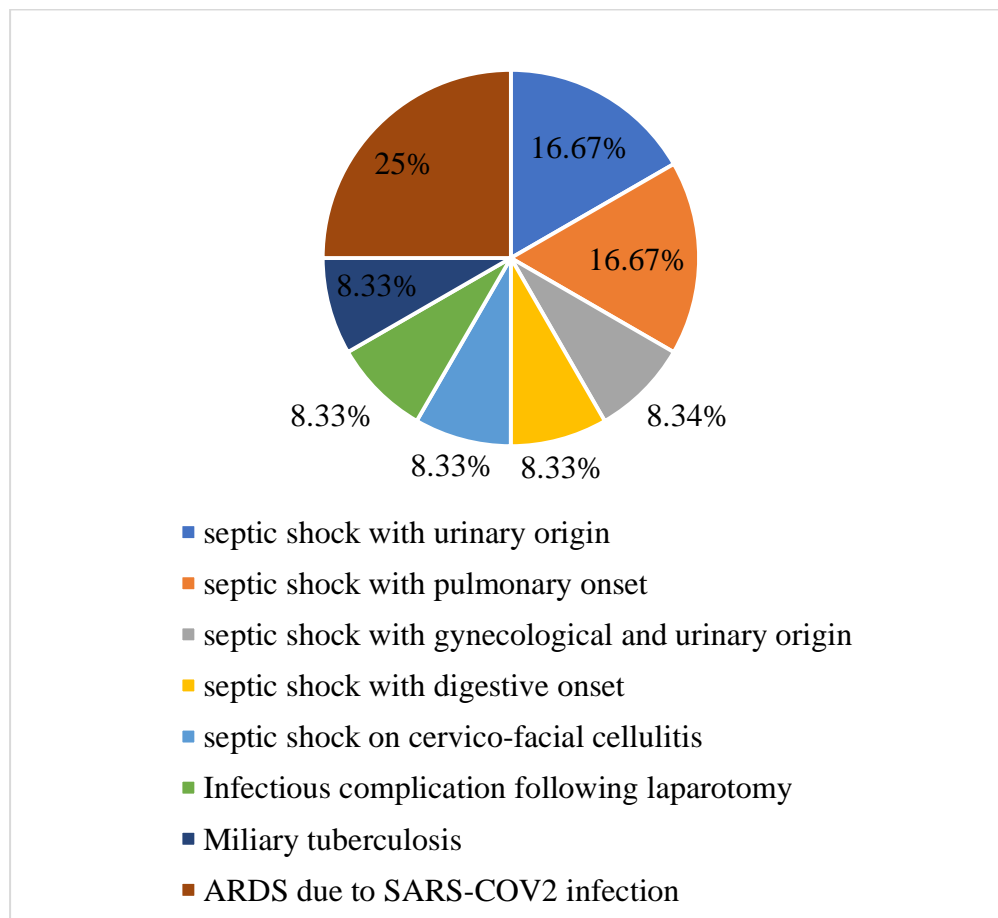


Figure 1: Distribution of patients who died according to infectious complications.

Complications linked to the progression of the disease were dominated by lupus nephropathy complicated by renal failure in 86.7% of patients.

Cardiovascular events accounted for 9.4% of causes of death. These were stroke in 66.7% of cases, and coronary insufficiency complicated by heart rhythm disorders in 33.3%.

In this study, six-point three percent of causes of death were unknown.

The factors associated with mortality identified in our series were: a history of arterial hypertension, tuberculosis infection, the presence of altered general condition, cardiovascular and nephrological impairment ($p \leq 0.05$).

Most lupus patients (40.6%) had died within 6 months of diagnosis. And in 34.4% of cases, death occurred 12 months after diagnosis (Table 2).

Table 2: Distribution of deceased patients according to the time between the date of diagnosis and the date of death.

Delay between diagnosis and death in months	N	Proportion (%)
1 à 6	13	40,6
7 à 12	8	25,0
Over 12	11	34,4

DISCUSSION

According to the present study, the overall mortality rate of lupus patients indexed during the study period (11 years) was 17.77%. This rate is relatively high compared with that reported in Tunisia by Jaziri F, et al. [3] in a 12-year study, who found a mortality rate of 12% [3].

According to the WHO, mortality during SLE appears to be extremely variable, being high in South America, Asia, and Africa. In contrast, the mortality rate in Europe had decreased between 2001 and 2014 [4]. Among the epidemiological factors involved in prognosis, the role of ethnic origin is widely described in the literature [5].

In this study, the mean age of deceased lupus patients was 41.18 years. This seems younger than the data from other studies. In a study by Truchetet and colleagues carried out in 2018, the mean age of deceased lupus patients was 53 years [4]. Similarly for this French study, Thomas, and his team found a mean age at death of 63.5 years [6]. This difference could be explained by the difficulty of access to care in developing countries such as Madagascar.

The present study reiterates the frequency of cutaneous and articular manifestations in SLE [7]. In addition, several authors have reported the severity of renal, cardiorespiratory, and neuropsychiatric involvement [8].

According to a study carried out by Hajji M, et al. [9] in Tunisia in 2014, renal involvement was found in 71.9% of patients, and constituted a severe and frequent visceral involvement [9].

Among biological parameters, thrombocytopenia and autoimmune haemolytic anemia are predictive factors of a fatal outcome [10]. These factors were not observed in the present study.

Immunological abnormalities have had little influence on the survival of lupus patients [11]. However, according to various studies, antinuclear antibodies predominated from the age of 40 onwards, and increased with age [12-13].

The short- and medium-term prognosis of lupus patients has improved considerably over the last four decades. This has been achieved thanks to improved knowledge of the disease and the use of immunosuppressants and glucocorticoids [14].

On the other hand, many studies have shown that lupus is still associated with excess mortality compared with the general population. Complications linked to the progression of the disease and infectious complications remain the main causes of death. This mortality is linked in the short term to infectious complications and in the long term to the severity of lupus disease [3]. Several studies have confirmed that renal damage is the leading cause of death linked to disease activity during lupus [9-16]. As this is still more pronounced in developing countries, due to poor access to healthcare.

Hypertension was associated with mortality in our study. In contrast, according to the study conducted by Somai M, et al. [17] Tunisia 2018, there was no association between death and hypertension [17]. During systemic lupus erythematosus, AH contributes to the increased cardiovascular risk factor.

Tuberculosis infection was a major cause of mortality. Indeed, the high endemicity of tuberculosis in developing countries increases the risk of exposure to the disease. A study carried out in Tunisia in 2021 by Ben Salem and colleagues showed that lupus patients had a higher risk of contracting tuberculosis than the general population [18].

CONCLUSION

Mortality in systemic lupus erythematosus remains high, especially in developing countries. This study confirmed the clinical polymorphism of SLE, its severity due to renal, cardiovascular, and infectious complications favoured by corticosteroid therapy. Early diagnosis and access to care and treatment determine the prognosis of lupus patients. Thus, this disease requires both early diagnostic and therapeutic management and regular monitoring to prevent its fatal complications.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHORS' CONTRIBUTIONS

AM Andrianiaina, RP Radinasoa, H Ramanandafy, S Nainanirina and RMF Randrianarisoa: Clinical data collection and report writing.

SJN Ratsimbazafy, MI Rahatamalala: Design and critical revision of the report.

HMD Vololontiana: Validated the report.

All authors have read and accepted the final version of the article.

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